

Abstracts of the Fourth World Parkinson Congress



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4th WORLD PARKINSON CONGRESS ABSTRACTS

Pre-Congress Oral Presentations

PCO01

Welcome and introduction to goals and overall course

Tom Isaacs
United Kingdom

Objectives

- To welcome everyone to the World Parkinson Congress 2016
- To run through the agenda for the day and to highlight the abundance of experience and expertise within the line-up of speakers on the day
- To provide an overview of the history of WPC and the increasing involvement of people with Parkinson's
- To set the tone of the meeting – the importance of having PwP's at the Congress and our role in making the conference a success
- "Do's and Don'ts" for WPC 2016

PCO02

Clinical features of Parkinson's disease

Anthony Lang
Toronto Western Hospital, Toronto, Ontario, Canada

Parkinson's disease is the second commonest neurodegenerative disorder after Alzheimer's disease. It is generally classified as a "movement disorder". However, non-movement features are now very well recognized. The classical neurological signs include Tremor (shaking movement), Rigidity (muscle stiffness), Akinesia for bradykinesia (slowness or loss of movement) and Postural disturbances (a flexion of the posture of trunk and limbs as well as reduction of balance) making up the acronym TRAP that is often taught to medical students. Generally the diagnosis cannot be made before some of these movement problems begin. However, we know the disease begins long before the initial motor manifestations become evident and many patients have "non-motor" symptoms that predate the motor complaints sometimes by many years (so-called prodromal symptoms). These can include loss of sense of smell, constipation, changes in mood and sleep disturbances. Once the motor features are evident, one of the most disturbing features is bradykinesia which can interfere with all physical activities. An important characteristic feature of these motor components of Parkinson's is a response (often striking) to dopamine replacement treatment, particularly levodopa. However, with time this response can be complicated by hour-to-hour fluctuations in motor benefit as well as involuntary movements known as dyskinesias. As Parkinson's disease progresses, the later course is complicated by the development of symptoms that are less or not responsive to levodopa (so-called "non-dopaminergic" features). These include motor symptoms such as speech and swallowing dysfunction as well as walking and balance disturbances, and non-motor features such as bladder and blood pressure problems and psychiatric and cognitive difficulties. This lecture will review the prodromal, early, middle- and later-stage clinical features of Parkinson's disease, setting the stage for subsequent lectures dealing with management of the disease.

PCO03

Treatments – overview, opening people's eyes to what's available and what's on the horizon: Talk #2: Therapies, personalized medicine, genetic testing & its impact on treatment

Joseph Friedman
Butler Hospital, Providence, Rhode Island, USA

Personalized medicine, strongly advocated by President Obama as the future of medicine, represents an idealized approach to treatment that might be achieved within this century, if the political will to invest research dollars while controlling costs of implementation can be achieved. It is highly likely that within the next decade or two, we will understand which genetic abnormalities and other factors lead to the development of PD and how their physiology. It is likely that as each cause is deciphered, a particular treatment, based on the genetic component or possible triggers, will be developed. Figuring out the different causes will likely explain why there is such a wide spectrum of problems seen: why some PD patients have tremors and others don't; why some get worse quickly and others slowly; why some have dyskinesias or dementia and others not. We will develop means to stop the progression of some of these forms of the disease. My fear is the cost. There may be a time when a treatment that stops progression becomes available but only to the wealthy. Currently there is no known way to slow progression but this is the focus of several new and promising approaches that are under investigation in people with PD.

PCO04

Nutrition

Heather Zwickey
National College of Natural Medicine, Portland, Oregon, USA

What if diet could not only influence Parkinson's symptoms but also slow disease progression? Would you be willing to change how you eat? There is growing research showing that nutrition has an impact on Parkinson's disease (PD). The neurodegeneration of PD is thought to be caused by inflammation and oxidative stress, which slowly damage neurons. As a result of this progressive process, the brain does not communicate as well with the body. Fortunately, inflammation and oxidative stress can be improved by diet. Many of the nutrients that are thought to improve PD reduce inflammation, contain high levels of anti-oxidants, and promote the production of dopamine to assist the body's natural processes. By choosing the right foods, those affected by PD can improve their symptoms and may even slow disease progression. For this reason, nutrition should be an essential part of the care plan for people with Parkinson's.

In this talk, we will discuss the current state of research for nutrition and Parkinson's. We'll identify foods that are thought to benefit or harm people with Parkinson's and why they have those effects. Finally, we'll suggest practical ways to integrate the lessons from nutrition research into daily life.

PCO05

Panel: So you want new treatments? How are you helping bring new treatments to the pharmacy? Or are you waiting for someone else to do the work?

Pat Davies¹, Michael Schwarzschild², Veronica Todaro³, Claire Schwarzschild⁴, Richard Windle⁵, Sohini Chowdhury⁶, Israel Robledo⁷

¹ Washington, USA

² Harvard Medical School, Boston, Massachusetts, USA

³ Parkinson's Disease Foundation, New York, New York, USA

⁴ Parkinson's UK, London, United Kingdom

⁵ St. Albans, United Kingdom

⁶ The Michael J. Fox Foundation for Parkinson's Research, New York, NY, USA

⁷ Parkinson's Movement, Midland, Texas, USA

In this session, members of the audience, along with a panel of researchers, representatives from organizations that support and fund clinical trials, and people with Parkinson's, will discuss opportunities to contribute to the search for a cure and improved therapies.

The session initially will focus on how to encourage participation in research and clinical trials. The majority of trials face delays because of insufficient volunteers, and many are never completed. The discussion will also focus on how to overcome the barriers to discovering what trials are available, and how and where people can participate.

In addition, the panel and the audience will discuss the growing movement in which clinicians, researchers and patients work in partnership to plan, shape and deliver PD research and clinical trials. This can include many different parts of the process—from identifying and prioritizing research questions, helping to design and manage the research, and evaluating how best to translate the outcomes into tangible benefits for people affected by the condition. Because Parkinson's is different for everyone, it is crucial that the research community work alongside patients and caregivers to understand the patient experience and perspective. This ensures that research will address issues that are important to people with Parkinson's, that studies are likely to recruit and retain participants and that results will be meaningful to people who live with the condition every day.

PCO07

How can SELF-care impact your Parkinson's?

Bob Kuhn

Trinity Western University, Canada

Seeing your neurologist for an hour or so once a year hardly seems enough given the extraordinary number and potential severity and impact of Parkinson's disease. And yet, not many of us spend a great deal of time or thought on the need for self-care for the other 8759 hours each year. Why is that? Will any self-care initiative really make a difference? How?

This session will focus on self-care in the context of Parkinson's disease by providing a reasonably comprehensive checklist of areas relevant to self-care, how to realize on the potential benefits, and taking back control of the most important things in life. Self-care is the personal plan to succeed in the face of challenges, both known and anticipated, resulting from Parkinson's disease.

"Self-care" is difficult to define, other than the relatively obvious idea of "taking good care of yourself". Of course, we don't always do that, often because we feel overwhelmed by the disease, its complexity and implications. Self-care seems to rank as a distant second to more comprehensive and competent professional health care. However, while it may present some difficulties in creating and sustaining a personalized self-care strategy, it is likely the most important aspect of responding to a Parkinson's disease diagnosis. Of course, like any other "self-help" remedy, plan or course of action, "self-care" requires discipline. But like similar personal challenges, it all starts with knowing what is required, designing a plan, and then sticking with it, whatever it takes. Remember, there are no failures, only opportunities to learn, adapt and try again.

Included in this presentation will be a number of creative and workable ideas to include in the self-care plan for a person with

Parkinson's. Together, we can develop a strategy for success, a focus for fulfillment, and a plan to take on Parkinson's.

PCO08

Panel: How to pick a good healthcare team and why it's so important to ask the right questions

Dilys Parker

New Zealand

People with Parkinson's (PWP) will do best when surrounded by a strong supportive network made up of caring individuals, all working to help them live well. Each person's team will be different depending on individual needs, age and stage of life but all will include health professionals.

Members of this panel are representative of the many health practitioners involved in the care of pwp. They include practitioners from the disciplines of physiotherapy, speech language pathology, occupational therapy, nursing, social work and neurology.

The purpose of this session is to demonstrate that a multi-disciplinary approach to managing PD is highly beneficial in addressing symptoms and in optimizing quality of life. A cornerstone of this approach is the development of a personalised health team with the person with Parkinson's actively involved in the process.

Communication is a key element in achieving this. It is important in the developmental phase but also in ensuring the ongoing effectiveness of the team. While members bring the core skills of their particular discipline to the group they will also bring their differing perspectives. We look at working with these differences to ensure there is effective communication and information sharing among participants.

The panel will use a scenario to model how a pwp might go from initial assessment by a neurologist or movement disorder specialist to the creation of their own personalized health team. This involves looking at both the construction of the team and the role of individual participants. Team development questions include exploring why the collaborative team approach is important, how to develop this, what happens if it fails and how to ensure it doesn't. More specific questions to practitioners will cover topics such as how a pwp can prepare for their visits with health team members, what they can expect from their visits, questions that need to be asked and issues that could arise.

At the end of the session it is hoped that forum attendees will be clearer about the place and composition of support teams, what makes a successful team and the essential part the pwp has in all of this.

PCO09

Panel: How to pick a good healthcare team and why it's so important to ask the right questions – Occupational therapist

Erin Foster

USA

Occupational therapists help people with Parkinson's disease perform and participate in their meaningful everyday activities and roles. This can range from basic self-care tasks, such as dressing and bathing, to engaging in social and leisure activities in the community. Occupational therapy takes a comprehensive and holistic view of the client, considering relevant motor, non-motor, personal and environmental factors during assessment and treatment. In addition to helping people build or maintain their capacity to perform daily activities, occupational therapists can help people modify their activities, routines and/or environments to accommodate their changing abilities and support continued performance and participation. Occupational therapists can also

address care partner concerns and provide education and training to care partners to enable them to support the person with Parkinson disease's daily performance and quality of life.

PCO10

Panel: How to pick a good healthcare team and why it's so important to ask the right questions – Nurse

Julie Carter
USA

Nurses are a core member of any multidisciplinary team. The expert PD nurse fulfills roles of assessor, educator, advocate, coordinator of care and team collaborator. Most importantly they are often the first link to medical care. In this talk we will discuss how best to utilize the role of the nurse from the perspective of the patient and family as well as other team members.

PCO11

Panel: How to pick a good healthcare team and why it's so important to ask the right questions – Social Worker

Lissa Kapust
Beth Israel Deaconess Medical Center, Harvard Medical School
Teaching Hospital, Boston, Massachusetts, USA

The clinical social worker (SW) is the "glue" in the PD multidisciplinary team; this is a critical role in light of the plethora of practical and emotional issues that follow the PD diagnosis. Today's healthcare system is better suited to respond to the needs of the person with acute illness than it is to provide specialized ongoing care necessary to meet the needs of the person with chronic illness. Popular terms in the literature include patient-centered care and patient self management. These approaches teach necessary skills to help patients become informed and proactive. Navigating the healthcare system takes great effort; SW is the link between patients, the medical institution and community resources. PD is a chronic illness; the relationship with SW may continue for years. Taking a careful psychosocial history guides the SW in formulating a care plan. The history sheds light on the impact of the diagnosis. Disclosing the diagnosis is often a starting point for discussion, following the diagnosis. Social workers wonder about current or future lifestyle changes to accommodate to PD. What will the "new normal" look like? Younger PWP may be concerned about different issues (work, childcare) than older PWP (financial/legal planning, potential move). Importantly, SW looks through the wide angle lens; including family members as "hidden patients". They facilitate open family discussions; attentive to mood for the PWP since untreated anxiety or depression can worsen PD symptoms. SW focuses on wellness in a broad way. They encourage exercise to promote wellbeing; recommendations range from Rock Steady Boxing to Mindfulness programs. In summary, SW maximizes coping by tapping into sources of resilience and strength for the PWP. They guide effective communication with the healthcare team and how to resolve the problems that inevitably arise. SW visits embrace approaches that goes "beyond the pillbox" maintaining the highest quality of life.

SW Questions:

- How often does SW meet with team members?
- Is SW someone I trust?
- Does SW convey ways to remain hopeful?
- How knowledgeable is SW about community resources?
- Will family be included in meetings?
- Does SW have access to PD support groups?

PCO12

Welcome and introduction: Why do we want interdisciplinary care?

Bastiaan Bloem
Parkinson Center Nijmegen (ParC), Nijmegen, Netherlands

Parkinson's disease is a complex neurological condition, characterized by a wide array of motor symptoms (e.g. tremor, walking problems, or balance difficulties) as well as so-called non-motor problems (e.g. difficulties with planning, disturbed sleep, or loss of smell). No two patients are the same, neither in terms of their clinical presentation (for example, some may have a tremor, others don't), nor in terms of their priorities for care. Recognition of the complexity and tremendous variability between patients can mean only one thing: that we need to move from the current model of care – which is largely a "one-size-fits-all" approach, to a much more personalized approach, with care delivery that is tailored exactly to each patient's individual needs. Given the tremendous complexity of Parkinson's disease, this new approach must be interdisciplinary in nature, with involvement of much more than just a neurologist. Indeed, over 20 different professional disciplines can potentially offer meaningful support to people with Parkinson's disease. Some of these disciplines are relatively well-known, such as the physiotherapist or Parkinson nurse specialist; others may be less familiar to patients (and even to medical professionals), such as the sleep expert or the sexologist. Additionally, new disciplines have been emerging and add to the growing team of experts that can help people with Parkinson's disease. These newer disciplines include a gastroenterologist and a pulmonologist. In this exciting pre-conference satellite session, we will address how modern care for people with Parkinson's disease could – and should – be organized. We will describe the complex presentation of Parkinson's disease, and the tremendous impact it can have on patients and their families. We will also highlight how an interdisciplinary team approach can benefit patients, reviewing the various team members, and also highlighting the mounting evidence to support a role in the clinical management of Parkinson's disease. New potential team members not previously emphasized will be introduced. We also emphasize how modern care should always involve the patients and their caregivers as true partners of the team, allowing them to participate in decision making, and supporting them in self-management. In what we expect to be an exciting part of the program, we will take this team approach to "the test," and present as well as discuss examples of everyday persons with Parkinson's disease along with an interdisciplinary team on stage. We will conclude by critically reviewing the scientific underpinnings of the interdisciplinary approach to Parkinson's disease, and by discussing the challenges on the road ahead of us; until we can make sure that every patient with Parkinson's disease receives the best possible care.

Suggested reading: 1–8

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- [4] van der Eijk M, Faber MJ, Post B, Okun MS, Schmidt P, Munneke M et al. Capturing patients' experiences to change Parkinson's disease care delivery: a multicenter study. *J Neurol* 2015.
- [5] van der Marck MA, Bloem BR, Borm GF, Overeem S, Munneke M, Guttman M. Effectiveness of multidisciplinary care for Parkinson's disease: a randomized, controlled trial. *Mov Disord* 2013; 28:605–611.

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[7] Ekker MS, Janssen S, Nonnekes J, Bloem BR, de Vries NM. Neurorehabilitation for Parkinson's disease: future perspectives for behavioural adaptation. *Parkinsonism Relat Disord* 2016; 22 Suppl 1:S73–S77.

[8] van der Eijk M, Nijhuis FA, Faber MJ, Bloem BR. Moving from physician-centered care towards patient-centered care for Parkinson's disease patients. *Parkinsonism Relat Disord* 2013; 19:923–927.

PCO14

Panel: Meet the “New Kids on the Block”: Why you need me on your Parkinson's team!

Dan Gold

John Hopkins Medicine, Baltimore, Maryland, USA

Visual symptoms in Parkinson's disease are very common, and stem from the simple (ocular surface irritation) to the more complex (eye movement disorders or subnormal vision from retinal dopamine depletion). A thorough ophthalmic/neuro-ophthalmic examination can offer an explanation for most visual symptoms in PD, and fortunately, treatments exist for many of these disorders. This talk will help patients/caregivers/clinicians to better understand these visual symptoms, as well as to emphasize the importance of routine visits with an eye care professional.

PCO15

Panel: Meet the “New Kids on the Block”: Why you need me on your Parkinson's team!

Jane Busch

USA

A healthy mouth is critical to chewing, tasting, swallowing and speaking. Oral health contributes to overall good health. A Parkinson patient-focused team needs a dentist who understands the complexity of oral function and how it relates to this neurological condition. There are a number of concerns that can affect and are affected by Parkinson's. Dysphagia (difficulty in swallowing), a symptom of Parkinson's may be worsened by a dry mouth or poor fitting dentures. Tremors and dyskinesia can cause bruxism (tooth grinding) which can lead to attrition and malocclusion. Xerostomia (dry mouth) is often a side effect of some Parkinson's medications. Saliva not only lubricates the oral cavity, but it provides enzymes for food digestion and antibodies to fight infection. Patients with xerostomia lose these benefits as well as increase their risk of dental caries and periodontal disease. Drooling (excess saliva) can result in angular cheilitis or cause denture instability. A neurologist-dentist team can address medication-local anesthesia interactions and modifications as well as medications that are contra-indicated in some PD patients. Patient cognitive ability and the need for caregiver involvement, emotional state and stage of disease (advanced PD may need sedation) are all information the dentist needs to provide optimal dental care. A dentist on the Parkinson team will provide a valuable service to both the team and the patient.

PCO16

Music as a therapy

Matthew Ford

Samford University, School of Health Professions, Birmingham, Alabama, USA

Music is therapeutic, and it's positive effects are no different in persons with PD. Music can be used to promote patient-centered care as health care providers (eg., music therapist, physical therapist, occupational therapist, exercise specialist) can allow the patient to choose the music used during therapy. For instance, research has shown that walking function still improves when a patient picks the music as opposed to the therapist. Persons with PD face many barriers to maintaining independence, health, and overall wellness. Music can be used across all disciplines to help a person overcome these barriers and have greater quality of life. Normally stressful events can be made more enjoyable. Patient's can set their medication alarm (on their smartphone) to play their favorite artist(s), while alerting them it's time for their medications. Physicians and nursing staff can play a patient's favorite music in the background during an appointment. Music has rhythmical structure and can be used to improve movement in persons with PD. A physical therapist can use it during gait training to improve upper and lower body coordination and walking speed. More fast-paced music can be used to motivate, and facilitate a person to move at exercise level intensities. Music embodies culture and community. Disease progression can lead to isolation and a cascade of events that decreases quality of life. Music and dance can remind people of their culture and promote community participation for both patient and care-partner(s). The aim of this pre-congress session is to show health care providers, persons with PD, and care partners how music can be used everyday to remove barriers and promote health living.

PCO17

Panel: Interdisciplinary care in real practice: case studies on best care delivery for patients

Lucie Lachance

McGill University Health Center, Montreal, Canada

The case studies will try to demonstrate what the nurse navigator model of care approach can do to explore the needs for PLWP. Given the multifaceted context of both medical and psychosocial needs of the PLWP, as well as difficult access to specialized care, the implementation of a nurse navigator is proposed as a vital part of the team. Most interactions with patients are completed via face to face visit and over the telephone allowing for rapid access to necessary support. The work of a navigator nurse is varied and addresses many challenges faced by the PLWP. Firstly, the nurse aims to obtain patient data such as past medical history, family history, life style, and medications. Secondly, she provides necessary referrals to other health care workers deemed relevant for each particular patient. Thirdly, the nurse assesses the patient and family concerns to allow prioritization of needs and development of care plans. In essence, the navigation nurse acts as the “go-to-person” for the patients.

PCO18

Panel: Interdisciplinary care in real practice: case studies on best care delivery for patients

Sue Lord¹, Lynn Rochester²

¹ Newcastle University Institute for Ageing, Newcastle upon Tyne, United Kingdom

² Newcastle University, Newcastle upon Tyne, United Kingdom

Evidence suggests that the optimal clinical management of PD is achieved via interdisciplinary input. PD is a multi-system disorder and although dopaminergic replacement therapies are highly effective for ameliorating motor symptoms, other features of the disease require a more holistic approach. Key to effective

interdisciplinary care is an understanding of these multi-system symptoms which are in a state of constant flux, integration and reintegration. With each clinical encounter it is essential to identify the primary presenting symptoms and those that are secondary. Does anxiety and depression, for example, occur in response to a situation or as a core feature of PD? How can it best be ameliorated? What are the limits of medication?

Delivering effective interdisciplinary care is challenging, and requires a flexible approach throughout the time course of the disease. One key feature around which management revolves is awareness of medication status. Response to medication is highly individual and may be heightened (or not) by external influences which are often subtle and more likely to be identified through an integrated team approach. For example, from a physical therapy perspective, exercise and activity has been shown to potentiate effects from dopaminergic therapy with better uptake and increased duration of effect. This positive effect is two-fold, in that outcomes from exercise also improve if it is carried out whilst on peak medication. However, this needs to be balanced against any detrimental coupling. For example, too much exercise may result in fatigue and as a result the benefits from medication are diminished.

This presentation draws on case studies to illustrate the advantages of an interdisciplinary team approach, with emphasis given to the gains that such an approach offers to physical therapy.

PCO19

Panel: Interdisciplinary care in real practice: case studies on best care delivery for patients

Daniel Weintraub

Perelman School of Medicine at the University of Pennsylvania, Philadelphia, USA

A multidisciplinary team is essential for the optimal care of Parkinson's disease (PD) patients. A key member of this team is a psychiatrist, who can help in the management of both psychiatric and cognitive complications that are common in PD. Common disorders are depression, anxiety, psychosis, impulse control disorders, apathy, mild cognitive impairment, and dementia. Specific clinical contexts include de novo patients, those undergoing DBS, and patients with non-motor fluctuations. Clinical experiences, including case studies, from a psychiatrist active in clinical care and clinical research will be utilized to discuss the assessment and management of psychiatric symptoms in PD.

PCO20

Panel: Interdisciplinary care in real practice: case studies on best care delivery for patients

Elaine Book

Pacific Parkinson's Research Centre, Vancouver, BC, Canada

With patients/family members, the role of the social worker on the PD team is to provide information, counseling and referral service to assist patients/family understand, adjust and manage the emotional, social and practical concerns that may arise as a result of PD. The social worker also plays a valuable role in providing collateral information about the patient's social situation to the team members in the clinic and in the community, facilitating collaborative work to optimize the patient centered approach to PD. Through a case study, the role of the social worker on the PD team will be demonstrated.

PCO21

Panel: Interdisciplinary care in real practice: case studies on best care delivery for patients

Paul Rabsztyl

Netherlands

As sex is for most people part of quality of life, sexual issues should be part of the interdisciplinary approach in Parkinson care. In this session we will show with case studies how an interdisciplinary approach on complex issues such as difference in sexual desire, hypersexuality, orgasm dysfunction the sexologist can contribute to the quality of Parkinson care.

PCO22

Shivering Tears

Hans Holtslag

Netherlands

Hans Holtslag quotes William Shakespeare (his pseudonym): 'The question having a diagnose is: to be or not to be'. The Parkinson's disease forces him to rewrite his script.

Without the Parkinson's disease he pretended everything was OK. Now he can't ignore what his body is telling him and others. He has to deal with a shaking body and shivering tears. This tears are the words which his heart can't tell.

The Parkinson's disease invites him to be in dialogue with his body; it tells him what he needs. The disease challenges him to change his ideas, his goals and activities. That gives him the opportunity to discover the world again.

This performance will challenge you to look through the eyes of a patient.

PCO23

Panel: Interdisciplinary care in real practice: case studies on best care delivery for patients

Jane Busch

USA

Parkinson's disease is complex disease that requires a team of healthcare professionals to deliver optimal care. Dentists are an integral component of this team because there is an important interplay between oral health and systemic health. Many symptoms of Parkinson's affect oral health, and dentists need medical information to provide safe and effective treatment.

Neurological concerns must be evaluated on a Parkinson person-to-person basis. Motor symptoms, such as bradykinesia, tremors and dysphagia affect the oral/facial structures. Non-motor symptoms include cognitive decline, depression, impulse control disorders, temperature regulation difficulties, sleep disorders, orthostatic hypotension and urinary dysfunction. In addition, dental treatment for the Parkinson patient may be affected by Parkinson medications. Negative drug interactions can occur with the use of local anesthetics containing epinephrine. Amounts must be reduced to prevent a rise in blood pressure. Pain medications must be chosen that are not contra-indicated for patients taking a MAO-B Inhibitors.

There are a number of recommendations for specifically treating the Parkinson dental patient. Full mouth restoration is best done in the early stage of PD. Appointments should be short and in the morning. The dental chair should not be reclined past 45 degrees. Rubber dam, bite blocks and saliva ejectors may offer comfort and safety. Dentists should evaluate for bruxism, tooth attrition, dental caries risk, TMJ dysfunction and denture fit. At appointment end, the chair should be raised slowly and patient assist given to avoid

syncope or falls. Advanced Parkinson patients may require sedation or general anesthesia in a hospital setting. In conclusion, dentists play an integral part in the overall optimal care of the Parkinson patient.

PCO24

Panel: Interdisciplinary care in real practice: case studies on best care delivery for patients

Dan Gold

John Hopkins Medicine, Baltimore, Maryland, USA

Visual symptoms in Parkinson's disease are very common, and stem from the simple (ocular surface irritation) to the more complex (eye movement disorders or subnormal vision from retinal dopamine depletion). A thorough ophthalmic/neuro-ophthalmic examination can offer an explanation for most visual symptoms in PD, and fortunately, treatments exist for many of these disorders. This talk will discuss why interdisciplinary collaboration with an eye care professional is beneficial to the patient with PD, and which type(s) of eye doctor would be most appropriate for each common visual complaint.

PCO25

Scientific basis & future perspectives of interdisciplinary care: Talk #1 – Collaborative care models: what's the evidence?

Marjolein van der Marck

Netherlands

The scientific evidence to support the merits of individual allied healthcare interventions is increasing, and, preferably, these specialists should work together as a team instead of working parallel to one another. Indeed, the multidimensional nature of Parkinson's disease and the shortcomings of current medical management to adequately control all symptoms call for a broad approach with input from multiple disciplines, as opposed to the single-clinician management which is still the dominant approach for many patients. A team-oriented approach is therefore widely suggested to represent the optimal treatment approach for complex disorders like Parkinson's disease. There is however no standard template on how to organize such an interdisciplinary approach to manage the wide spectrum of motor and non-motor symptoms that patients experience throughout the course of the disease. As a result, the organization of team-based approaches differs widely across different Parkinson centers worldwide. This presentation will cover the scientific evidence of multidisciplinary approaches in care for patients with Parkinson's disease. Shared common elements of organizations of team-based models will be highlighted as well as the differences regarding actual implementation of care. Also, challenges to clinical research on multifaceted care will be discussed including methodological and practical difficulties that have to be faced when designing and implementing trials on complex interventions like multispecialty approaches.

PCO26

Panel: Evidence for mono-disciplinary care: physical, occupational and speech therapy

Lynn Rochester

Newcastle University, Newcastle upon Tyne, United Kingdom

Parkinson's disease (PD) is a complex multisystem neurodegenerative condition which impacts physical function (e.g. gait, postural control and falls risk amongst other motor complaints). The

response to therapy is heterogenous and limited highlighting the need for therapies to complement existing treatment and augment motor function. Physical therapy plays an important role in the management of Parkinson's in this respect. Increased evidence supports the role of physiotherapy to address a wide range of physical symptoms and evidence based guidelines have been published to support the provision of physical therapy and provide a benchmark for standard of care. Physical therapy can be divided into two main approaches: exercise and compensatory strategy training. Exercise addresses the secondary effects of movement disorders related to de-conditioning. Exercise targets strength, endurance, balance and co-ordination and flexibility. There is a large body of evidence that supports the use of exercise to reduce gait impairments, improve balance and overall mobility and emerging evidence for falls reduction. Compensatory strategies or movement strategy training also shows important therapeutic benefits for gait and functional activities. Studies show that cueing (attentional, visual and auditory) improves gait performance and is also useful to reduce and prevent FOG. This presentation will summarise the latest evidence for physical therapy in PD, together with an optimal timeline for intervention.

PCO27

Panel: Evidence for mono-disciplinary care: physical, occupational and speech therapy

Hanneke Kalfe

Netherlands

The characteristic motor and non-motor changes in persons with Parkinson's disease (PwP) also worsen speaking and swallowing in a typical manner. Hypokinesia and rigidity reduce breathing, voice quality and loudness, articulation, prosody, swallowing speed and swallowing frequency. This may result in worsening of intelligibility, intake of food and liquid, up to reduced conversation and social participation. The key component of behavioural treatment, similar to other activities (walking, dressing etc.) is to train a PwP to overcome hypokinesia.

To overcome hypokinetic speech, PwPs in short need to learn to speak louder, despite their changed auditory feedback. Although Cochrane reviews show insufficient evidence to support the efficacy of any form of speech treatment for Parkinson's disease (PD) there is evidence from small studies that intensive training techniques like Lee Silverman Voice Treatment (LSVT) and Pitch Limiting Voice Treatment (PLVT), that aim to train PwPs to speak louder, do improve speech loudness resulting in intelligible speech. Nevertheless, there is a need for larger trials to demonstrate who may profit from such approaches, measured with functional outcomes. Communication may further be hampered by slowness of word finding, for which treatment options are scarcely published.

Difficulty with swallowing (dysphagia) in general is not an early sign of PD and may start with occasional choking when drinking coffee. In advanced PD, choking, struggling with food residue after swallowing and difficulty with taking pills may put PwPs at risk for aspiration pneumonia or less benefit from medication. Although the pathophysiology of hypokinetic dysphagia is not fully understood yet, behavioural treatment (similar to dysarthria) is aimed at overcoming hypokinesie. There is evidence for the efficacy of exercises to swallow with more effort or to improve expiratory strength, but more studies with functional outcomes and longer follow-up are required.

Drooling (loss of saliva) is a multi-factorial symptom, partially caused to hypokinetic dysphagia. Except for making PwPs aware of factors that can be compensated, there is paucity in the literature regarding behavioural treatment options.

PCO28**Panel: Evidence for mono-disciplinary care: physical, occupational and speech therapy***Linda Tickle-Degnen*

Tufts University, Medford, Massachusetts, USA

Parkinson's disease affects participation in valued life activities in the home, community and workplace. Occupational therapists use models of assessment and intervention that are targeted at maximizing the fit between a person's capacities and preferences, the task requirements needed to perform the person's valued activities, and the physical and social environment where these activities are performed in daily life. Occupational therapists analyze activity performance in order to adjust activities and their settings for optimal performance. The evidence for the outcomes of occupational therapy in Parkinson's disease is emerging. Current evidence suggests that occupational therapy at the early to middle stages of the disease is suitable for helping people with Parkinson's and their care partners to learn how to self-manage and adapt daily life activities and routines to maintain and promote their quality of life. There is considerable evidence that engaging in valued social activities and roles in home and community is health protective in older adults in general and likely to be protective of quality of life in Parkinson's as well. This presentation will discuss the current evidence for occupational therapy with Parkinson's.

PCO29**Perspectives on psychosis in Parkinson's disease – Talk #1: Recent developments in our understanding of Parkinson's psychosis***Daniel Weintraub*

Perelman School of Medicine at the University of Pennsylvania, Philadelphia, USA

Psychosis in Parkinson's is a common and sometimes disabling (leading cause of institutionalization) psychiatric complication in Parkinson's disease (PD). The cumulative prevalence rates are higher than previously thought (50-60%). Recent research documents that psychosis is not uncommon even at disease onset. The occurrence of "minor" symptoms (passage, presence, illusions) may be harbingers of more severe psychosis in the future. Psychosis in PD is not just visual hallucinations, but also auditory, tactile, and olfactory. And not just hallucinations either, but also delusions too in a subset. Psychosis is different than RBD, vivid dreams, and sleep-emergent symptoms such as hypnagogic/hypnopompic (psychosis occurs during full waking state). There is a complex etiology for PD psychosis. Once thought to simply be a side effect of dopaminergic therapy, recent data in de novo PD and also dementia with Lewy bodies (DLB; where psychosis occurs in 75% of patients at time of diagnosis without dopaminergic therapy) suggests that disease pathology plays an important role too. There is also now recognition of importance of serotonin system in PD psychosis based on PET imaging pathology studies too. There is a strong association between psychosis and cognitive impairment, with psychosis becoming more common in older patients with advanced disease.

PCO30**Perspectives on psychosis in Parkinson's disease – Talk #4: Modern treatment for psychosis today***Stuart Isaacson*

Parkinson's Disease and Movement Disorders Center of Boca Raton, Boca Raton, Florida, USA

Over the past several years there has been a shift in how we think about the underlying cause of PDP. Rather than merely attributing PDP to a side effect of medications used to treat PD, more recently it has become apparent that PDP is really part of the underlying disease process of PD. Approximately 50 percent of patients with PD will develop PDP during the decades-long course of their disease, yet many caregivers and providers are surprised by the onset of psychotic symptoms. These symptoms may initially be mild, but tend to gradually increase in frequency and severity. Typical symptoms may include visual hallucinations (ie seeing children, visitors at dinner), delusions (ie, spousal infidelity, stealing money), and paranoia (ie, being watched). It can sometimes be difficult to get an accurate history. Specific questioning about psychosis symptoms of hallucinations, paranoia, and delusions is often needed to identify PDP. Often, patients and caregivers will not associate psychosis symptoms with PD.

The treatment of PDP is multifaceted. Reassurance is useful, and cognitive behavioral therapy can help. Reducing potentially offending dopaminergic and anticholinergic medications can lessen psychosis. An antipsychotic medication is sometimes needed. Most currently available antipsychotics worsen the motor symptoms of PD, as they block postsynaptic D2 dopamine receptors in the brain. The ultimate goal would be to improve PDP without worsening motor symptoms. Only clozapine (Clozaril), which requires weekly blood tests, and quetiapine (Seroquel), which can cause sedation, will not worsen motor symptoms.

With a greater understanding of PDP as a common part of PD, and with the recognition of the role of serotonin in PDP, new treatment options are being evaluated. One new serotonin inverse agonist medication that has recently been approved by the FDA for the treatment of PDP is pimavanserin (Nuplazid), which targets serotonin 5HT-2a receptors that play a key role in psychosis, without blocking dopamine. In clinical studies, pimavanserin was found to improve PDP symptoms, with demonstrated tolerability without worsening motor function. With its recent approval, pimavanserin is a much awaited and needed novel treatment option for patients with PDP.

Oral Sessions**O1****Targeted modulation of motor and mood circuits using deep brain stimulation: complementary studies in Parkinson's disease and major depression***Helen Mayberg*
USA

Deep Brain Stimulation (DBS), the therapeutic modulation of discrete neural circuits using implanted electrodes, is an established treatment for severe Parkinson's disease and an emerging strategy for intractable major depression. Catalyzed by availability of next generation devices that allow ongoing recording of local field potentials in the targeted circuit of interest, recent work now combines multi-modal neuroimaging with real-time behavioral and electrophysiological measurements, providing a more precise method to identify the optimal target location and stimulation parameters for individual patients. Together these studies offer a unique perspective on critical pathways and mechanisms mediating clinical effects of DBS, and on the pathophysiology of both Parkinson's Disease and Major Depression more generally.

O2

What is new in DBS – a clinical perspective: notions of decision-making, early vs. late

Andres Lozano
Canada

For many patients with Parkinson's disease who continue to be disabled despite medical therapy, Deep Brain Stimulation (DBS) can provide significant benefit. So far, more than 100,000 patients throughout the world with Parkinson's disease have received DBS. There have been significant advances in this field including the selection of the best target whether it be STN or GPI, the introduction of directional leads to better direct the current to get optimal results and avoid side effects. Other emerging strategies include the possibility of closed loop feedback systems that turn on and deliver electrical stimulation only when required. These advances plus the possibility of doing procedures with MR guidance with the patients awake or asleep and reducing the time of operations are also significant developments

O3

Outcome: what can you expect in the short term and long term?

Michael Okun
UF Center for Movement Disorders and Neurorestoration,
Gainesville, Florida, USA

Patients considering deep brain stimulation (DBS) for Parkinson disease (PD) may be exposed to videotapes, media coverage, or literature which show dramatic improvements in PD symptoms after surgical intervention. Based on this information, patients may seek a medical center with expertise in DBS for an evaluation and assessment of their candidacy for surgery. If patients receive a device, they may be disappointed or despondent following surgery because of a failure to achieve a preconceived and unrealistic outcome. There are ways to address the important issue of patient misconception of potential outcome. Expectation information should be reviewed with patients and families both before and after surgery. Persons with Parkinson's disease and families should be given the time necessary to consider and alter the perception of perceived benefit. This education can help to ensure that outcome meets or exceeds expectation, and as a result persons with Parkinson's disease become a more satisfied and easy-to-manage partner. Finally, education from multiple members of the DBS team during the screening process can also be a useful and reinforcing approach.

O4

DBS: the lived experience

Andy McDowell
New Zealand

My presentation will cover

- my life before Parkinsons
- my experience with diagnosis and dealing with it
- my lead up to DBS
- the procedure and aftermath
- the (Life changing) results

I will then introduce "Lessons from Brain surgery – for beginners" and complete the session with a "exercise in gratitude"

O5

Levodopa: where we've come and where we are going

John Nutt
Oregon Health & Science University, Oregon, USA

Levodopa (LD) is a marvelous treatment for Parkinson's disease (PD). However, its clinical use poses challenges. LD is absorbed only from the small intestine; it has a short half-life so blood levels vary minute to minute making delivery to the brain variable and finally, its entry into the brain is influenced by amino acids in food. These factors contribute to the fluctuating response to LD. A variety of methods to produce continuous delivery of LD via the gastrointestinal tract or to bypass the gastrointestinal tract altogether are entering the market or are in early clinical trials. Methods to improve entry into the brain by altering LD blood-brain transport system are imaginable. But will overcoming these pharmacokinetic challenges be sufficient to produce a continuous "on" state? Even with constant blood LD patients still have "off" periods.

The response to LD changes with long-term administration and progression of the disease. Motor fluctuations which have been mild and often unnoticed early in the treatment appear. Onset of response is shortened and the magnitude is increased. But another change is the long-duration response, a response to dopaminergic drugs that develops and decays over weeks with repeated dosing. The long-duration response may be the same magnitude as the immediate response to LD and early in treatment may obscure the short-duration response. If the origin of the long-duration response was understood it could be manipulated to therapeutic benefit.

Oral administration and even new methods to administer LD continuously can not mimic the normal pattern of tonic and phasic release of dopamine from nerve terminals. Feedback loops based on physical or brain activity could tailor delivery of LD in relation to need. In advanced PD, conversion of LD to dopamine likely occurs in serotonergic nerve terminals and other cells in the striatum leading to release of dopamine in no relation to normal targets or physiological needs. Further, decarboxylation to dopamine may become limiting in advanced PD. Remodeling the striatum by grafting or gene therapy may overcome these limitations.

Fifty years later, challenges abound but many opportunities also exist to improve our use of LD in PD.

O6

Lecture #1: The psychological journey of Parkinson's – the importance of a positive attitude

Bob Kuhn
Trinity Western University, Canada

No wonder many people with Parkinson's disease suffer from depression. PD is a vicious and unpredictable threat to any otherwise well-adjusted person with Parkinson's (PWP). It affects your physical, mental, emotional and relational life. It inevitably takes charge of virtually all aspects of living. Everything seems to slip out of your control. Despite the medication, therapy, and even DBS, you feel invaded, helpless, frightened, discouraged, defeated, and even hopeless. But this degenerative and debilitating disease lacks control over one thing. It is something that you have complete control over. Something that makes all the difference.

This talk will focus on the importance of attitude in response to Parkinson's disease. It is the one thing that you can control. Attitude is your Basic Choice. Success, relationships, quality of life and even your health itself are directly affected by your choice of attitude. But how can you develop and maintain the right attitude?

If you feel like you're losing the fight against Parkinson's disease and its myriad of symptoms, this session will challenge you to

consider how to get “back in the ring”. Even if you are a caregiver or healthcare professional, your attitude can have a significant impact on the person with PD. Attitude leads to Action which results in Accomplishment.

Studies prove that one of the most significant issues in dealing with major health challenges is a person’s attitude. Yet, it is rarely discussed. Why is that? Are we afraid to be “Positively Parkinson’s”?

O7

Lecture #2: Living well with Parkinson’s – a framework for self-care

Jane Busch
USA

Coming to grips with the reality of Parkinson’s disease is not easy or quick. It creates a cascade of emotions from shock and denial to anger and fear. Hopefully it leads to acceptance. It takes time. Your physicians ask you to accept this diagnosis after simply watching you walk, tap your fingers together and falter when pushed from behind. It would be easier to believe something more tangible, like an x-ray or lab test. Sometimes it takes time for physicians to accurately diagnose. Young women are not the garden variety of Parkinson’s and doctors are taught to look for horses, not zebras. I was a zebra. I have Parkinson’s.

In time, I accepted my new identity and I committed myself to creating a positive framework for self-care. I found a physician who gave me the 5 keys to living well with Parkinson’s. I adopted the keys and they surprised me by opening doors to new experiences and strong friendships. The keys are 1) feed your body good nutrition 2) supplement your life with vitamins 3) there is magic in movement, exercise, 4) live in the present with mindfulness and 5) volunteer, it gives riches to the spirit and purpose to life. These keys have unlocked the freedom to be the new me, to nurture myself and my health, to appreciate new friendships. They are my framework for living well with Parkinson’s.

O8

Lecture #3: Communication, communication, communication

Dilys Parker
New Zealand

Many factors contribute to how we can live well with Parkinson’s and one vital area is communication, the focus of this session. The language we use can define us and our world in a way that can be liberating but language can also be restricting. How we speak of Parkinson’s and how others speak of it to us shapes our understanding and can have implications far beyond the words used.

Diagnosis is often a time of high emotions as we are faced with redefining ourselves and adjusting to a new and different sense of who we are in the world. What we were told, by whom and how we were told become important milestones in our PD journey. We must then make decisions about when, where and to whom we communicate this news.

As we are finding our place in this new reality our family, colleagues and friends are also adjusting. Communication is at the centre of this time of change. The spoken word is just one element in this as so much of how we communicate is non verbal. In addition there is the wider societal context to consider. All this contributes to the way our life is viewed by ourselves and by others.

Being aware of how we communicate and the factors that influence communication opens up the possibility of choice. Having choice means we can decide how we might live our lives in ways that are personally fulfilling.

O9

Lecture #1: Why did previous neuroprotective trials fail and what are we doing to address these issues?

Kalpna Merchant
Indianapolis, Indiana, USA

Recent years have seen tremendous advances in the understanding of the pathogenesis and pathophysiology of Parkinson’s Disease (PD). In parallel, a large number of investigational drugs have been tested in PD patients, with none showing medically relevant efficacy at slowing the disease progression. This talk will focus on key reasons underlying the clinical failures and ways to improve the success rate of future clinical trials. These include: (a) methods to assess and establish the validity of the mechanism of the investigational therapy, (b) dose selection strategy and associated necessity to demonstrate modulation of the intended target/pathway in early phase clinical trials, (c) considerations for selection of patients most likely to respond, (d) other clinical trial design components such data-informed adaptive trials, futility analyses, length of the treatment duration, etc., and finally (e) end-points selected for assessment of neuroprotection/disease modification. Through integration of appropriate biomarkers, clinical end-points and informative trial design, it is possible to translate breakthroughs in basic science to effective therapies for PD patients.

O10

Lecture #3: Drug repurposing: calcium channel blockers and beyond

Richard Wyse
The Cure Parkinson Trust, United Kingdom

To identify and clinically test disease-modifying drugs for PD patients we used an approach so far unique to any other therapeutic area. We assembled an international committee comprised of 15 acknowledged PD experts who have amongst them a wide range of complementary PD clinical, biochemical and pharmaceutical skills. Focusing on >65 candidate biological targets known to be relevant for PD, and often drawing from cutting-edge breakthroughs in other therapeutic areas, over the past 5 years we have compiled for this committee extremely detailed dossiers on >120 candidate drugs each with strong potential, and compelling biochemical arguments, for repurposing as disease-modifying therapeutics for PD patients. Partially feeding this unique initiative, several drugs for repurposing (such as Parkin agonists, PARIS inhibitors and mitochondrial modulators) have been specifically identified for this clinical PD program via various dedicated drug screening programs that we have commissioned from laboratories worldwide.

With the highly comprehensive drug dossiers as their startpoint, members of the PD expert committee are tasked during a month-long assessment process culminating in extended face-to-face meetings, with prioritizing (on the basis of safety, efficacy, pre-clinical justification and rationale, target engagement, bioavailability etc) which therapeutics should enter proof-of-concept Phase II adaptive clinical trials in PD patients in many of the specialist neurological hospitals around the world. So far, around 30 of these 120 drugs have now been actively prioritized by this committee. Included amongst these therapeutics, many of which were previously unknown to PD researchers, are 4 different mitochondrial-specific drugs, a wide range of enzyme inhibitors and agonists, drugs which impact on cellular energy homeostasis, as well as several drugs which each impact on various other PD-relevant biological targets. Many of the drugs not prioritized have returned for additional pre-clinical testing, or for further patient safety or dose-finding studies, as requested by the committee and

may well enter PD trials later after further detailed scrutiny via this rigorous assessment process.

Several of these prioritized PD clinical trials have already started, 4 of which will finish during 2016, with others finishing in 2017, 2018 and 2019. We believe the best way to develop fundamental new disease-modifying treatments for PD is to bring together a very large A-team of PD experts to select, by rigorous mutual consensus, highly promising therapeutics for testing clinically in PD patients. Only this way can we determine which of the many highly creditable pharmaceutical approaches will emerge from this exacting process as being superior for long-term therapeutic use in PD patients, or for particular PD patient groups. We are now working on repurposed drug combinations to enter clinical trials that will cohesively tackle separate biochemical elements of the disease simultaneously, and that we hope will build even further on the excellent results we have enjoyed so far. This forward-looking presentation will describe our unique global approach to run multiple PD trials in parallel, and will update to Q3/2016 on the progress and results of these vital disease-modifying PD trials.

O11

Lecture #1: Phenotypic spectrum and biomarkers of cognitive deficits in Parkinson's disease

David Burn

Newcastle University, Newcastle, United Kingdom

Up to 40% of people with early Parkinson's (PD) will display cognitive deficits on formal testing, but in a majority these deficits have little impact upon activities of daily living. "Mild cognitive impairment (MCI)" associated with PD affects different cognitive domains (e.g. memory, attention, visuospatial function). PD-MCI affects quality of life in the person with PD and their carers. Attentional impairments may be most important in determining poorer quality of life. The pathophysiological substrate underpinning the early cognitive deficits in PD is varied both neurochemically and neuropathologically. Cognitive deficits mediated by dopaminergic dysfunction (particularly via the caudate nucleus) are common but may not necessarily predict cognitive decline. The role of norepinephrine is yet to fully established, but is likely to be important in mediating attentional function. Perhaps the most "malignant" substrate relates to cholinergic deficiency, which is also a key player in the symptoms of dementia associated with PD.

Progression to dementia in PD is by no means inevitable, but occurs around six times more commonly than in age-matched people without PD. Current age is the biggest risk factor for dementia in PD, but other factors, including motor phenotype and genotypic background are also involved.

Research has focused upon phenotypic, "wet" (e.g. cerebrospinal fluid, CSF) and "dry" (e.g. neuroimaging) biomarkers that may more accurately predict and monitor cognitive decline in people with PD. Although progress has been made there remain issues with regard to predictive value in the individual subject, rather than in a group setting, as well as the availability (and to some degree acceptability) of some investigations. From the phenotypic perspective, a postural instability-gait difficulty motor pattern, autonomic dysfunction and presence of REM Sleep Behaviour Disorder appear to predict cognitive decline. Low levels CSF beta-amyloid, above median retention of 11C-PIB on PET scanning, and reduced inhibition of short-latency afferent inhibition, amongst others, may all indicate a greater likelihood of dementia. Future research should focus upon establishing more robust biomarkers that may be applied widely, with high levels of acceptability. Ultimately, identifying individuals at high risk of dementia will allow earlier and more focused use of disease-modifying treatments.

O12

Genetic risk for cognitive impairment in Parkinson's disease

Thomas Montine, Cyrus Zabetian, Brenna Cholerton, Ignacio Mata
USA

Parkinson's disease (PD) is a growing global health problem that causes untold suffering for patients and their loved ones, and challenges health care systems. Motor symptoms are the classic features for which there are effective interventions; however, non-motor symptoms, especially cognitive impairment, are very common, may precede motor symptoms, and do not respond well to existing therapies. The Pacific Northwest Udall Center (PANUC) and its collaborators in the PD Cognitive Genetics Consortium (PDCGC) are investigating the genetic risk for cognitive impairment in PD to hasten the day of precision medicine for this common, debilitating non-motor symptom of PD, using a candidate gene approach to examine SNCA, MAPT, APOE, LRRK2 and GBA. In cross-sectional analyses of baseline psychometric data, variation in two genes (APOE and GBA) was found to have an important, negative impact on cognitive performance in PD. The APOE e4 allele predicted lower performance across multiple domains including memory, executive function, and verbal fluency. When subjects with dementia were excluded, the effects of APOE e4 were restricted to declarative memory and semantic verbal fluency, a pattern that is consistent with deficits in frequently observed in early AD. In contrast, GBA variants were primarily associated with lower performance on tests of working memory/executive function and visuospatial abilities. Conversely, LRRK2 variants were associated with better working memory and a lower prevalence of dementia among PD patients. Variants in SNCA and MAPT that increase risk for PD motor symptoms did not influence risk for cognitive impairment. These findings are foundational to our proposal and represent an important step in clarifying the molecules that underlie the cognitive heterogeneity in PD.

O13

Lecture #3: Patients with Parkinson's disease show impaired use of priors in conditions of sensory uncertainty

Michele Basso

University of California, Los Angeles, Los Angeles, California, USA

Good decisions arise after carefully considering the available sensory evidence. When sensory information is unreliable a good strategy is to rely on previous experience in similar situations to guide decisions. We used a novel, perceptual decision-making task and manipulated the statistics of the sensory stimuli presented to patients with Parkinson's disease and healthy participants to determine the influence of past experience on decision-making in the presence of sensory uncertainty. We also modeled the data using the drift diffusion model, a popular model of decision-making. We found that patients with Parkinson's disease on medication were impaired at using prior information to guide choices in the presence of sensory uncertainty and that this impairment resulted from a failure to adjust their starting point of evidence accumulation, consistent with an impairment in adjusting the amount of evidence needed to make a decision. A change in the starting point of evidence accumulation reflects an asymmetric adjustment in the amount of sensory evidence that needs to be collected for each of the options before committing to a choice. Interestingly, patients were able to adjust their drift rate according to the prior experience, consistent with an ability to learn from feedback and in some cases this adjustment was sufficient to overcome the "frozen" starting point of evidence accumulation leading to some benefit of the prior experience. Together these results suggest a general impairment in decision-making in patients with Parkinson's disease when those

decisions require the combination of multiple sources of information; in this case sensory and previously learned information. Furthermore, the general deficit patients exhibited in adjusting their starting point of evidence accumulation could explain some of the motor symptoms seen in patients such as paradoxical movement and freezing of gait and may represent a common mechanism underlying dysfunction in patients with Parkinson's disease.

O14

Lecture #1: Dysregulation of mRNA translation by PD-associated LRRK2 mutations

Ian Martin¹(Presenter), Jungwoo Kim¹, Byoung Dae Lee², Hochul Kang², Jinchong Xu¹, Hao Jia¹, Min Sik Kim¹, Jun Zhong¹, Dennis Dickson¹, Zbigniew Wszolek¹, Akhilesh Pandey¹, Ted Dawson¹, Valina Dawson¹

¹ USA

² Korea

Mutations in LRRK2 (leucine-rich repeat kinase 2) are the most common genetic cause of PD. While the biology of LRRK2 remains unclear, mutations that segregate with the disease are found in its ROC-COR and kinase domains indicating that altered enzymatic output contributes to disease development. Prominent kinase domain mutations (G2019S and I2020T) bestow elevated kinase activity to LRRK2 which, when blocked, can prevent mutant LRRK2 toxicity in cell and animal disease models. Screening for LRRK2 kinase substrates revealed ribosomal protein s15 as a key pathogenic substrate and led to the observation of a substantial increase in bulk mRNA translation caused by G2019S LRRK2 which is mediated via s15 phosphorylation. This induction of translation is central to the neurodegenerative phenotypes exhibited by aged LRRK2 transgenic *Drosophila*, as evidenced by a rescue effect of treatment with protein synthesis inhibitors of expression of phospho-deficient T136A s15. Current work is focused on better understanding the link between dysregulated mRNA translation and neurodegeneration with the ultimate goal of identifying therapeutic targets to combat disease progression.

O15

Lecture #2: Interplay of LRRK2 and alpha-synuclein in the pathogenesis of PD

Andrew West

University of Alabama, Birmingham, Alabama, USA

α -Synuclein is genetically linked to Parkinson disease (PD) susceptibility and encodes the protein that composes Lewy inclusions that define PD pathology. The most common genetic cause of PD is the G2019S LRRK2 mutation that upregulates kinase activity in the encoded protein. The molecular interaction between α -synuclein neurotoxicity and LRRK2 in PD susceptibility is not clear. We have used several model systems in rodents to show that LRRK2 deficiency protects from α -synuclein neurotoxicity whereas the G2019S LRRK2 mutation exacerbates α -synuclein neurotoxicity. In normal brain tissue, LRRK2 protein localizes to neurons, but in the presence of abnormal α -synuclein, LRRK2 protein accumulates in cells of the innate immune system. In neurons in culture and in the brain, we have found that G2019S-LRRK2 protein may accelerate the progression of α -synuclein inclusion formation in axons and in the cytosol, but did not change the probability of initiation formation of these inclusions. In macrophages that are recruited to the brain in response to neurons that harbor abnormal α -synuclein, we found that G2019S-LRRK2 expression in the macrophages may accelerate macrophage mobility and chemotactic responses. Through enhanced mobility,

G2019S-LRRK2 expression in macrophages may lead to the accumulation of excessive numbers of pro-inflammatory cells in the brain that fail to quiesce and can produce neurotoxic oxidative products and cytokines. We hypothesize that these LRRK2 actions in both neurons and macrophages may lead to the acceleration of neurodegenerative effects attributed to abnormal α -synuclein in PD.

O16

Lecture #3: LRRK2 regulation of synaptic function

Patrik Verstreken

KU Leuven, Leuven, Belgium

Neurodegeneration is characterized by misfolded proteins and dysfunctional synapses. However, how synaptic compartments normally cope with proteopathic stress resulting from synaptic activity is not understood. We found that the most commonly mutated protein in Parkinson's disease, LRRK2, regulates macroautophagy at presynaptic terminals by phosphorylating a synapse specific protein involved in endocytosis. This function is evolutionary conserved from flies to embryonic stem cell-derived human neurons. Specific targeted dysregulation of synaptic and LRRK2-dependent autophagy causes age-dependent decline in synaptic function and neurodegeneration, demonstrating the existence of a previously unknown, evolutionary conserved branch of autophagy critical for neuronal survival. Given the connections between several Parkinson's disease genes, vesicle trafficking and autophagy (LRRK2, Parkin, Synaptojanin, auxilin, etc), dysfunction of synapse-specific autophagy may be a common theme in this disorder.

O17

Talk #1: Gut-microbiome-brain connections

Sarkis Mazmanian

Caltech, Pasadena, CA, USA

Neurodevelopmental disorders, including autism spectrum disorder (ASD), are defined by core behavioral impairments; however, subsets of individuals display a spectrum of gastrointestinal (GI) abnormalities. We demonstrate GI barrier defects and microbiota alterations in the maternal immune activation (MIA) mouse model that is known to display features of ASD. Oral treatment of MIA offspring with the human commensal *Bacteroides fragilis* corrects gut permeability, alters microbial composition, and ameliorates defects in communicative, stereotypic, anxiety-like and sensorimotor behaviors. MIA offspring display an altered serum metabolomic profile, and *B. fragilis* modulates levels of several metabolites. Treating naive mice with a metabolite that is increased by MIA and restored by *B. fragilis* causes certain behavioral abnormalities, suggesting that gut bacterial effects on the host metabolome impact behavior. Taken together, these findings support a gut-microbiome-brain connection in a mouse model of ASD and identify a potential probiotic therapy for GI and particular behavioral symptoms in human neurodevelopmental disorders. The talk will also introduce how the concepts defined by this work may be extended to neurodegenerative disorders such as Parkinson's disease.

O18

Talk #2: Changes in gut microbiome as a biomarker for Parkinson's disease

Filip Scheperjans

Department of Neurology, Helsinki University Central Hospital, Helsinki, Finland

Biomarkers for PD are urgently needed, in particular markers for early (premotor) disease and disease progression. Such markers might enable a correct diagnosis and prognosis estimate as early as possible in the disease course so that future disease modifying therapies could achieve maximum efficacy. Gastrointestinal (GI) dysfunction affects up to 80% of PD-patients and may precede the onset of motor symptoms by years. Therefore, the GI tract is an intriguing site to search for promising premotor PD-biomarkers. Alpha-synuclein related changes in the enteric nervous system (ENS) can be found in earliest stages of PD. However, the sensitivity and specificity of these findings are not yet unequivocally established and an invasive sampling procedure is required. The pathogenesis leading to these pathological changes is still poorly understood, but mucosal barrier impairment and inflammation seem to be associated with it. Gut microbiota is in close physiological interaction with the mucosal immune system and as well the enteric and central nervous system. Alterations of microbiota composition and microbiota-host-interactions have been described in numerous diseases fuelling hope for better biomarkers, understanding of pathogenesis, and eventually treatments. Recently, we described reduced Prevotellaceae abundance and other alterations of gut microbiota in PD patients as compared to control subjects. Depending on the bacterial taxa included in the analysis, gut microbiota composition provided up to 86% sensitivity and 90% specificity for identifying PD patients. Two independent studies later confirmed microbiota alterations in PD, but comparisons are difficult due to major methodological differences between studies. Nevertheless, initial results provide proof-of-concept that gut microbiota analysis is worth being explored further regarding its biomarker potential for PD. In the future, it will be crucial to investigate whether gut microbiota composition and function are associated with clinically relevant questions in PD. Such questions include the presence and analytic accuracy of microbiota alterations in the premotor phase of PD, associations with disease progression, and its usability for differential diagnosis of parkinsonian syndromes. Larger longitudinal studies of international cohorts with well standardized protocols for recruitment and analysis could be the key to better understand the role of microbiota in PD and its biomarker potential.

O19

Talk #3: Linking changes in gut microbiome to alpha-synuclein misfolding as an early trigger of the disease process in Parkinson's

Kathleen Shannon

Department of Neurological Sciences, Rush Medical College, Chicago, Illinois, USA

Epidemiological and some neuropathological studies suggest that the gastrointestinal system may be an early site of involvement in Parkinson's disease. We and others have found multiple gastrointestinal abnormalities in early and more advanced PD subjects including: (1) increased intestinal permeability; (2) abnormal integrity of tight junction proteins; (3) evidence of increased inflammatory cytokines in intestinal tissue; (4) evidence of systemic exposure to the bacterial endotoxin lipopolysaccharide and (5) deranged microbiome compared to healthy controls; and (6) immunohistochemical evidence of mucosal and submucosal synuclein in PD subjects and some control subjects. In vitro and in vivo evidence suggests there may be a link between these intestinal abnormalities, particularly lipopolysaccharide exposure, and synuclein aggregation. Some have postulated that there may be a prion-like spread of synuclein from the enteric nervous system to the central nervous system. This presentation will review preclinical evidence linking intestinal abnormalities to synuclein aggregation and spread, as well as important human studies in this area,

highlighting variability in reported results and providing direction for future studies.

O20

Talk #1: Updates on the course, assessment and biological management of depression

Daniel Weintraub

Perelman School of Medicine at the University of Pennsylvania, Philadelphia, USA

Depression is among the first, most common, and most studied non-motor symptoms in Parkinson's disease (PD). It is associated with worse quality of life, caregiver burden, and poorer long-term outcomes. In recent years there have been numerous randomized clinical trials, both pharmacologic and non-pharmacologic, that provide an evidence base on which to base the treatment of depression in PD. In addition, there has been progress in our understanding of the neurobiology of depression in PD, its occurrence in de novo and at-risk PD, the impact of DBS on depressive symptoms, dysphoria as a symptoms of non-motor fluctuations, and further understanding of the relationship between depression and anxiety.

O21

Talk #2: Assessment and treatment of generalized anxiety, anxiety attacks, agoraphobia and social anxiety

Albert Leentjens

Maastricht University Medical Centre, Maastricht, Netherlands

Anxiety disorders are common in patients with Parkinson's disease (PD), and have a significant impact on the quality of life. Thirty-one percent of PD patients meet the diagnostic criteria for at least one anxiety disorder. Because of the overlap of symptoms of anxiety with depressive, autonomous and motor symptoms, assessment of anxiety may be difficult. Another factor complicating the assessment of anxiety is the fact that the DSM IV classification of anxiety disorders does not seem to reflect the clinical reality of the different presentations of anxiety in Parkinson's disease. Clinically there is evidence for persistent anxiety, which may either be generalized or situational, and episodic anxiety, and both forms may co-occur. Especially the persistent form of anxiety is frequently associated with depression. In addition, anxiety may be associated with motor fluctuations or 'wearing-off' of medication.

The severity and symptom range of anxiety can be assessed with anxiety rating scales. Although the reliability of the most commonly used anxiety rating scales is acceptable, construct validity is often a problem. For instance, the Hamilton Anxiety Rating Scale and the Beck Anxiety Inventory are differentially sensitive for generalized anxiety and panic attacks, and do not identify the same patients. The Parkinson Anxiety Scale has different subscales for these presentations and is best validated in this respect. It is the only anxiety scale that incorporates questions about avoidance behaviour.

Over 50% of PD patients with anxiety receive pharmacological treatment for anxiety symptoms. There is no scientific evidence to guide the choice of treatment however, since no study concerning the treatment of anxiety in PD has been published yet. One small pilot study of Cognitive Behavioural Therapy (CBT) in 16 PD patients with anxiety or depression has been published and reported improvement in depression and a trend towards improvement in anxiety (n=7). Studies involving CBT, buspirone and rotigotine, that specifically address anxiety in PD are ongoing.

O22

Talk #3: Non-pharmacological management of depression*Roseanne Dobkin*

RUTGERS, The State University of New Jersey, Piscataway, New Jersey, USA

This session describes non-pharmacological treatments that have been shown to be effective for reducing depressive disturbances in people with Parkinson's disease (PWP). Treatments range from relatively simple behavioral techniques, such as deep breathing, to longer-duration formal cognitive behavioral therapies (CBT) that can be provided in person or using telephone and internet-based methods. In brief, CBT works by teaching PWP the coping skills needed to manage their emotional reactions to the numerous challenges they face daily. Specifically, the treatment targets negative thoughts (e.g., I have no control; I am helpless) and behaviors (e.g., avoiding friends and family, lack of exercise, poor sleep habits, excessive worry) associated with depression. It also trains care-partners to help PWP practice healthy habits at home. Relevant clinical trials data, as well as strategies for overcoming barriers to effective mental health care utilization, will be highlighted throughout the presentation. As depression is associated with increased rates of physical, cognitive, and functional decline for PWP, the effective treatment of depression has the potential to enhance the overall quality and impact of all aspects of PD care.

O23

Talk #1: Gait dysfunction in early PD and implications for treatment*Sue Lord¹, Brook Galna², Rosie Morris², David Burn², Lynn Rochester²*¹ Newcastle University Institute for Ageing, Newcastle upon Tyne, United Kingdom² Institute of Neuroscience, Newcastle University, Newcastle upon Tyne, United Kingdom

Knowledge of gait dysfunction in early Parkinson's disease has been refined in recent years by two key areas. The first is greater awareness of the role of non-motor aspects (principally cognition) to gait and how these influence performance. The second is through measurement of discrete gait characteristics which allows a more nuanced approach to understanding the neural basis to gait deficit and the mechanisms that drive it. Advances in both fields influence treatment and help inform disease trajectory. For example, some features of gait (such as step hypokinesia) respond to medication which is the primary therapy of choice in the early stages of PD, whilst others (such as gait characteristics associated with postural control) are refractory. Similarly, physical therapy has a selective impact on gait. Understanding the non-motor and motor aspects of early gait disturbance, their change over time, and their response to treatment is important to optimise outcome. Cognitive-based physical therapy (eg movement strategy training and cue-based interventions) is effective but may be time-limited due to cognitive decline or because motor deficit becomes too great. Of further interest is the role of secondary features that arise from reduced mobility (such as attenuated muscle strength and loss of aerobic conditioning) which is an early and persistent feature of PD. Targetting primary and second features of gait disturbance is critical. This presentation discusses contributory features of gait dysfunction in early PD, and provides evidence for interventions to improve gait including pharma and non-pharma approaches, along with broader aspects of management.

O24

Talk #2: Facial masking: what are the social implications?*Linda Tickle-Degnen*

Tufts University, Medford, Massachusetts, USA

The face rapidly expresses emotion, personality, social vitality and cognitive status to other people. Facial masking (hypomimia or masked facies) is a reduction of facial expressiveness due to Parkinson's disease. A person with facial masking who is happy, friendly, socially engaged, and cognitively intact can appear incorrectly to be sad, withdrawn, apathetic or cognitively impaired. This incorrect impression can lead to stigmatization and difficulty sustaining one's personal relationships, social roles and daily activities that are the fabric of purposeful and satisfying living. The aims of this talk are to describe: (1) social daily function of the face, (2) emerging research findings on facial movement in Parkinson's, and (3) tips for optimizing one's ability to express oneself through the face and other means

O25

Talk #3: Impact of early training to improve vocalization in PD*Cynthia Fox*

LSVT Global, Tuscon, Arizona, USA

Voice, speech and communication problems are extremely common in people with PD with reports as high as 89% of people with PD suffering from speech dysfunction. In contrast to historical observations suggesting a mid or late-stage onset of speech symptoms, more recent investigations with sensitive and valid measures consistently report speech symptoms early in the course of PD with such notable consequences as exclusion from conversations, loss of dignity, and feelings of isolation. Given the early onset of voice and speech disorders in many people with PD, it is important to have a speech-language evaluation upon diagnosis and, if necessary, speech treatment early in the course of PD. Evidence-based treatments for speech changes in early PD, such as the Lee Silverman Voice Treatment (LSVT LOUD), exist. Data post LSVT LOUD in people with early PD have demonstrated improvements in both acoustic aspects of the speech signal (e.g., improved vocal loudness) as well as self-reported improvements in communication effectiveness. Identifying early changes in voice and speech, treating these symptoms with evidence-based approaches, and maintaining vocal exercise over time can collectively minimize the negative impact of PD on communication.

O26

Roundtable #1: Hallucinations and PD*Joseph Friedman*

Butler Hospital, Providence, Rhode Island, USA

Hallucinations occur in 20–30% of PD patients treated with PD medications. These are usually visual, but may affect any of the special senses (hearing, smell, taste or touch). They are surprisingly stereotypic, in that most are of people, often children, or smaller than normal people, who ignore the patient and simply go about their business, as if the patient didn't exist. Another type of false sensation, called "presence hallucinations," are a feeling that someone or something is behind or nearby, when there is no one there. These are rarely associated with any feeling of distress or fear, but are simply annoying. The presence of hallucinations are a deterrent for increases in medications for PD motor symptoms as all of these medications may worsen the hallucinations. The importance of recognizing hallucinations as part of the illness, and

the fact that these rarely may even occur before PD medications are started, is important because patients often fear that they are "going crazy," and are reluctant to share their experience with others. This session will discuss the phenomenology of hallucinations, what importance they signal for future treatment and prognosis, and when and how they should be treated. Effective medications are available.

O27

Roundtable #2: Cannabis and Parkinson's?: what's all the fuss?

Benzi Kluger

Denver, Colorado, USA

There is growing interest in the Parkinson's disease (PD) community regarding the therapeutic potential of marijuana (cannabis) and cannabinoid-based chemicals for specific symptoms of PD as well as slowing disease progression. This interest has been driven both by changes in the legal status of cannabis in many areas and increasing research into the roles of endocannabinoids within the central nervous system. In this Roundtable Session we will review the current status of both basic science and clinical studies as they relate to the symptoms of PD and the therapeutic potential of cannabinoids for PD. As there are over 60 neuroactive cannabinoids identified to date this is a complex field and there is much research to be done before definitive conclusions can be drawn. The endocannabinoid system is known to modulate neurotransmission involved in motor function, particularly within the basal ganglia. Preclinical research in animal models have shown variable evidence for symptomatic benefits, but suggest potential neuroprotective effects in several animal models of Parkinson's (PD). Clinical observations of cannabinoid-based therapies suggest a possible benefit of cannabinoids for both motor and nonmotor symptoms in PD but controlled clinical trials to date have failed to demonstrate symptomatic benefits, at least for the compounds and doses tested. Despite the widespread publicity about the medical benefits of cannabinoids the current evidence available is either negative or inconclusive. Further preclinical and clinical research is needed to better characterize the pharmacological, physiological, and therapeutic effects of this class of drugs for PD.

O28

Roundtable #3: Living alone with PD

Ryan Tripp¹, Elaine Book²

¹ World Parkinson Congress, Bracebridge, Ontario, Canada

² Pacific Parkinson's Research Centre, NPF Center of Excellence, Vancouver, Canada

Living single with Parkinson's disease presents challenges that require careful planning in the immediate and foreseeable future. Many people with Parkinson's live alone and are quite successful. In order to accomplish this, adjustments in the home environment and activities of daily living may be needed to increase safety, and improve quality of life. This session will provide an opportunity for attendees to share common concerns and challenges of living alone at home with Parkinson's on a daily basis.

A guided discussion will be facilitated by a person who lives at home alone and a clinical social worker. The discussion will focus on strategies to modify and equip the home, build a support system to deal with motor and non-motor symptoms, and identify important personal human and financial resources.

Eventually and ultimately, the summary and conclusion will segway from, not just physically living alone or flying solo, but also the need and importance of your Parkinson's Team. This "Team" enables you to live alone in a safe environment and maintain a quality of life that

acceptable and meaningful for you, your family and friends and the surrounding community.

Acronyms:

Alone: A – attitude L – laughter O – organization N – nutrition E – exercise

Flying: F – freedom L – listen Y – yahoo I – independence N – network G – goal setting

Solo: S – safety O – openness L – laugh O – often

PD Team: P – positive D – direction T – team E – engagement A – a M – must

O29

Roundtable #4: Managing PD motor symptoms

Sotirios Parashos

University of Minnesota, Minneapolis, Minnesota, USA

Parkinson's disease affects lives in many different ways, yet mobility challenges continue to be one of the foremost sources of disability for persons with Parkinson's. Although medications can help many of the motor symptoms, most people with Parkinson's will have either motor symptoms that are not fully controlled despite best medical treatment, or motor symptoms that are not helped by medications or DBS surgery at all. In this round table we will review whether medical treatment may or may not help certain motor symptoms, discuss strategies and techniques that will help persons with Parkinson's manage motor symptoms, either by using a training approach, or by pursuing compensatory strategies. Exercise, rehabilitation treatments, and the philosophy behind these treatments will be discussed, but also tools that can be used in day-to-day activities. We will pay particular attention to some motor symptoms that are notoriously fickle when it comes to response to medications, such as freezing of gait, and falling and balance troubles. We will explore new ways to perform certain tasks and discuss the role of adaptive equipment.

O30

Roundtable #5: Sex and PD: how to stay close to your partner

Gila Bronner

Center for Sexual Medicine, Israel

Introduction: Staying close to a partner and keeping intimate relationship requires a lot of time and effort. Intimacy plays a central role in the human experience and quality of life. Intimacy doesn't only refer to erotic events. It includes a basic need to belong, to be close (mentally and physically), to be significant and to be loved. People with Parkinson's disease (PD) and their partners have to cope with multi-faceted challenges and their intimacy may be impaired.

Objectives of this roundtable: To enable the participants an opportunity to discuss openly suggestions for how to stay connected with a spouse and increase intimacy and intimate communication.

Methods and Results: Participants will discuss various options to increase intimacy and stay close within their relationship. Verbal and non-verbal communication will be practiced and evaluated. Effective, accessible and practical strategies will be presented, and implementation modes will be discussed. This interactive dialog may enable couples living with PD to communicate more intimately and increase their motivation to make efforts to stay close.

Conclusions and recommendations: People who are open to share their feelings, thoughts and ideas without the fears of being misunderstood, can achieve intimacy in their relationship. Maintaining intimate communication in a relationship will have a positive impact on the long-term effects of PD and may assist patients and their partners in staying close and feeling good with one another.

O31

Roundtable #6: PD for a day: how to help others understand what it's like to live with PDJean Burns¹, Peter Schmidt²¹ Sun Lakes, AZ, USA² NPF, Miami, FL, USA

Discussion of the program: PD for a day. A person with PD (pwp) spends a day with a learner (scientist, member of PD community, neurologist, etc). Throughout a day, the pwp and learner communicate. The pwp tells the learner how they feel, and how they go about their day. For instance, if the pwp is freezing, they might have their learner walk backwards. Or to show difficulty typing, wear 2 pair of rubber gloves. The goal is for learners to get a feel – and have real empathy – on what it is like to have PD 24/7. This roundtable describes what happened in a PD for a day in 2015 with Smart patients. We want to teach others how to do this.

O32

Roundtable #6: PD for a day: how to help others understand what it's like to live with PD

Peter Schmidt

National Parkinson Foundation, USA

Researchers and clinicians may know the biology and treatment of Parkinson's, but what is it really like to experience Parkinson's? A group of patient leaders, with the help of some experts in patient empowerment, decided to give a group of clinicians, researchers, and patient advocacy group executives each a one-day experience of what Parkinson's is like. Using props, sharing experiences, and guided role-playing, this group of people who thought they knew a lot about Parkinson's found they had a lot more to learn. In this session, patient guides and their partners will share what they learned and offer guidance on how you can share the Parkinson's experience. Roundtable participants will share what they learned from each other, what aspects of the experience were the most powerful, and how sharing Parkinson's for a day helped them to better understand each other. People with Parkinson's will learn how they, too, can share their experience with Parkinson's with others and researchers, clinicians, and community organization staff will have the opportunity to engage with members of the community and arrange their own Parkinson's One Day experiences.

O33

Roundtable #7: Shame and PD: how to recognize it and address itJulio Angulo¹, Paul Krack²¹ Mesa, Arizona, USA² University Hospital, Grenoble, France

Shame is a self-conscious emotion. It can be an intensely self-critical feeling leading to self-devalorization or even self-loathing with suicidal risk. Shame is about fear, anxiety, hiding, avoiding. Observations and experience with the disease indicate that it is not rare to encounter PD patients in which the emotion of shame is significantly distressing, with consequential vulnerability to self-solation, social anxiety, depression, and substance abuse. Given its obvious impact on quality of life, the topic of shame and PD might be of interest to PwP's, their families, as well as researchers and health professionals focused on PD. And yet, shame is hardly dealt with in the PD literature. There are a few quantitative works on shame and PD, typically from a sociological perspective. The work most often cited is on stigma, labeling theory and studies on the

social construction of health and illness. There are, however, abundant empirical articles in psychology on shame outside the specific context of PD. Concerning psychological literatures on management/intervention of shame, there are many empirical studies pointing out the efficacy of exposure therapy, CBT and, more recently, mindfulness. We are not aware of studies directly focused on managing PD-related shame.

During this round-table, the co-chairs will describe shame as felt experience, and as construct defined in the psychological and sociological literature, then comment on what we do know/not know specifically about shame and PD and present a short review of the most promising evidence-based shame-reducing interventions for shame in general. The audience can contribute with own personal experience or observations. The workshop is meant to raise awareness on shame on PD and hopefully stimulate research on prevalence, causes and interventions in what seems a neglected area of patient management in PD.

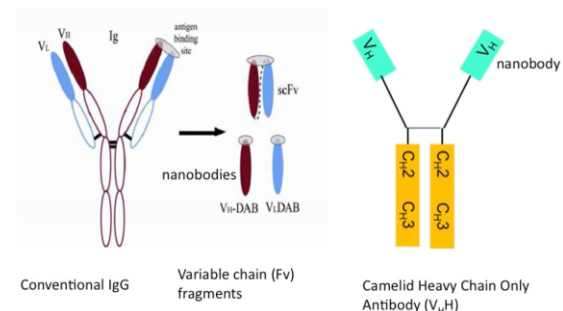
O34

Roundtable #8: Harnessing antibody engineering to counteract effects of excess protein accumulation in PD

Anne Messer

Neural Stem Cell Institute/Regenerative Research Foundation and University at Albany, Albany, New York, USA

This Roundtable will discuss current and future therapeutic directions using fragments of antibodies. The diagram shows how these single-chain (nanobody) and single-domain antibody fragments relate to full-length antibodies. When expressed within cells, the fragments are also collectively referred to as intrabodies. These can be engineered to target some of the earliest critical pathology in PD and related disorders of abnormal proteins; they may also allow protection of transplanted stem cells. Powerful molecular technologies allow engineering of the binding and interaction domains of antibody proteins to provide a powerful new pathway for highly specific drug candidates. Because the engineering initially takes place at the gene level, it is also possible to create innovative fusions. These can then be used to alter intracellular solubility, cellular localization, turnover, and binding to multiple or complex targets. Antibody fragments also offer multiple options for delivery as genes or proteins.

Classical IgG and Camelid-Heavy-Chain-Antibody

From-- Messer et al. Expert Opinion on Biological Therapy, 2009

O35

Lecture #1: Immunization against synuclein: challenges and lessons learned*Martin Ingelsson*

Uppsala University, Department of Public Health and Caring Sciences, 751 85 Uppsala, Sweden

Immunotherapy targeting α -synuclein has evolved as a potential therapeutic strategy for Parkinson's disease and a number of studies on cellular and animal models have demonstrated promising results. For example, α -synuclein vaccination of transgenic mice has been shown to reduce the number of brain inclusions containing α -synuclein, whereas passive immunization studies indicated that antibodies against the C-terminus of α -synuclein can pass the blood-brain barrier and ameliorate the neuropathology. Moreover, assessment of antibodies that target presumably toxic α -synuclein oligomers have demonstrated a reduction of pathological features in the central nervous system of different transgenic mouse models. Although the underlying mechanisms of immunotherapy are not yet fully understood, these may include antibody-mediated clearance of intraneuronal α -synuclein deposits, prevention of cell-to-cell propagation of toxic species and microglia-dependent protein clearance. Thus, immunotherapy targeting α -synuclein holds promise but needs to be further developed as a future disease-modifying treatment in Parkinson's disease and other α -synucleinopathies.

O37

Lecture #3: Engineered multifunctional nanobody fragments as neurodegenerative disease therapeutics*Anne Messer*

State University of New York, Albany, New York, USA

Nanobodies are single-domain fragments of the variable binding regions of antibodies. They are particularly valuable for engineering multi-functional constructs due to their small size and defined structures. We have previously shown that intrabodies fused to a proteasomal targeting PEST degron can degrade their intracellular target in both Huntington's and Parkinson's diseases. In recent studies, we have investigated functional effects of candidate bifunctional nanobodies for their ability to modulate effects of overexpressed α -Syn in situ and in vivo. VH14 is a fully human single domain intrabody selected against the non-amyloid component (NAC) hydrophobic interaction region of α -Syn, which is critical for initial α -Syn aggregation. A VH14PEST fusion construct is sufficiently solubilized to function intracellularly, and can reduce levels of overexpressed target. In situ, it can counteract the heterologous proteostatic effects of mutant α -Syn on mutant huntingtin, and protect against toxicity. We compared this anti-NAC candidate to NbSyn87, a nanobody that binds to the C-terminus of α -Syn, a target that has shown in vivo efficacy with full-length antibodies. NbSyn87PEST degrades α -Syn as well or better than VH14PEST; however, VH14PEST appears more effective in proteostatic stress and toxicity assays in situ. Carrying the candidate nanobodies forward to an in vivo AAV rat model of PD, similar effects were found. Both AAV-nanobody-PESTs improved motor function in AAV-SYN treated rats. Nigral phospho-serine-129 was reduced with VH14PEST>Nbsyn87PEST, matched by dopamine (DA), tyrosine hydroxylase, and DA transporter recovery. Differences could be a function of relative doses, affinities, binding to different isoforms of α -Syn, or construct-specific inflammation. These data validate the NAC region as a nanobody target. They also illustrate the power of multifunctional engineered nanobodies as a valuable therapeutic strategy to reduce abnormal α -Syn accumulation in synucleinopathies such as Parkinson's disease.

O38

Lecture #1: Mechanisms of impulse control disorders in PD*Celeste Napier¹ (Presenter), Amanda Persons²*¹ Rush Medical College, Chicago, Illinois, USA² Rush University Medical Center, Chicago, IL, USA

The existence of impulse control disorders (ICDs) in some patients with Parkinson's disease or restless legs syndrome on dopamine agonist therapy is well-appreciated. However, these behaviors remain poorly understood, and the neuroanatomical substrates and molecular mechanisms that underlie their development and expression are largely unknown. Dopamine agonists (e.g., pramipexole, ropinirole) exhibit high affinity for the D3 receptor (D3R), and this receptor is highly expressed in limbic brain regions. As theorized for drug addictions, ICDs likely encompass learning and memory that involve strengthening of glutamatergic synapses via enrichment of AMPA receptors (AMPA). AMPAR trafficking is a tightly controlled process that involves several intracellular signals, including the Akt/GSK-3 β pathway, which can be engaged by activation of D3Rs. To provide new insight into how dopamine agonists may promote ICDs, we hypothesized that dopamine agonists, acting via D3R-Akt/GSK-3 β , would increase AMPAR trafficking in limbic cortico-striatal-pallidal systems. To test this hypothesis, male Sprague-Dawley rats were treated with 2mg/kg intraperitoneal pramipexole. One hour later, brain tissues (i.e., medial prefrontal cortex, nucleus accumbens and ventral pallidum) were harvested. A modified Western blot protocol was used to determine surface and intracellular levels of AMPAR subunits (GluA1, GluA2) and Akt/GSK-3 β . No changes were noted in the medial prefrontal cortex, but surface expression of GluA1 and GluA2 was increased in the nucleus accumbens and ventral pallidum. These changes were paralleled by decreased phosphorylation of Akt and GSK-3 β , leading to increased constitutively active GSK-3 β . All three outcomes were blunted by pretreating the rats with the competitive D3R-prefering antagonist PG01037 (30mg/kg). These findings suggest increases in D3R-driven, AMPAR-mediated synaptic strengthening occurs within subcortical limbic regions that involve Akt/GSK-3 β signal transduction. Many of these proteins offer druggable targets. As the nucleus accumbens and ventral pallidum are involved in reward-motivated behaviors, the studies also indicate the value of further evaluations on potential utility of employing pharmacotherapy targeted toward these proteins as a means to blunt pramipexole-induced ICDs.

O39

Lecture #2: Imaging of impulse control disorders in PD: what have we learned?*Antonio Strafella*

University of Toronto, Toronto, Ontario, Canada

In Parkinson's disease (PD) the decision of which action to take, and the inhibition of harmful behaviour, can be impaired and further worsened by dopaminergic therapy. We often need to adapt behaviour to changing circumstances – to plan novel actions or inhibit pre-potent ones. Abnormalities in this process can lead to impulse control disorders. The combination of PET and fMRI is beginning to reveal the mechanisms of poor impulse control in PD. Here, we show the results of neuroimaging studies conducted in PD patients with and without ICDs or DDS providing evidence of significant abnormalities in those prefrontal-striatal areas associated with decision making and reward. Proposed mechanisms include abnormal functioning of mesolimbic structures resulting in dysregulation of dopamine.

O40

Lecture #3: Clinical management of ICDs in PD

Angelo Antonini
Italy

Impulse control disorders (ICDs), such as pathological gambling, hypersexuality, compulsive shopping, and compulsive eating, and other impulsive behaviours, such as punting and hobbyism, are an increasingly recognised psychiatric complication in patients with Parkinson's disease (PD). These behaviours encompass a wide range of severity, but in general ICD-related behaviours in PD are associated with a decreased quality of life, greater functional impairment, and increased caregiver burden. Thus, patient and caregiver education is important, as is routine monitoring for the early detection of ICD development. The DOMINION study, a cross-sectional study of 3090 patients with PD, reported a point prevalence estimate of 13.6%; however, the prevalence varies between studies because of differences in assessment methods and sociocultural background of study populations. An Italian study reported that approximately 14% of PD patients have predisposing personality traits already at diagnosis, before treatment is initiated.

Introduction of medication is likely to be the primary risk factor, with dopamine agonists (DAs) most strongly associated with their development. For example, the DOMINION study reported a prevalence of 17.1% in patients receiving a DA vs 6.9% in those not receiving a DA. In addition, longer duration of treatment with DAs may also add to the risk of developing ICDs.

The first step in the management of ICDs and related disorders is counseling and surveillance to facilitate early diagnosis and treatment. Dopamine agonist taper and substitution of other classes of PD medications can be highly effective in some patients, but not all patients tolerate this because of DAWs or other clinical factors. When this approach is unsuccessful, then other pharmacological or nonpharmacological approaches can be considered. At this time only anecdotal evidence exists for efficacy. Advances in the management of these disabling conditions can be made by including ICDs as a specific outcome measure in trials of medical or surgical therapies for PD. Future studies are needed to clarify the underlying pathophysiology of ICDs and identify novel therapeutic targets, to facilitate the development of safe and effective evidence-based treatments for ICDs.

O41

Lecture #1: Role of transcription factors in maintenance and function of midbrain DA neurons

Marten Smidt
Netherlands

Dopaminergic (DA) neurons in the ventral mesodiencephalon control locomotion and emotion and are affected in psychiatric and neurodegenerative diseases, such as Parkinson's Disease (PD). A clinical hallmark of PD is the specific degeneration of DA neurons located within the Substantia Nigra (SNc), whereas neurons in the Ventral Tegmental Area (VTA) remain relative unaffected. Recent advances have highlighted that the selective vulnerability of the SNc may originate in subset specific molecular programming during DA neuron development, and significantly increased our understanding of the molecular code that drives specific SNc development. Here we present an up-to-date overview of molecular mechanisms that direct DA subset specification, integrating our current knowledge about subset specific roles of transcription factors. We will discuss the underlying role of subset specific gene regulatory networks, the clinical promise of fundamental knowledge about subset specification of DA neurons and new directions towards the role of epigenetic programming and stability with regards to cell-type specific vulnerability in PD.

O42

Lecture #2: Engrailed1 and the survival of dopaminergic neurons

Patrik Brundin
Van Andel Institute, Grand Rapids, Michigan, USA

Engrailed 1 (En1), a homeobox transcription factor crucial for both the development and survival of midbrain dopaminergic neurons. Mice that lack both copies of the gene die at an embryonic stage. By contrast, mice that lack one En1 allele (En1^{+/-} mice) have a normal lifespan. The En1^{+/-} mice are born with normal numbers of dopamine neurons, display decreased mitochondrial complex I activity, changes in DNA repair and progressive midbrain dopamine neuron degeneration in adulthood. These features are all relevant to Parkinson's disease (PD). Akin to PD, the loss of dopamine neurons is more pronounced and occurs earlier in the substantia nigra than in the adjacent ventral tegmental area. Prior to loss of the nigral cell bodies, the nigrostriatal terminals are dystrophic and swollen. We analysed the 3D morphology of nigrostriatal axons in En1^{+/-} mice using CLARITY and found that they were fragmented. This is consistent with axonal degeneration, which is also suggested to occur in PD and precede the demise of the cell bodies by several months or years. At the ultrastructural level, the degenerating axons exhibit electron dense bodies resembling abnormal autophagic vacuoles. In line with these observations indicating changes in autophagy in the midbrain dopamine neurons, we detected an up-regulation of mTOR pathway markers, concurrent with a downregulation of the autophagic marker LC3B. We also found that the nigrostriatal axons are dysfunctional long before they have died. Thus, using *in vivo* electrochemistry, we observed that nigrostriatal terminals in the dorsal (but not ventral) striatum were severely deficient in dopamine release and reuptake. Finally, we have found that the nigral degeneration were coupled to an activation of microglia, indicative of an ongoing neuroinflammation. In short, the En1^{+/-} mouse replicates several key features of PD nigrostriatal pathology. This suggests that the mouse is a relevant and powerful PD animal model. The results are also particularly interesting for two additional reasons. First, studies have identified a single nucleotide polymorphism close to the En1 gene locus that may be associated with altered PD risk. Second, the En1 protein has been shown to protect neurons against various neurotoxic insults that are relevant to PD pathogenesis. Taken together, further studies are warranted into the role of molecular pathways regulated by En1 in PD pathogenesis.

O43

Lecture #3: WNT/ β -catenin-regulated genetic networks in midbrain dopaminergic neuron differentiation and survival

Nilima Prakash
Hamm-Lippstadt University of Applied Sciences, Hamm, Germany

Dopamine (DA)-synthesizing nerve cells located in the mammalian midbrain and caudal forebrain are involved in the control and modulation of voluntary movements, rewarding/aversive behaviors and other cognitive functions of the brain. The age-dependent and progressive degeneration of these neurons leads to the motor symptoms of Parkinson's Disease (PD), whereas their dysfunction is associated with neuropsychiatric disorders such as addiction, schizophrenia, attention deficit hyperactivity disorder and depression. The etiology of these diseases, in particular of the neuropsychiatric disorders, is thought to have a neurodevelopmental component. Moreover, a precise understanding of the developmental cues that regulate the generation of these neurons is needed to devise new stem cell-based regenerative therapies for PD.

The mesodiencephalic dopaminergic (mdDA) neurons arise from the ventral midline of the mesencephalon (midbrain) and caudal diencephalon (forebrain) between embryonic day 9.5 to 12.5 (E9.5–12.5) of mouse development. Several cell signaling pathways are implicated in these early steps of mdDA neuron development, the most important of all being the WNT1/beta-catenin pathway. Initially (around E9.5), WNT1/b-catenin signaling promotes the proliferation of ventral midline (mdDA) progenitors. From E11.5 onwards, this signaling pathway directs the specification of the mdDA cell fate in these progenitors and their correct differentiation into particularly a Substantia nigra pars compacta (SNc) mdDA neuron subset, the most affected neurons in PD. Moreover, WNT1/b-catenin signaling promotes the survival of mature mdDA neurons through a network of downstream transcription, neurotrophic and enzymatic factors. I will review our earlier data about WNT1/b-catenin-regulated genetic networks in mdDA neuron development, and focus on our more recent data showing that the sustained expression of WNT1 in mdDA neurons of a genetic mouse model for PD (the *En1+/-* mouse) protects these neurons from their premature degeneration by activating a similar neuroprotective gene cascade as during development. I will also discuss our most recent work about Dickkopf 3 (*DKK3*), a secreted modulator of WNT1/b-catenin signaling, which both in the mouse and in cultured pluripotent stem cells promotes the differentiation and survival of a rostralateral mdDA precursor subset giving rise to the SNc DA neurons. Thus, WNT1/b-catenin-regulated genetic networks may open new avenues to the treatment of PD.

O44

Lecture #2: Focus on non-motor symptoms not often recognized: fatigue, apathy and daytime somnolence in PD

Ron Pfeiffer

Oregon Health & Science University, Portland, Oregon, USA

Parkinson's disease (PD) is a multisystemic disorder causing motor and non-motor symptoms. Non-motor symptoms can remain undetected by patients due to misconception or embarrassment, for example, and undetected by doctors due to lack of a systematic search. Fatigue, apathy, and daytime somnolence, share some correlates and a strong impact on patients quality of life (QoL) and caregivers burden (CB).

Fatigue, referred as "difficulty initiating or sustaining physical or mental voluntary activity" is present in around 30–60% of PD patients. Potential causal factors are many and its pathophysiology remains quite unknown. Several scales (e.g., Fatigue Severity Scale, Parkinson Fatigue Scale) help to detect and measure this symptom. Patients QoL and CB are negatively influenced by fatigue, which could be improved by doxepin, rasagiline, and perhaps amantadine.

Apathy, reported in 7–70% of PD patients, is defined as a "lack of motivation, characterized by reduced goal-directed behavior, goal-directed cognitive activity, and emotional responsiveness". It may be associated with depression, dementia, anhedonia, and fatigue. For screening and evaluation of apathy in PD, the Apathy Scale and the Lille Apathy Rating Scale are "recommended". Apathy deteriorates patients and caregivers QoL, increasing the CB. Psychotherapy, dopamine-eliciting activities and drugs (e.g., priribedil, ropinirole) can improve apathy, whereas it may appear or increase after STN-DBS.

Daytime somnolence, a "chronic state of inability to stay awake during the day", affects around 12-50% of PD patients. It may be related with dopaminergic medication, pain, depression, obesity, high apnea/hypopnea index, and fatigue. Daytime sleepiness also impacts hardly on patients QoL and CB and its severity can be assessed using rating scales (e.g., Epworth Sleepiness Scale) and objective measures (e.g., multiple sleep latency test). Treatment

includes reduction of obesity, pain, sleep apnea, and optimization of dopamine agonists dosage.

For these three symptoms, most relevant unmet needs are: to progress in the knowledge of their intimate causes and mechanisms; to improve the awareness on them and on their importance among patients, carers, and health professionals; to have available better means for detection, precise diagnosis, and evaluation; and to develop efficacious therapies for preventing and neutralizing their negative effects on patients and caregivers.

O45

Lecture #3: State-of-the-art latest clinical trials addressing non-motor symptoms of PD

Susan Fox

University Health Network, Toronto, Ontario, Canada

The importance of non-motor symptoms in PD is reflected in the increasing number of studies evaluating therapies for these bothersome symptoms. Thus over the past decade, approximately 150 RCTS have been published in a range of non-motor symptoms, with many more open label studies. This reflects an increased understanding of the pathophysiology of many non-motor symptoms and the availability of new drugs or more commonly, indication-switching of clinically available drugs. However, many challenges exist in designing such studies and thus determining true efficacy. These issues include a lack of PD-specific rating scales for both diagnosing and measuring severity of many non-motor symptoms; the large placebo effects in some non-motor symptoms especially mood-related and the difficulty in dealing with overlapping features of some symptoms (eg. depression, cognition, apathy). The largest area of successful trials has been into neuropsychiatric symptoms, including mood, cognition and psychosis. Less studied areas are in autonomic problems, sleep and pain where most currently used drugs come from the non-PD field. Although the field is moving forward, more studies need to be done particularly in defining PD-specific non-motor symptoms and understanding the pathological causes.

O46

Talk #1: Regulation of ATP13A2 via PHD2-HIF1alpha signaling is critical for cellular iron homeostasis: Implications for Parkinson's disease

Julie Andersen

The Buck Institute, Novato, California, USA

We previously reported that pharmacological inhibition of a class of enzymes known as prolyl hydroxylase domain proteins (PHDs) has neuroprotective effects in various in vitro and in vivo models of Parkinson's disease (PD). We hypothesized that this was due to inhibition of the PHD2 isoform, preventing it from hydroxylating the transcription factor hypoxia-inducible factor 1 alpha (HIF1alpha), targeting it for eventual proteasomal degradation. HIF1alpha itself induces the transcription of various cellular stress genes, including several involved in iron metabolism. Although all three isoforms of PHD are expressed within vulnerable dopaminergic (DAergic) substantia nigra pars compacta neurons, only select downregulation of the PHD2 isoform was found to protect against in vivo neurodegenerative effects associated with the mitochondrial neurotoxin 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine. These findings were corroborated in induced pluripotent stem cell-derived neurons, providing validation in a pertinent human cell model. PHD2 inhibition was found to result in increased expression of ATP13A2, mutation of which is responsible for a rare juvenile form of PD known as Kufor-Rakeb syndrome. Knockdown of ATP13A2

expression within human DAergic cells was found to abrogate restoration of cellular iron homeostasis and neuronal cell viability elicited by inhibition of PHD2 under conditions of mitochondrial stress, likely via effects on lysosomal iron storage. These data suggest that regulation of ATP13A2 by the PHD2-HIF1 α signaling pathway affects cellular iron homeostasis and DAergic neuronal survival. This constitutes a heretofore unrecognized process associated with loss of ATP13A2 function that could have wide-ranging implications for it as a therapeutic target for PD and other related conditions.

O47

Talk #2: Ceruloplasmin dysfunction in PD animal models and PD brain: therapeutic implications

David Finkelstein

Florey Institute of Neuroscience and Mental Health, Melbourne, Australia

Ceruloplasmin is an iron-export ferroxidase that is abundant in plasma and also expressed in glia. We found an approximately 80% loss of ceruloplasmin ferroxidase activity in the substantia nigra of idiopathic Parkinson disease (PD) cases, which could contribute to the pro-oxidant iron accumulation that characterizes the pathology. Consistent with a role for ceruloplasmin in PD pathogenesis, ceruloplasmin knockout mice developed parkinsonism that was rescued by iron chelation. Additionally, peripheral infusion of ceruloplasmin attenuated neurodegeneration and nigral iron elevation in the MPTP mouse model. Recent studies by others in PD patients have shown that chelation with deferiprone showed increases CSF and serum ceruloplasmin activity. These findings show, in principle, that intravenous ceruloplasmin may have therapeutic potential in PD.

O48

Talk #3: Iron chelation treatment of PD

David Devos

Lille, France

Background: Excess iron is primarily detected in the substantia nigra pars compacta, where dopaminergic neurons are exposed to high levels of oxidative stress produced by mitochondrial disorders and dopamine metabolism.

Aims: The pathophysiological role of iron in PD was assessed by a chelation strategy aimed at reducing oxidative damage associated with regional iron deposition without affecting circulating metals. Translational cell and animal models provided concept proofs and a delayed-start treatment paradigm the basis for preliminary clinical assessments.

FAIRPARK-I. For translational studies we assessed the effect of oxidative insults in mice systemically pre-chelated with deferiprone (DFP) by following motor functions, striatal dopamine and brain iron deposition (relaxation-R2*-MRI) aided by spectroscopic measurements of neuronal labile iron and oxidative damage by markers of protein, lipid and DNA modification. DFP significantly reduced labile iron and biological damage in oxidation-stressed cells and animals, improving motor functions while raising striatal-dopamine. For a pilot double-blind, placebo-controlled- randomized clinical trial, early-stage Parkinson's patients on stabilized dopamine regimens enrolled in a 12-months single-center study with DFP (30 mg/kg/day). Based on a 6-month delayed-start paradigm, early-start compared to delayed-start patients (37/40 completed) responded significantly earlier and sustainably to treatment in both substantia-nigra iron deposits (R2* MRI) and UPDRS motor indicators of

disease progression. Apart from three rapidly resolved neutropenia cases, safety was maintained throughout the trial.

Novelty. A moderate iron chelation regimen that avoids changes in systemic iron levels may constitute a novel therapeutic modality for PD.

FAIRPARK-II. This project seeks to demonstrate that conservative iron chelation therapy (i.e. with iron chelation and redeployment) with moderate dose DFP slows the progression of handicap in de novo PD patients. The 9-month, parallel-group, randomized, placebo-controlled, multicentre trial will be followed by a one-month wash-out period. The primary efficacy criterion will be the change in motor and non-motor handicap scores on the Total MDS-UPDRS between baseline and 36 weeks (i.e. disease-modifying and symptomatic effects). The secondary efficacy criterion will be the change in score between baseline and 40 weeks (i.e. disease-modifying effect only). The study results might prompt academic and industrial research on iron chelation as a disease-modifying treatment in neurodegenerative diseases.

O49

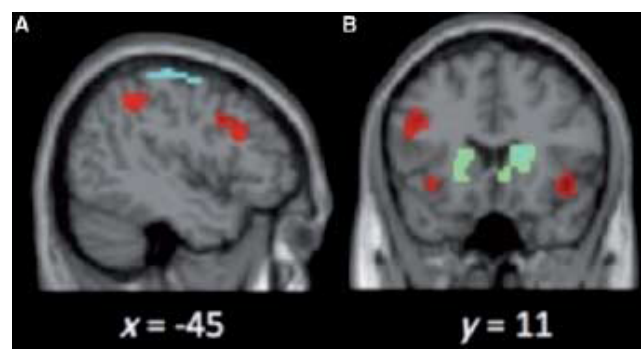
Talk #1: Neural mechanisms underlying freezing of gait in PD

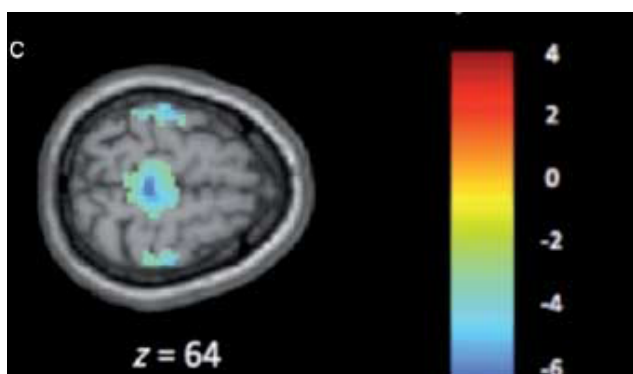
Simon Lewis

University of Sydney and Royal Prince Alfred Hospital, Sydney, Australia

Despite being one of the most common and debilitating symptoms in PD, the phenomenology underlying freezing of gait (FOG) remains poorly understood with only limited benefits from currently available treatments. It is well known that freezing can be provoked by a wide range of disparate triggers including turning, dual tasking and doorways as well as being relieved by strategies such as cueing. These findings indicate that the paroxysmal "brain failure" resulting in FOG must be more than just a simple failure in one region and most likely arises from a breakdown in complex connections. Trying to identify the underlying regions of the brain that account for FOG has been a challenge.

This presentation will cover some of the innovative approaches used in recent research to identify the neural mechanisms underlying FOG. Obviously brain scanning techniques have been limited by the inability of having patients actually walking during a study. This has been addressed to some extent by using novel functional MRI techniques in combination with Virtual Reality environments to monitor the activity of the brain during episodes of freezing and also during periods when patients are presented with triggers that provoke FOG. In addition, neurophysiological advances have been made through recording cortical brain activity with technology such as ambulatory electroencephalography and from electrodes placed within the brain during Deep Brain Stimulation. It is hoped that the insights gained from this novel avenue of research will lead to a greater understanding of FOG in PD, which will in turn lead to improved treatments.





O50

Talk #2: What goes wrong to explain freezing of gait?

Alice Nieuwboer

Department of Rehabilitation Sciences, Belgium

Explaining the paroxysmal nature of freezing of gait (FOG) remains one of the most challenging research questions in Parkinson's Disease (PD). Several components of motor control go wrong during FOG. First, the inability to fine tune the scale and timing of repetitive movements induces motor breakdown, making freezers vulnerable to amplitude and frequency modulations. This core motor problem also explains freezing in different motor effectors, such as when writing sequential loops or during tapping tasks. Second, de-automatization exacerbates these motor difficulties. Even in the brain at rest, freezers have reduced functional connectivity and white matter integrity between subcortical and cortical regions, associated with worse dual task performance. As patients with FOG have greater difficulties with executive function, compensatory switching from automatic to goal-directed motor control and vice versa is therefore affected. Third, freezing is triggered by motor adaptation, often when anticipating on the upcoming adaptive response (exaggerated anticipatory inhibition) or when adaptation is required implicitly. Fourth, postural instability is a contributing factor to freezing. Just before FOG during turning, a reduced medial center of mass deviation and lack of forward shift were found. In a recent longitudinal study, we showed that postural instability as measured with the Mini-BESTest declined more in freezers than in non-freezers over a period of 12 months, a decline which was not apparent in gait outcomes. In line, postural instability deteriorated more in patients in whom FOG emerged over 1 year, i.e. in converters. However, the exact freezing-related postural abnormalities still need elucidation.

O51

Talk #3: Innovative approaches to improve walking and reduce freezing of gait in PD

Fay Horak

Oregon Health & Science University, Oregon, USA

This presentation will summarize new research on the promise of innovative approaches to improve walking and freezing of gait for Parkinson's disease.

Although walking problems and freezing of gait are the most common reasons for falls and reduced quality of life in people with Parkinson's disease (PD), current antiparkinson medications and deep brain stimulation (DBS) have limited effects. In fact, although levodopa and DBS often improves gait speed, balance does not improve and falls may increase with treatment. Unlike other

neurological diseases, gait in people with PD often does not improve with a cane or walker. Currently, many laboratories are exploring innovative approaches to improve walking and reduce freezing of gait based on new: 1) medications, 2) technologies, or 3) exercise programs.

Medication: Recent studies suggest that balance does not improve with levodopa because it may depend more on the neurotransmitter, acetylcholine and recent studies with Rivostigmine and Donepezil that increase the amount of acetylcholine in the brain can improve gait and reduce falls.

Technologies: Augmenting sensory inputs during gait with biofeedback shows promise in reducing freezing of gait. Traditionally, external cues have been shown to overcome freezing (ie; a line on the ground) but new technology can link sensory cues to real-time measurement of walking. For example, studies are showing that vibrotactile or visual or auditory feedback about how a person is actually walking could improve gait and reduce freezing. However, most of these studies are limited to short term changes in a laboratory environment and need to be translated and tested in real life conditions.

Exercise: There is good evidence that exercise can improve gait speed and stride length but less evidence that exercise can improve freezing. Since freezing is associated with specific types of cognitive deficits, we developed and are testing a new type of agility training with cognitive challenges. Preliminary results show significantly reduced freezing of gait after a 6-week (18 session) agility group exercise program. In addition, this improvement is associated with improved functional connectivity between locomotor and cognitive areas of the brain.

O52

Talk #1: Nutrition and malnutrition in PD: prevalence, importance & ramifications

Matthew Brodsky

Oregon Health & Science University, Portland, Oregon, USA

The important role nutrition plays in the etiology and treatment of Parkinson's disease (PD) has only recently been recognized. The standard definition of nutrition is the process of taking in nutrients from the foods you eat, and the science that interprets the interaction of these nutrients in food in relation to health and disease of an organism. However this definition may be expanded to include what one breathes, and also may include the emerging field of the effects of the microbiome in health and disease.

Well-designed population-based epidemiologic studies spanning the globe have demonstrated an increased prevalence of malnutrition in PD. There is now a body of evidence that not only those with PD are at greater risk for malnutrition, but that poor nutrition may increase the risk of developing PD or hasten its progression. Thus, the impact between PD and nutrition is bidirectional.

A number of other studies have described various dietary risk factors for developing PD. There is recent evidence that the makeup of the human microbiome may also confer risk of developing PD.

Further, it is well established that managing nutrition appropriately can help improve the treatment of the motor symptoms of PD, including response to dopamine replacement therapies. There is also evidence that modifying nutrition may improve some of the nonmotor symptoms of PD.

Finally, there are ongoing efforts to investigate nutritional strategies that may slow the progression of PD. This presentation will cover the evidence for prevalence of malnutrition in PD and the effects of nutrition on etiology and management of PD.

O53

Talk #2: Is there a role for nutrition in the management of PD symptoms?*Heather Zwickey*

National College of Natural Medicine, Portland, Oregon, USA

It's widely recognized that good nutrition is important for general health. Can nutrition play a larger role in health, such as managing symptoms of a disease like Parkinson's? Symptoms are the body's indicator that an internal process isn't functioning properly. Since nutrition is essential for the proper function of every cell, it's likely that nutrition plays a role in the symptoms of any disease, and Parkinson's is no exception. While the research on nutrition and PD symptoms is limited, there are lessons we can learn from this existing research, as well as nutrition research in other fields. In this talk, we'll discuss examples of foods and nutrients that may impact PD symptoms and why they have these effects.

O54

Talk #3: Is there a role for nutrition altering progression of PD?*John Duda*

Veteran's Administration Medical Center, Philadelphia, Pennsylvania, USA

Many mechanisms have been implicated in the pathogenesis of PD including oxidative stress, mitochondrial dysfunction, protein aggregation, and inflammation. Current treatment strategies focus on symptomatic improvement by mitigating the consequences of these mechanisms, which is the dysfunction or loss of dopaminergic and other neuronal populations in the brain. However, these therapies have not been proven to modify disease progression. Therefore, alternative strategies, which directly address some of the underlying mechanisms involved in PD pathophysiology are being developed and tested. A whole food, plant-based diet contains innumerable compounds that have been shown to counteract the putative mechanisms involved. Flavonoids, one of the largest groups of phytochemicals, have been shown to have the ability to reduce free radicals, to stimulate antioxidant enzyme expression, and to inhibit reactive oxygen species formation, all leading to less oxidative damage. Phytochemicals such as isoflavonoids may modify the inflammatory response by inhibiting the production of pro-inflammatory cytokines while other flavonols reduce the amount of circulating inflammatory markers. Sulforaphane, a phytochemical found in cruciferous vegetables, has been shown to cross the blood brain barrier and increase intracellular glutathione levels thus reducing oxidative stress, and L-ergothioneine, a compound found mostly in mushrooms, has its own receptor and functions similarly to glutathione. Other phytochemicals have been shown to prevent the aggregation of alpha-synuclein while several plant-based phytochemicals including caffeine, curcumin and resveratrol inhibit the mammalian target of rapamycin (mTOR) which could increase autophagy and lead to the clearance of accumulated alpha-synuclein. Some isoflavonoids modify the inflammatory response by inhibiting the production of pro-inflammatory cytokines while other flavonols reduce the amount of circulating inflammatory markers. In addition, a whole foods, plant based diet, rich in dietary fiber, may alter the gut microbiome, decreasing inflammation and promoting production of beneficial short chain fatty acids that may inhibit the gut permeability hypothesized to play a role in PD pathogenesis. In summary, phytochemicals in plant-based whole foods may contribute to neuroprotection in PD by alleviating many of the underlying pathophysiologic mechanisms and adopting a plant-based diet may alter disease progression in PD.

O55

Roundtable #1: Tools for living with young-onset PD*Jon Stamford¹, Ruth Hagestuen²*¹ Parkinson's Movement, London, United Kingdom² National Parkinson Foundation, Miami, Florida, USA

Taking the physical aspects first, the principal tools are exercise, diet and medication. The single most important tool at the disposal of all, but particularly YOPD, is exercise. It is easier to maintain physical health than it is to regain it. Thus exercise, especially if initiated early, can have significant benefit on overall well-being as well as ameliorating Parkinson's specific symptoms such as rigidity and bradykinesia. There has been much discussion and/or speculation in relation to the types of exercise that are most effective. A pragmatic answer is that the exercise one chooses most often is the exercise that is most likely to be sustained. Diet is another critical aspect of physical maintenance. PD patients have a propensity to constipation and careful attention to diet can help obviate this as well as ensuring that medication is most effective. Medication itself is of course vitally important and again, attention to timing and impact helps manage and minimize drug side effects. The mental toolkit is a little more difficult. Principal tools are support networks, knowledge base and communication. First and foremost is support. PD is difficult enough but YOPD carries a significant burden of isolation even from the rest of the PD community. It is important to build your own support network as early as possible. Knowledge about the condition is empowering and, in turn, has been shown to improve long-term outcomes. Finding credible sources of information and establishing relationships with a PD specialized, patient centered care team for assistance with management over time are essential for all persons with YOPD. Finally, the value communication cannot be underestimated. PD patients in general and YOPD patients specifically need to find ways of communicating their needs and expectations to those around them whether these are family members, work colleagues or the general public. Each presents specific communication challenges. This roundtable will discuss individual strategies and approaches for each of the tools mentioned.

O56

Roundtable #2: Patient advocates at work around the world: how to get involved around Europe*Tom Isaacs*

United Kingdom

Parkinson's is often associated with apathy, low morale and lack of energy. People with Parkinson's (PwP) who experience such feelings often find it very difficult to motivate themselves to communicate to those around them or to have a positive attitude about their future. By contrast, PwP who take an active interest in their own Parkinson's often gain a sense of fulfilment by getting involved with and contributing to the wider Parkinson's community. In the US, patient advocates are a recognised feature of the clinical and scientific landscape. Yet often these groups struggle to exert the influence they would like, and the medical sector is still reticent to involve/include the patient voice in shaping the Parkinson's community's agenda. In Europe, there is a more open and collaborative culture adopted by those involved in the Parkinson's field. Nevertheless, patient advocacy in Europe is not as well established as it is in the US and the organisational structures needed to enable PwP to exert influence within the wider European Parkinson's community (i.e. scientific and clinical sectors) have never really been developed effectively. In this roundtable, Fulvio and Tom will start the conversation by briefly summarising their own journeys with Parkinson's from

diagnosis to present day, together with their experiences of advocacy in both the US and Europe. After this, there will be a discussion on the numerous different ways that PwP can, through responding more positively to their own Parkinson's, contribute to progress in the wider Parkinson's community.

An interactive discussion will follow looking at the ways that PwP within Europe can take a more active involvement and have greater influence on progress in the Parkinson's field in Europe. The group will then discuss ways to improve and grow patient advocacy within Europe and how best to overcome the cultural and language barriers that exist.

The objective for the group will be to think up new ideas to create a more cohesive and constructive approach to advocacy in Europe which exerts greater influence and increased patient-centricity to all parts of the Parkinson's community.

O57

Roundtable #3: Vision & PD: challenges and tips

Dan Gold

John Hopkins Medicine, Baltimore, Maryland, USA

Visual symptoms in Parkinson's disease are very common, although oftentimes the eye care provider is unfamiliar with PD and its influence on the visual system. Therefore, many symptoms remain unexplained and untreated, thus negatively affecting patient quality of life. This talk discusses Pearls (i.e., tips) & Pitfalls (i.e., challenges) associated with vision & PD.

O58

Roundtable #4: Occupational therapy and PD: how it can improve your daily life

Erin Foster, Linda Tickle-Degnen

USA

In this roundtable session, participants will become more informed regarding the role and benefits of occupational therapy in the management of Parkinson disease. The session will include a discussion of the nature of interventions provided by occupational therapists and the goals of occupational therapy intervention. The overarching approach of self-management will be explained. The evidence for occupational therapy related interventions for persons with Parkinson disease will be summarized and the impact on reducing disability and enhancing participation and quality of life will be reviewed.

O59

Roundtable #5: How to face impulse control disorders & get help

Daniel Suwyn

Savannah, Georgia, USA

Parkinson's is a brain disorder, not just a movement disorder. All treatment options, whether Sinemet or DBS, interfere in the brain's natural handling of Dopamine and other chemicals which play a critical role in addictions. The absence of awareness around these issues can ruin lives – from the priest who gambled away his church's savings to the bank president who became a sex addict or the professional golfer who gained 110 lbs. I'll share my experience with Dopamine Agonist induced addiction and subsequent depression and how it took a team of family members and professionals to get me back on track.

O60

Roundtable #5: How to face impulse control disorders & get help

Daniel Weintraub

Perelman School of Medicine at the University of Pennsylvania, Philadelphia, USA

Impulse control disorders (e.g., compulsive gambling, buying, sexual behavior and eating) and related disorders (e.g., punding, dopamine dysregulation syndrome) are increasingly recognized as common and clinically significant psychiatric complications of dopaminergic medications in Parkinson's disease (PD). ICDs and related disorders appear to be under-recognized, in part due to poor insight among some patients, embarrassment over symptoms, secondary gain by not reporting symptoms, and unawareness of connection between PD medications and the symptoms. In addition, patients and family members may report symptoms differently, with patients under-endorsing some symptoms and over-endorsing others. Specific clinical contexts include initiation of medications and consideration of DBS. There are parallels to the treatment of ICDs and substance-related and addictive disorders, and a multidisciplinary team that includes both a neurologist and a psychiatrist or psychotherapist is optimal.

O61

Roundtable #6: PD and children: how does PD impact children?

Amy Lemen¹, Soania Mathur²

¹ The Fresco Institute for Parkinson, New York, New York, USA

² Canada

When a parent, grandparent or loved one is diagnosed with Parkinson's disease, they are not the only ones affected. Instead whole family units struggle with this challenge. Of particular concern are the children and their ability to cope with having a loved one with a progressive illness.

Some of the changes associated with Parkinson's disease can alter both appearance and ability. Tasks and movements accomplished easily at one time become increasingly challenging as this neurological disease progresses. This can be a monumentally difficult adjustment for both the person afflicted and for the children witnessing these changes, particularly if not acknowledged or left unexplained. Children are extremely intuitive and can often sense there is something wrong which becomes even more distressing if they feel a parent or loved one is keeping a secret. They rely on reassurances by trusted adults and their reactions will often mirror the family's attitude. Therefore creating a positive family environment through truthful dialogue, education and optimism is vital.

Mathur and Lemen will lead a discussion on how from their experience, this disease affects children and will suggest strategies to approach a number of concerns. How to have that first conversation about the diagnosis, how to keep the lines of communication open as new questions or worries arise, educating kids about the disease at an age level appropriate for their understanding and insight and providing concrete ways that children can help, will be addressed.

Ultimately this session hopes to spark meaningful dialogue on how to remain engaged and inspired as adults living with Parkinson's as well as finding ways to help the children affected to feel empowered despite this family challenge.

O62

Care Partner Lounge: Intimacy and maintaining a relationship with your partner*Lissa Kapust*

Beth Israel Deaconess Medical Center, Harvard Medical School Teaching Hospital, Boston, Massachusetts, USA

"...til death do us part" is a critical part of the marriage vows; how does this impact on relationships when one partner has PD? There are many aspects to close relationships that are strained by PD; maintaining intimacy is probably the most challenging. Chronic medical conditions compound the sexual issues that people face during the natural aging process. Ms. Kapust will bring decades of clinical experience to bear for this important presentation and discussion. For this talk, intimacy is broadly defined. While intimacy includes sexual intimacy, for many is more broadly defined. Ms. Kapust will present an overview of the literature on this topic. Importantly, the physical and emotional aspects of PD that affect relationships will be highlighted in a way that promotes open and frank discussion. Included in the talk will be gender differences for the person with PD. Men and women with PD are affected by different physical and hormonal factors. Additionally, men and women may be anxious about different aspects of maintaining intimate relationships. Similarly, there are differences between the concerns of male care partners versus female care partners. The impact of PD medications on sexuality also needs to be considered. Mood and other non motor aspects of PD play an important role in maintaining intimacy. For care partners, strong feelings emerge in the context wearing "two hats"; one of spouse and the other of caregiver. Guilt and anger are normal feelings in this situation, but they complicate the caring relationship. Both PWP and care partners talk passionately about the importance of maintaining connections with their partners. These connections promote quality of life, self worth and self esteem. Intimacy may involve hugs and hand holding, hearing that familiar belly laugh or continued sexual relationships. Strategies to keep critical loving bonds sustained will be shared.

O63

Talk #1: How are genes studied that are involved in PD, from causing genes to risk factors*Tom Gasser*

Germany

In the last years it has become apparent that, in a small proportion of patients, Parkinson's disease (PD) is inherited in families as a single-gene ("Mendelian") disorder with autosomal-dominant or – recessive inheritance patterns. In these families, a research strategy called "positional cloning" has been extremely successful in identifying causative genes and mutations. The identification of these genes has led to a remarkable increase in our knowledge of the specific molecular pathways leading to PD. Abnormalities of the correct folding of proteins and their turn-over, but also disturbances of vesicular transport and mitochondrial integrity are some of these crucial cellular functions which, when impaired, can lead to PD.

While causative mutations are rare, genome-wide association studies (GWAS) have shown that common DNA variants contribute to the risk to develop PD in the large group of patients with sporadic disease. Remarkably, rare mutations and common variants can affect some of the same genes, indicating that the identified pathways are relevant in both genetic and in sporadic cases. While rare mutations usually affect the coding region of the gene and lead to a change of the amino acid sequence of the encoded protein, most of the common variants reside in regulatory regions and are thought to act via alterations of gene expression.

Despite these remarkable findings, a considerable proportion of the heritability of PD is still unaccounted for. At least a fraction of this "missing heritability" is thought to reside in rare variants of moderate effect strength that are now being identified by whole exome and whole genome sequencing strategies. This is a daunting task for current research, as the variability of the human genome appears to be much greater than anticipated.

It is hoped that these advances will lead to an increased understanding of the complex etiology of PD and other neurodegenerative disorders and eventually to the development of specific treatments targeted not at the clinical syndrome, but rather at the underlying specific molecular pathology, thus enabling more effective approaches of "precision medicine" for these devastating disorders.

O64

Talk #2: How does genetic susceptibility interact with environmental exposures to influence PD risk?*Beate Ritz*

Fielding School of Public Health, USA

In the post-genomics era, much of Parkinson's disease (PD) etiology still cannot be explained by genetic or environmental factors. Some of the unexplained PD etiology has been referred to as 'missing genetic heritability' and attributed to undiscovered rare genetic variants conferring large risks, though this explanation has not been supported by data. We argue that gene-environment (GxE) interactions may have a large contribution that remains underexplored. For more than a decade, we have explored GxE interactions that may explain how genetic as well as environmental factors together influence PD risk. To do so, we assembled a very large population-based PD study for which we created three objective pesticide exposure measures (ambient due to agricultural applications, home and garden use, occupational use), confirmed PD diagnoses during multiple medical examinations, and genotyped biologic samples. We assessed interactions between specific classes and types of pesticides with genes responsible for pesticide metabolism (PON1); transport across the blood brain barrier (ABCB1); pesticides interfering with or depending on dopamine transporter activity (DAT) and dopamine metabolism (ALDH2); impacting mitochondrial function via oxidative/nitrosative stress (NOS1) or proteasome inhibition (SKP1); and contributing to immune dysregulation (HLA-DR). These studies established specificity for pesticides' neurodegenerative actions in humans contributing biologic plausibility to epidemiologic findings and are poised to help us identify those genetically susceptible to PD if exposed to neurotoxic agents.

O65

Talk #3: What can you do with this information, and what will it do to you?*Jason Karlawish*

University of Pennsylvania, USA

The definition of sporadic PD has historically been grounded on the solid foundation of a clinical disorder defined by signs and symptoms such as troubles walking, a tremor and a response to dopamine replacement therapy. The discovery of the genes and mechanisms, also called biomarkers, of sporadic PD are remodeling this foundation. Researchers are creating a new definition grounded in the presence of genes or biomarkers and their response to a drug intervention. This definition is essential to develop method to prevent PD. Progress to achieve this presents patients both short and long term challenges. Short term challenges engage matters of

research ethics. Studies that enroll persons on the basis of their genetic or biomarker profiles present potential subjects an ethical dilemma over whether to enroll in the study. If they enroll, they will advance progress in diagnostics and therapeutics but learning gene or biomarker information may be harmful. If they don't enroll they will avoid leaning this information but also not help to advance the field. Making this decision engages values about risk tolerance and also understanding how this information may affect an individual's affective and neuropsychological function. Long term challenges include how society interprets this new model of sporadic PD. Interpretations will shape how patients experience their diagnosis. They may, for example, find the information threatening to relationships and therefore information they choose to keep private from family and friends. They may also experience changes in how they perceive themselves and their abilities. Other challenges of a biomarker-based diagnosis in an otherwise asymptomatic person include the way people and society responds to the person, causing, for example, discrimination in the workplace or insurance, and changes in social interactions.

O66**Talk #4: Genetic testing: empowerment or risk for people with Parkinson's?**

Alice Lazzarini
USA

The struggle to determine just who we are at any given point in time creates a lifelong process of changing identity for each one of us with Parkinson disease. A diagnosis of Parkinson's bisects a life into "Before Parkinson's" and "After Parkinson's"—genetic testing can do that in an instant.

With the ever increasing availability of genetic information one now finds direct to consumer (DTC) genetics being widely advertised on television. Protocols for predictive testing—to determine gene-carrier status of persons at-risk for late onset neurogenetic disorders—began back in 1983 with the localization of the gene for Huntington disease. Predictive testing for other diseases has turned out to be more complex, yet demand is widespread enough so as to necessitate a new paradigm for genetic counseling.

Genetic testing for Parkinson disease among high-risk populations can identify cohorts that will help clarify the prodromal stages of Parkinson's as well as contribute to the advancement of therapeutic discovery. Individuals identified as gene carriers gain information for life-planning decision making and may stand to benefit from early clinical testing of preventive therapeutics. Knowledge IS power, and persons have a right to available information about their own health. The days when professionals presumed to direct an individual's reproductive decision-making are, hopefully, long gone. Nevertheless, some constants remain that are dictated by the very nature of the intellectual and the emotional components of assimilating information with such an import. Several predictive testing scenarios will be used to illustrate measures to be considered as we anxiously await the development of an intervention capable of altering the course of Parkinson disease.

O67**Living well with Parkinson's**

Brian Grant

The Brian Grant Foundation, Portland, Oregon, USA

I have faced the challenge of Parkinson's with the same approach that I have with other challenges in my life. As a former NBA player, I dealt with adversity head on, consistently educating myself about my opponents' strengths and weaknesses and formulating an

efficient way to attack. Parkinson's has become the next opponent. When I was first diagnosed, I feared how it would affect my everyday life. The most important question I needed an answer to: would I be around to watch my kids grow? Once I was educated by my doctors, I learned that I could live with this illness and create a new reality of existence. Parkinson's is a monster that does not have one direction. Rather, it is a serpent that attacks different parts of me without warning and regard to my preparedness. Each day I worry about which tentacle of the serpent will attempt to rule me. Through fitness and nutrition I am attacking my opponent every day—all the while knowing that it has the ability to change those directions at any moment. My plan is fluid, rapidly changing, yet does not deviate from the core values of fitness and strength that I have armed and dedicated myself with. My commitment to react to change and directly face adversity has put me in a position to stay in front of something that I once believed was preying on me. I am now chasing what I once feared.

O68**Living well with Parkinson's**

Tim Hague

Winnipeg, Manitoba, Canada

Living well with Parkinson's is a lesson in learning to live with a new best friend whom the writer hates. This friend who has brought so much good into his world and yet holds every likelihood of wrecking his life. Lessons learned from having run and won The Amazing Race Canada will be shared. Living with this disease has boiled down to an understanding of what it means to Live Your Best every day. How does one live their best despite what this disease does to their life? What does one's best look like in the face of physical decline, emotional challenges, and what can seem to be a frightening future? Three key phrases will be explored; simplicity, contentment and perseverance. The hope is that of providing the listener with tools that will allow them to persevere in the face of difficulty. To understand that they too can run and win their personal race with this disease.

O69**Living well with Parkinson's**

Andy McDowell

New Zealand

I will offer my 10 lessons for living well with Parkinson's.

1. Exercise is mission critical
2. Rest is a weapon
3. Diet is a tool
4. Take care of what you can
5. Walking is gold
6. Learn what YOU need to
7. Attend to your soul
8. Share the load
9. Did I mention exercise?
10. Make your own list

O70**Living well with Parkinson's**

Linda Olson

San Diego, California, USA

I'd like to introduce myself this morning in a fashion I heard over and over while I was hospitalized 37 years ago. "This 29-year-old

Caucasian female was admitted via ambulance after an auto versus train accident in Berchtesgaden, Germany. Vital signs upon arrival were blood pressure of 60/40, pulse rate 140, respirations 30. Physical exam revealed a young female in acute distress with obvious traumatic amputation of the right arm just below the shoulder, total amputation of the left leg above the knee and an incomplete amputation of the right leg above the knee. Radiographs of the spine documented a moderate T-12 and L-1 fracture. Extensive debridement and completion amputations were performed on all three extremities after which the patient was transferred to the ICU."

And so began my life as a "severely disabled person". It was also the beginning of a wonderfully rewarding life, overflowing with opportunities and challenges. Within the first twenty-four hours we chose to honor our promise of "to have and to hold...for better for worse...in sickness and in health...till death do us part...". We chose to spend our energy on being happy rather than angry, not to worry about how we looked, to laugh often—particularly at ourselves, to keep adapting, to get up and go, and to make others happy along with us. It has been an adventure shared by my husband, our two children who were born after the accident, our friends and professional colleagues.

O71

Lecture #1: Update on evidence that alpha-synuclein is transmitted between neurons

Donato Di Monte

German Center for Neurodegenerative Diseases, Bonn, Germany

Neuropathological and experimental evidence of neuron-to-neuron transfer of alpha-synuclein is abundant and convincing. Relatively less clear are the mechanisms and conditions that promote this transmission and may play a critical role in triggering alpha-synuclein pathology and facilitating its progression. The relevance of this issue is underscored by the consideration that cell-to-cell protein transfer may explain the spreading of pathological lesions (Lewy bodies and Lewy neurites) in Parkinson's disease brains and could contribute to the progressive exacerbation of motor and extramotor symptoms in patients. From the mechanistic standpoint, recent emphasis has been given to the possibility that neuron-to-neuron propagation of alpha-synuclein may be a consequence of prion-like properties of the protein. This hypothesis also bears significant clinical implications since, for example, classification of alpha-synuclein as a prion may imply that Parkinson's disease should be considered potentially transmissible. Our work has recently focused on conditions that trigger inter-neuronal passage and long-distance brain spreading of alpha-synuclein. We tested the hypothesis that increased neuronal expression may be one of these conditions. It is known that enhanced alpha-synuclein levels are causally associated with familial parkinsonism in individuals with alpha-synuclein gene multiplication (SNCA). Furthermore, clinical and experimental evidence suggests that one of the mechanisms by which Parkinson's disease risk factors (e.g., toxic exposures and aging) could augment neuronal vulnerability to pathological processes is through an increase in intracellular alpha-synuclein. Thus, our experimental work on the relationship between expression and spreading of alpha-synuclein is likely to have translational relevance. Using novel animal models we were able to show that, under conditions of increased neuronal alpha-synuclein, the protein passed from one neuron to another and spread throughout the brain following a pattern that mimicked the progression of alpha-synuclein pathology seen in Parkinson's disease brains. Quite importantly, features of alpha-synuclein transmission in our models apparently contrasted with typical features of prion proteins, consistent with the interpretation that mechanisms alternative or complementary to a

prion-like behavior of the protein can underlie Parkinson's disease pathogenesis.

O72

Lecture #2: What form(s) of alpha-synuclein is transmitted from cell to cell? Evidence from animal models

Veerle Baekelandt

KU Leuven, Leuven, Belgium

Misfolded protein aggregates represent a continuum with overlapping features in neurodegenerative diseases, but differences in protein components and affected brain regions. The recent discovery of the transmissible nature of amyloidogenic proteins suggests a hypothesis of a pathogenic trigger which might spread throughout the nervous system underlying the progression of the disease. Furthermore, evidence is emerging that these protein aggregates can adopt distinct conformations or 'strains' with remarkable differences in structural and phenotypic traits. α -Synuclein aggregation is considered to play a central role in multiple neurodegenerative diseases, such as Parkinson's disease (PD), Multiple System Atrophy (MSA) and Dementia with Lewy Bodies (DLB). These synucleinopathies are determined by the deposition of α -synuclein aggregates but segregate in distinct pathological phenotypes and diagnostic criteria. α -Synuclein is recently shown to aggregate into different polymorphs or 'strains'. This has led to the hypothesis that strains might account for the distinct clinicopathological traits within synucleinopathies. We have shown that alpha-synuclein strain conformation and seeding propensity lead to distinct histopathological and behavioural phenotypes. We assessed the properties of structurally well-defined alpha-synuclein assemblies (oligomers, ribbons and fibrils) after injection in rat brain. We proved that alpha-synuclein strains amplify in vivo. Fibrils seemed to be the major toxic strain, resulting in progressive motor impairment and cell death, whereas ribbons caused a distinct histopathological phenotype displaying Parkinson's disease and multiple system atrophy traits. Additionally, we showed that alpha-synuclein assemblies cross the blood-brain barrier and distribute to the central nervous system after intravenous injection. Our results demonstrate that distinct alpha-synuclein strains display differential seeding capacities, inducing strain-specific pathology and neurotoxic phenotypes. These distinctive neurotoxic and pathological prion-like effects of alpha-synuclein strains might provide a basis for the heterogeneity observed in synucleinopathies and open new therapeutic opportunities such as targeting the degradation of alpha-synuclein higher molecular weight species.

O73

Lecture #3: Mechanisms of transmission of alpha-synuclein and therapeutic development

Pamela McLean

Mayo Clinic Florida, Jacksonville, Florida, USA

Aggregation of alpha-synuclein and resulting cytotoxicity is a hallmark of sporadic and familial Parkinson's disease (PD) as well as dementia with Lewy bodies. The paradoxical appearance of aggregated alpha-synuclein in naive transplanted embryonic stem cells in Parkinson's disease (PD) brains highlights the possibility that neuron to neuron transmission of alpha-synuclein plays a role in disease progression. In support of this hypothesis, alpha-synuclein pathology spreads throughout the neuraxis in a hierarchical distribution with its epicenter in the brainstem, extending to the mesolimbic cortex and associated areas. As yet, the underlying mechanisms of disease spread in PD remain to be determined. Recent studies indicate that alpha-synuclein oligomers can be

released from neuronal cells by nonconventional exocytosis involving extracellular vesicles such as exosomes whereas other studies implicate fibrillar asyn species in cell to cell propagation. Here we will discuss potential mechanisms of cell-to-cell transmission of alpha-synuclein as it pertains to disease progression and therapeutic development.

O74**Lecture #1: Visual dysfunction**

Dan Gold

John Hopkins Medicine, Baltimore, Maryland, USA

Visual symptoms in Parkinson's disease are very common, and stem from the simple (ocular surface irritation) to the more complex (eye movement disorders or subnormal vision from retinal dopamine depletion). A thorough ophthalmic/neuro-ophthalmic examination can offer an explanation for most visual symptoms in PD, and fortunately, treatments exist for many of these disorders. This talk will describe the most common visual (input) and eye movement (output) disorders in PD, including how to identify/diagnose each, as well as a discussion of treatments.

O75**Lecture #2: Pain and PD: measuring it and addressing it**

Santiago Perez-Lloret

Argentina

Pain affects between 40% to 80% of patients with Parkinson's Disease (PD). Quality of Life is severely compromised in painful patients, therefore timely assessment and management of pain syndromes in PD is recommended. Pain can have several origins in PD. Musculoskeletal pain is the most frequent one and includes aching, cramping, arthralgic, myalgic sensations in joints, and muscles. Pain can also be associated with dystonia or with restlessness. Finally, neuropathic pain can have a peripheral (radicular) or central origin. Clinical assessment of pain should be accomplished by using rating scales. Scales will most typically allow for the evaluation of pain localization, intensity, and syndromic classification (i.e. neuropathic or nociceptive). Some pain scales originally validated for pain assessment in the general population have been used in PD. This is the case of the Brief Pain Inventory, McGill Pain Questionnaire, Pain-O-Meter, Neuropathic Pain Symptom Inventory, or 100-mm Visual Analog Scale or 11-point Numerical Rating Scale, which can be used to rate pain intensity. Pain syndromic classification can be achieved by means of the Douleur Neuropathique 4 (DN4) scale. Scales specifically developed for PD may offer some advantages, including assessment of multiple pain syndromes at the same time, evaluation of PD-related pain syndromes, or assessment of the response to antiparkinsonian treatment. Currently, the only validated pain PD scale is the King's PD Pain Scale. There is a paucity of double-blind randomized controlled trials and thus firm recommendations for the management of pain in PD are difficult at the present time. Musculoskeletal pain may respond to optimization of dopaminergic therapy, and in case of failure, analgesics or physical therapy may be used. Dystonic pain and some forms of neuropathic pain may also respond well to optimization of dopaminergic therapy. Recent double-blind, randomized, controlled trials showed positive effects of rotigotine transdermal patch and prolonged-release oxycodone–naloxone, which did not attain statistical significance, in patients with moderate-to-severe pain in PD of any origin. Further trials are needed to confirm these findings. Hopefully, more well-designed trials with other drugs for pain in PD will be conducted in the near future.

O76**Lecture #1: Sleep disturbances in PD**

Amy Amara

University of Alabama, Birmingham, Alabama, USA

Sleep disorders are common among patients with Parkinson's disease and have an adverse impact on quality of life. Sleep disturbances in PD include sleep fragmentation, daytime sleepiness, nocturnal limb movements, difficulty rolling over in bed, and parasomnias, such as REM Sleep Behavior Disorder. These disorders are influenced by motor symptoms, medications, and by other non-motor symptoms, such as mood, memory, or hallucinations. Further, sleep dysfunction also impacts many aspects of the disease. In this session, we will discuss the features and impact of sleep dysfunction in PD, diagnostic methods, and potential therapeutic options.

O77**Lecture #2: Sleep in prodromal PD**

Alex Iranzo

Spain

Parkinson disease (PD) has a prodromal phase where neurodegeneration occurs before parkinsonism becomes apparent. Sleep disorders, depression, constipation and smell loss may precede the onset of the cardinal motor symptoms of PD. This is in line with a proposed staging model of pathology in PD where the neurodegenerative process occurs first in the peripheral autonomic nervous system, lower brainstem and olfactory bulb before reaching the substantia nigra in the midbrain and causing parkinsonism. Two sleep disorders, namely hypersomnia and REM sleep behavior disorder (RBD), are thought to increase the risk of PD. The association of hypersomnia as a predictor of PD comes from two population studies where this symptom was defined as "being sleepy most of the day" or "daytime napping during more than hour". After several years of follow-up, it was shown that hypersomnia at baseline increased the risk for developing PD. However, several studies have shown that hypersomnia in untreated de novo PD patients is not more frequent than in matched healthy controls. The association between RBD and future appearance of PD is much more robust. RBD is characterized by abnormal motor and vocal behaviors (e.g., jerking, kicking, shouting, crying, laughing) and nightmares (e.g., being attacked or chased by people) linked to REM sleep without atonia. RBD is the result of the dysfunction of the brainstem structures that regulate REM sleep. Polysomnography with audiovisual recording is needed to confirm the diagnosis of RBD. There is the following evidence that the idiopathic form of RBD (IRBD) represents the prodromal stage of PD and other synucleinopathies. First, IRBD patients show clinical and subclinical abnormalities that are characteristic of the synucleinopathies including subtle parkinsonian signs, asymptomatic cognitive deficits, hyposmia, constipation, depression and mneuroimaging of the nigrostriatal system. Second, the majority of IRBD subjects develop the cardinal signs and symptoms of PD and other synucleinopathies with time. Finally in vivo and postmortem examination of subjects with IRBD demonstrates alpha-synuclein pathology. This indicates that IRBD may be a good candidate to test disease-modifying interventions to stop the neurodegenerative process in prodromal PD.

O78

Lecture #1: Maladaptive immune responses in face of vulnerable neurons in Parkinson's disease*Sheela Vyas*

UPMC, Paris, France

Evidence from epidemiological, genetic, postmortem and animal studies of Parkinson disease (PD) suggests that inflammatory processes primarily associated with glial activation could be intricately linked not just to disease progression but also to selectivity of neurodegeneration. In addition to these now well-recognized culprits, latest developments in the field of neurodegeneration have revealed the importance of perivascular brain macrophages as well as extravasation and migration of peripheral immune cells (both myeloid and T cells) to lesioned regions, the latter process largely dependent on the chemokine axis.

In chronic PD pathology, the inability of these immune-competent cells to resolve inflammatory processes and help repair the lesion suggests that inflammatory controls may be impaired. One such control possibly affected is glucocorticoid signaling via glucocorticoid receptor. Several reports have consistently shown significantly high basal levels of cortisol in PD patients suggesting that adaptive functions of glucocorticoids are compromised. We show how dopamine neurons of substantia nigra are particularly vulnerable to absence of glucocorticoid receptor actions in myeloid cells and in astrocytes. Thus for example, in the absence of glucocorticoid receptor in microglia/myeloid cells, dopamine neurons are selectively vulnerable to TLR9 activation by its synthetic ligand or mitochondrial DNA.

In view that aging is known to affect immune functions promoting also microglial priming, elucidating the precise functions of each of the above immune cell type in PD pathology is important to harness their beneficial roles for therapeutic strategies.

O79

Lecture #2: Microglia, a dynamic player in the neurodegenerative process of Parkinson's disease*Marina Romero Ramos*

Denmark

While the occurrence of the so called microgliosis has been long well known in Parkinson's disease (PD), little is still understood about the role of the microglia in the disease. Development in the recent years has revealed that the immune response in neurodegenerative disease is dynamic and involves not only brain microglia, but also peripheral immune cells. These cells would interact with the brain cells, neurons and glia, therefore modulating the immune response, which will have consequences in the disease progression. Of especial relevance are the evidences supporting a pro-inflammatory property for the alpha-synuclein protein and the key role played by microglia in the clearance of extracellular alpha-synuclein.

Our lab has been focusing in the last years on characterizing the changes of microglia during alpha-synuclein induced neurodegeneration in the dopaminergic neurons. Our data suggest that the microglia is activated early in PD but that this response is not static and will develop as the neuropathology progress as a result of local and peripheral cues. The response of microglia will be different in the presence or absence of cell death, but will not depend on this one to happen. We have also shown that the modulation of this process can be achieved not only by modifying brain events, but also by approaching peripheral immune system. Altogether this has opened new therapeutic possibilities that are being explored nowadays by both, basic and clinical researchers.

O80

Lecture #3: Neuroinflammation in Parkinson's disease: a risk factor and a therapeutic opportunity*Malu Tansey (Presenter), George T. Kannarkat, Darcie A. Cook, Lori N. Eidson, Amarallys F. Cintron, Kathryn P. MacPherson, Christopher Carr, W. Michael Caudle, Stewart A. Factor, Jeremy Boss*

Emory University, Atlanta, Georgia, USA

Gene-environment interactions determine an individual's life-long risk for Parkinson's disease (PD). Defense against environmental exposures and invading pathogens requires immunocompetence, a process that declines as we age. Moreover, the aging process is accompanied by alterations in immune cell responses and a pro-inflammatory state. The research interests of our laboratory include studies aimed at gaining a deeper understanding of the physiological alterations in innate and adaptive immune system activation that contribute to neuroinflammation and risk for development of PD with the long-term goal of informing development of mechanism-based immunomodulatory interventions to delay or prevent development of PD. Important questions under investigation include the extent to which inflammatory markers in central or peripheral biofluids could serve as bona fide biomarkers to diagnose or monitor PD pathophysiology or responses to therapy and whether deep immunophenotypic analysis of cells in central and peripheral compartments could reveal important clues about disease pathogenesis. Recent findings from our group and others indicate that environmental exposures synergize with genetic variability in HLA genes, which are involved in antigen presentation and activation of the adaptive immune system, and modify an individual's risk for late-onset Parkinson's disease. Specifically, pyrethroid insecticides have direct effects on immune cell profiles *in vivo* and *in vitro* and this immune dysregulation may increase the risk for neurodegeneration. Although the field has primarily focused on studying mechanisms in neurons, PD-related genes such as LRRK2 are highly expressed in the immune system and are likely to be involved in regulation of immune and inflammatory responses. Recent studies from our group reveal alterations in LRRK2 expression in immune cells from individuals with late-onset PD relative to that in immune cells from healthy age-matched controls. Ongoing immunophenotype analyses of individuals with sporadic and autosomal dominant forms of PD (including those with G2019S LRRK2 mutations) are likely to reveal opportunities for immunomodulatory intervention (including use of LRRK2 kinase inhibitors) that could delay the onset or slow the progression of PD [Funding from the Michael J. Fox Foundation for Parkinson's Research and the NIH/NINDS].

O81

Talk #1: The role of autophagy in PD*Sheng-Han Kuo*

Columbia University, New York, NY, USA

"Autophagy" is used to mean degradation by a cell of its own components within lysosomes. There are multiple means by which this process occurs, including via formation of vacuoles that swallow cargo and then fuse with lysosomes, or "macroautophagy"; recognition of specific proteins by chaperones that are targeted directly to the lysosome ("chaperone-mediated autophagy"); and other forms that remain poorly characterized in neurons. Over the past 15 years, autophagic mechanisms have been implicated in normal and diseased neuronal functions. We will discuss the formation of neuromelanin, a normal autophagic component in substantia nigra; the degradation of alpha-synuclein by chaperone-mediated autophagy and how that might be perturbed for its mutant

forms, reaction with cytosolic dopamine, by mutations for LRRK2; roles for autophagy in the turnover of mitochondria and its possible regulation by PD-related genes; regulation of dopamine neurotransmission and neurophysiology by autophagy; and multiple directions that may provide therapy for patients.

O82

Talk #2: Glucocerebrosidase and its role in the pathogenesis of PD

Joe Mazzulli

Northwestern University Feinberg School of Medicine, Department of Neurology, Chicago, Illinois, USA

It is well established that Lewy body inclusions comprised of aggregated alpha-synuclein (a-syn) define the histopathology of Parkinson's disease (PD), however no treatments exist that are capable of clearing a-syn. Recent genetic analysis has indicated that loss-of-function mutations in the GBA1 gene that encodes lysosomal glucocerebrosidase (GCase) lead to increased risk for the development of PD and dementia with Lewy bodies. This indicates that lysosomal dysfunction and accumulation of the GCase substrate, glucosylceramide (GluCer), may play a key role in pathogenesis of synucleinopathies. While previous studies have indicated that expression of GBA1 mutants result in the accumulation of a-syn, the mechanisms have not been clearly defined. Here, recent developments in the role of GCase mutations in PD pathogenesis will be discussed with an emphasis on how loss-of-function mechanisms and GluCer accumulation may contribute to pathologic structural changes in a-syn. Data from our group indicates that loss of GCase function, in the absence of GBA1 mutations, results in the accumulation of protease resistant oligomeric forms of a-syn in human midbrain dopamine neurons. Reducing cellular GluCer levels through enzyme activation results in reduction of pathological a-syn in midbrain neurons derived from genetic PD patients. Our data suggests that GluCer reducing agents may provide therapeutic benefit in PD and related synucleinopathies.

O83

Talk #3: Therapeutic prospects of enhancing chaperone-mediated autophagy in synucleinopathies

Leonidas Stefanis

Greece

A number of studies have shown that the Parkinson's Disease (PD)-linked protein alpha-synuclein is degraded, at least in part, by the lysosomal process of Chaperone-Mediated Autophagy (CMA) in cultured cells. Furthermore, aberrant alpha-synuclein can inhibit this process, creating a vicious cycle of pathogenicity. We have proposed that enhancing CMA through overexpression of its rate-limiting step, the lysosomal transmembrane protein Lamp-2a, may represent a viable therapeutic strategy for PD and related synucleinopathies, as it would theoretically enhance alpha-synuclein turnover, while at the same time limiting its detrimental effects on lysosomal function, thus "hitting two birds with one stone". In support of this notion, we have shown that, in cultured neuronal cells and in vivo, in the rat substantia nigra, viral-mediated induction of Lamp-2a levels and resultant CMA enhancement prevents the neurodegeneration associated with alpha-synuclein overexpression via Adeno-Associated Virus (AAV) and limits its neurotoxic species. Importantly, in the in vivo model, this neuroprotection was observed not only at the level of the cell bodies, but also at the terminals. We are in the process of performing experiments to investigate the temporal window in which such a neuroprotective intervention may

be beneficial in alpha-synuclein overexpression models, including transgenic rodents. In more recent work, we have examined the effects of in vivo Lamp-2a downregulation via relevant AAV-shRNA injections in the rat substantia nigra. We have observed a dying-back type of axonopathy and eventual profound dopaminergic neuron degeneration, accompanied by an accumulation of alpha-synuclein aggregates in surviving neurons and intense neuroinflammatory effects. Thus, this model replicates certain aspects of PD. These findings suggest that CMA impairment may indeed play a role in the pathogenesis of PD, especially as regards nigral dopaminergic neuron vulnerability. Strategies that counteract this dysfunction could be beneficial in PD and related synucleinopathies.

O84

Talk #1: PINK1/Parkin-mediated mechanisms

Leo Pallanck

Department of Genome Sciences, University of Washington, Seattle, Washington, USA

Mitochondria perform a number of essential cellular functions, but their damage can lead to bioenergetic failure and the release of cytotoxins that are implicated in aging and in neurodegenerative disease. Fortunately, eukaryotes have evolved a number of cellular pathways to prevent and repair damaged mitochondria, and in extreme circumstances, to discard extensively damaged mitochondria altogether through a process termed mitophagy. Although the molecular mechanisms underlying the prevention and repair of damaged mitochondria have been long studied, the machinery tasked with the detection and degradation of damaged mitochondria emerged only recently through studies of the PINK1 and Parkin genes, mutations of which cause Parkinson's disease. My talk will provide an overview of the current model by which damaged mitochondria are detected and degraded. I will also describe some of our recent proteomic and genetic data that bears on the mechanisms by which mitochondria are damaged and degraded, and that allows us to quantify the contribution of mitophagy to mitochondrial protein turnover.

O85

Talk #2: Parkin/PINK1 interplay and pathological consequences of their mutations

Miratul Muqit

School of Medicine, University of Dundee, Dundee, United Kingdom

Clues to the molecular origins of Parkinson's have been transformed by spectacular advances in genetics that have to date uncovered nearly 20 genes or loci that are linked to Mendelian inherited forms of Parkinson's. For the most part, the function of these genes remains poorly understood and in particular the central pathways mediating dopaminergic neurodegeneration remain unknown. Mutations in PTEN-induced kinase 1 (PINK1) and Parkin cause autosomal recessive Parkinson's and in recent years these genes have been strongly implicated in a mitochondrial quality control pathway. Over the last few years our laboratory and others have elaborated a novel signalling pathway for PINK1 and Parkin. In particular we have identified that PINK1 phosphorylates Parkin and the modifier, ubiquitin, at an equivalent residue, Serine 65, and this leads to maximal activation of Parkin E3 ligase activity at mitochondria. Current work in the laboratory is directed at understanding the pathophysiological consequence of mutations in PINK1 and Parkin in disrupting both signalling and mitochondrial quality control pathways in both human cell lines and Parkinson's derived cells and tissues.

O86

Talk #1: What is palliative care and why is it relevant to PD?*Benzi Kluger*

Denver, Colorado, USA

Palliative care is an approach to the care of patients and families affected by chronic or life-threatening illnesses that focuses on the relief of suffering through the management of medical symptoms, psychosocial issues, spiritual wellbeing and planning for the future. As Parkinson's disease (PD) may be associated with difficult to treat nonmotor symptoms, caregiver distress, reductions in life expectancy and challenges to individuals and relationships we feel that palliative care provides essential services which are complementary to traditional PD care. In this talk we will address several common misconceptions regarding palliative care and discuss why palliative care is relevant to PD patients, caregivers and healthcare providers. We will specifically address: (1) What is palliative care and what is hospice care? (2) What are the palliative care needs of PD patients and their families? (3) What palliative care issues should all PD patients be aware of? and (4) How can palliative care be integrated into the care of PD patients?

O87

Talk #2: Approaches to providing palliative care to the PD community*Indu Subramanian*

USA

Palliative care is a relatively new concept in the Parkinson Disease (PD) treatment arena. There have been a number of barriers in providing robust palliative care to the Parkinson disease patient and in supporting their care partners. In this talk we will specifically address:

1. Barriers to providing palliative care and how to address them
2. Description of the multidisciplinary team approach to delivering palliative care in different care settings
3. Using novel technology to deliver care to palliative care patients in remote settings- eg. telemedicine
4. Utilizing complementary and alternative approaches in palliative care of PD patients
5. Practical issues that arise in the care of Parkinson disease patients in the palliative care/hospice setting focusing on what the palliative care/hospice provider needs to know about PD-symptoms covered will include dementia, psychosis, pain, swallow, immobility and orthostasis.
6. How to deliver care giver support and care

O88

Talk #3: Palliative care and PD: a patient perspective*Kirk Hall*

USA

Palliative care is commonly associated with cancer patients and confused with hospice. As the ramifications of Parkinson's (PD) issues become better understood, palliative care specifically designed for PD is a topic that is getting considerable attention in the medical world. Clearly, palliative care has significant potential for improving quality of life for PD patients, caregivers, and their families at every stage of the disease. A vision proposal created by patients and caregivers participating as stakeholders in a PD palliative care clinical research study will be the focus of this presentation. The palliative care spectrum is broken down into three stages for the purpose of this discussion:

- Early: Diagnosis-5 years (typical honeymoon period)
- Middle: 5 years-Advent of symptoms that substantially affect daily living
- Late: Advent of symptoms that substantially affect daily living/hospice – death/bereavement

Key issues that will be covered include:

- confusion regarding the palliative care term
- potential benefits of a unified, consistent approach to regional PD support organizations nationwide
- need for changes designed to minimize patient/caregiver angst at time of diagnosis and the months that follow as well as finding ways to reach more patients and caregivers with education that will facilitate engagement and ownership (early stage)
- assistance to help begin planning for late-stage issues (medical, legal, financial, spiritual and personal) in advance of late stage symptoms (middle stage)
- caregiver needs, under-utilization of hospice and patient control over the setting and manner in which they die (late stage)

Fundamental changes in the mindset and training of doctors are also proposed, including:

- ethical aspects of referring patients for services that better meet their needs
- taking time to understand patient/caregiver needs and wants
- sensitivity/empathy with regard to communication of difficult news
- how their role changes (and does not end) when they are no longer able to prolong life
- how to recognize and deal with caregiver needs
- strategies for providing services to patients in remote areas or who would benefit from non-traditional approaches including telemedicine

Recommendations for short-term priorities are included in recognition of the volume of change being recommended.

O89

Roundtable #1: Advocacy: patient advocates at work around the world – how to get involved in North America*Israel Robledo*

USA

The voice of the patient-advocate is becoming more important as new therapies and treatments are sought. Many opportunities for patient-advocate engagement are available in North America, including regional, national, and international organizations. Patient advocates can focus on their areas of interest and become involved to the extent that they can, while knowing that they are making a difference in the lives of those living with Parkinson's Disease. Specific opportunities for involvement will be discussed, along with contact information for various organizations.

O90

Roundtable #2: Is the future really about immunization against PD? What have we learned so far?*Martin Ingelsson*

Uppsala University, Department of Public Health and Caring Sciences, Uppsala, Sweden

Immunotherapy against amyloid- β (A β) has evolved as the most promising therapeutic strategy for Alzheimer's disease (AD) and several monoclonal antibodies are currently assessed in various clinical trials. The pathophysiological similarities between AD and Parkinson's disease (PD) have now led researchers to believe that also PD can be treated with a similar strategy. In PD, aggregating

species of the α -synuclein protein are targeted as they are believed to play a causative role in the disease. By applying different forms of vaccines and antibodies directed against α -synuclein on various cellular and animal models, we have gained knowledge as to what properties that the compounds should have. Monoclonal antibodies directed against either the C-terminal of the native protein or against a particular oligomeric conformation of α -synuclein seem to give the best effects on transgenic mouse brain pathology and newly designed anti- α -synuclein single chain antibodies also seem to reduce brain pathology in mouse models. So far, four phase I clinical trials have been initiated, based on peripheral administration of either peptides that are mimicking certain α -synuclein epitopes or of α -synuclein monoclonal antibodies, targeting the C-terminal. The trials have shown a satisfactory safety profile and ongoing studies will demonstrate whether these therapies also could have an effect on PD symptoms. Here, a major challenge will be to recruit patients at a disease stage where the α -synuclein pathology and the related neuronal loss have not yet become too extensive.

O91

Roundtable #3: Living alone with PD

Pat Davies

Washington, USA

In January 2009 I was diagnosed with Parkinson's Disease. I knew very little about it, so began to read as much as I could. Soon I noticed that whenever a Person with Parkinson's (PwP) was mentioned there were three other words "and their Caregiver." I live alone, have no Caregiver, and don't even have any family to provide support, so I wondered what would become of me. I searched the internet for "living alone with Parkinson's Disease", but the search yielded nothing – no comforting words of advice, no list of useful resources – zero!

So I decided that I would be my own caregiver and advocate, that I would continue to live life to the full by doing as much as I could for as long as possible, and that I would ensure that I am well prepared for whatever the future might bring.

My personal strategy is to be actively involved with several different organizations/projects, some are associated with Parkinson's Disease, and others are totally unrelated. More importantly I have assembled a group of practitioners and friends who can treat and support me, from my movement disorder specialist, my acupuncturist, and my clinical social worker, to my dog walker, and my friends who will intervene if they see that I am no longer able to cope alone, or that I am a danger to myself and others on the road! Staying engaged in your community, striving not to become isolated, and learning that living alone need not mean that you are lonely, are very important, and often particularly difficult for some PwPs, for example if depression and difficulty with speech are among your symptoms.

At this session I will share what getting prepared for the future means for me, especially from a practical point of view, such as organizing documents so that others can navigate them when the time comes, appointing medical and financial powers of attorney, and ensuring that I have options for assisted living or nursing home care when this becomes necessary. We will also explore other issues for PwPs who live alone in different circumstances.

O92

Roundtable #3: Living alone with PD

David Burn

Newcastle University, Newcastle, United Kingdom

"Every hour, someone in the UK is told they have Parkinson's. Because we're here, no one has to face Parkinson's alone" (Parkinson's UK).

By pure coincidence, I woke this morning to an item on the BBC about loneliness. The interviewee was not an older person, but a man in his mid-50s who had separated from his wife, and having lost a lot of confidence, had ended up having very little social interaction. It must be even more difficult to be living alone with Parkinson's. Although the human spirit is resilient, there is a limit to the mental and physical challenges that we can endure alone, and this resilience clearly varies between different people. Patient advocacy groups like Parkinson's UK can do a huge amount to support people with Parkinson's throughout their journey, but along with health care professionals I do not think they can be expected to "treat or manage" loneliness. Some people, of course, like to be alone, and would not regard this as a negative in their lives. So as a doctor involved in the care of people with Parkinson's I suggest that some broad "principles" on the issue of living alone with Parkinson's would be as follows:

1. Consider every person as an individual and do not assume or generalise.
2. Encourage society as a whole to be less selfish and "silo-ed" in its approach. It costs nothing to be kind or to call in on a neighbour occasionally.
3. Facilitate independent living as far as possible for someone with PD to make their lives easier – the role of a multidisciplinary team is essential in this regard.
4. Be aware that some symptoms may be caused or exacerbated by loneliness. Do not just focus on the "mechanistic" aspects in the consultation, but put them in social context.

O93

Roundtable #4: DBS: advice from one PwP to another

Allison Smith

USA

This roundtable provides an opportunity for PwP who are considering or who have had Deep Brain Stimulation surgery to share their questions and experiences. The co-facilitators of the roundtable have both had DBS surgery, although their stories are quite different.

Marilyn Veomett had DBS surgery in May of 2015, at age 68, after living with PD for 18 years. She had electrodes implanted on both sides of the brain, in the GPi region, under general anesthesia (asleep DBS). Wires from both electrodes connect to a single impulse generator, which was implanted in her abdomen during a second surgery. She is very happy with the results of her surgery, although she found the entire DBS journey from initial decision to look into the procedure through programming of the neurostimulator to be more stressful and lengthy than she had anticipated.

Allison Smith had DBS surgery in April of 2010 after being diagnosed the previous month at age 32. Allison had bilateral DBS surgery while being awake to ensure the electrodes were placed in the best location to control her Parkinson's symptoms. Allison's Neurosurgeon breaks down the procedure into 3 surgeries, a week apart and did not require her to shave her head. Allison, being a young-onset Parkie, chose to do DBS early into her disease, to help slow the progression of PD.

O94

Roundtable #5: Dyskinesia: impact, treatment and the future

Oscar Gershanik

Argentina

Levodopa induced dyskinesias is one of the most frequent adverse events observed after long-term treatment in Parkinson's disease. It is estimated that up to 50% of the patients develop dyskinesias after 5 years of treatment, reaching almost 100% after 10 years. Impact on motor function and quality of life is variable and depends on severity and duration of this complication during the "on" period. Its presence may be just socially stigmatizing while on the other hand if it is severe enough may contribute to subjective discomfort and functional impairment on activities of daily living and even participate in the mechanisms leading to postural instability and falls. At present, available strategies include prevention through a rational and cautious use of dopaminergic agents and use of the NMDA antagonist amantadine, which is not devoid of side-effects. Research on the pathophysiology and molecular underpinnings of dyskinesia has been quite active in the last several years, leading to the identification of potential targets for therapeutic intervention. Many of the drugs presently under research and development are targeted to interfere with the mechanisms leading to the occurrence of dyskinesias or to the reduction of already established dyskinesias. The forecast in this regard appears quite promising.

O95

Roundtable #6: Self-care: how can technology help you take control of your own care?

Sara Riggare
Sweden

In this roundtable discussion, Sara Riggare will share her experiences with using technology to learn more about her Parkinson. This has enabled her to engage with her neurologist and other healthcare professionals on a higher level and asking better questions as well as being able to work as equals. Sara will also talk about the research she does as a doctoral student in health informatics at Karolinska Institutet in Stockholm, Sweden. She works on investigating and developing different aspects of selfcare for Parkinson.

O96

Roundtable #7: Nutrition and PD: what's the big deal?

Laurie Mischley
Bastyr University, USA

Nutrients are those molecules and minerals that must be obtained from our environment in order to survive. In addition to those from food, nutrients include vitamin D from sunlight, vitamin K from intestinal bacteria, and oxygen from the air.

A substantial body of research suggests dietary choices made early in life affect risk of developing PD; consumption of dairy products has been consistently associated with an increased risk of diagnosis, while green and black tea, coffee, dark berries, and a prudent diet have been shown to be protective. Just because a nutrient or food increases or decreases risk of developing PD does not mean that consumption, or avoidance, will shape the rate of disease progression if you already have PD. No attempts have been made to evaluate the effect of dietary modification on PD symptoms or progression in a randomized clinical trial.

Individuals with PD have been shown to be at increased risk of vitamin D, B12, folic acid, and coenzyme Q10 deficiency. Constipation and small intestinal bacterial overgrowth (SIBO) are common. PD medications, such as levodopa, interfere with nutrient absorption. While there is evidence that individuals with PD have unique nutritional needs, few attempts have been made to comprehensively describe the nutrient requirements specific to individuals with PD.

Neurologists receive little training in nutrition as part of their medical school curriculum and naturopathic physicians, well trained in nutritional medicine, often lack PD-specific expertise. Patients often find themselves attempting to navigate questions about diet and supplements without supervision. Online resources and well-intended friends and family suggest a wide variety of special diets, such as gluten-free, low carbohydrate, ketogenic, vegetarian, vegan, organic, nutrient-dense, calorie restricted, low-protein, and macrobiotic. Many of these recommendations conflict with one another or with PD medications, while others are not financially feasible or sustainable. Dietary modification and use of supplements can be a safe, accessible, and empowering strategy for improving health, although numerous questions remain about the effect of nutrition on PD progression.

O97

Lecture #1: Overview: Update on latest of data repositories, CSF and other biological samples

Tanya Sumini
Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA

There is an urgent and still unmet need to develop biomarkers of Parkinson's disease (PD) diagnosis and progression. While a substantial progress has been made in the symptomatic treatment of PD, there still is not treatment to slow or halt disease progression. One of the major obstacles to development of such therapies is lack of biomarkers (objective measures) of PD diagnosis and progression. In the last 5 years there has been a substantial global effort to discover and validate PD biomarkers.

This talk will provide overview of the major PD biomarkers discovery and validation programs, focusing on the National Institute of Health PD Biomarker Program (PDBP) and Michael J Fox Foundation Parkinson Progression Biomarker Initiative (PPMI). The talk will highlight achievements and obstacles and outline the paths to the future development.

O98

Lecture #1: (Mis)perception of PD

Joseph Friedman
Butler Hospital, Providence, Rhode Island, USA

There are several common misperceptions in PD patients that often are baffling to the observer but not apparent to the patient. One of the most common is the difference between what many patients hear when they speak and what others hear. PD patients often believe they are speaking at a normal volume while others think they are talking too softly. Another common misperception is the feeling that dyskinesias are not as prominent as others think they are. Patients will sometimes be surprised when they view videos of themselves when dyskinetic. This is much less common for tremors. They are thus mis-perceiving. Another common problem is the misperception by the patient of the location of their center of gravity. Many patients will attempt to stand up from a chair without putting their center of gravity over their feet, so that when they start to stand they rise a little then fall backwards. This probably explains why some PD patients walk faster than they want to, or even start running, and why they have difficulty getting up from their bed. They are strong but they cannot position themselves properly to take advantage of available leverage. Many patients are unaware of their stooped posture or that they tilt to one side. Many family members will report that the patient, although driving safely, will always be on either the right or the left side of the lane but never in the middle. The patient insists he is in the middle, when he is not. He

misperceives where the middle is. In driving studies PD patients often fail to notice as many things in the environment than non-PD drivers. And, unbeknownst to the patient, two studies have found that PD patients are often misperceived by others, including doctors, and are thought to be angry, hostile, or unpleasant, simply based on their facial expressions. This talk will discuss some misperceptions in PD and their effects on the patient and loved ones.

O99

Lecture #3: Drooling and excessive sweating

Anne-Louise Lafontaine

McGill University, Montreal, Quebec, Canada

Drooling and excessive sweating are common dysautonomic symptoms that negatively impact the quality of life of Parkinson patients. Both contribute to social embarrassment and isolation.

Drooling also known as sialorrhoea, is among the most important determinants of health related quality of life in patients with Parkinson disease. Its exact mechanism is unclear but in many instances it is a byproduct of dysphagia, rather than an overproduction of saliva.

Management requires a multidisciplinary approach. Reducing "off" time can improve "off" related drooling. Botulinum toxin has proved effective for sialorrhoea and certain drugs like the anticholinergics and antihistaminics are also employed with some success. Speech and swallowing therapy can be beneficial in helping to improve posture and teach good swallowing techniques. Improving the stooped or flexed head posture can also be of great help.

Sweating disturbances, either hypohidrosis or, in particular, hyperhidrosis occur in more than half of the patients. Like intolerance to cold and heat, they are a consequence of thermoregulation, common in more than half of PD patients. Excessive sweating occurs frequently in the "off" state but also may in the "on" state in patient with severe dyskinesias, and accordingly adjustments of PD medications to reduce motor complications can be useful. Botulinum toxin injections may reduce focal sweating and deep brain stimulation has also been shown to be beneficial. Practical measure such as avoiding getting overheated or strenuous activity in the heat and to wear well-ventilated clothes should be encouraged

O100

Lecture #1: Levodopa-induced dyskinesia: impact on quality of life

Oscar Gershanik

Argentina

Reduced QoL significantly correlates with disease progression and duration in Parkinson's disease, however, the impact of dyskinesias on QoL remains controversial. There are published reports which have found that dyskinesias do have a significant impact on the QoL of PD patients. Dyskinesias adversely affect various dimensions of QoL – including mobility, activities of daily living, stigma, communications, and bodily discomfort. Increasing severity of dyskinesias is also associated with increasing depression. Other studies have shown that dyskinesias can seriously interfere with the performance of activities of daily living, ambulation, and balance, and that they can be associated with increased falls and unintended weight loss. On the other hand, other investigators have reported that dyskinesias do not have a significant impact on QoL and may not pose a major concern for patients who prefer to be in the on state with dyskinesias rather than in the off state. Differences in QoL study results may be attributed to variability in methodology and to the patient populations studied. Despite this controversy,

dyskinesias, being highly prevalent in patients under long-term levodopa treatment, pose a therapeutic challenge that needs to be addressed. The pathophysiological mechanisms underlying its development and the search for targets for intervention is at present a very active field of research.

O101

Lecture #3: Novel targets for treatment of dyskinesia: what is in the pipeline?

Erwan Bézard

Institut des Maladies Neurod, 33076 Bordeaux cedex, France

Involuntary movements, or dyskinesia, represent a debilitating complication of levodopa (L-dopa) therapy for Parkinson's disease (PD). L-dopa-induced dyskinesia (LID) are ultimately experienced by the vast majority of patients. In addition, psychiatric conditions often manifested as compulsive behaviours, are emerging as a serious problem in the management of L-DOPA therapy. The presentation attempts to provide an overview of our current understanding of dyskinesia and other L-DOPA-induced dysfunctions, a field that dramatically evolved in the past twenty years. In view of the extensive literature on LID, there appeared a critical need to re-frame the concepts, to highlight the most suitable models, to review the central nervous system (CNS) circuitry that may be involved, and to propose a pathophysiological framework was timely and necessary. An updated review to clarify our understanding of LID and other L-dopa-related side effects was therefore timely and necessary, a task that was recently achieved at consortium level. We review the novel targets for treatment of dyskinesia, some of them being relatively advanced in the pipeline.

O102

Lecture #1: Non-invasive imaging of progression in PD and Parkinsonian disorders

David Vaillancourt

University of Florida, Gainesville, USA

Parkinson's disease (PD) is a progressive neurodegenerative syndrome that is characterized by the loss of dopaminergic cells in the substantia nigra (SN) and reduced dopamine levels in the putamen. In PD, a major goal has been to develop therapies that modify disease progression. Unfortunately, despite dozens of clinical trials in PD over the past several decades, identifying a disease-modifying drug for PD has not been achieved. A major reason for this failure is because prior studies have relied upon subjective clinical ratings as outcome measures. Sensitive and objective markers of PD progression that directly relate to basal ganglia and cortical neuroanatomy are critically needed. Over the past decade, our group has developed two non-invasive imaging techniques that show excellent promise at 3 Tesla for assessing the progression of the substantia nigra, putamen, and motor cortex in PD and Parkinsonism. The lecture will describe recent progress using free-water diffusion imaging and motor task-based functional magnetic resonance imaging, in studies that assess progression over one year for PD and Parkinsonism.

O103

Lecture #2: Effects of dopaminergic treatments on brain function in PD

Vesna Sossi

Canada

L-dopa remains the most widely used treatment in PD. While effective in improving motor symptoms in early disease, its effects on other aspects of PD, such as cognition and behaviour, are variable and the significant cognitive and motor side effects often present in the later stages of treatment are still incompletely understood. There is increasing evidence coming from imaging studies that dopaminergic treatment affects the brain at the regional and network levels and that response to treatment is likely highly dependent on the topography of dopaminergic denervation. PET and resting state fMRI studies have identified PD-related alterations in functional and metabolic networks and have shown that, initially, L-dopa and other dopamine replacement therapies, reduce the aberrations, especially as related to motor performance. Dopaminergic treatment induces cognitive improvement in some patients and worsening in others. Imaging studies suggest that a large dynamic range in the level of dopaminergic denervation may partially explain such variability; an excess of treatment-induced dopaminergic stimulus may be detrimental to regions with relatively preserved dopaminergic function. Accordingly, patients with larger baseline deficits in caudate dopaminergic innervation have been found to more likely cognitively benefit from L-dopa. Similarly, differences between the nigrostriatal and mesolimbic dopaminergic denervation, coupled with an increase in L-dopa-induced dopamine release in the ventral striatum, are deemed associated with treatment-induced compulsive behaviours. Abnormal L-dopa-induced dopamine release in the putamen, possibly mediated by serotonergic terminals, has been implicated in the emergence of dyskinesias. L-dopa was also found to induce dissociation between metabolic and hemodynamic networks, which was exacerbated for subjects suffering from L-dopa-induced dyskinesia; while L-dopa reduced PD-related alterations in metabolic patterns, it led to higher cerebral blood flow network alterations. Such dissociation was not observed when subthalamic nucleus deep brain stimulation was successfully used as treatment, indicating a direct link between L-dopa treatment and neurovascular uncoupling. Improvement in imaging techniques and data analysis methods have significantly augmented our understanding on how dopaminergic treatment, and L-dopa in particular, affect brain function, but more information is needed to develop effective strategies. Multi-modality imaging approaches are expected to play a key role in this effort.

O104

Lecture #3: Novel insights from imaging the cholinergic system in PD

Nicolaas Bohnen

University of Michigan Radiology Nuclear Medicine, Ann Arbor, Michigan, USA

There is increasing interest in the clinical effects of cholinergic basal forebrain and tegmental pedunculo-pontine complex (PPN) projection degeneration in Parkinson's disease (PD). Recent evidence supports an expanded cholinergic role beyond cognitive impairment, including effects on olfaction, mood, REM sleep behavior disorder, and motor functions. Cholinergic denervation is variable in PD without dementia and may contribute to clinical symptom heterogeneity. In vivo imaging evidence shows that impaired cholinergic integrity of the PPN associates with frequent falling and that degeneration of basal forebrain cholinergic projections correlates with decreased gait speed and increased gait variability. These findings suggest that in the dopamine-depleted PD brain, cholinergic cell loss reveals the full impact of striatal dopamine loss on motor performance, reflecting loss of compensatory attentional supervision of monitoring of gait, posture and complex movements. Although cholinergic system dysfunction has been implicated in more episodic or capacity processing-

dependent components of postural and gait changes in PD, in particular falls or freezing, it has not been selectively associated with overall 'trait' severity of axial motor impairments. Interactive effects between loss of dopaminergic nerve terminals and cholinergic integrity have been shown to underlie cognitive impairment in PD. The so-called 'compensatory' hypothesis of the cholinergic system in the dopamine-denervated PD brain underscore the communality between cognition and postural instability and gait difficulties in PD. Cholinergic compensation – or its breakdown – appears to affect brain regions differentially and may involve cerebellar circuitry.

O105

Talk #1: Overview of defects in protein clearance in PD

Vivek K. Unni

Parkinson Center of Oregon, Oregon Health & Science University, Portland, Oregon, USA

Aggregation of α -synuclein protein in the brains of patients with Parkinson's Disease (PD) is the hallmark neuropathological inclusion of PD and several related disorders. Why this occurs and how it relates to disease pathogenesis is still a major unanswered question in the field. Increased intracellular levels of α -synuclein are specifically implicated and may be potentially caused by alterations in several different protein clearance pathways. Intense effort has been focused on the role of traditional protein degradation pathways, such as the ubiquitin-proteasome system (UPS) and the autophagy-lysosomal pathway (ALP), in the clearance of α -synuclein and other potential disease players. However, more recently, several non-traditional pathways for protein clearance from the cell have garnered increasing attention, including the possible role of exosomes and/or trans-synaptic transport, for removing harmful protein species from the cell. This talk will give an overview of the field with regard to both traditional and non-traditional protein clearance pathways and their possible role in Parkinson's Disease development and progression.

O106

Talk #2: Traffic jams and the molecular basis of Parkinson's disease

Tiago Fleming Outeiro

University Medical Center Göttingen, 37073 Göttingen, Germany

The misfolding and aggregation of alpha-Synuclein (aSyn) are common events in several neurodegenerative diseases, including Parkinson's disease (PD) and dementia with Lewy bodies, disorders known as synucleinopathies. Accumulating evidence suggests that secretion and cell-to-cell trafficking of pathological forms of aSyn may explain the typical patterns of disease progression. However, the precise molecular mechanisms controlling aSyn aggregation and spreading of pathology are still elusive. aSyn impairs ER-to-Golgi trafficking, a defect that can be rescued by the expression of Rab1. In order to obtain unbiased information about the process of aSyn oligomerization, we performed a microscopy-based large-scale RNAi screen in living cells. Interestingly, we identified nine Rab GTPase and kinase genes that modulated aSyn aggregation, toxicity and levels. From those, Rab8b, Rab11a, Rab13 and Slp5 were able to promote the clearance of aSyn inclusions and rescue aSyn induced toxicity. Furthermore, we found that endocytic recycling and secretion of aSyn was enhanced upon Rab11a and Rab13 expression in cells accumulating aSyn inclusions. Notably, Rab11 also ameliorates aSyn-associated phenotypes in vivo, in fruit flies. Overall, our study resulted in the identification of new molecular players involved in the aggregation, toxicity, and secretion

of aSyn, opening novel avenues for our understanding of the molecular basis of PD and other synucleinopathies and for the design of future strategies for therapeutic intervention.

O107

Talk #3: Proteasomal dysfunction in PD

Pamela McLean

Mayo Clinic Florida, Dept. of Neuroscience, Jacksonville, Florida, USA

Within cells, proteins are continually degraded into amino acids and replaced by newly synthesized proteins. However, in the cellular environment these newly synthesized proteins are at great risk of aberrant folding and aggregation. Protein misfolding can lead to the formation of toxic substrates including oligomers, protofibrils, and fibrillar deposits. Therefore protein quality control and the maintenance of proteostasis are crucial steps for cellular health.

Increased intracellular levels of alpha-synuclein are implicated in Parkinson's disease and is thought to be caused by alterations in the ubiquitin-proteasome system (UPS) or the autophagy-lysosomal pathway (ALP). To handle a build-up of abnormal proteins, cells employ different processes and machinery. Molecular chaperones and their regulators (co-chaperones) are a group of molecules that contribute to the prevention of aggregation and enhance

the efficiency of de novo protein folding. We and others have demonstrated molecular chaperones to be effective in preventing alpha-synuclein aggregation in model systems. Here we will discuss how dysfunction of cellular proteostasis contributes to PD pathogenesis and the potential for therapeutic development targeting the proteasome degradation machinery.

O108

Talk #1: Swallowing & cough

Michelle Ciucci

University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin, USA

Oropharyngeal swallowing requires fine sensorimotor control of the muscles of the head and neck. The highly coordinated and rapid event must be integrated with respiration in order to protect the airway and safely transport the bolus to the esophagus. Further, the ability to cough is vital for airway clearance. The neuropathology in PD that causes deficits in swallow and cough is widespread, including areas in the central nervous system, such as the brainstem, and peripheral nerves and muscles. Currently, standard treatments such as levodopa and deep brain stimulation do not effectively treat swallow and airway deficits in persons with PD. However, exercise-based treatments hold promise. This session will cover current theories on the onset, progression, and neuropathology of swallowing and airway clearance dysfunction, as well as potential therapeutic techniques that should be considered.

O109

Talk #3: Speech production – neural mechanisms in normal and Parkinsonian states

Kristina Simonyan

USA

In the past few years, several studies have been directed to understanding the complexity of functional interactions between different brain regions during various human behaviors. Among these, neuroimaging research installed the notion that speech and

language require an orchestration of brain regions for comprehension, planning, and integration of a heard sound with a spoken word. These studies mapped the neural correlates of separate speech elements, examined distinct cortical or subcortical circuits involved in different aspects of speech control, and quantified the large-scale speech network topology. With an advance of our knowledge about the neural organization controlling normal speech production, it is becoming increasingly important to clarify the neural mechanisms underlying the speech control in disordered states, such as Parkinson's disease. The overview will be given on the current state of knowledge about speech-related brain functioning in patients with Parkinson's disease and the therapeutic challenges these patients face in terms of the limited improvement of their speech symptoms.

O110

Talk #1: Apathy in PD: from diagnosis to management

Paul Krack

France

Normal maintenance of human motivation depends on the integrity of subcortical structures that link the prefrontal cortex with the limbic system. Structural and functional disruption of different networks within these circuits alters the maintenance of spontaneous mental activity and the capacity of affected individuals to associate emotions with complex stimuli. The clinical manifestations of these changes include a continuum of abnormalities in goal-oriented behaviours known as apathy. Apathy is highly prevalent in Parkinson's disease, which can be explained by degeneration of monoaminergic systems and particularly of dopamine, activating the motivation network, but degeneration of serotonine neurons are also contributing to the clinical syndrome. Apathy can easily be missed by the treating physician, if not specifically screened for. This is important as apathy can severely affect the quality of life of both patients and caregivers and is accessible to treatment. Differentiation of apathy from depression is important for its management. Discrimination of its cognitive, emotional, and auto-activation components can guide an individualised approach to the treatment of symptoms.

O111

Talk #2: Clinical features and diagnosis of MCI in PD

Jennifer Goldman

Rush Medical College, Chicago, IL, USA

Cognitive decline is one of the most frequent and disabling non-motor features of Parkinson's disease (PD). However, it is only in recent decades that cognitive impairment has become recognized as a relevant clinical manifestation of PD, the prevalence of dementia reaching 80% in long-term patients. Mild cognitive impairment (MCI) is also highly prevalent in PD (PD-MCI) (around 38% in most of series) and it is known to be a risk factor for dementia (PDD). PD-MCI is defined as cognitive decline that is not normal for the age and educational level of the patient but that is not associated with impaired functional activity. Identifying PD patients with MCI is important from clinical and scientific perspectives, since these patients appear to represent the early stage of a progressive cognitive decline. Until recently, there were no formal criteria for the diagnosis of this entity and different study groups used a variety of criteria trying to identify PD patients having a cognitive dysfunction of this type. Recently, a set of criteria and guidelines for the ascertainment and definition of MCI in PD has been proposed allowing the diagnosis of this entity in a uniform way. However, MCI in patients with PD is a heterogeneous entity that involves different

types and extents of cognitive deficits depending upon the number and type of cognitive domains affected. Currently it is not known which type/s of PD-MCI confer a higher risk of progression to dementia. Hopefully, ongoing longitudinal studies in large cohorts of patients with this diagnosis will allow clarifying this critically important aspect. Currently, there is no validated treatment for PD-MCI and drugs used to treat dementia associated with PD are been used in these patients. In this sense, a few on going trials with pharmacological and non-pharmacological therapies will clarify whether certain interventions are indicated in PD-MCI patients or even in specific MCI subtypes.

O112

Talk #3: Neuroimaging of apathy and MCI

Joel Perlmutter

Washington University in St. Louis, St. Louis, Missouri, USA

Parkinson's disease (PD) leads to substantial nonmotor complications including apathy and cognitive impairment. Neuroimaging has provided several key insights into the pathophysiology underlying these behavioral manifestations. These studies employ several different imaging modalities including molecular imaging of metabolism, neurotransmitter pathways and abnormal protein deposition as well as structural and functional imaging with magnetic resonance (MR) methods. However, the most revealing studies combine multimodality approaches – not only across imaging modalities but also combining imaging with other tools. Investigations of apathy in people with PD have included SPECT studies of dopamine transporter, PET studies of glucose metabolism, structural studies with MR and resting state functional connectivity MR. Each of these has focused on specific brain regions or networks associated with apathy. Furthermore, molecular imaging studies combined with postmortem brain measures in a nonhuman primate model of apathetic behaviors has provided additional insights into potential pathophysiologic mechanisms. Studies of cognitive impairment have frequently addressed mild cognitive impairment (MCI) in PD with the goal of identifying biomarkers that either correspond with MCI, predict subsequent cognitive impairment or attempt to identify new targets of engagement for therapeutic interventions. These studies also encompass the gamut of neuroimaging modalities. However, the rationale for many of these studies, indeed even the notion of MCI in PD, derives from comparable studies in Alzheimer disease. This has helped guide the PD field but perhaps may mislead the field as well. The literature contains key examples of each. The extraordinarily high risk for development of cognitive impairment in each person with PD makes it more important to identify underlying pathophysiology of and predict risk of dysfunction in specific cognitive domains. Recent neuroimaging investigations have been bringing us closer to this goal.

O113

Roundtable #1: Tools for living with young-onset PD

Fulvio Capitanio

Udidos contra el Parkinson, Spain

Although most people associate Parkinson's with the elderly, Parkinson's disease can affect people of all ages. Young Onset Parkinson's (YOPD) begins before the age of 40. People with YOPD will live with the disease for many years and need to find ways to adapt to Parkinson's and its effect on their lives. They need to consider how to manage a chronic disease while engaged in career, perhaps raising a family – or even starting a

family – and maintaining as high a degree of wellness as possible for as long as possible.

Family and friends, Employment & Finance, Keep active, became an advocate, volunteer for research on Parkinson's. This is only a short list of things you should do... and there is another list of things you shouldn't

O114

Roundtable #3: DBS: lessons learned after DBS

Andy McDowell

New Zealand

I will share my experiences with the DBS procedure as a patient. In particular the effect on one's mind and how both physical and mental preparation contributed significantly to my recovery.

O115

Roundtable #3: DBS: lessons learned after DBS

Michael Okun

UF Center for Movement Disorders and Neurorestoration, Gainesville, Florida, USA

This session will offer access to an experienced DBS neurologist to discuss all aspects of the procedure, the follow-up, and short and long-term outcomes in a patient friendly and completely open-ended session. Additionally, in this session we will also address new technologies and any patient or family concerns with mixing therapies (e.g. DBS plus drug/vaccine/growth factor/stem cell).

O116

Roundtable #4: Sex and PD: things you should know but are too afraid to ask

Sheila Silver

Portland, Oregon, USA

This roundtable will offer an informal time to discuss sexual challenges you may be experiencing as a person with PD or as a partner of someone who has PD. It will be an interactive presentation in which you can share your concerns and ask anything. You will leave with ideas about how to create a closer and more intimate life with your partner.

O117

Roundtable #5: Dental care and Parkinson's

Jane Busch

USA

Parkinson's disease (PD) is a complex and progressive neurological disease. It affects the entire body including the mouth. Dentists need to understand how this disease affects the care they provide to their PD patients. Parkinson Patients need to be an active participant in their own comfort and safety. Motor symptoms, such as bradykinesia, tremors and dysphagia affect the oral/facial structures. Non-motor symptoms include cognitive decline, depression, temperature regulation difficulties, sleep disorders and orthostatic hypotension. Oral/facial effects of Parkinson's may include difficulty in mouth opening, dry mouth and/or drooling Dental treatment for the Parkinson patient may be affected by Parkinson medications. There are a number of recommendations for treating the Parkinson dental patient. Full mouth restoration is best done in

the early stage of PD. Appointments should be short and in the morning. The dental chair should not be reclined past 45 degrees. Rubber dam, bite blocks and saliva ejectors may offer comfort and safety. Dentists should evaluate for bruxism, tooth attrition, dental caries risk, TMJ dysfunction and denture fit. At appointment end, patient assist should be given to avoid syncope or falls.

Patient oral home care needs to fit the abilities of the Parkinson patients. PD patient may need to use a large-handled toothbrush or electric toothbrush, brushing at least twice daily. Flossing may be easier with a floss aid or caregiver assistance. Denture wearers should brush or soak their dentures and leave them out at night. Decay concerns may necessitate additional fluoride and a chlorhexidine mouthwash be prescribed for periodontal disease. Soda and sugary snacks should be limited. In conclusion, Parkinson patients and their dentists need to work together for optimal oral health.

O118

Roundtable #6: Living well with Parkinson's: it starts at the diagnosis

Tim Hague

Winnipeg, Manitoba, Canada

Life is not always what you expect. Those living with Parkinson's likely never imagined that life would take them on this journey. Living well with Parkinson's will be enhanced when we have the ability to be nimble with our emotional well being. This talk will focus on the need to know the game, know ourselves, know how to respond to the loser clap and have a clear sense of purpose. Attitude. Expectations. Goals. We will explore the importance of these three key concepts and how proper implementation at diagnosis can radically change the trajectory of the experience with Parkinson's. The goal of this talk is to provide tools to help the person with Parkinson's and their loved ones Live Your Best right from diagnosis.

O119

Roundtable #7: Parenting and PD: the joys and challenges of raising kids while navigating Parkinson's

Elaine Book¹, Rebecca Miller²

¹ Pacific Parkinson's Research Centre, Vancouver, BC, Canada

² Yale School of Medicine, New Haven, Connecticut, USA

Parkinson's Disease (PD) is a family affair and as a result, everyone in the family is affected by the disease. As a parent of children/adolescents/young adults or as a professional working with families with PD, it is important to consider how PD specifically impacts children and family life. There is a great deal of research in the area of parental illness and its impact on children. However, the specific area of parental PD and its effect on children is ripe for further understanding as well as for the development of support and resources. This roundtable session will plan to address the issues related to disclosure of diagnosis, how, what and when to share information and strategies to manage the impact of daily life for children. There will be opportunity to gain insight into common emotions and reactions of younger family members and to discuss options for support. The session will also provide a venue to explore and generate ideas for the future development of resources critical to meeting the needs of children/adolescents/young adults of parents with Parkinson's Disease.

O120

Care Partner Lounge: Cognitive challenges: how to recognize them and get the help you need

Amy Lemen

The Fresco Institute for Parkinson, New York, New York, USA

When someone you love is living with Parkinson's disease, your life changes too. Caregivers, spouses, partners, friends and family can all face enormous and unexpected change when the diagnosis hits home.

As the disease progresses, caregivers can face specific challenges related to changes and fluctuations in cognition. Some caregivers say that these changes are among the most difficult that they face. They may also be the hardest to talk about. Too often, caregiver needs are overlooked and they may develop complex feelings of grief, loss, anger, confusion, sadness and guilt. Without tools to actively cope, caregivers can begin to feel frustrated, isolated and alienated from their loved one and from those around them.

Keeping the lines of communication open is crucial for the Parkinson's caregiver. Adaptation to the changes that come with cognition is possible and caregiver's can develop effective ways to manage their own stress through new avenues of support. There's no greater support than the kind you get from someone who knows just what you're going through.

Join Amy Lemen as she gives information on the cognitive changes that can accompany the progression of Parkinson's disease and fosters an interactive dialogue between the true, day to day Parkinson's care professionals – the Parkinson's caregivers. This informative discussion aims to help get caregivers connected to one another to share their ideas, expertise and know-how with one another in a safe and supported environment.

O121

Talk #1: Overview: What's the difference between stem cells and IPs cells?

Malin Parmar

Sweden

The ability to reprogram cell fate is a new and rapidly emerging field where somatic cells can be turned into pluripotent stem cells or other somatic cell types simply by overexpression of specific combinations of genes. This remarkable discovery makes it possible to generate patient specific cell lines that will serve as major tools for understanding how diseases arise, develop and progress. The cells can also be useful for other biomedical applications including drug screens and early and differential diagnostics. As cellular reprogramming becomes more finely controlled, efficient and safe, it seems inevitable that many diseases will some day be treated with new healthy versions of the individuals own cells obtained via reprogramming. But, we are not there yet.

In this talk I will discuss the current status of cellular reprogramming with focus on:

1. What is the difference between a pluripotent stem cell derived from a fertilized egg and a reprogrammed skin cell?
2. How do we best make and test dopamine neurons for cell replacement in PD?
3. Which is the best cell to go forward with in the pioneering first in human trials and for the first clinical trial for PD?

I will also discuss the key challenges remaining for any stem cell based therapy before clinical trials can be initiated and how we can best navigate the cells towards this goal to ensure safe and effective cells and better treatments.

The authors own work is funded by the EUs 7th framework program, ERC, Swedish Research Council, and Swedish Parkinson Foundation

O122**Talk #2: Disease modeling in iPSC cells***Steve Finkbeiner*

Gladstone Institute of Neurological Disease, San Francisco, California, USA

The discovery of methods to generate induced pluripotent stem cells from patients using adult cells has opened up new avenues for research into the causes and treatments for Parkinson's disease (PD). For the first time, it is possible to collect skin or blood cells from patients with sporadic or familial causes of PD and differentiate them into a variety of cell types, including dopaminergic neurons and other types of brain cells. In this talk, we will discuss our efforts to create fully human models of disease from patient iPSCs and their applications to understand mechanisms of disease, find therapeutic targets, and to develop small molecule therapeutics. Importantly, caveats and challenges inherent to iPSCs will also be discussed.

O123**Talk #3: Transplantation in humans: an update***Roger Barker*

United Kingdom

The ability to successfully treat Parkinson's Disease (PD) patients with dopaminergic drugs for many years means that dopaminergic cell based therapies should be able to achieve the same with the theoretical advantage that they will;

(i) deliver dopamine in a more normal fashion and thus avoid the long term complications of some of these drugs in terms of involuntary movements and dyskinesias; and

(ii) not cause off target effects and thereby avoid side effects including some of the psychiatric and cognitive problems seen with these agents.

However the ability to do this with fetal ventral mesencephalic allografts has been variable. Some patients have shown dramatic improvements for decades in the face of their anti-PD therapy being stopped whilst others have shown no benefits and side effects such as graft induced dyskinesias (GIDs) necessitating further neurosurgical interventions. The reasons for this have been debated for many years but the recent EU funded TRANSEURO study has attempted to test some of these hypotheses through undertaking a new trial in younger patients with PD at an earlier stage of disease using better defined protocols for tissue preparation, grafting and the immunosuppression they receive post transplantation. This trial has also been useful in better defining a road map to take the next generation of stem cell derived dopamine cells to patients in first in human clinical trials. These trials are now being planned with efforts to better co-ordinate them being done through the newly formed global GFORCE-PD initiative.

In this talk I will review the current status of the TRANSEURO trial as well as the planned trials looking at stem cell derived dopaminergic neurons. I will highlight some of the challenges that face the field and how international efforts to harmonise the approach appear to be the optimal way by which to take these new experimental therapies to the clinic.

The authors own work is funded by the EU, Cure-PD, PUK, NIHR and the Rosetrees Trust.

O124**Talk #4: What it means for people with Parkinson's***Tom Isaacs*

United Kingdom

This session will explore the current attitudes and perceptions of people with Parkinson's (PwP) to cell therapies in terms of existing treatments being offered, the likely timescales envisaged and the sense and extent of progress being made. The presentation will also demonstrate the value of "hope" for PwP and the importance of accuracy and clarity of information supplied about the science and news of the current clinical trials underway.

For PwP, understanding about the different types of cell therapy and the respective, ethical and regulatory issues involved can prove difficult and accurate and robust information is difficult to find. Currently science has not advanced far enough for scientists to be able to communicate the prospect of breakthroughs in the short term. Despite this, the internet is awash with spurious claims from commercially run private stem cell clinics. How can the Parkinson's community better cope with this divergence of information so that it is less harmful to PwP? And how will scientists, clinicians and PwP be able to validate their decisions about novel therapies as they move into mainstream medicine.

Finally, this talk will cover the importance of good communication and education if stem cell therapy is to fulfil its promise. In particular, the following issues will be addressed:

- The dangers of miscommunication and misrepresentation of cell therapy
- The importance of clarity and transparency of information exchange between scientists and PwP and the need for clinicians to articulate the science effectively so that PwP can make informed decisions about the potential risks and benefits of a variety of prospective treatment options falling under the category of regenerative medicine.
- Issues arising with patient to doctor and doctor to patient communication
- Managing the expectations or destroying hope
- Patient to patient communication – opportunities and risks
- Managing progress in cell therapy – dealing with the ever narrowing gap between "fake" therapies and genuine "shake" therapies
- The benefits of involving PwP in ensuring only robust evidence-based science is observed, disseminated and practised

O125**Lecture #1: Serotonergic mechanisms of dyskinesia***Manolo Carta*

University of Cagliari, Cagliari, Italy

The appearance of dyskinesias remains a major burden for the management of motor symptoms in Parkinson's disease (PD) patients. During the last decade, the use of animal models of L-DOPA-induced dyskinesia (LID) allowed a major advance in the understanding of the mechanisms underlying the emergence of this motor complication due to chronic L-DOPA administration.

Overwhelming evidence points to the serotonin system as a key player in the emergence of LID in animal models of PD. In fact, it has been suggested that dopamine released from the serotonin neurons, after L-DOPA administration, contributes to abnormal swings in synaptic dopamine levels, leading to pulsatile stimulation of supersensitive dopamine receptors. Accordingly, toxin lesion or pharmacological inhibition of serotonin neurons produce striking suppression of LID both in the rat and monkey models of PD. Clinical evidence are accumulating showing that serotonin neurons may also play a pivotal role in the appearance of LID in patients. Thus, it has been reported that the 5-HT_{1A} receptor agonist buspirone can reduce LID as well as L-DOPA-induced extracellular dopamine levels in the caudate-putamen of dyskinetic patients. Moreover, the 5-HT_{1A/1B} receptor agonist eltopazine, which has been previously shown to suppress LID in animal models, has been acutely tested in dyskinetic patients, producing significant reduction

of the involuntary movements. Long-term clinical investigations are needed to understand if silencing of serotonin neurons by selective auto-receptor activation can be a feasible and convenient approach for the treatment of dyskinesias in PD patients.

O126**Lecture #2: Synaptic and signaling dysfunction leading to f LID**

Dalton James Surmeier

Northwestern University, Evanston, Illinois, USA

A balanced interaction between dopaminergic and cholinergic signaling in the striatum is critical to goal-directed behavior. But how this interaction modulates corticostriatal synaptic plasticity underlying learned actions remains unclear – particularly in direct-pathway spiny projection neurons (dSPNs) thought to drive levodopa-induced dyskinesia (LID). We found that cholinergic signaling through M4 muscarinic receptors (M4Rs) promoted long-term depression of corticostriatal glutamatergic synapses and blocked D1 dopamine receptor (D1R) dependent long-term potentiation (LTP) in dSPNs. In a mouse model of LID, boosting M4R signaling with positive allosteric modulator blocked aberrant LTP in dSPNs, enabled LTP reversal, and attenuated dyskinetic behaviors. The anti-dyskinetic effect was also validated in a monkey model. These studies identify an important signaling pathway controlling striatal synaptic plasticity and point to a novel pharmacological strategy for alleviating dyskinesia in PD patients.

O127**Lecture #3: Glutamatergic pathways as a target for the treatment of dyskinesias in Parkinson's disease**

M. Angela Cenci Nilsson

Sweden

Multiple lines of evidence indicate that L-DOPA-induced dyskinesia (LID) is associated with an increased activation of glutamate receptors in the basal ganglia. For example, positron emission tomography studies in dyskinetic PD patients have revealed high activity at NMDA-type glutamate receptors in the striatum shortly after L-DOPA administration. Furthermore, post-mortem studies of striatal tissue from both PD patients and parkinsonian animals have revealed upregulation of metabotropic glutamate receptor type 5 (mGluR5) in cases affected by LID. Compounds that reduce the activity of mGluR5 ('antagonists') have clear antidyskinetic effects in both rodent and non-human primate models of LID, and normalize aberrant molecular responses to L-DOPA in striatal neurons. Both NMDA and mGluR5 antagonists have been shown to ameliorate LID in proof-of-concept trials performed in PD patients. However, the promising preclinical and early-clinical data have not yet materialized as new antidyskinetic treatments on the market. Three major obstacles appear to have halted the clinical development process: a difficulty in defining the effective drug dosage, adverse events, and variability in clinical responses. After reviewing the available clinical information, this lecture will focus on the issue of response variability. I will present recent results from animal models of LID showing that NMDA- and mGluR5 antagonists alleviate dyskinesia via distinct mechanisms, and that the targeted mechanism must be causal to the dyskinetic behaviour in order for the treatment to have an effect. Based on these findings, I will propose that roadblocks to the clinical translation of antidyskinetic drugs can be overcome by tailoring treatments to critical pathophysiological pathways. To this end, approaches should be developed to probe specific pathophysiological mechanisms in patients affected by LID before recruiting them to clinical trials.

O128**Lecture #1: Cardiovascular dysautonomia in PD**

Horacio Kaufmann

New York, New York, USA

Abnormal autonomic control of the cardiovascular system, a frequent problem in patients with Parkinson disease (PD), causes orthostatic and postprandial hypotension. Symptoms can be disabling but its severity varies widely among patients. Hypertension while supine can also occur and further complicates clinical management. Dopaminergic agents can induce or worsen orthostatic hypotension but, more often, their hypotensive effects are unmasked by the presence of an underlying autonomic neuropathy. Indeed, there is increasing evidence that peripheral sympathetic nerves are compromised in patients with PD impairing norepinephrine release on standing, a defect that explains the orthostatic hypotension. Non-pharmacologic measures are the first line of treatment. Volume expansion, short acting pressor agents and abdominal binders are frequently useful. More recently, using a strategy similar to dopamine replacement with L-dopa, treatment with the orally active artificial aminoacid L-threo-dihydroxyphenylserine (droxidopa) which is converted to norepinephrine by dopa decarboxylase, showed significant symptomatic improvement in PD patients with orthostatic hypotension. Concomitant administration of high doses of carbidopa, a peripheral dopa decarboxylase inhibitor, blocks the pressor effect of droxidopa but enhances its CNS penetration. Combining droxidopa with inhibitors of other enzymes/transporters involved in catecholamine metabolism, as has been tried with levodopa, is an attractive therapeutic strategy to investigate.

O129**Lecture #2: Gastrointestinal dysfunction**

Kathleen Shannon

Rush Medical College, Chicago, Illinois, USA

Gastrointestinal (GI) symptoms, including drooling, disorders of swallowing, delayed gastric emptying, bloating, excessive gas, constipation and difficulty evacuating the bowels affect more than 50 percent of all Parkinson's disease (PD) patients. The GI tract has a rich population of nerve cells that is second only to the brain. It is believed that GI nerve cells are affected by the same cellular processes as are seen in PD brain, and that this involvement gives rise to the troublesome GI symptoms. GI symptoms may be present years before the characteristic motor symptoms emerge, suggesting they may in the future be useful in identifying person destined to get PD. The symptoms typically become more prevalent and severe with disease progression. Gastrointestinal distress may significantly impair quality of life, but has been largely ignored until recently. This presentation will review the types of GI dysfunction typically seen in PD, discuss the frequency and underlying causes of specific symptoms, and will present therapeutic dietary, over-the-counter, and prescribing strategies that can be used to reduce the impact of GI symptoms.

O130**Lecture #3: Skin-related dysautonomia and bladder dysfunction in PD**

Hirohisa Watanabe¹, Masahisa Katsuno², Gen Sobue³

¹ Japan

² Department of Neurology, Nagoya University Graduate School of Medicine, Japan

³ Nagoya University Graduate School of Medicine, Japan

27–80% of patients with Parkinson's disease (PD) complaints of lower urinary tract (LUT) dysfunction. Overactive bladder (OAB) is the most frequently observed LUT symptom in PD. Particularly, nocturia is observed in more than 60% of PD patients and can be associated with sleep disturbance and daytime sleepiness. Since LUT dysfunction significantly influences QOL and health economics, appropriate management of bladder dysfunction is necessary. As for treatment, dopaminergic drugs can improve or worsen LUT symptom. Acute D2 receptor activation worsens bladder function but tonic D1 receptors activation inhibits bladder voiding. It is generally difficult to treat LUT symptoms with dopaminergic therapy alone. Therefore, an add-on therapy for OAB including anticholinergic drugs or beta 3 receptor agonist is frequently required. Since classical non-selective antagonist of the M1, M2, and M3 subtypes of the muscarinic acetylcholine receptor will increase the risk for cognitive-related adverse events, selective M3 receptor anticholinergic drugs are widely used. More recently, adrenergic beta 3 receptor agonist which has little to no central cognitive events is another option for treatment. Several researchers reported that deep brain stimulation of subthalamic nucleus may be useful to improve bladder dysfunction in PD. Botulinum toxin injections can be used to treat intractable urinary incontinence in PD but invasive approach. With respect to skin-related dysautonomia, sweating dysfunction is another troublesome problem in PD patients. Daily use of an antiparkinsonian drug does not affect sweating. As the autonomic disturbance becomes more advanced, dyshidrosis becomes more common. Hyperhidrosis may develop with dyskinesia or off stage. Thus, dopaminergic therapy or deep brain stimulation may ameliorate the symptom in association with improvement of motor symptom. Botulinum toxin injections may be effective for palmar and axillary hyperhidrosis. In addition, there are several clinical issues about skin-related dysautonomia. Seborrheic dermatitis which may occur as one of the premotor symptoms in PD may influence on the impairment of patients' QOL. Dermatological side effects of dopaminergic therapy such as livedo reticularis and pedal oedema also are important clinical problems. The melanoma risk in PD will require further analysis.

O131

Lecture #1: Biological effects of exercise in Parkinson's disease

Giselle Petzinger¹, Daniel Holschneider², Halliday Matt², William Toy², Beth Fisher², Zhou Wang², John Walsh², Michael Jakowec²

¹ USA

² University of Southern California, Los Angeles, CA, USA

Epidemiological studies examining the effects of exercise have suggested that regular strenuous physical activity can reduce the risk of developing Parkinson's disease (PD). Utilizing animal models of PD, research from our lab and others has been instrumental in providing evidence for exercise's role in neuroplasticity of corticostriatal circuits that are profoundly affected in Parkinson's disease. Neuroplasticity is the ability of the brain to change and adapt (structurally and functionally) in an experience-dependent manner. This evidence includes exercise's role in modulating dopamine and glutamate neurotransmission, altering synaptogenesis, and increasing cerebral blood flow. In addition, recent evidence supports that the type of exercise may have regional effects on brain circuitry, with skilled exercise differentially affecting frontal related circuits more so than pure aerobic exercise. The purpose of this presentation is to provide an overview of exercise-induced neuroplasticity in models of dopamine depletion with the focus on how exercise can influence dorsal lateral striatum and prefrontal related circuitry underlying motor and cognitive impairment in PD. Although clearly more research is needed to address major gaps in our knowledge, we hypothesize that the

potential effects of exercise on inducing neuroplasticity may occur through parallel mechanistic pathways that include increasing neuronal metabolic demand and increased blood flow. Elucidation of these mechanisms may provide important new targets for facilitating brain repair and modifying the course of disease in PD.

O132

Lecture #2: The impact of exercise on physical and cognitive function in PD

Lynn Rochester

Newcastle University, Newcastle upon Tyne, United Kingdom

Parkinson's disease (PD) is a complex multisystem neurodegenerative condition which impacts physical function (e.g. gait, postural control and falls risk amongst other motor complaints), cognitive function and mood amongst others. The diverse range of symptoms are driven by a complex blend of neurotransmitter disturbance (e.g. dopaminergic, cholinergic, noradrenergic, and glutamatergic), dual-pathology (e.g. associated cardiovascular risk factors and white matter lesions, osteoarthritis) and de-conditioning (due to reduced mobility). It is therefore unsurprising that the response to therapy is heterogenous and limited highlighting the urgent need for therapies to address motor function and cognitive function. In this respect there is considerable interest in the role of exercise as a therapy with the potential to target both physical and cognitive symptoms independently and simultaneously. The benefits of exercise on physical function (such as gait, postural control and other physical functions) are well recognised evidence in PD. However evidence is also emerging in PD which demonstrates the benefits of exercise on cognitive function and mood. Moreover there is considerable interest (although currently limited evidence) of the potential of exercise to protect the brain or modify symptom progression. Exercise is broad incorporating aerobic, strength, balance and flexibility training in isolation or combination. More recently a focus on complex cognitive motor training has emerged where both systems are targeted simultaneously, a shift in focus that reflects the emerging recognition of the integrated nature of motor and cognitive functions. Finally simply aiming for an active lifestyle has also demonstrated benefits. This presentation will define a framework for exercise and summarise the evidence within this framework to support exercise/activity as a therapy to target physical and cognitive function in isolation or together. The optimal type of exercise will be discussed, challenges to exercise adherence and adoption of an active lifestyle will be identified, and finally recommendations will be made to optimise clinical and self-management.

O133

Lecture #3: Practical implications: integration of exercise into everyday life

Gammon Earhart

Washington University in St. Louis, St. Louis, Missouri, USA

Growing evidence supports the key role of exercise in the management of Parkinson disease (PD), yet many people with PD do not achieve recommended levels of physical activity. As such, it is critical that we combine scientific evidence with practical knowledge to optimize exercise participation for people with PD. This presentation will review current literature related to barriers and motivations to exercise, specifically addressing key factors like self-efficacy that influence exercise behavior in people with PD. Subsequently, strategies to address barriers, enhance motivation and effectively integrate exercise into everyday life will be discussed. The presentation will focus not just on getting started with regular exercise, but also on maintaining healthful long-term

habits through use of social support, community resources and technology. The information presented will draw from the latest evidence and have practical implications for people with PD, care partners and clinicians alike.

O134**Lecture #1: How Parkinson's disease affects sexuality and intimacy**

Gila Bronner

Center for Sexual Medicine, Israel

The physical and emotional changes as well as the various treatments may have a major effect on sexuality, sexual functioning and intimacy in couples living with Parkinson's disease (PD). Sexual functioning is a complex process that requires functioning of the body's autonomic, sensory, and motor systems and depends on the neurological, vascular, and endocrine systems, allowing sufficient blood supply to and from genital organs, a balanced hormonal system and a healthy emotional state.

Four main factors are involved in sexual dysfunction in people with PD: (1) the disease itself and comorbid illness; (2) medications and other treatments, (3) general consequences of PD (fatigue, weakness, impaired mobility, sleep disturbances and concentration problems) and (4) psychosocial problems (depression, anxiety, reduced self-esteem and body image, role changes and relationship difficulties). For example, muscle rigidity, bradykinesia, "clumsiness" in fine motor control make intimate touching, hugging and sexual arousal difficult. Tremor and dyskinesias may interfere with sexual activities and positioning. Hypomimia and speech difficulties may impair intimate communication and reduce attractiveness, negatively influencing self-esteem of patients and partners.

Consequently, patients and their partners report on frequent sexual problems, ranging from hypo-sexuality (decreased desire, erectile dysfunction, pain, difficulties reaching orgasm) to hyper-sexuality (compulsive sexual behaviour as part of impulse control disorders involving compulsive and reward-based behaviors).

O135**Lecture #2: Sexual medicine therapies and interventions**

Paul Rabsztyl

Netherlands

Parkinson's disease can have a severe impact not only on patient's daily life, but also on the life of the partner. The impact involves various aspects of life: not in the least the sex life. As sex is for many patients and couples part of quality of life they often seek for a solution for a sexual problem and / or dysfunction. Besides partner relation and individual sex therapy also medical and instrumental technical treatment options are available that can contribute to a solution and a better sex life. But they are often not efficacious as a single agent therapy. How to introduce, use and guide them? How can patients and partners benefit from these treatment options? In this session we will go through the available treatment options for men and woman where the pro's and con's will be discussed.

O136**Lecture #3: Creating and keeping intimacy in your relationship**

Sheila Silver

Portland, Oregon, USA

Living with Parkinson's challenges patients and their partners to talk about sexuality with each other in ways they may have never needed to before. This presentation will offer practical tools to have

these types of conversations. It will also help all those affected by Parkinson's, to broaden the way they think about sex, and offer tools to increase both physical and emotional intimacy. Patients, partners, social workers, and health care professionals will increase their confidence and comfort with this topic.

O137**Talk #1: In vivo cell specific striatal manipulations and behavior**

Alexandra Nelson

San Francisco, California, USA

Long-term dopamine replacement therapy in Parkinson's Disease is often complicated by the development of levodopa-induced dyskinesia (LID). The cellular mechanisms of LID are unknown, but the combination of advanced disease and chronic intermittent dopamine exposure may lead to basal ganglia circuit alterations, which in turn predispose to dopamine-driven aberrant striatal firing. The standard model of basal ganglia function posits that dopamine has opposing effects on striatal direct and indirect pathway neurons, and that in Parkinson's Disease, the loss of dopamine leads to decreased firing of direct pathway neurons and increased firing of indirect pathway neurons, respectively. Levodopa is predicted to trigger opposing firing rate changes, and perhaps at the extremes, causes dyskinesia. Given the challenges in labeling the two pathways in vivo, direct testing of these hypotheses has not been possible until recently. We have taken advantage of genetic and optogenetic tools to perform single-unit recordings of optically identified striatal direct and indirect pathway neurons, before and after levodopa administration in freely moving hemi-parkinsonian mice. We found that in the parkinsonian condition there were modest differences in the firing of direct and indirect pathway neurons, but in a direction supporting the standard model. Levodopa treatment triggered markedly increased firing in direct pathway and decreased firing in the indirect pathway. Interestingly, unit responses to levodopa could be subdivided into those which correlated with therapeutic (prokinetic) versus pathological (dyskinetic) behavior. While changes in rate in both pathways correlate with dyskinesia, we hypothesized that increased striatal direct pathway activity was responsible for dyskinesia. To test this hypothesis, we optogenetically stimulated direct pathway neurons in the dorsolateral striatum in vivo. In both normal and parkinsonian animals, stimulation was sufficient to trigger dyskinesia in the absence of levodopa. These results confirm the bidirectional effects of dopamine on striatal neuron firing in parkinsonism, and also provide evidence for the hypothesized role of aberrant striatal firing in dyskinesia. The existence of distinct striatal subpopulations with prokinetic versus dyskinetic features suggests an opportunity to improve pharmacological therapies in the future.

O138**Talk #2: Maladaptive synaptic and cellular plasticity in the subthalamic nucleus in experimental Parkinson's disease**

Mark Bevan

Canada

The subthalamic nucleus (STN) is a key component of the cortico-basal ganglia-thalamo-cortical circuit and plays an important role in suppressing and terminating movement during normal motor behavior. In Parkinson's disease (PD), STN hyperactivity and abnormal, coherent, rhythmic firing in the STN and its related structures are associated with motor dysfunction. Interestingly, in acute lesion models of PD, abnormal STN activity emerges 2–3 weeks after the loss of dopamine, implying that plasticity within the cortico-basal ganglia-thalamo-cortical circuit is critical for its emergence.

Using the unilateral 6-hydroxydopamine lesion mouse model of PD in combination with electrophysiological, molecular, anatomical, optogenetic and chemogenetic approaches, we report that following the loss of dopamine: 1) hyperactive D2 receptor-expressing striatal projection neurons excessively inhibit GABAergic pallido-subthalamic neurons leading to less restricted cortical excitation of the STN; 2) GABAergic pallido-subthalamic inputs proliferate; 3) cortico-STN inputs diminish in number and potency; 4) the distal dendrites and dendritic spines of STN neurons, which are the normal targets of cortico-STN inputs, are lost; 5) the autonomous activity of STN neurons is disrupted; 6) knockdown of STN NMDARs prevents synaptic and cellular plasticity in the STN and improves motor function; 7) chemogenetic rescue of intrinsic STN activity similarly ameliorates motor dysfunction.

Together, these data suggest that following the loss of dopamine, increased indirect pathway activity leads to excessive cortical excitation of STN NMDARs, which triggers compensatory but ultimately maladaptive synaptic and cellular plasticity in the STN. This plasticity results in an abnormal balance of synaptic inhibition, excitation and intrinsic excitability in the STN, which promotes parkinsonian circuit activity. Finally, interventions, which prevent or compensate for maladaptive STN plasticity ameliorate motor dysfunction.

O139

Talk #3: Pathway-specific remodeling of thalamostriatal synapses in Parkinsonian mice

Anatol Kreitzer

Gladstone Institute of Neurological Disease, San Francisco, California, USA

Movement suppression in Parkinson's disease (PD) is thought to arise from increased efficacy of the indirect pathway basal ganglia circuit, relative to the direct pathway. However, the underlying pathophysiological mechanisms remain elusive. To examine whether changes in the strength of synaptic inputs to these circuits contribute to this imbalance, we obtained paired whole-cell recordings from striatal direct- and indirect-pathway medium spiny neurons (dMSNs and iMSNs) and optically stimulated inputs from sensorimotor cortex or intralaminar thalamus in brain slices from control and dopamine-depleted mice. We found that dopamine depletion selectively decreased synaptic strength at thalamic inputs to dMSNs, suggesting that thalamus drives asymmetric activation of basal ganglia circuitry underlying parkinsonian motor impairments. Consistent with this hypothesis, *in vivo* chemogenetic and optogenetic inhibition of thalamostriatal terminals reversed motor deficits in dopamine-depleted mice. These results implicate thalamostriatal projections in the pathophysiology of PD and support interventions targeting thalamus as a potential therapeutic strategy.

O140

Talk #1: An overview – The nuts and bolts of clinical trials

Soania Mathur

Canada

How does a drug or any other intervention go from being an idea in a researcher's mind to a viable treatment? The development of a new neurologic therapy takes a significant investment of time and resources. It is a long and arduous journey in which clinical trials are an integral part.

Clinical trials simply refer to those research studies that involve human volunteers and are conducted to add to our understanding of certain diseases. They are necessary to see how effective or safe certain treatments, interventions or diagnostic tests are in humans.

They are also important in gaining information about the disease, how it manifests and the clinical course that it takes. Clinical trials are an essential part of the therapeutic development process.

But yet it is estimated that fewer than 10% of Parkinson's patients actually participate in clinical studies and without enough volunteers the development of better treatments and ultimately a cure will not be possible. Information regarding the importance of clinical trials in the therapeutic development process and how they work is important knowledge to have when making a decision to enrol in a particular study.

The types of trials, from observational to interventional and the different phases of interventional studies from phase I to phase IV will be discussed. Specific types of research such as treatment or prevention trials, screening, genetic and quality of life studies will be distinguished. Also misinformation and myths regarding the clinical trial process, patient safety and the patient experience will be addressed. Throughout, terms related to clinical research, which may be unfamiliar to many patients, will be defined.

Regardless of the outcome, every clinical study adds to our knowledge of Parkinson's which benefits not only the individual participant but the global Parkinson's community. Understanding the clinical trial process is the first step to becoming involved.

O141

Talk #2: On the road to better treatments and a cure – why is it taking so long?

Kalpana Merchant

Indianapolis, Indiana, USA

Despite advances, there remain many impediments to development of disease-modifying therapies and ultimately, a cure for Parkinson's disease. This talk will focus challenges of identification and validation of druggable pathways, development of predictive cellular and animal models and finally, biomarkers to monitor disease progression and enrich patient populations. The solutions require initiating translational research on patient-derived samples and deep insights into natural history of the disease using multiple modalities of biomarkers and clinical end-points. By their very nature, such studies are large, multidisciplinary and expensive and are best conducted in a collaborative, pre-competitive environment that leverages participation by patients, clinicians, basic and translational research scientists. The resulting understanding of molecular pathobiology of the disease in individual patient populations would lead to identification drug targets or pathways, as well as more predictive cellular and animal models that can be taken advantage of for drug discovery. Secondly, such translational research will provide the ability to conduct clinical trials in patients that are most likely to benefit from a specific therapeutic mechanism and monitor their therapeutic response using objective biomarkers. With the advent in genomic and analytical technologies, the goal to cure Parkinson's disease is within reach but will require collaborative engagement of all stakeholders – from patients to researchers to drug companies, funding agencies and regulators.

O142

Talk #3: From lab to pharmacy shelf

Jon Stamford

Parkinson, London, United Kingdom

The path from drug discovery to medicine is a long one with a high rate of attrition. Estimates vary widely depending on the field of health but a development period of up to 15 years is not exceptional. Moreover it can be necessary to screen as many as 10,000 compounds before a single commercially available medicine

results from the process. The path from lab to pharmacy shelf is also a significant financial journey for a drug company, with decisions to endorse or abort a development programme taken on pragmatic and/or political grounds. The input of many different stakeholders influences such decisions.

The principal point of convergence between a drug company's novel compound(s) and the target stakeholders currently occurs mainly during the clinical trial program where both healthy controls and patients are exposed to the compound(s). Until relatively recently, the involvement of patients was restricted to being experimental subjects, providing data about new medicines. This role remains pivotal. Without such volunteers there will be no new medicines. Patients can get involved via their local hospital, drug companies and university departments.

But the perception of patients and patient roles is expanding. Patients are no longer simply sources of data. Patients, through individual and collective advocacy, are increasingly seeking more active roles and at more stages in the process. Patients have a role to play in the selection of research programs, serving on advisory boards to influence decision-making by advocacy. Patients increasingly expect a more participatory role in the process of drug development, an expectation fuelled by the invested risk for anticipated benefit that clinical trials comprise. More drug companies are recognising the value to be gained from such an arrangement. Patients also have a role to play in the promotion of clinical trials to their peers. Trials which have been designed at least in part by fellow patients are often seen by the patient community as more appropriate to their needs. In summary, opportunities are presenting all the time for patients to be involved in an increasingly wide range of roles – participant, partner, driver, and promoter.

O143

Talk #1: Challenges in clinical trials in PD: essential role of regulatory science

Diane Stephenson¹, Arthur Roach², Steve Ford²

¹ Tuscon, Arizona, USA

² Parkinson's UK, London, United Kingdom

Development of safe and effective medicines represent a high unmet need for people living with Parkinson's. There is a growing recognition from all stakeholders that the sharing of patient data will create more efficient clinical trials by enabling precision medicine approaches aimed at advancing the right drug for the right patient at the right time.

Critical Path for Parkinson's (CPP), funded by Parkinson's UK and the pharmaceutical industry, and led by Critical Path Institute (C-Path) is a coalition of industry members, regulatory agencies, academic experts and patient advocacy groups all collectively working together. CPP aims to integrate patient level data from worldwide observational cohorts and randomized controlled clinical trials into a database that will improve knowledge and generate tools that promise to accelerate new ways to treat Parkinson's.

Global Regulatory agencies including FDA and EMA are dedicated first and foremost to patient safety. The early 2016 events of unexpected toxicities in early clinical development of a neuroinflammation target being advanced for Parkinson's is a tragic example of the essential role that regulators have in assuring that promising new treatments being tested are safe. In addition, regulators own the decision making required to approving new therapies based on effects of drugs in showing clinically meaningful treatment benefit. Assessing drug efficacy is challenging in Parkinson's due to many factors including the slow nature of disease progression, true unique heterogeneity between subjects, lack of diagnostic tools, unpredictable placebo response and the need for polypharmacy approaches. Regulatory agencies worldwide have proactively identified innovative approaches to accelerating

treatments to people living with diseases such as Parkinson's. Quantitative disease models and biomarkers have been identified as valuable drug development platforms to advancing new therapies more efficiently by avoiding duplication of effort and reducing the risk that each sponsor takes in advancing a single therapy forward.

CPP will bring together a panel which will include researchers, clinical experts and people affected by Parkinson's. The panel will focus on what we can achieve as a coalition inclusive of regulatory agencies to streamline and improve efficiency of clinical trials in development of new treatments for Parkinson's.

O144

Talk #2: How precompetitive data sharing can bring benefits when delivering new treatments for PD

Arthur Roach

United Kingdom

Important advances in the understanding of the pathophysiology of Parkinson's have emerged from studies in genetics, histopathology, biochemistry and cell biology over the last decade. The challenge of converting these discoveries into important new treatments is now being taken up by stakeholders including patient organizations, universities, government, regulatory agencies and biotech and pharma companies. The design and implementation of efficient and effective clinical testing programmes for experimental treatments is a critically important element of this undertaking, and is closely linked to scientific, financial, clinical and regulatory aspects of this challenge.

To achieve this, a sound foundation in relevant patient-level clinical data is needed. A recent consensus paper has identified that testing in early stages of the condition (earlier than six years from diagnosis) is expected to become increasingly important for potential disease-course modifying therapies in Parkinson's. However, patient-level clinical data on early disease stages are fragmentary, collected in a small number of drug trials and in a number of disease cohort studies conducted by academic investigators. Combining patient-level data from these studies can create a robust foundation for modelling aspects of disease progression to aid in a data-driven design of clinical testing strategies.

Control of the data and resources required for this task reside with a wide range of parties including some that may compete with others in certain areas of work. Experience in other fields facing similar challenges has shown that bringing these organisations together in a precompetitive data sharing consortium to work with regulatory agencies can produce tools and consensus that benefit all stakeholders through new and improved approaches to drug testing. The Critical Path for Parkinson's consortium was launched less than a year ago for this purpose and has the objective of delivering data, tools and regulatory guidance to improve trials and advance the search for new treatments for Parkinson's.

O145

Roundtable #1: Advocacy: patient advocates at work around the world – Asia/South Pacific

Dilys Parker¹, Samuel Ng²

¹ New Zealand

² Malaysia

There are commonalities about advocacy work around the globe but there will also be specific regional factors that influence the way things are done. This round table discussion is an opportunity for sharing aspects of the work of the two WPC Ambassadors who live in the Southern Hemisphere, Dilys from New Zealand and Samuel from Malaysia.

Dilys lived in the UK for a number of years and this contributes to her perspective on work in her country in the South Pacific. Samuel brings his uniquely Asian perspective to the work he is doing organising educational events and support services for people with Parkinsons in Malaysia.

They will share their experiences and invite you to join in with questions, information and stories that may be unique to where you live.

O146

Roundtable #1: Advocacy: patient advocates at work around the world – Asia/South Pacific

Samuel Ng

Perak Parkinson's Association, Malaysia

Parkinson's disease (PD) is debilitating movement disorder disease, which takes away one's mobility day by day. The disease is neither preventable nor curable. It is estimated about 4–6 million people around the world suffer from PD. In Malaysia at least 50,000 people are suffering from PD.

I am battling with Young Onset Parkinson's Disease (YOPD) since 42 years of age which made me to resign from a 16-years stint with the top pharmaceutical company. My sufferings has created a deeper understanding for People with Parkinson's (PWP). Life with PD changed my attitude, made me a better person and enhanced my self-confident and caring. I recognized that my life is extraordinary demanding me to accomplish meaningful goals despite of living with disabilities.

Objectives:

- To share the experience of my extraordinary life with YOPD.
- To motivate PWP to change their life perspective.

Methods:

- Changing one's mindset in three ways 3Ps – Positive Thinking, Positive Attitude and Positive Action.
- Expanding enormous support from family and friends.
- Emphasizing the important of exercise on daily routine, like a food to us.
- Establishing Perak Parkinson's Association (PPA) on 3rd December 2012.
- Extending rehabilitation services to PWP at PPA.
- Ensuring spirit of team work among the committee members.
- Organizing events like Awareness & Fundraising Parkinson's Open day, 3in1 event Cycling, Food Fair and Pet event and The Victory Summit.

I am blessed with gorgeous supportive wife, bountiful family and friends, most importantly team of highly motivated and dedicated committee members streamlined me to a successful life organizing fruitful events to improve the quality of life of PWP.

Conclusion: It is possible to live well with PD. I being a YOPD recognized the importance of changing myself as an exemplary so that I can change others to live well with PD.

O147

Roundtable #2: Placebo effect and Parkinson's: impact on trials and what it all means

Alberto Espay

Center for Parkinson's Disease and Movement Disorders, Ohio, USA

In randomized controlled clinical trials, the therapeutic efficacy of interventions is measured against the response elicited by a placebo. Such response, driven by heightened expectations of efficacy, is referred to as the placebo response. The placebo response may be influenced by non-intrinsic attributes of interventions such as price, brand, and other "inactive" traits and

may be associated with neurobiological alterations, including release of endogenous dopamine from both the dorsal and ventral striatum, which is correlated with positive anticipation, motivation, and response to novelty in normal subjects. Saline injections given to patients with Parkinson's disease (PD) believing to have received an active drug and, thus, demonstrating an "expectation of reward" response, is associated with dopamine release in the nucleus accumbens similar to the response to reward itself. Strategies to harness placebo responses to enhance benefits of treatment are to be encouraged during clinical practice but managing patients' expectations during clinical trials can alter the assessment of effect size of experimental therapies. Pharmacological and surgical clinical trials may be augmented by the synergistic addition of superimposed placebo responses in order to maximize benefits while reducing dosage and toxicity. Given that the benevolent use of deception to generate a placebo response is in conflict with the principle of respect for patient autonomy, preliminary data suggest that the use of "non blind placebo" (inert content disclosed) may be effective and eliminate the need for deception or concealment even in a randomized clinical trial setting. The potentially large benefit of placebo is waiting to be untapped for patients with PD in both clinical trials and clinical practice.

O148

Roundtable #3: Self-care: how can technology help you take control of your own care?

Peter Schmidt

National Parkinson Foundation, USA

New technologies are giving us the ability to monitor and track changes in our health in ways most people never imagined possible. Consumer electronics can monitor sleep, heart rate, temperature, and motion continuously. There are tools available to allow people to administer their own motor tests and web-based tools to track health status and quality of life. New research is focusing on how we can draw insight into Parkinson's generally using technology-enabled remote monitoring and treatment. Other groups are taking these new tools to empower patients to conduct "n=1" experiments – research on how what you do affects your own life. Several questions have emerged from these efforts:

1. Can we use these tools to give us better insight into Parkinson's disease?
2. Can people with Parkinson's use technology to better understand and manage their own care?
3. How can we best integrate technology-enabled self monitoring into a model of care where clinicians and patients collaborate using communications and monitoring tools to enable the very best care to reach more people, to help those people to be empowered to take charge of their own care, and to ensure that when problems happen, great care is available right away.

At this session, participants are invited to bring their own insight and experience to share with others and to inform efforts to develop a technology-enabled model of care.

O149

Roundtable #4: Pain & PD: how to manage it

Santiago Perez-Lloret

Argentina

Pain affects between 40% to 80% of patients with Parkinson's Disease (PD). Quality of Life is severely compromised in painful patients, therefore timely assessment and management of pain syndromes in PD is recommended. Pain can have several origins in PD. Musculoskeletal pain is the most frequent one and includes aching, cramping, arthralgic, myalgic sensations in joints, and

muscles. Pain can also be associated with dystonia or with restlessness. Finally, neuropathic pain can have a peripheral (radicular) or central origin. There is a paucity of double-blind randomized controlled trials and thus firm recommendations for the management of pain in PD are difficult at the present time. Musculoskeletal pain may respond to optimization of dopaminergic therapy, and in case of failure, analgesics or physical therapy may be used. Dystonic pain and some forms of neuropathic pain may also respond well to optimization of dopaminergic therapy. A recent double-blind, randomized, controlled trial showed that rotigotine transdermal patch may be effective for the treatment of fluctuation-related pain. Prolonged-release oxycodone–naloxone has shown non-significant positive effects in severe pain in a well-designed clinical trial. Levodopa was effective for reducing pain thresholds in an acute challenge. Duloxetine has also shown positive effects for neuropathic pain in an uncontrolled, open-label trial. Deep Brain Stimulation of the Subthalamic nucleus showed some efficacy for dystonic or musculoskeletal pain in an uncontrolled, open-label trial. Cranial Electro Stimulation was effective for musculoskeletal pain in a small double-blind randomized controlled trial. Physical therapy plus botulinum toxin alleviated pain related to Pisa syndrome in a small double-blind, randomized, controlled trial. Finally, aerobic physical exercise reduced pain intensity in a 6-m open-label, randomized, controlled trial. Further trials are needed to confirm these findings. Hopefully, more well-designed trials with other drugs for pain in PD will be conducted in the near future.

O150

Roundtable #5: What's up with glutathione and why does it get a bad wrap?

Laurie Mischley

Bastyr University, USA

Glutathione (GSH) is an essential brain nutrient that is both produced in the body and obtained through diet. Several studies have demonstrated that GSH depletion occurs early in the PD brain and laboratory research suggests GSH deficiency contributes to free radical damage, inflammation, mitochondrial dysfunction, and dopaminergic cell death. Social media has popularized anecdotal reports of symptomatic improvement in PD symptoms following GSH administration.

While there is substantial evidence for GSH deficiency in PD, few attempts have been to evaluate whether deficiency is associated with disease severity or whether fortification strategies are capable of treating symptoms or slowing disease. Oral GSH is Generally Recognized As Safe (GRAS) by the Food and Drug Administration (FDA), although it is poorly absorbed and no data exists to support the idea that oral supplementation effectively raises brain GSH concentrations. In recent years, researchers have attempted to supplement GSH via intravenous and intranasal routes to individuals with PD. While both of these forms of administration have been shown to be safe and tolerable, whether or not they offer sustainable symptomatic improvement or slow the rate of disease progression has yet to be determined.

The strong biological plausibility, ready availability, and preliminary reports of symptomatic improvement have resulted in public demand for GSH therapy. As a safe, naturally occurring molecule, patients and providers are in a unique position to use GSH therapeutically, before the appropriate research studies have been done to determine effectiveness. Providers are commonly asked for opinions and prescriptions for various forms of GSH and must decide on a case-by-case basis whether the potential benefits may outweigh the potential risks of supplementation, knowing the appropriate studies have yet to be conducted. When conventional providers discourage oral GSH, or refuse to prescribe intravenous or intranasal GSH, patients often treat themselves with over-the-counter oral GSH or seek the therapy from alternative medicine

providers. Patients turning to different physicians when they don't get the answer they want from the first, poor communication between providers, and a lack of long-term efficacy data all contribute to the frustration surrounding GSH as a therapy in PD.

O151

Roundtable #6: Palliative care treatment options: what works best from the health professional and patient perspectives

Julie Carter

USA

Palliative care is the relief of physical, emotional and spiritual suffering of patients and their families from diagnosis to the end of life. The focus is on quality of life at each stage of the disease. In this roundtable we will discuss some of the issues that occur at each stage of disease for both the patient and the family. We will specifically address: 1) How the shift from restorative care to palliative care is advantageous at each stage of disease. 2) How health professionals would benefit from changes in mindset and training in palliative care. 3) How patients and families can improve their own care by understanding the value and purpose of palliative care and by effectively communicating their future wishes and goals.

O152

Lecture #1: Cholinergic interneurons and the control of movement

Antonio Pisani

University of Rome Tor Vergata, Rome, Italy

The striatum is the primary input nucleus of the basal ganglia, integrating excitatory inputs from the thalamus and cortex with dopaminergic input from the substantia nigra pars compacta. A major neuronal component is represented by spiny projection neurons, whereas the remaining <10% of striatal neurons are interneurons: GABAergic (including parvalbumin, calretinin, and neuropeptide Y-expressing subtypes) and acetylcholine-releasing interneurons. Cholinergic interneurons powerfully regulate locomotion and procedural learning by modulating the excitability of spiny neurons, the plasticity of corticostriatal synapses, and striatal dopamine levels. Indeed, the close proximity of striatal dopaminergic and cholinergic terminals ensures interactions between the dopaminergic and cholinergic systems, a functional interplay which is crucial for the proper functioning of the striatum. Fluctuations in levels of both transmitters are believed to contribute to pathological circuit activity and symptom generation in pathological conditions such as Parkinson's Disease, dystonia, and Huntington's Disease, and indeed represent a potential target of current therapeutic agents. The complex acetylcholine-dopamine interaction can be variable and bidirectional in an activity-dependent manner, and occurs via different striatal nicotinic and muscarinic receptors, which might facilitate region-specific receptor targeting. Although antimuscarinic drugs represented the first accepted treatment for Parkinson's disease, and still remain one of the few treatment choices that are useful in dystonia, their utilization is limited because of serious side effects. Thus, it is essential to improve our understanding of the underlying cholinergic mechanisms in order to seek improved therapies. The development of new animal models is moving research to a level in which the physiology of the receptor subtypes could be addressed in vivo, offering new perspectives for their pharmacological manipulation.

O153

Lecture #2: Regulation of dopamine by cholinergic interneurons: implication for PD

Sarah Threlfell
United Kingdom

The degeneration of dopamine (DA) neurons is central to the motor disturbances observed in Parkinson's Disease (PD). DA neuron degeneration leads to a critical loss of DA within the striatum; a major projection target of DA neurons where DA acts to facilitate voluntary movement. DA neurons are incredibly large neurons with huge overlapping axonal arbours in striatum. Alongside these DA axons in striatum are axons from local interneurons containing acetylcholine (ACh) – cholinergic interneurons (ChIs), and a balance between striatal DA and ACh has long been thought to be crucial for the normal regulation of movement and to be disrupted in PD. Indeed, DA axons are adorned with nicotinic acetylcholine receptors where ACh acts to tightly control DA release. We have previously identified that striatal ACh released from ChIs can powerfully regulate DA transmission, however new findings place ChIs more central than ever to our understanding of DA function and potentially, dysfunction.

Using optogenetic approaches we identified that single action potentials synchronised in a small network of ChIs powerfully drives DA transmission directly within striatum, bypassing activity in midbrain DA neurons. Moreover, activation of thalamic inputs to these ChIs is also sufficient to drive this ChI-driven DA release. These findings suggest that ChIs and their related circuits could be key targets for therapies in PD. Notably, ChIs are thought to change their functional properties in PD; ChIs have been shown to change characteristic properties including afterhyperpolarization conductances, muscarinic autoreceptor control and synchronized pause responses that result in/from a dysregulation and desynchronisation of their spiking in acute toxin PD models. Such changes, contribute to striatal dysfunction and might also compromise the normal triggering of DA release and DA function. Manipulations targeting ChI activity might help to restore PD deficits, including through the ability to drive DA directly.

In this presentation I will review our current understanding of striatal acetylcholine regulation of dopamine and outline our latest research exploring the ACh-DA axis in a promising new transgenic model of PD.

O154

Lecture #1: Falls risk: A complex and evolving picture

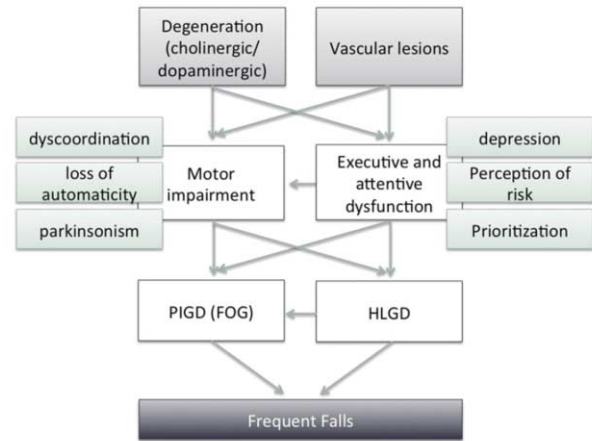
Alfonso Fasano
University of Toronto, Toronto, Ontario, Canada

Parkinson's disease (PD) is a known risk factor for recurrent falls, a major clinical problem as it often leads to fractures, immobilization, poor quality of life and life-span reduction.

In recent years, research on falls has completely changed and new instruments and definitions have been formulated, definitively building the 'science of falling'. A translational approach has contributed to developing the construct of the neurobiology of falling (Figure), which sees the interaction of 4 pathophysiological moments: 1) parkinsonism (and particularly freezing of gait); 2) failure of automaticity or inter-limbs coordination/symmetry during walking; 3) impairment of executive and attentive resources; 4) extra-dopaminergic pathology (e.g. vascular lesions or other ageing processes).

More recently, new insights have come from the animal model of falls (rats with both dopaminergic and cholinergic pathology), long-term monitoring of patients (clinical or based on instruments, such as videorecordings of actual falls), categorization of falls (useful to

understand the heterogeneity of this complex problem), and efforts of a dedicated task force. Furthermore, different contributing factors have been linked to falls in PD patients: incorrect weight shifting, co-occurrence of urinary urgency (but not frequency), impaired executive function, impulsivity, and cardiovascular comorbidities.



In addition, a number of other tools have been explored in order to detect the risk of future falls, particularly the variable combinations of rating scales, such as Activities-specific Balance Confidence scale, Falls Efficacy Scale-International, Berg Balance Scale, Dynamic Gait Index, Functional Reach Test, Mini-BESTest, Timed Up and Go. The strongest predictor of future falls seems to be fear of falling, followed by a history of near falls and retropulsion. Others have proposed a composite score considering the fall history in the previous year, freezing of gait in the past month, and gait velocity <1.1 m/s. Other interesting scenarios are related to assessments during both off and on L-dopa conditions as well as during dual tasking.

O155

Lecture #2: Measuring and classifying falls: From technology to clinical tools

Jeff Hausdorff
Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel

People with Parkinson's disease suffer from frequent and often debilitating falls. This presentation will review the methods and approaches that have been used to measure and classify falls, fall frequency, and fall risk. The patient characteristics that have been associated with falls in Parkinson's disease (e.g., disease severity and freezing of gait) will be discussed along with relatively simple tools that have been applied to address these issues in Parkinson's disease and related cohorts. The most important question that should be asked when assessing fall risk will be described and we will review the utility of performance-based measures like the mini-BEST, Timed Up and Go, and the Four Square Step Test. In addition, emerging approaches based on the application of Smartphones, body-fixed sensors and wearable technology will be covered. These devices are becoming smaller, less expensive and more ubiquitous. We will describe how this form of technology can be used to assess fall risk by augmenting performance-based tests (e.g., the instrumented Timed Up and Go) in the clinic and will also show how long-term, 24x7 monitoring using wearables can be used to capture and objectively characterize falls and fall risk. The advantages and disadvantages of the different approaches will be summarized along with gaps in our understanding and the need for future studies.

O156

Lecture #3: Preventing falls: What is the evidence?*Colleen Canning*

The University of Sydney, Lidcombe, Australia

People with Parkinson's disease (PD) fall frequently, with 60% falling annually and two-thirds of these falling recurrently. Historically, falls have been monitored as adverse events in drug and exercise trials, however, recently interventions have been designed and tested with the specific purpose of reducing falls in people with PD. This presentation will provide an overview of the current evidence for falls prevention, including non-pharmacological and pharmacological approaches, and identify clinical recommendations.

Commonly identified fall risk factors include previous falls, higher disease severity, freezing of gait, poor balance, mobility and lower limb strength and poor cognition. While some risk factors cannot be changed, others have the potential to be modified with targeted interventions. To date, five large-scale randomized controlled trials of exercise interventions have been reported (Ashburn 2007, Canning 2015, Goodwin 2011, Li 2012, Morris 2015). These studies show that challenging balance exercises (including Tai Chi), progressive strengthening exercises and movement strategy training (including cueing) are effective in reducing falls in people with PD without significant cognitive impairment. In addition, two studies with minimally supervised physiotherapy programs show greater reductions in falls in people with milder disease severity (Ashburn 2007, Canning 2015). Furthermore, the three economic analyses that have been conducted to date provide evidence of cost-effectiveness of these exercise interventions (Farag 2016, Fletcher 2012, Li 2015). Finally, two large-scale randomized controlled trials of drug interventions provide promising results, with bisphosphonates reducing hip fractures (Sato 2011) and anticholinesterase inhibitors reducing falls (Henderson 2016).

Minimally-supervised exercise is both effective and cost-saving in people with mild PD without significant cognitive impairment. Therefore, exercise for falls prevention in people with PD should be initiated early in the disease process in combination with optimal drug therapy. As the disease progresses multifactorial interventions including more closely supervised exercise, avoidance of high-risk activities and environmental modifications should be considered and high quality trials are needed to test for effectiveness of these interventions.

O157

Lecture #2: Use of technology to support patients with Parkinson's*Sara Riggare*

Sweden

We have all seen how the field of technology in health and healthcare is increasing with sensors, apps, devices, online services and more. In Parkinson, the field has really exploded with technology like online genetic testing (23andme), assistive technologies (for example the Lift spoon, canes/shoes/walkers with laser to help during freezing-of-gait), apps and more.

This presentation will give an overview of the use of technology for Parkinson with a special focus on how people with Parkinson can make use of technology to learn more about their condition and improve their health.

O158

Lecture #3: Opportunities and challenges of using wearable technology to facilitate clinical trials in the field of PD*Alberto Espay*

Center for Parkinson's Disease and Movement Disorders, Ohio, USA

In both daily practice and clinical trials, it remains difficult to reliably evaluate patients' functioning in everyday life, over long periods of time, and using methods sensitive to relevant milestones. Examples include fluctuating events (e.g., response to medication), rare incidents (e.g., falls), and non-motor complications (e.g., orthostatic hypotension). The miniaturization, sophistication, proliferation, and accessibility of sensing technologies are now enabling the acquisition of data suitable to capture more and previously inaccessible phenomena in Parkinson disease (PD). However, a gap remains between the amount of information gathered using these technologies and the corresponding insights into disease complexity that should be gained to satisfy diagnostic and therapeutic needs. Challenges include the variety of non-compatible technology platforms, the feasibility of wide-scale and long-term deployment of sensor technology (in particular among vulnerable elderly patients), and the gap between the "big data" acquired with sensitive measurement technologies and their limited clinical application. Major opportunities could be realized if new technologies are developed as part of open-source and/or open-hardware platforms enabling multi-channel data capture, sensitive to the broad range of motor and non-motor problems that characterize PD, and adaptable into self-adjusting, individualized treatment delivery systems. With the support of the International Parkinson and Movement Disorders Society Task Force on Technology work has begun to convene engineers, clinical researchers, and patients to promote the development of integrated measurement and closed-loop therapeutic systems with high patient adherence that also serve to: 1) encourage the adoption of clinico-pathophysiologic phenotyping and early detection of critical disease milestones; 2) enhance tailoring of symptomatic therapy; 3) improve subgroup targeting of patients for future testing of disease modifying treatments; and 4) identify objective biomarkers to improve longitudinal tracking of impairments in clinical care and research. This session will delve into identifying the challenges and opportunities in the development of technologies with potential for improving the clinical management and quality of life of individuals with PD.

O159

Talk #1: Research on cannabis: Is there any evidence?*Benzi Kluger*

Denver, Colorado, USA

There is growing interest in the therapeutic potential of marijuana (cannabis) and cannabinoid-based chemicals within the medical community and, particularly, for neurological conditions including Parkinson's disease (PD), due in part to changes in the legal status of cannabis in many regions and increasing research into the roles of endocannabinoids within the central nervous system. We review basic science as well as preclinical and clinical studies on the therapeutic potential of cannabinoids specifically as it relates to PD. The pharmacology of cannabis is complex, with over 60 neuroactive chemicals identified to date. The endocannabinoid system modulates neurotransmission involved in motor function, particularly within the basal ganglia. Preclinical research in animal models of several movement disorders have shown variable evidence for symptomatic benefits and also suggest potential neuroprotective effects in several animal models of Parkinson's (PD). Clinical

observations suggest that cannabinoids may be helpful for several nonmotor and motor symptoms in PD. However, clinical trials to date have failed to replicate these uncontrolled observations. Despite the widespread publicity about the medical benefits of cannabinoids, further preclinical and clinical research is needed to better characterize the pharmacological, physiological, and therapeutic effects of this class of drugs in PD.

O160

Talk #2: Yoga as therapy: What is the research telling us?

Indu Subramanian
USA

There has been an increasing interest in exercise in the treatment of Parkinson Disease (PD). Yoga is a unique type of exercise in that it marries the "Mind, Breath and Body" and may be extremely beneficial in both the motor and non-motor symptoms of PD. The following objectives will be covered:

1. A review of the current evidence in the research literature for Yoga in PD
2. Identifying the barriers to designing and implementing studies on Yoga in PD
3. Strategies to improve future studies on Yoga in PD.
4. Identifying outcome measures that would be relevant to studies of Yoga in PD

O161

Talk #3: Where does "music therapy" fit in the complementary care world?

Matthew Ford
Samford University, School of Health Professions, Birmingham, Alabama, USA

Persons with PD love music like everyone else. When presented with array of artist's people can quickly identify with music they enjoy, as well as music they don't. There are so many music genre's that persons with PD, if given the opportunity, can find music that improves their mood, movement, and overall quality of life. The brain is our internal rhythm generator, while music can provide external rhythmical structure. The fit between the two is natural. Patient's love music and it therapeutic effect because it is immediate. Persons with PD lose some ability for internal rhythm generation and a music (external cue) can help. Living with PD, persons deal with daily fluctuations in their symptoms and overall functional abilities. However, the presence of music provides immediate enjoyment (wellness) and can facilitate movement (health). Unfortunately, the effects of this external timer are not permanent. If music is removed, symptoms and function can return to previous levels. Thankfully, we have readily available technology that allows us enjoy our favorite music and receive it's therapeutic effects just about anywhere we go. This technology allows health care providers to design effective programs that persons with PD can use at home or in their community.

O162

Talk #4: Research on glutathione

Laurie Mischley
Bastyr University, USA

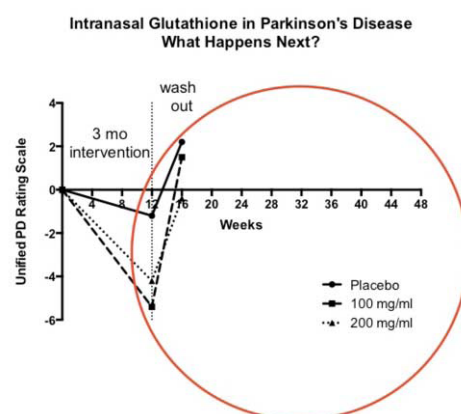
The first formal suggestion that Parkinson's disease (PD) may be caused by a deficiency of brain glutathione (GSH) was published in 1982. The questionable absorption of oral GSH led researchers to

intravenous (iv)GSH in 1996. Nine patients with early, untreated PD were administered (iv)GSH twice daily for 30 days. The authors concluded that all patients improved significantly after (iv)GSH therapy (42% decline in disability) and the therapeutic effect lasted for 2-4 month after stopping.

The biological plausibility, record of safety, legal access, and the preliminary suggestion of symptomatic improvement led some providers to begin using (iv)GSH in clinical practice ~2002. Social media circulated YouTube videos demonstrating improvement in motor symptoms following (iv)GSH, perpetuating demand among patients. In 2009, a double-blind study of 21 individuals compared (iv)GSH thrice weekly to placebo; their results suggested GSH was safe and symptom scores were suggestive of a mild symptomatic effect in those receiving (iv)GSH.

Oral GSH is poorly absorbed and (iv)GSH is invasive, expensive, and inconvenient. Thus, clinicians began using intranasal GSH, (in)GSH, as a strategy for boosting brain GSH concentrations in 2004. A safety survey of (in)GSH was published in 2011; of the seven individuals with PD responding to the survey, 57% reported an overall positive experience with (in)GSH after an average 9 months of use.

In 2015, a randomized, double-blind study of (in)GSH to 30 individuals with PD demonstrated it was safe, tolerable, and both the low- and high-dose GSH treatment arms demonstrated symptomatic improvement over placebo. In 2016, researchers confirmed that (in)GSH is capable of boosting brain GSH concentrations. Ongoing research is attempting to identify whether the symptomatic improvement resulting from (in)GSH administration is reproducible, and if so, identify the symptoms that benefit most. Future trials will evaluate whether long-term use of (in)GSH improves symptoms or slows progression of PD.



O163

Talk #1: Mitochondria in axon terminals and PD pathology

Thomas Schwarz
USA

The axon typically contains most of the volume of a neuron and indeed represents more than 99% for many neurons, including the vulnerable population in the substantia nigra. Consequently, neurons depend heavily on the long distance transport of mitochondria and need to constantly refresh the extensive population of mitochondria that provides ATP in axons and synapses. Defects in the processes that sustain a healthy mitochondrial population can prove pathogenic in neurons while tolerated in much smaller cells. The significance of these

phenomena for the etiology of Parkinson's is demonstrated by the involvement of PINK1 (PARK6) and Parkin (PARK2) in the movement and clearance of axonal mitochondria. This presentation will describe the proteins needed to move mitochondria in axons and the mechanism by which mitochondrial movement is regulated by PINK1 and Parkin, including the influence of Miro phosphorylation on the process. In addition, the talk will present evidence that PINK1 and Parkin are required for the local autophagic clearance of mitochondria in axons as an acute response to mitochondrial damage. This process is rapid and can result in mitophagic clearance by an axonal lysosomes in 30–60 minutes. By locally arresting damaged mitochondria the PINK1/Parkin pathway can quarantine them and prevent them from fusing with healthy mitochondria or spreading reactive oxygen species throughout the cell. Finally, the fact that axons can extend long distances from the major sites of protein synthesis will be considered and the implications of this fact for the PINK1/Parkin system and for the etiology of PD will be discussed.

O164

Talk #2: Mitochondrial antigen presentation in PD

Heidi McBride¹, Michel Desjardins², Diana Matheoud², Ayumu Sugiura¹

¹ McGill University, Montreal, Quebec, Canada

² University of Montreal, Montreal, Quebec, Canada

Mutations in two genes coding for proteins involved in mitophagy, Parkin and PINK1, are linked with the autosomal form of Parkinson's disease. The role played by mitophagy in the progression of the disease is still under debate. In the present study we demonstrate that, unlike other autophagic pathways, mitophagy is a poor inducer of antigen presentation in macrophages, a feature that may allow the clearance of damaged mitochondria without alerting the immune system. Remarkably, in the absence of PINK1 and/or Parkin, peptides from mitochondrial proteins are highly presented on MHC class I molecules in response to stress *in vitro* and *in vivo*. This novel antigen presentation pathway involves the formation of vesicular structures derived from mitochondria through a process requiring Sorting nexin 9 and the small GTPase Rab9, which are recruited to mitochondria upon stress. A second GTPase, Rab7, is needed for the clearance of mitochondrial vesicles through late endocytic organelles. Conditions that promote an inflammatory response, such as heat stress and exposure to lipopolysaccharide, increase vesicle formation and mitochondrial antigen presentation. Altogether, our data indicate that PINK1 and Parkin are key modulators of the immune system playing a "protective" role by preventing the presentation of mitochondrial antigens. Our data further suggest that part of the etiology of Parkinson's disease is linked to autoimmune reactions. The link between adaptive immunity and Parkinson's disease opens new avenues for the development of effective treatments.

O165

Talk #3: Targeting mitochondrial electron transport chain dysfunction in Parkinson's

Patrik Verstreken

KU Leuven, Leuven, Belgium

PINK1 mutations cause Parkinson's disease, but how the protein affects mitochondrial function under endogenous conditions is incompletely understood. Using genetic analyses in flies and mice and biochemical studies based on mass spec we found that Pink1 affects the enzymatic activity of Complex1 of the mitochondrial electron transport chain. Pink1 maintains the phosphorylation status

of a specific subunit of Complex I: NDUFA10. Phosphorylated NDUFA10 is required for the effective coupling of electron transport between Complex I and ubiquinone. I will discuss our recent efforts of large scale genetic screens in fruit flies to modulate these Pink1-induced defects and talk about unexplored but evolutionary conserved connections between Pink1, Complex1 and lipid biosynthesis as well as about pharmacological approaches to revert the Pink1 defects in flies, mice and human cells. Our work suggests that Complex1 defects are a major culprit in Pink1 mutants and that targeting this defect may constitute a viable therapeutic avenue.

O166

Impulse control disorder: a team strategy with the patient, family and doctor

Daniel Weintraub

Perelman School of Medicine at the University of Pennsylvania, Philadelphia, USA

Impulse control disorders (ICDs; e.g., compulsive gambling, buying, sexual behavior and eating) and related disorders (e.g., punding, hobbyism and dopamine dysregulation syndrome) are common and difficult-to-manage psychiatric disorders in approximately 20% of Parkinson's disease (PD) patients. These disorders can be difficult to diagnose and manage, and can have devastating consequences in some cases. It is important that both patients and family members (when available) be educated about the possibility of developing of ICD symptoms after initiation of a range of PD medications, and routine monitoring, including use of corroborative sources, is essential throughout the disease course. Including a psychiatrist as part of the treatment team can help in the management of these symptoms, which are difficult to treat and can generate significant interpersonal difficulties.

O167

Talk #1: What are impulse control disorders (ICD), why do they occur and what are the common presentations?

Mark Stacy

Duke University School of Medicine, Durham, North Carolina, USA

Impulse control disorders (ICDs), including compulsive gambling or spending, hyperlibidinous behavior, and binge eating, were first recognized in the context of Parkinson's disease (PD) in the late 1990's. At about the same time additional impulsive-compulsive behaviors such as, punding (stereotyped, repetitive, purposeless behaviors) and dopamine dysregulation syndrome (DDS; compulsive PD medication overuse, medication hoarding, secrecy and "walkabouts") were also described. While the etiology of these behaviors may be linked to personality trait and changes in the basal ganglia, ICDs have been most closely related to the use of dopamine agonists (DAs), perhaps more so at higher doses. Interestingly, punding behaviors seem to emerge at peak times for levodopa dosing, and also be linked to cognitive decline. The DDS is also more tightly linked to levodopa, but is also seen with the shorter-acting DA, apomorphine. Possible risk factors for ICDs include male sex, younger age and younger age at PD onset, a prior history of ICDs, and a personal or family history of substance abuse, bipolar disorder; or gambling problems.

This presentation will review specific examples of ICDs, and in some cases the devastating consequences of these behaviors, as well as strategies to avoid and manage these syndromes.

O168

Talk #3: Treatment strategies*Mayela Rodríguez Violante*

Instituto Nacional de Neurolog, La Fama, Mexico

Impulse Control Disorders in subjects with Parkinson's disease may have deleterious effects on their activities of daily living and, consequently, in their quality of life. Moreover, impulse control disorder may also have a direct impact on the strain and burden of the primary caregiver. Treatment of impulse control disorder involves a team strategy involving the neurologist, the family and caregiver, as well as the patient himself.

From the neurologist viewpoint, patient and caregiver education is essential. Proper surveillance of symptoms suggestive of an impulse control disorder is key for an early diagnosis. Involvement of caregivers and other family members is needed in order to detect early and minor symptoms, but also is important to aid them to understand the nature and impact the disorder.

Once the diagnosis is made, adjustment of PD medications is needed, but it is also important to consider psychiatric or psychological consultation. Common strategies involve the dose reduction of dopamine agonist or even gradually withdrawing it. As a consequence, worsening of motor symptoms may happen and further adjusts, such switching from oral to transdermal or subcutaneous dopamine agonist administration can be warranted. In some cases, deep brain stimulation should be considered.

As mentioned before, psychiatric consultation is usually advisable, not only for the impulse control disorder, but also because of the possibility of other psychiatric comorbidities. Medications such as antidepressants, anxiolytics and antipsychotics can be added to the pharmacological treatment. Psychological treatment, such as cognitive behavior therapy, may be helpful in some cases.

Efforts should be made to involve the patient, the family and the health-related professionals in the management of impulse control disorders associated with Parkinson's disease.

O169

Roundtable #1: Exercise & PD: what's really on the horizon?*Giselle Petzinger*

USA

Exercise is emerging as a standard of care for the treatment of Parkinson's disease and other common neurological disorders. Patients, caregivers and physicians often ask what type of exercise and how much should I do? The purpose of the roundtable discussion is to discuss studies supporting the role of aerobic vs goal-based exercise vs. cognitive training plus exercise approach for treating cognitive and motor impairment in Parkinson's disease (PD) and aging. Additionally, we will discuss potential practice parameters of exercise including the role of variable practice and contextual shifting that may be important for facilitating cognitive/motor learning in PD. Another critical gap in knowledge is understanding the underlying molecular and cellular mechanisms by which exercise can facilitate neuroplasticity in the PD brain. Thus, we will discuss studies examining potential peripheral effects of exercise, such as neurotrophic factors and insulin-like receptors, that may be important for promoting exercise induced neuroplasticity in the brain.

O170

Roundtable #2: Swallowing, coughing and PD*Michelle Ciucci*

University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin, USA

Disordered swallowing, or dysphagia, can occur at any time during the disease process and can in fact, be one of the first signs of PD. PD-related dysphagia includes difficulty with coordinated lip, jaw, and tongue movements, making chewing and swallowing difficult. Importantly, safe swallowing requires closure of the airway while transporting the bolus to the esophagus. Failure to do so results in aspiration; aspiration pneumonia is the leading cause of death in PD. The ability to cough is a key feature of airway protection, and strengthening the cough/respiratory mechanism has helped reduce aspiration. This discussion will focus on newly emerging diagnostic and therapeutic techniques that hold promise to provide earlier detection and directed therapies based on hypothesis-driven research. The impact of dysphagia on quality of life and resilience will also be discussed.

O171

Roundtable #3: Sex and PD: things you should know but are too afraid to ask*Paul Rabsztyrn*

Netherlands

Healthcare professionals are often reluctant to ask Parkinson patients if they suffer from sexual problems and dysfunctions. They are afraid to get an insight in the sex life of the Parkinson patient, to embarrass the patient or for inappropriate questions. Why is it important to bring up the subject with Parkinson patients? What are the appropriate questions to ask to get an insight in the unmet needs and to be able to deliver good and tailored care. In this session we will focus on the fears for the wrong sex questions, tips and tricks and the questions you certainly should ask.

O172

Roundtable #4: Genetics & environment: where are we headed?*Beate Ritz*

Fielding School of Public Health, USA

Parkinson's disease (PD) is most likely caused by both genetic and environmental factors. While geneticists refer to the unexplained PD etiology as a 'missing genetic heritability', we argue that the environment plays a major role and contributes to gene-environment (GxE) interactions that can have very large contributions. In California and Denmark, we have explored GxE interactions that may explain how genetic as well as environmental factors together influence PD risk. To do so, we assembled a two very large population-based PD study for which we created objective environmental exposure measures, confirmed PD diagnoses with medical examinations or record review, and genotyped biologic samples. We assessed interactions between specific classes and types of pesticides with genes responsible for pesticide metabolism (PON1); transport across the blood brain barrier (ABCB1); pesticides interfering with or depending on dopamine transporter activity (DAT) and dopamine metabolism (ALDH2); impacting mitochondrial function via oxidative/nitrosative stress (NOS1) or proteasome inhibition (SKP1); and contributing to immune dysregulation (HLA-DR), between head trauma and the synuclein gene (SNCA), head trauma and paraquat exposures in farmers, and air pollution in Denmark and inflammatory gene variants. These studies established specificity for the actions of environmental factors and described how they contribute to neurodegeneration in humans or provided biologic plausibility to epidemiologic findings. These results in the long run may also help to identify those more susceptible to PD when encountering certain environments and neurotoxic agents.

O173

Roundtable #5: Fatigue, sleep & PD*Amy Amara*

University of Alabama, Birmingham, Birmingham, Alabama, USA

Sleep disorders, fatigue, and daytime sleepiness affect many patients with Parkinson's disease (PD). These symptoms and disorders have significant impact on quality of life, daily functions, and safety. The most common sleep disorders among PD patients include fragmented sleep, insomnia, parasomnias (acting out dreams, sleep walking, and sleep talking), daytime sleepiness, and leg kicks during sleep. These sleep disorders can be influenced by medications, PD motor symptoms, memory problems, mood problems, and other factors. In this session, we will discuss these sleep disorders, talk about how they affect patients with PD, and address questions about strategies to improve sleep and fatigue.

O174

Roundtable #6: Chemical exposure and neurodegenerative disease*Caroline Tanner*

Parkinson's Disease Research Education and Clinical Center, San Francisco, California, USA

Parkinson's disease (PD) and other neurodegenerative disorders of late life are in most cases thought to have complex etiologies – that is, a combination of factors determines whether or not an individual will develop disease. Studies in human populations and in the laboratory suggest that exposures to certain chemicals years or decades before diagnosis can trigger the processes that ultimately result in a neurodegenerative disease in some people. Certain pesticides, solvents and other persistent pollutants have been associated with PD. Head injury and a sedentary lifestyle have also been associated with an increased risk of developing PD. Other factors may reduce the risk of developing PD. An individual's genetic makeup is an additional important determinant of disease risk. The combination of harmful and beneficial environmental factors, along with genetic make up, will determine an individual's risk of PD. Identifying risk factors for PD can help in developing ways to prevent disease, as well as strategies to slow progression in people with PD.

O175

Care Partner Lounge: Tips for managing your own health*Lissa Kapust*

Beth Israel Deaconess Medical Center, Harvard Medical School Teaching Hospital, Boston, Massachusetts, USA

"When one is sick, two need care". This is an old adage. It is wisdom for many situations, but for it is as the heart of caregiving for People with Parkinsons (PWP). The PWP care partner is at risk: we know this from our clinical experience and this is born out in published research on caregiving. Caregiver burnout is not just an overused concept. Without attention to self care individuals are at heightened risk for a decreased immune system, premature aging, higher mortality, depression, sleep deprivation and not getting proper medical care. In this discussion, we will examine in an open and non judgmental atmosphere, how care partners must work to juggle their own health needs with the demands for care of their partners. A group exercise will help each participant consider how they are doing with this juggling challenge.

How are you doing with keeping multiple balls in the air? How good are you at asking for what you need? What do you do to lower your

stress? How do you rate your physical health? How well is your emotional wellbeing? Everyone in this discussion group is an expert and everyone is a learner. Join this workshop. Bring your expertise and teach others. Bring your curiosity and learn from others. You will leave this discussion understanding that self care is a necessity; not a luxury.

O176

Care vs cure: Allocating scarce resources*David Iverson¹, Jon Palfreman²*¹ Menlo Park, California, USA,² Lexington, Massachusetts, USA

While everyone in the Parkinson's community, from research scientists to clinicians to those living with the disease and their families, is focused on the importance of finding a way to alter disease progression, there's another key question that doesn't receive the same attention: Are we doing enough to provide the best ongoing care options for people with Parkinson's? By "care options" we mean both the need to develop better drugs for symptomatic treatment as well as the need to provide exercise and physical or movement therapy opportunities. It's a key question for anyone who is at mid or late stage disease since disease modifying therapies aren't likely to be on the market any time soon. For these individuals, really good care options, for all practical purposes, are disease modifying. It's understandable that funding disease modifying research has been a priority, but has it come at the expense of developing improved levodopa delivery systems or providing adequate access to exercise facilities or other therapeutic approaches? This isn't so much a debate over "care vs. cure" as it is an exploration of what more we can do to make sure the "care" part of the equation isn't neglected.

Poster Presentations**BASIC SCIENCE: ETIOLOGY, GENETICS, EPIDEMIOLOGY AND TOXICANTS**

P01.01

Diabetes mellitus type two and decreased relative risk for Parkinson's Disease: a community based cross-sectional study*Fawzi Abukhalil, Raffi Djenderedjian, Bijal Mehta, Erin K Saito, Natalie Diaz, Julia Chung, Aaron M McMurtray*
USA

Introduction: As both the number of people affected by Parkinson's disease (PD) and the costs in caring for them increase, identifying alterable risk factors for development of PD is essential. Previous studies disagree on whether type 2 diabetes mellitus (DM) poses an increased or decreased risk in the development of PD.

Objective: To determine if the prevalence of diabetes observed in a community based sample of outpatients with Parkinson's disease is more consistent with an increased or decreased risk for development of Parkinson's disease among diabetics.

Methods: Cross-sectional analysis of all patients treated for Parkinson's disease in a community based outpatient clinic during a three-year period. Estimates of expected diabetes prevalence were calculated separately for increased and decreased risk models.

Results: A total of 105 patients with Parkinson's disease were included in this study. The observed diabetes prevalence among

outpatients with Parkinson's disease (18.10%) fell within the 95% confidence interval for the expected value in the decreased risk model (95% CI=16.86%–25.52%) but not for the increased risk model (95% CI=29.72%–35.14%).

Conclusions: The results of this study support a decreased risk for development of Parkinson's disease associated with type 2 diabetes mellitus. Further research into the potential mechanisms through which diabetes may exert a protective effect in the development of Parkinson's disease is needed.

P01.02

First report of LRRK2-G2019S mutation in Parkinson's disease patients from Ecuador.

Brennie Andree Munoz¹, Jorge Chang Castello², Ramiro Burgos³, Hector Zambrano⁴, Cyrus Zabetian⁵, Ignacio Mata⁵

¹ Service of Neurology, Hospital Luis Vernaza, Guayaquil, Guayas, Ecuador

² Ecuador

³ Laboratory of Molecular Biology, SOLCA, Guayaquil, Guayas, Ecuador

⁴ Laboratory of Molecular Biology, Hospital Luis Vernaza, Guayaquil, Guayas, Ecuador

⁵ Veterans Affairs Puget Sound Health Care System, Seattle, WA; Department of Neurology, University of Washington School of Medicine, Seattle, WA, Seattle, WA, USA

Background: The LRRK2-G2019S mutation is the most frequent genetic cause of Parkinson's disease (PD) reported to date. Its frequency have been studied extensively in both North America and Europa, however its role in populations from South America and especially in Ecuador is still unknown. This is, to the best of our knowledge, the first report on the frequency of LRRK2-G2019S mutations in PD patients from Ecuador.

Objective: To address this gap in knowledge, our aim was to investigate the presence of LRRK2-G2019S mutation in Ecuador.

Methods: We screened 61 (34 men; 27 women; mean age at onset 62 years, only one with family history of PD) patients with Parkinson's disease from all over Ecuador as part of the Latin American Research Consortium on the Genetics of PD (LARGE-PD). We obtained peripheral blood samples and extracted DNA. We subsequently amplified the entire coding region of exon 41 using polymerase chain reaction. The amplicons were purified and quantified for Sanger sequencing on an ABI-3170XL following manufacturer's recommendations. The sequences were then analyzed using BioEdit and Clustal-W free software packages. TaqMan® genotyping was performed on an ABI 7900 to verify our sequencing results.

The study was approved by the Ethics Committee and informed consent was provided by all participants.

Results: Genetic analysis show the presence of LRRK2-G2019S mutation in 1 (1.6%) of the 61 cases studied. A 71 years old (63 years old age of onset) female patient with no family history of PD.

Conclusions: The frequency of the LRRK2-G2019S mutation in this cohort in Ecuador appears to be low, similar to other studies conducted in admixed populations from other South American countries like Peru, which are of large Amerindian ancestry. However a larger number of patients should be screened to better estimate the real frequency in our country. We also think that further studies should include the sequencing of the entire gene looking for novel mutations specific to our population as well other known genes associated to Parkinson's disease.

P01.03

Air pollution and Parkinson's disease: mechanisms of diesel exhaust neuronal toxicity

Lisa Barnhill¹, Aaron Lulla¹, Sataree Khuansuwan², Jesus Araujo³, Jeff Bronstein²

¹ University of California Los Angeles Department of Molecular Toxicology, Los Angeles, CA, USA

² University of California Los Angeles Department of Neurology, Los Angeles, California, USA

³ University of California Los Angeles Department of Cardiology, Los Angeles, California, USA

Objective: Parkinson's disease (PD) is caused by a combination of genetic and environmental interactions. Known environmental and genetic influencers of PD risk cannot account for the majority of cases and therefore, it is likely that there remain significant, but yet unidentified, environmental factors. Recent epidemiological studies have found associations between long-term exposure to traffic-related air pollutants and PD that could account for a large portion of PD cases. Animal studies have shown that components of air pollution can cause neuroinflammation, which has been associated with PD. This project examines the mechanisms of action that link diesel exhaust (DE), a major component of urban air pollution, with dopaminergic neuron toxicity.

Methods: To understand the impacts of DE extract (DEX) on neuron survival, we utilized a zebrafish (ZF) model. Neuron counts were conducting via confocal microscopy using a transgenic line (VMAT2:EGFP) labeling aminergic neurons. Gene expression of synuclein was measured in cell culture after DEX exposure by rtPCR. Western blots were conducted on ZF embryo heads after DEX wash-out to determine levels of endogenous tyrosine hydroxylase (TH), a marker of dopaminergic neurons, as well as sncg1, a zebrafish synuclein gene. Additionally, to explore the impact of DEX exposure on neuroinflammation, a transgenic zebrafish line (mpeg1:mcherry) labeling microglial immune cells in the brain, was imaged via confocal microscopy.

Results: Exposure to DEX causes a significant decrease in number of GFP-positive aminergic neurons in VMAT2:EGFP embryos in a dose- and time-dependent manner. Western blot analysis demonstrated an increase in synuclein protein after treatment and, at higher doses, showed a reduction in the amount of TH protein, indicative of dopaminergic neuron toxicity. DEX showed an increase in alpha synuclein expression in cell culture. Additionally, exposure of mpeg1:mcherry embryos caused a change in localization and morphology of microglial cells in the brain, but the association between microglial changes and neuron toxicity has not been determined. The data suggest that exposure to components of traffic-related air pollution can lead to dopaminergic neuronal toxicity and has the potential to dysregulate the synuclein in ways that contribute to the development of neurodegenerative disorders such as Parkinson's disease.

P01.04

Prevalence of Parkinson's disease in North America: a nationwide epidemiological study sharing available databases

James Beck¹, Roy Alcalay², James Bower³, Hongle Chen⁴, Connie Marras⁵, Brad Racette⁶, Beate Ritz⁷, G. Webster Ross⁸, Rodolfo Savica⁹, Michael Schwarzschild¹⁰, Caroline Tanner¹¹, Stephen Van Den Eeden¹², Allison Willis¹³, Bill Wilson¹⁴

¹ Parkinson's Disease Foundation, New York, NY, USA

² Movement Disorders Division, Dept of Neurology, Columbia University Medical Center, New York, NY, USA

³ Dept of Neurology, Mayo Clinic, Rochester, MN, USA

⁴ Aging & Neuroepidemiology Group, National Institute of

Environmental Health Sciences, Research Triangle Park, NC, USA

⁵ Toronto Western Hospital Morton and Gloria Shulman Movement Disorders Centre and the Edmond J. Safra Program in Parkinson's Disease, University of Toronto, Toronto, ON, Canada

⁶ Dept of Neurology, Washington University School of Medicine, St. Louis, MO, USA

⁷ Center for Occupational and Environmental Health, Fielding School of Public Health, UCLA, Los Angeles, CA, USA

⁸ Pacific Health Research and Education Institute, Honolulu, HI, USA

⁹ Dept of Neurology, Mayo Clinic, Rochester, MN, USA

¹⁰ MassGeneral Institute for Neurodegenerative Disease, Charlestown, MA, USA

¹¹ Parkinson's Disease Research Education and Clinical Center, San Francisco Veteran's Affairs Medical Center; Dept. of Neurology, University of California, San Francisco, San Francisco, CA, USA

¹² Division of Research, Kaiser Permanente, Oakland, CA, USA

¹³ Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania School of Medicine, Philadelphia, PA, USA

¹⁴ Research Advocate, Parkinson's Disease Foundation, New York, NY, USA

Objectives: To estimate the prevalence of Parkinson's disease (PD) in North America using databases from different geographic areas. To date, there is no estimate of PD prevalence incorporating data from different regions of North America.

Design: We took advantage of six North American databases: Rochester epidemiology project (REP) in Olmsted County, MN; California PD Registry Pilot Project (CPDR-PP) in 4 California counties, the Honolulu-Asia Aging Study in Hawaii; Kaiser Permanente Northern California; the health administrative databases in Ontario, Canada; and CMS/Medicare administrative data for the USA. The investigators gathered to discuss the methodologies and data available from the different studies to guide interpretation of the resulting estimates. The goals were to compare the prevalence data of PD in the different projects and to derive a best estimate for PD prevalence incorporating data from each. Despite the great heterogeneity of the different studies, all the investigators agreed on a common strategy to report the prevalence of PD. We limit our current report to preliminary estimates from 3 databases with available information.

Results: 298 cases of PD were identified in the REP, 6,881 cases in the CAPDR-PP and 28,191 cases of parkinsonism were identified in Ontario. The crude prevalence rate for PD for all ages in MN on January 2006 was 0.21%, in CPDR-PP in 2010 was 0.17%, and in Ontario in 2010 the prevalence of parkinsonism was 0.43%. We observed a consistent increase in prevalence of PD as age progresses.

Conclusions: In this work-in-progress, our preliminary estimates of the prevalence of PD in North America show an age-associated increase. Adjustment to a standard population will account for different demographic characteristics of the underlying populations, and facilitate comparisons. Consideration of the methodological differences among studies may provide insight into the influence of geographic area, population setting (urban vs rural) and case ascertainment (prospective collection vs medical records review vs medical database) on the estimates. Incorporating information from additional studies will improve reliability of the prevalence estimates. As the world population ages, the burden of PD is expected to increase, and accurately measuring PD incidence and prevalence will be critical.

P01.05

Movement disorders after stroke in third level hospital Marrakech, Morocco

Abderrahmane Chahidi¹, Mohamed Chraa², Najib Kissani²

¹ Sorbonne University & Basic and Clinical Neurosciences Research Laboratory of UCA, Tagzirt, Beni Mellal, Morocco

² Neurology Department, University Hospital Mohammed VI, Marrakech, Morocco

Objectives: The goal of this study is to describe the clinical, paraclinical and evolutive features of patients having suffered a movement disorder in the aftermath of an ischemic stroke

Methods: Authors report a retrospective study from January 2000 to December 2009. This study collected 442 stroke cases. Data were collected 442 patient's folders who were hospitalized for ischemic stroke in the Neurology Department, Mohammed VI university hospital in Marrakesh, Morocco. Our department is a third level structure which covers much of southern Morocco. The diagnosis of ischemic stroke was established in base of clinical and CT scan criteria. Only patients who presented with a movement disorder in the aftermath of stroke were included.

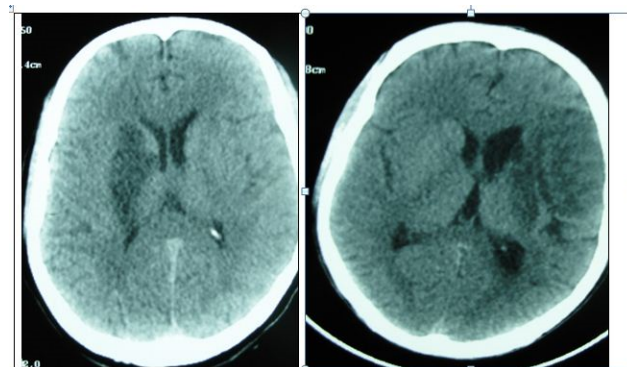
Results: Within our 442 stroke patients with ischemic stroke, 18 presented a movement disorder. There was 10 man and 8 women. The mean age was 59 years. Patients presented this complication 3 days to 1 year after the acute episode. We had 8 patients who developed a parkinsonism syndrome, 4 patients had a chorea, 3 others had an isolated tremor and 3 presented a dystonia. Parkinsonism was the later to develop in our patients whereas chorea developed whiting days after the stroke. CT scan showed a subcortical ischemic stroke interesting the basal ganglia in all cases. Finally, the evolution was marked by a resolution of all cases of dystonia and chorea, in the other hand patients who had a parkinsonism were being followed in our department for up to 6 years without any major improvement.

Conclusions: The present series report the clinical, paraclinical and the outcomes of patients who presented a movement disorder after an ischemic stroke. Even with the small number of patients in this study, many finding and suggestions may be developed.

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P01.06

Hallervorden-Spatz disease with psychotic symptoms

Eu Jene Choi¹, Dong Goo Lee²

¹ Department of Neurology, Asan Medical Center, Ulsan University, Seoul, South Korea

² Department of Biomedical Sciences, University of Waterloo, Waterloo, Ontario, Canada

Hallervorden-Spatz disease (HSD) is a rare degenerative, autosomal-recessive, and neurological disorder associated with progressive motor impairment and mental deterioration. The

diagnosis of HSD consists of clinical features and magnetic resonance imaging evidence of iron accumulation in the brain and mutations in the PANK2 gene. Typically, clinical features show motor symptoms including dystonia, involuntary movement, rigidity and dysarthria, as well as psychiatric symptoms like anxiety, depression and mental retardation. Although it is unusual for patients with HSD to have psychotic symptoms, this patient showed anxiety, startling and rapidly deteriorating memory impairment. T2-weighted magnetic resonance imaging (MRI) of the patient's brain indicated a specific pattern of hyperintensity within the hypointense medial globus pallidus with a mutation in the gene encoding pantothenate kinase 2 (PANK2). Interestingly, in the case of schizophrenia, pathology in the basal ganglia is central to the psychiatric symptoms because the basal ganglia play a key role on motor functioning, cognition, affect and mood. In the case of HSD, however, lesions caused by abnormal iron deposition in the globus pallidus and the substantia nigra pars reticulata can aggravate various psychotic symptoms, cognitive function impairment and mood disorders.

P01.07

GBA mutations and the E326K polymorphism are associated with faster rate of motor and cognitive progression in Parkinson's Disease

Marie Davis

University of Washington, Seattle, WA, USA

Parkinson's disease (PD) is heterogeneous in symptom manifestation and disease progression. Identifying factors underlying this heterogeneity will lead to better understanding of the underlying disease mechanism, improved prognosis and potential new therapeutic targets.

To determine whether GBA mutations and the E326K polymorphism modify the rate of symptom progression in PD, we analyzed detailed longitudinal motor and cognitive assessments from a prospective cohort of 733 PD patients enrolled at 7 U.S. sites. Patients were examined in the "on" state if receiving medication for PD, and were followed for an average of 3.0±1.7 years. The entire GBA coding region was sequenced in all participants to ascertain genotypes for all known pathogenic mutations and the functional polymorphism E326K.

To test for the association of GBA genotype and rate of motor progression, we performed linear regression with MDS-UPDRS III score at the last assessment as the outcome and GBA genotype as the independent variable, adjusting for levodopa equivalent dose, sex, age, disease duration, MDS-UPDRS III score at the first assessment, site, and the length of time between the first and last assessments. We performed similar linear regression to examine whether GBA genotype associated with progression of tremor, or gait and balance scores. To test for the association of GBA genotype and rate of cognitive progression, we performed logistic regression of subjects dichotomized to progressors and nonprogressors of cognitive decline with GBA genotype as the independent variable, adjusting for sex, age, disease duration, MDS-UPDRS III score at the first assessment, site, and the length of time between the first and last assessments.

GBA pathogenic mutations ($P=.002$), E326K ($P=.02$), and GBA variants combined as a single group ($P=1.5 \times 10^{-4}$) were associated with a faster rate of change in MDS-UPDRS III score. E326K and GBA variants were associated with faster rate of change in balance and gait ($P=.002$, $P=.01$, respectively) but not tremor. E326K was also associated with faster decline in cognition ($P=.02$).

Our data suggest that motor and cognitive symptoms progress more rapidly in PD patients carrying GBA variants, including the E326K variant, compared to noncarriers. These findings provide evidence that GBA mutations and E326K influence the heterogeneity in symptom progression observed in PD.

P01.08

Polychlorinated biphenyls (PCBs) are associated with Parkinson's disease risk in two populations

Samuel Goldman¹, Freya Kamel², Cheryl Meng³, Monica Korell³, Kathleen Comyns³, David Umbach², Jane Hoppin⁴, Connie Marras⁵, Anabel Chade⁶, Meike Kasten⁷, Dale Sandler², Aaron Blair⁸, G. Webster Ross⁹, Caroline Tanner¹

¹ San Francisco Veterans Affairs Health Care System; University of California-San Francisco, San Francisco, CA, USA

² National Institute of Environmental Health Sciences (NIEHS), Research Triangle Park, NC, USA

³ University of California-San Francisco, San Francisco, CA, USA

⁴ North Carolina State University, Raleigh, NC, USA

⁵ Toronto Western Hospital, Toronto, Ontario, Canada

⁶ Favaloro University, Buenos Aires, Argentina

⁷ University of Luebeck, Luebeck, Germany

⁸ National Cancer Institute, Bethesda, MD, USA

⁹ Pacific Health Research and Education Institute, Honolulu, HI, USA

Objective: To investigate whether previously observed associations of serum PCBs and Parkinson's disease (PD) replicate in an independent study population.

Background: PCBs are persistent environmental pollutants detectable in most humans despite a worldwide production ban over 20 years ago. They cause selective dopaminergic toxicity in animal models, but have been minimally studied in PD. We recently reported a significantly increased risk of PD associated with higher levels of serum PCBs in a case control study of Alaska Native people. Here we investigate this association in a demographically dissimilar study population.

Methods: We identified people with PD (PwPD) from the Agricultural Health Study (AHS), a cohort of pesticide applicators and their spouses in Iowa and North Carolina. We randomly selected controls matched for age, sex and state. PD was confirmed by in-person neurologist evaluation and consensus review. PCB congeners 118, 138, 153 and 180 were measured as ng/g lipid in serum using gas chromatography-mass spectroscopy (GC-MS). The analytic approach paralleled that of the prior study in AK. To assess dose-response, we constructed quartiles for each congener and for the sum of congeners. We calculated odds ratios (ORs) and 95% confidence intervals (95%CI) using logistic regression adjusting for age, gender and state.

Results: 97 PwPD and 103 controls were analyzed. PD was associated with higher levels of PCBs, with significant dose-responses across quartiles (Table). ORs were similar in the AHS and AK studies. In both studies, PCB levels correlated positively with age, but not with disease duration.

Conclusions: Higher serum levels of PCBs are associated with increased risk of PD in two independent study populations. Lack of association with PD duration argues against reverse causation.

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Current study in AHS	PCB quartile ORs (95%CI), except where specified				p-trend
	Q1 (ref)	Q2	Q3	Q4	
PCB118	1.0	2.1 (0.9-4.7)	1.9 (0.8-4.4)	2.3 (0.9-5.8)	0.1
PCB138	1.0	1.2 (0.5-2.8)	3.1 (1.3-7.2)	2.7 (1.1-6.3)	0.006
PCB153	1.0	1.4 (0.6-3.1)	2.1 (0.9-4.8)	2.2 (0.9-5.2)	0.055
PCB180	1.0	2.2 (1.0-4.9)	1.3 (0.5-3.2)	3.1 (1.3-7.6)	0.044
PCB sum	1.0	1.7 (0.7-3.9)	2.4 (1.0-5.5)	2.7 (1.1-6.6)	0.022
Prior AK Study (n=65 PwPD, 168 controls)					
PCB118 ¹	1.0		2.3 (1.02-5.0)		0.045
PCB138	1.0	1.6 (0.6-4.6)	3.1 (1.1-8.5)	3.7 (1.3-10.8)	0.008
PCB153 ²	1.0	1.0 (0.4-2.2)	2.0 (0.93-4.4)		0.099
PCB180	1.0	0.9 (0.4-2.5)	1.25 (0.5-3.1)	3.0 (1.3-7.1)	0.015
PCB sum	1.0	1.3 (0.5-3.7)	2.0 (0.7-5.5)	3.1 (1.1-8.6)	0.019

¹Binary (detected vs non-detected); ²Tertiles

P01.09

Cigarettes, lithium and Parkinson's disease

Thomas Guttuso, Edward Russak, Miriam Tamano De Blanco, Murali Ramanathan
University at Buffalo, Buffalo, NY, USA

Introduction: Cigarette smoking has been associated with a reduced risk of developing Parkinson's disease (PD). This association may be due to a reduced rate of smoking in people at increased risk of developing PD or due to one or more neuroprotective compounds in tobacco. In 1980, Jathar et al. (J Postgrad Med 1980;26:39-44.) reported lithium concentrations in tobacco to be 12.0µg/gm, which was over 10x that of 56 other foods, beverages and spices tested in Bombay, India. Lithium has a wide array of neuroprotective actions and its use has been associated with a 50-60% reduced risk of dementia. Because inhaled lithium from cigarette smoke would likely enter into circulation, lithium could be a neuroprotective element in cigarettes. Most of the epidemiologic studies on smoking and risk of developing PD have been performed in western societies. We sought to assay the lithium concentrations in popular brands of western cigarettes to compare with the results from Jathar et al.

Methods: Tobacco samples from five brands of cigarettes were analyzed for lithium content using inductively coupled plasma optical emission spectrometry (ICP-OES). A 100 mg aliquot of tobacco from each cigarette was digested overnight in 69% trace metal analysis grade nitric acid at room temperature. After digestion, the suspension was centrifuged and filtered. A 1ml aliquot of the filtrate was diluted to 10 ml with 2% nitric acid for ICP-OES analysis. Certified lithium standards (Perkin Elmer) were used for instrument calibration. Yttrium (Perkin Elmer) was added to all blank, standard, and sample solutions as an internal standard. All solutions were analyzed in triplicate by ICP-OES (Perkin Elmer, Optima 2000 DV) running argon as the plasma gas and nitrogen as the purge gas. Lithium concentrations were computed from measurements of the 670.784 nm lithium emission line from the calibration curve after correcting for sample dilution.

Conclusion: Popular brands of western cigarettes were found to have high concentrations of lithium compared to many foods and beverages previously assayed. Inhaled lithium from cigarette smoking could be a neuroprotective element partially accounting for the inverse association between smoking and risk of developing PD.

Results:

Tobacco Source	Lithium Concentration (µg/gm)
American Spirit	3.2
Camel Blue	21.2
Camel Turkish Gold	18.0
Marlboro Red	15.8
Marlboro Gold	14.8
Indian Tobacco (Jathar et al. 1980)	12.0

P01.11

Clinical profile and outcome of acute Parkinsonism in a tertiary care south Indian hospital.

Venkatraman Karthikeyan¹, Chandramouleeswaran Venkatraman², Gobinathan Shankar³

¹ Second year resident in Neurology, Chennai, Tamilnadu, India

² Professor of Neurology, Institute of Neurology, Madras Medical College, Chennai, Tamilnadu, India

³ Director, Institute of Neurology, Madras Medical College, Chennai, Chennai, Tamilnadu, India

Background: Acute Parkinsonism is a neurological emergency caused by numerous reversible etiological factors. Outcome of this

condition depends on the etiology, clinical picture and time to diagnosis/treatment. Treatment of the etiological factors recovers the patients out of this life threatening condition, albeit residual sequel can be present in some cases.

Objectives: To identify the etiological factors, clinical profile and outcomes of patients presenting with acute Parkinsonian syndrome. **Methods and Materials:** Young patients (<40 years) presenting with acute akinetic rigid state (<2 weeks duration) were enrolled. Patients were investigated for the etiological factors and treated accordingly. The outcomes were documented as mortality, residual sequel and completely recovered based on the clinical examination during a 6 month follow up.

Results: A total of 17 cases presenting with axial and appendicular rigidity of less than 2 weeks duration were included. Their etiologies were as follows – 7 cases were due to infective causes (Japanese encephalitis(4), Varicella zoster(2), measles(1)), 2 cases each due to cerebrovascular disease, osmotic demyelination syndrome and Neuroleptic Malignant syndrome, 1 case each due to acute hydrocephalus secondary to VP shunt dysfunction, SLE, paraneoplastic syndrome associated with lung cancer and Wilsons disease. 8(47%) cases had resting tremor along with rigidity. 16(94%) cases had higher cognitive dysfunction (reduced level of consciousness, poor attention and language disturbances). 5(29%) cases died, 6(35%) cases recovered completely and 6(35%) cases had residual rigidity and bradykinesia at the end of 3 month follow up. Patients with residual rigidity, were managed with levodopa and clonazepam. 4(66%) cases showed favourable responses in UPDRS and modified bradykinesia rating scale at the end of 6 month follow up.

Conclusions: Acute Parkinsonism is a potentially treatable, yet life threatening condition. Rapid onset, mental status disturbance and toxic presentations helps to distinguish them from insidious onset idiopathic Parkinson Disease. Sequel of the condition behaves as idiopathic Parkinsonism clinically and responds favourably to dopaminergic treatment. High degree of suspicion is required to rule out secondary causes of Parkinsonism in young patients presenting as a sequel to an acute presentation before labelling them as idiopathic Parkinson Disease

P01.12

Variable frequency of LRRK2 mutations in Latin America, a case of ancestry

Ignacio Mata¹, Mario Comejo-Olivas², Luis Torres², Mario Velit-Salazar², Miguel Inca-Martinez², Pilar Mazzetti², Carlos Cosentino², Federico Micheli³, Claudia Perandones³, Elena Dieguez⁴, Victor Raggio⁴, Vitor Tumas⁵, Vanderci Borges⁵, Carlos Rieder⁵, Artur Shumacher-Schuh⁵, Carlos Velez-Pardo⁶, Marlene Jimenez-Del-Rio⁶, Francisco Lopera⁶, Jorge Chang Castello⁷, Brennie Andreé Muñoz⁷, Sarah Waldherr¹, Dora Yearout¹, Cyrus Zabetian¹

¹ USA

² Peru

³ Argentina

⁴ Uruguay

⁵ Brazil

⁶ Colombia

⁷ Ecuador

Objective: To further elucidate the frequency of the p.R1441G/C/H/S, p.G2019S and p.Q1111H Leucine Repeat Rich Kinase 2 (LRRK2) variants in Latin America.

Background: Mutations within LRRK2 represent the most common genetic cause of typical Parkinson's disease (PD) especially in European and North African derived populations. Two codons, G2019 and R1441 harbor the majority of these mutations. While LRRK2-p.G2019S and p.R1441G/C are very rare or absent in Asian populations, little is known about their frequency in Latin American

populations. On the other hand, LRRK2-p.Q1111H is only present in Latinos, however whether or not has is a risk factor for PD is not clear.

Methods: We screened a total of 2,843 individuals (1,739 PD patients) from Peru, Colombia, Brazil, Uruguay, Argentina and Ecuador as part of the Latin American Research Consortium for genetics in Parkinson's disease (LARGE-PD). All samples were screened for the p.G2019S and p.Q1111H variant by Taqman and the cluster of three substitutions in codon 1441(R1441C/G/H) by sequencing LRRK2 exon 31.

Results: We identified 29 PD patients (29/1712; 1.7%) carrying the p.G2019S mutation. Interestingly frequency varied greatly amongst sites, ranging from 0.02% in Peru to 4% in Uruguay. We also identified 5 healthy controls carrying this mutation (3 of them from Uruguay). Surprisingly we only detected 2 PD patients, from Uruguay and Peru, carrying the p.R1441G mutation. One patient from Brazil carried the p.R1441C mutation. We also observed an increased frequency of p.Q1111H in patients (3.8%) compared to controls (3.1%) although this difference was not significant (OR 1.02, $p=0.873$).

Conclusions: We identified LRRK2-p.G2019S carriers in all our cohorts thru Latin America, however the frequency varied greatly between countries. LRRK2-p.R1441 mutations are rare in Latin America despite the fact that many of these countries have been historically influenced by Spanish colonizers where p.R1441G is relatively common. We did identify a very interesting family in Peru carrying the LRRK2-p.R1441G in which the affected proband presents with early onset typical PD while his octogenarian mother and his 54 year-old brother, who are also carriers, remain without PD symptoms showing variable penetrance for this mutation; similar to that shown for the most common LRRK2-p.G2019S

P01.13

The roles of diet, exercise, & supplements in Parkinson's disease progression

Laurie Mischley¹, Richard Lau²

¹ Bastyr University, Kenmore, WA, USA

² Oregon State University, College of Public Health and Human Sciences, Corvallis, OR, USA

Background: Studies show that those who consume green tea, coffee, blueberries, and avoid dairy are less likely to be diagnosed with Parkinson's disease (PD). That which protects does not necessarily treat, and those already diagnosed want to know, "Does my diet and lifestyle affect the course of my disease?" Thus far, no studies have attempted to evaluate whether nutrition is associated with disease progression.

Objective: The goal of this study was to describe whether any modifiable aspects of lifestyle are associated with rate of PD progression.

Methods: An internet-based natural history study was designed to generate information useful to patients and providers. An assessment tool, the Patient-Reported Outcomes in PD (PRO-PD) scale, was designed to assess PD severity and was validated against the existing measures of disease severity. Disease progression was defined as PRO-PD, adjusted for age and years since diagnosis. Baseline food frequency questionnaires (FFQ) were used to quantify dietary intake in the cross-sectional analysis.

Results: 844 participants participated in the study, with a mean age of 62.8 years and an average 5 years since diagnosis. The following foods were associated with a statistically significant improvement in PRO-PD score: fresh fruit, fresh vegetables, nuts and seeds, olive oil, fish (non-fried), wine, eggs, fresh herbs. The following foods were associated with worse outcomes: Fried foods, beef, diet soda, canned fruits, canned vegetables. Dairy consumption was not associated with disease severity. Of the 33 supplements studied,

only oral glutathione and coenzyme Q10 were associated with improved outcomes; iron and melatonin supplementation were associated with worse outcomes. There was a dose response curve with exercise, with at least 30 minutes per day 7 days per week was associated with the greatest reduction in disease progression.

Conclusions: The foods shown here to protect against PD progression are common to the Mediterranean diet and support an existing body of literature. Fried food, beef, and diet soda should be avoided. Further research is warranted regarding the association between canned foods and melatonin, which may be a surrogate for low income and sleep disorders, respectively. Patients should be advised to exercise 30 minutes daily.

P01.14

NFE2L2, PPARGC1 α , and oxidative stress in Parkinson's Disease susceptibility and progression

Kimberly Paul¹, Janet Sinsheimer¹, Myles Cockburn², Jeff Bronstein¹, Yvette Bordelon¹, Beate Ritz¹, Cynthia Kusters¹

¹ UCLA, USA

² USC, USA

Background: Nuclear factor-erythroid 2 related factor 2 (Nrf2) and peroxisome proliferator activator receptor γ coactivator 1 α (PGC-1 α) are important transcription factors that activate multiple antioxidant defense mechanisms in response to oxidative stress and, thus, are of interest for Parkinson's disease (PD) etiology.

Objective: To investigate the influence of common variants in the genes NFE2L2 and PPARGC1 α on PD susceptibility and progression of symptoms, and assess gene variant-pesticide interactions specifically with oxidative stress inducing co-exposures to the pesticides maneb and paraquat (MB/PQ).

Methods: In 472 PD patients and 532 population-based controls of European ancestry, we investigated the influence of haplotypes for NFE2L2 (rs35652124, rs6706649, rs6721961) and PPARGC1 α (rs6821591, rs8192678, rs2970848, rs4235308) and their interactions with MB/PQ exposure on PD occurrence (using logistic regression models) and also on progression of motor symptoms and cognitive decline in patients followed prospectively ($n=192$; repeated measures models). Ambient agricultural MB/PQ exposures were generated with a geographic information system (GIS) based exposure assessment tool.

Results: Assuming an allelic genetic model, two NFE2L2 haplotypes were associated with significant increases in the risk of developing PD ($p<0.04$) and with faster cognitive decline as measured with the Mini-Mental State Exam (MMSE) ($p<0.0006$). None of the PPARGC1 α haplotypes were marginally associated with PD risk. However, one haplotype interacted with MB/PQ exposure ($p=0.03$), such that highly exposed haplotype carriers showed no increased risk of PD while these pesticides increased PD risk in wildtype haplotype carriers. Additionally, three PPARGC1 α haplotypes were associated with differing rates of motor symptom progression.

Conclusion: Our study provides support for the involvement of NFE2L2 in both PD susceptibility and cognitive symptom progression. PPARGC1 α seems to modify PD risk in MB/PQ exposed subjects and influences motor symptom progression. The observations are consistent with the hypothesis that oxidative stress-inducing mechanisms influence PD risk and progression.

P01.15

Association of brain organochlorines with Lewy pathology

G. Webster Ross¹, Robert D. Abbott², Petrovitch Helen³, John Duda⁴, Caroline M Tanner⁵, Zarow Chris⁶, Jane Uyehara-Lock⁷, Kamal Masaki⁸, Lenore Launer⁹, Lon R White³

¹ Veterans Affairs Pacific Islands Health Care System, Honolulu, Hawaii, USA

² Center for Epidemiologic Research in Asia, Shiga University of Medical Science, Shiga, Japan

³ Pacific Health Research and Education Institute, Honolulu, Hawaii, USA

⁴ Parkinson's Disease Research, Education and Clinical Center, Corporal Michael J. Crescenz VA Medical Center, Philadelphia, Pennsylvania, USA

⁵ Parkinson's Disease Research, Education, and Clinical Center, San Francisco Veterans Affairs Medical Center, San Francisco, California, USA

⁶ Department of Neurology, Keck School of Medicine, University of Southern California, Los Angeles, California, USA

⁷ Dept. of Pathology, University of Hawaii, John A. Burns School of Medicine, Honolulu, Hawaii, USA

⁸ Dept. of Geriatrics, University of Hawaii, John A. Burns School of Medicine, Honolulu, Hawaii, USA

⁹ National Institute on Aging, National Institutes of Health, Bethesda, Maryland, USA

Background: Organochlorine pesticides are associated with an increased risk of Parkinson's disease (PD). Recent data suggest that heptachlor epoxide, a metabolite from a pesticide extensively used by pineapple growers in Hawaii may be especially important. The mechanism of this relationship is uncertain. While a previous report from the Honolulu-Asia Aging Study (HAAS) suggested a strong association of some organochlorines with presence of Lewy pathology in the brain, findings were too imprecise to definitively support a relationship.

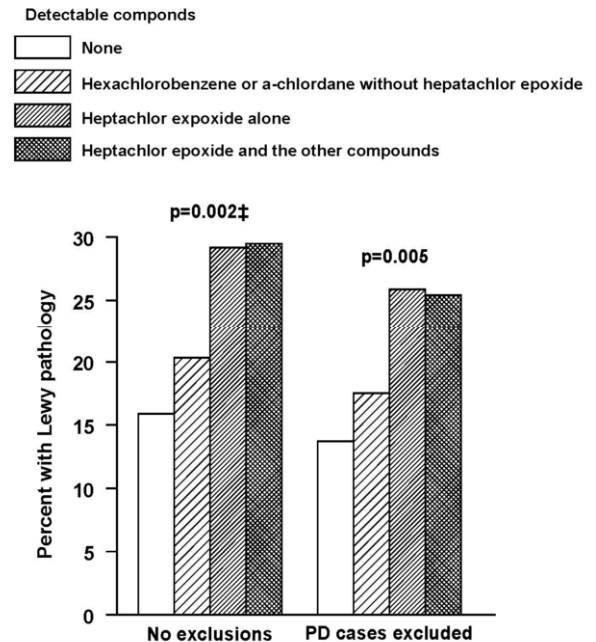
Purpose: To evaluate the association of brain organochlorines with Lewy pathology in an enriched sample of brains from the HAAS.

Methods: Organochlorines were measured in frozen occipital or temporal lobes in 705 brains using high resolution gas chromatography. Lewy pathology was identified utilizing alpha-synuclein immunohistochemistry and H&E staining of the substantia nigra and locus ceruleus.

Results: Of 16 organochlorines, 3 were associated with high prevalence of Lewy pathology. They included heptachlor epoxide ($P < 0.001$), hexachlorobenzene ($P = 0.003$), and a-chlordane ($P = 0.009$). The association with heptachlor epoxide was especially strong. Among the brains, the percent of decedents with Lewy pathology was nearly doubled in the presence versus the absence of detectable levels of heptachlor epoxide (30.1% [120/399] versus 16.3% [50/306], $p < 0.001$). In order to understand the relative importance of the 3 compounds, the relationship of their combination with presence of Lewy pathology was evaluated. After adjustment for age and other characteristics, presence of Lewy pathology was 15.9% in decedents with no detectable levels of any compound, 20.3% in decedents with detectable levels of hexachlorobenzene or a-chlordane but not heptachlor epoxide, and 29.2% in decedents with detectable levels of heptachlor epoxide alone ($p = 0.002$ for trend). In the latter group, detectable levels of another compound increased the percent of decedents with Lewy pathology only modestly (to 29.5%). Removing cases of PD had negligible effects on these findings ($p = 0.005$ for trend).

Conclusion: Three organochlorines were significantly associated with Lewy pathology with heptachlor epoxide having the strongest effect.

Adjusted† percent of decedents with Lewy pathology by selected combinations of detectable levels of heptachlor epoxide, hexachlorobenzene, and a-chlordane.



P01.16

Nonsteroidal anti-inflammatory drugs (NSAIDs) and penetrance of LRRK2 Parkinson's disease (PD)

Caroline Tanner¹, Connie L Marras², Cheryl Chen Meng³, Samuel Goldman⁴, Anthony E Lang², Monica Korell⁵, Marta San Luciano Palenzuela³, Eduardo Tolosa⁶, Birgitt Schuele⁷, J William Langston⁷, Alexis Brice⁸, Stefano Goldwurm⁹, Giulio Riboldazzi¹⁰, Christine Klein¹¹, Kathrin Brockmann¹², Daniella Berg¹², Joachim J Ferreira¹³, Meriem Tazir¹⁴, George Mellick¹⁵, Carolyn Sue¹⁶, Kazuko Hasegawa¹⁷, Eng King Tan¹⁸, Michael J Fox^{19,20}

¹ Parkinson's Disease Research Education and Clinical Center, SFVAMC & University of California – San Francisco, San Francisco, CA, USA

² Toronto Western Hospital, University of Toronto, Toronto, Ontario, Canada

³ University of California – San Francisco, San Francisco, California, USA

⁴ University of California – San Francisco & San Francisco Veterans Affairs Health Care System, San Francisco, California, USA

⁵ Northwestern University Medical Center, Chicago, Illinois, USA

⁶ Universitat de Barcelona, Barcelona, Spain

⁷ Parkinson's Institute, Sunnyvale, California, USA

⁸ CRICM UPMC, Inserm UMR_S975/CNRS UMR 7225, Paris, France

⁹ Parkinson Institute, ASST G.Pini – CTO, ex ICP, Milano, Italy

¹⁰ Center for Parkinson's Disease, Macchi Foundation, Varese and Department of Rehabilitation, "Le Terrazze" Hospital, Cunardo, Italy

¹¹ University of Luebeck, Luebeck, Germany

¹² University Hospital in Tübingen, Tübingen, Germany

¹³ Instituto de Medicina Molecular & University of Lisbon, Lisbon, Portugal

¹⁴ CHU Mustapha Bacha, Université d'Alger, Algiers, Algeria

¹⁵ Griffith University, Brisbane, Australia

¹⁶ University of Sydney, Sydney, New South Wales, Australia

¹⁷ National Sagami Hospital, Kanagawa, Japan

¹⁸ National Neuroscience Institute & Duke-NUS Graduate Medical School Singapore, Singapore, Singapore

¹⁹ Foundation LRRK2 Cohort Consortium

Background: The penetrance of LRRK2 mutations is reduced for PD [1]. Environment and/or other genes may influence penetrance. NSAID use may reduce inflammation and lower PD risk [2], but has not been studied in LRRK2 PD.

Objective: To determine the role of NSAIDs on penetrance in LRRK2 Parkinson's disease

Methods: Symptomatic ("LRRK2-PD") and asymptomatic ("LRRK2-nonPD") persons with the G2019S, R1441x, or I2020T mutations ("pathogenic carriers") or G2385R or R1628P variants ("risk variant carriers") in LRRK2 who were members of 2 international LRRK2 studies provided information on regular NSAID use (defined as >2 pills/week for >6 months) prior to index date (diagnosis date in PD, interview date in nonPD). The relationship between regular NSAID use and PD was determined for any NSAID, and separately for ibuprofen use or aspirin use, in all carriers and separately in pathogenic and risk variant groups, using Cox regression models, adjusted for gender, to calculate hazard ratios (HR).

Results: 247 LRRK2-PD (51% men) and 318 LRRK2-nonPD (38.7% men) were enrolled. NSAID use was associated with a reduced hazard of PD (Table).

	LRRK2 PD	LRRK2 nonPD	HR	95%CI	
				lower	upper
Overall	%	%			
Any NSAID	10.9	31.8	0.28	0.19	0.42
Ibuprofen	2.5	7.3	0.61	0.27	1.37
Aspirin	8.2	24.2	0.26	0.16	0.40
Pathogenic Carriers					
Any NSAID	11.4	22.5	0.42	0.28	0.64
Ibuprofen	2.8	11.9	0.40	0.18	0.91
Aspirin	8.3	8.9	0.54	0.33	0.89
Risk Variant Carriers					
Any NSAID	7.1	42.3	0.13	0.03	0.56
Ibuprofen	0.0	2.0	0.00		
Aspirin	7.1	41.6	0.14	0.03	0.58

Conclusion: Regular NSAID use is associated with reduced penetrance in LRRK2 associated PD. Similar patterns are seen when pathogenic mutations and risk mutations are studied separately. Anti-inflammatory drugs may be useful as disease modifying treatments in LRRK2 PD.

[1] Marder, K., et al., *Neurology*, 2015. 85:89–95.

[2] Chen, H., et al., *Arch Neurol*, 2003. 60:1059–64.

** www.michaeljfox.org/lccinvestigators

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P01.17

Current status of Parkinson's disease in Mongolia

Bayasgalan Tserensodnom

Department of neurology of Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia

Objective: To assess patterns of drug use and age specific prevalence of Parkinson's disease (PD) in Mongolia based on National Center Health Development (NCHD) statistics.

Background: No epidemiological data of Parkinson's disease (PD) is available in Mongolia.

Method: Total number of PD patient and Demographic data were obtained from National Center of Health Development (NCHD). To assess the patterns of drug use in Parkinson's disease (PD) in Mongolia information about the clinical characteristics and current treatment of patients with PD was obtained from regional neurologists.

Results: The calculated prevalence rate of PD based on National Center Health Development (NCHD) statistics is 5.5 per 100.000 in 2005. Considering significant increase of PD with age, the age specific prevalence of PD 33/100.000 at the aged 50 and above, which is much lower than that in Taiwan, Japan, Korea, European countries and close to the data in China, People's Republic of, and Nigeria. There are several factors influencing these statistics is the fact that misdiagnosis, under diagnosis of PD patients, age specific characteristics and life expectancy of population in Mongolia. Few antiparkinsonian medications including levodopa, amantadine, anticholinergics, are currently available in Mongolia where as widely used new dopamine agonists, deprenyl and COMT inhibitors are still not available. Substantial number of patients (38.5%) is still unable to receive appropriate treatment. Levodopa is the most frequently used treatment and about 80% of PD patients received this drug. Although in 2003 Ministry of Health approved of free dispensing of levodopa, only 20% PD patients are able to receive free levodopa. Rest of the patients with PD has to buy throughout their life, which burdened them economically.

Conclusion: The age specific prevalence of PD based on National Center Health Development (NCHD) statistics 33/100.000 at the aged 50 and above. Our study shows the Mongolian therapeutic trends in PD in the common practice. Substantial number of patients is still unable to receive appropriate treatment. Role of regional health care organization and neurologists is essential for free dispensing of levodopa to patients with PD living in rural area.

BASIC SCIENCE: CELL DEATH, NEUROPROTECTION AND TROPHIC FACTORS

P02.01

Marinesco bodies and substantia nigra neuron density in Parkinson's disease

Robert D. Abbott¹, James S. Nelson², G. Webster Ross², Caroline M. Tanner³, Kamal H. Masaki⁴, Lenore J. Launer⁵, Lon R. White², Helen Petrovitch²

¹ Shiga University of Medical Science, Otsu, Shiga, Japan

² Pacific Health Research and Education Institute, Honolulu, Hawaii, USA

³ Department of Neurology, University of California, San Francisco, California, USA

⁴ Department of Geriatric Medicine, University of Hawaii, Honolulu, Hawaii, USA

⁵ National Institute on Aging, Bethesda, Maryland, USA

Background: Marinesco bodies (MB) are intranuclear inclusions in pigmented neurons of the substantia nigra (SN). While absent or rarely found in children, MB frequency increases with age. Relative to young controls, MB frequency in the elderly remains high in the presence of several neurodegenerative disorders, including Alzheimer's disease and dementia with Lewy bodies. In contrast to MB, pigmented neurons in the SN decline 5 to 10% per decade of life. Whether the accumulation of MB with advancing age has a role in this decline is uncertain.

Purpose: To examine the association of MB frequency with SN neuron density in Parkinson's disease (PD) based on findings from the Honolulu-Asia Aging Study (HAAS).

Methods: Data on MB and SN neuron density were collected from a HAAS sample of 131 men with postmortem examinations from 1992 to 2007. Men were aged 73 to 99 years at the time of death. Neuron density was measured in quadrants from scaled tracings of the SN. MB frequency was measured as the overall percent of neurons containing MB in a cross-section of the SN contralateral to the section used in deriving neuron density. Diagnosis of PD was clinically and pathologically confirmed. Additional features include data collected from physical examinations during middle adulthood and late-life.

Results: Frequency of MB was more than 60% lower in decedents with PD versus those without PD (2.4 versus 6.5%, $p < 0.001$). Low MB frequency was unique to PD as its high frequency in non PD cases was unrelated to parkinsonian signs and incidental Lewy bodies. High MB frequency was also common in the presence of Alzheimer's disease and apolipoprotein e4 alleles. For those with PD, MB frequency continued to decline as PD duration increased. For each year of PD duration, MB frequency declined by an average of 12% ($p = 0.008$). Similar patterns were also observed for SN neuron density. Within the SN ventrolateral quadrant, neuron density declined an average of 14% for each year of PD duration ($p < 0.001$).

Conclusions: Elevations in MB frequency are common in the elderly but are low in cases of PD. Low frequency of MB in elderly individuals where MB frequency is expected to be high could be a phase of PD progression that is distinct from the development of incidental Lewy bodies and other neurodegenerative disorders. Whether MB have a pathological role in age-related declines in SN neuron density warrants consideration.

P02.02

Effects of alpha-synuclein fibrils on dopamine neurodegeneration in young and one year old mice: neuroprotective study with CDNF.

Katrina Albert¹, Merja H. Voutilainen¹, Jenni Siekkinen¹, Kelvin C. Luk², Virginia M.-Y. Lee², Mart Saarma¹, Mikko Airavaara¹

¹ Institute of Biotechnology, University of Helsinki, Helsinki, Finland

² Department of Pathology and Laboratory Medicine, Institute on Aging and Center for Neurodegenerative Disease Research, University of Pennsylvania School of Medicine, Philadelphia, PA, USA

Parkinson's disease is a progressive neurodegenerative disorder that affects over 7 million people worldwide. α -synuclein (α -syn) is mutated in certain patients with familial forms of Parkinson's disease (PD), and it is a major component of insoluble protein aggregates called Lewy bodies, present in all patients. Therefore, α -syn is strongly considered to be one of the major causes of dopamine neuron degeneration in PD. Injection of preformed fibrils consisting of purified α -syn (PFFs) into rodents is a promising model of the disease due to the presence of Lewy bodies and the slow onset of motor symptoms.

Recently discovered cerebral dopamine neurotrophic factor (CDNF) has been shown to be neurorestorative in neurotoxin models of PD. Importantly, it is able to rescue neurons from endoplasmic reticulum-induced cell death, a process associated with aggregation of α -syn. The objective was first to create an α -syn-based model of dopamine neurodegeneration in our laboratory using PFFs and then to test the ability of CDNF to decrease α -syn-induced neurodegeneration.

Mouse PFFs were injected to the striatum of 3 month or 1 year old mice and their behaviour was measured at 1, 3 and 6 months. At 1 month, CDNF was also injected to the striatum. For behaviour,

cylinder test, rotarod, wire hanger and beam walking tests were performed. Brains were immunostained for tyrosine hydroxylase (TH) and α -syn.

From 1 to 3 months there was a tendency for PFF-injected mice to stay on the rotarod for less time, indicating motor deficits. For cylinder test performed at 3 months with mice injected with CDNF or vehicle, CDNF injected mice showed significant restoration in ipsilateral vs. contralateral paw use (ie. mice were using both paws equally). The direct outcome measures for quantifying dopamine loss are striatal dopamine concentration, TH optical density and number of TH+ cells from substantia nigra, and will be presented in the poster.

P02.03

Neuroprotective epigenetic and molecular mechanisms of selected iron-chelating antiinflammatory antioxidant PARP-1 Inhibitors against 6-OHDA-induced neurotoxicity in aged rats

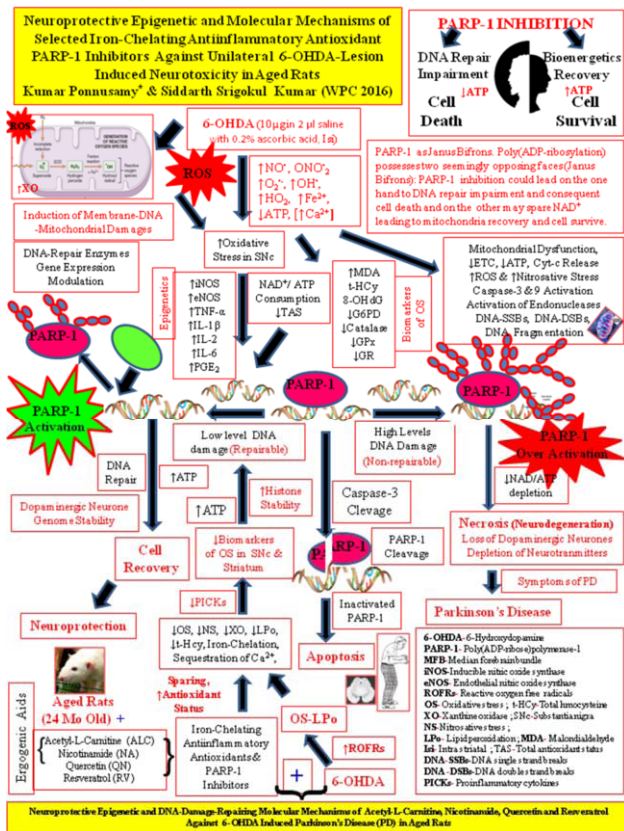
Sindhu Babulogaiah¹, Kumar Ponnusamy², Siddarth Srigoikul Kumar², Jegathambigai Rameshwar Naidu³

¹ Department of Biomedical & Electronic Engineering, Vellore, Tamilnadu, India

² International Medical University (IMU), Kuala Lumpur, Selonghor, Malaysia

³ Asia Metropolitan University (AMU), Johor Bharu, Malaysia

Parkinson's disease (PD) is a neurodegenerative disorder associated with progressive loss of dopaminergic neurones of the substantia-nigra pars compacta (SNc) and associated depletion of dopamine in the terminal region, the caudate-putamen, with major signs of oxidative stress (OS). ROS plays an important role in the ageing and age-related progressive neurodegenerative disorders such as Senile Dementia, Alzheimer's disease and PD. Present study was designed to investigate the neuroprotective-epigenetic and DNA-damage-repair molecular-mechanisms of selected ergogenic-aid "iron-chelating antiinflammatory-antioxidant Poly(ADP-ribose) polymerase-1 (PARP-1) inhibitors (ICAAP-Is)" such as acetyl-L-carnitine (ALC), nicotinamide (NA), quercetin (QN) and resveratrol (RV) against 6-OHDA-induced neurotoxicity in aged rats. Aged male albino rats (24-month-old) were divided into 7-groups. Group-1: Control; Group-2: OHDA-alone (10 μ g in saline, intrastriatal); Group-3: OHDA+ALC (300mg/kg b.wt for 21 days, i.p, ICAAP-Is started 3-days prior to OHDA-administration); Group-4: OHDA+NA (100mg/kg b.wt., i.p); Group-5: OHDA+QN (50mg/kg b.wt., i.p); Group-6: OHDA+RV (100mg/kg b.wt., i.p); Group-7: (ALC+NA+QN+RV). Effect of ICAAP-Is on oxidative-stress biomarkers, proinflammatory cytokines (PICKs), total antioxidant-status (TAS), DNA, ATP and dopamine contents, DNA-repair enzyme levels and genome-stability in SNc and corpus striatum were estimated. OHDA-challenged rats elicited a significant increase ($p < 0.01$) in lipidperoxidation (LPO), protein-carbonyl-content (PCC), 8-hydroxy-2'-deoxyguanosine (8-OHdG), xanthine oxidase (XO), PICKs, nitric oxide synthase (NOS), caspase-3, PARP-1 and DNA-SSBs when compared with control rats. There was a significant decrease ($p < 0.001$) in TAS, superoxide-dismutase, GPx and catalase levels in OHDA-treated group. Co-administration of ICAAP-Is to the experimental groups elicited a significant ($p < 0.01$) reduction in LPO, PCC, PICKs, NOS, caspase-3, PARP-1 and a significant increase ($p < 0.01$) in TAS and antioxidant enzymes, DNA, ATP and dopamine contents and exerted a neuroprotection evidenced by a significant ($p < 0.01$) reduction in DNA-SSBs and 8-OHdG. PARP-1 activity regulated differently, in severe-OS and severe OS-DNA damages coupled with ATP-depletion and cleavage-autolysis of PARP-1 occurs. Administration of ICAAP-Is enhances genome-stability against neurotoxins and hence will be beneficial in the treatment of PD.



P02.04

Neuroprotective potential of transcription factors Lmx1a and Lmx1b in mouse models of Parkinson's disease

Hélène Doucet-Beaupré¹, Aurore Voisin², Louis-Eric Trudeau², Martin Lévesque¹

¹ Centre de Recherche de l'Institut universitaire en santé mentale de Québec; Département de Psychiatrie & Neuroscience, Université Laval., Québec, Québec, Canada

² Université de Montréal, Montréal, Québec, Canada

Degeneration of midbrain dopamine neurons is the main pathological hallmark of Parkinson's disease. Identifying transcriptional programs that maintained these neurons in the adult brain will help understand their specific vulnerability. The LIM-homeodomain transcription factors Lmx1a and Lmx1b play critical roles during the development of midbrain dopaminergic progenitors, but their functions remain poorly understood in the adult brain.

We show here that sustained expression of Lmx1a and Lmx1b is required for the survival of adult midbrain dopaminergic neurons. Strikingly, inactivation of Lmx1a and Lmx1b recreates cellular features observed in Parkinson's disease. We found that Lmx1a and Lmx1b control expression of key genes involved in mitochondrial functions and their ablation results in impaired respiratory chain activity, increased oxidative stress and mitochondrial DNA damage. Lmx1a and Lmx1b deficiency caused axonal pathology characterized by alpha-synuclein positive inclusions, followed by a progressive loss of dopaminergic neurons. These results reveal the key role of these transcription factors beyond early developmental stages and provide mechanistic links between mitochondrial

dysfunctions, alpha-synuclein aggregation and survival of dopaminergic neurons.

Our results also suggest that disturbed function of LMX1A and LMX1B contributes to Parkinson's disease. Therefore, we are also testing the hypothesis that AAV-mediated overexpression of Lmx1a and/or Lmx1b in adult nigral dopaminergic neurons is neuroprotective in mouse models of Parkinson disease.

P02.05

Tools and technologies for the production of midbrain dopaminergic neurons from human pluripotent stem cells

Nicola J. Drummond¹, Maurice A., Canham², Yixi Chen², Karamjit Singh Dolt², David J. Harrison³, Ngoc-Nga Vinh³, John Morris⁴, Mariah J. Lelos³, Tilo Kunath²

¹ United Kingdom

² The University of Edinburgh, United Kingdom

³ Cardiff University, United Kingdom

⁴ Asymptote Ltd, United Kingdom

Parkinson's disease is characterised by the loss of midbrain dopaminergic (mDA) neurons. The loss of these neurons causes the motor symptoms associated with the disease. Therefore in the early 1990's the potential of cell replacement therapy was examined. Human fetal ventral midbrain from aborted fetuses was transplanted into Parkinson's disease patient's brains to replace the cells lost. There were mixed results but some patients did show improved dopaminergic function and reduced motor symptoms. However, there are problems with using fetal tissue, as there is a limit to the availability and logistical issues with getting the appropriate amount of tissue as well as the ethical issues. Therefore, an alternative source of cells is pluripotent stem cells (PSCs).

Here we show that human PSCs can be differentiated into a homogenous population of mDA precursors based on CORIN FACS and LMX1A/FOXA2/EN1 immunostaining. These precursors can be matured in vitro to give rise to cells expressing mature midbrain markers, including TH, Nurr1 and Pitx3. In addition, these mDA precursors are capable of survival, outgrowth and robust rescue in rat 6-OHDA model of Parkinson's disease.

If these cells are to be used in cell therapy a cryopreservation step is required to allow quality assurance to be performed. We investigated the cryopreservation of these midbrain dopaminergic precursors. We tested seven different cryopreservation media and different freezing rates to determine which gave the best post-thaw survival. We have identified the optimal cryopreservation conditions that minimally affect the ability of cells to differentiate in vitro.

We have also identified a novel secreted biomarker of mDA neurons that is predictive of cultures that are on the correct trajectory to produce homogenous cultures of mDA precursors. ELISA for this biomarker in the conditioned-medium within the first week of the PSC-to-mDA protocol gives quantitative read-outs of the efficiency of differentiation.

The cryopreservation methods and non-invasive real-time monitoring of mDA progenitor production will advance the efforts to bring a cell therapy for PD to the clinic.

P02.06

Accumulation of PARIS (ZNF746) plays a role in alpha-synuclein-induced neurodegeneration

Preston Ge, Saurav Brahmachari, Changqing Yuan, Senthilkumar Karuppagounder, Haisong Jiang, Yunjong Lee, Hanseok Ko, Valina Dawson, Ted Dawson

Institute for Cell Engineering, Johns Hopkins University School of Medicine, Baltimore, MD, USA

The development of effective neuroprotective therapies in Parkinson's disease (PD) has proven challenging due to the heterogeneity of PD disease processes and pathogenesis. Thus, identifying pathologic mediators that play a crucial role in both the familial and sporadic disease is essential for developing effective neuroprotective drugs. Recent work has demonstrated that accumulation of parkin substrate PARIS (ZNF746) is necessary for neurodegeneration following parkin inactivation. Here, we demonstrate that accumulation of PARIS (ZNF746) is also critical for neurodegeneration in two different α -synuclein mouse models of PD. We show that overexpression of human (h)A53T α -synuclein leads to parkin inactivation, and a corresponding accumulation of parkin substrates AIMP2 and PARIS. PGC-1 α , a target of PARIS transcriptional repression and promoter of mitochondrial biogenesis, is likewise downregulated. We further find that PARIS-KO substantially reduces accumulation of aggregated and phosphorylated α -synuclein, ameliorates motor deficits, and restores average lifespan by 50 percent in hA53T α -synuclein overexpressing mice. Finally, PARIS-KO protects against dopaminergic cell death in the SNpc caused by virally-induced overexpression of hA53T α -synuclein. Together, these data indicate that PARIS accumulation is an important pathological process in α -synuclein-induced neurodegeneration, and could prove to be an attractive therapeutic target in cases of PD characterized by accumulation of misfolded α -synuclein.

P02.07

E3 ligase GIP1 contributes to neurodegeneration in Parkinson's disease by regulating GCase protein turnover

Donghoon Kim, Sang Ho Kwon, Seulah Choi, Heehong Hwang, Olga Plentnikova, Juan Troncoso, Valina Dawson, Ted Dawson, Han Seok Ko

The Johns Hopkins University School of Medicine, Baltimore, MD, USA

Genetic and biochemical abnormalities of GCase are implicated in Gaucher's disease (GD) and α -synucleinopathies including Parkinson's disease (PD) and Dementia with Lewy bodies (DLB). The loss of catalytic activity of GCase due to its quantitative protein reduction are linked the neurodegeneration, but the regulator that connects the reduction in GCase protein levels and activity to the neurodegeneration is still unknown. Here, we show that E3 ligase GIP1, a new GCase interacting protein 1, interacts, ubiquitinates, and regulates the ubiquitin proteasomal degradation of GCase. Overexpression of GIP1 both in vitro and in vivo leads to reduction in protein levels and activity of GCase, a substantial accumulation of the α -synuclein proteins, which is reversed in knockdown condition of GIP1. In human postmortem PD brain and A53T α -synuclein transgenic mice and α -synuclein preformed fibrils (pffs) induced PD neurons and mouse, GIP1 is accumulated, GCase protein levels and activity is decreased, and α -synuclein accumulates. Strikingly, knockdown of GIP1 protects against neuronal toxicity due to transmission of LB-like pathology induced by α -synuclein pffs in neurons. Moreover, in vivo α -synuclein pffs inoculation recapitulates PD phenotypes such as loss of dopaminergic neurons and LB-like pathology, and motor deficits, notably which is rescued by increasing GCase protein levels and activity via knockdown of GIP1. Taken all together, ubiquitination of GCase by GIP1 is a major posttranslational modification that regulates GCase protein turnover and activity possibly contributing to pathogenesis of sporadic PD. The identification of E3 ligase GIP1 provides a molecular mechanism for the neurodegeneration due to GCase deficiency correlated with its quantitative protein reduction. Thus, boosting of GCase activity via blocking of GIP1 E3 ligase activity may be a neuroprotective strategy for treatment of PD.

P02.08

Modulation and mechanism for the neuroprotective effects of 17-beta-estradiol: relevance to depressive symptoms in Parkinson's disease.

Pardeep Kumar, Najma Baquer

Jawaharlal Nehru University, New Delhi, Delhi, India

Parkinson's disease (PD) is a neurodegenerative disease and a movement disorder characterized by loss of dopaminergic neurons in the substantia nigra causing dopamine depletion in the striatum. Aging in females and males is considered as the end of natural protection against age related diseases like osteoporosis, coronary heart disease, diabetes, Alzheimer's disease and Parkinson's disease. These changes increase during menopausal condition in females when the level of estradiol is decreased. The objective of this study was to investigate neuroprotective potential of 17 β estradiol (E2) treatment on the activities of acetylcholinesterase and monoamine oxidase, membrane fluidity, neurolipofuscin, glucose transporter-3 (GLUT3) expression and testing learning memory, occurring in brains of female rats of 3 months (young), 12 months (adult) and 24 months (old) age groups, and to see whether these changes are restored to normal levels after exogenous administration of 17 β estradiol (E2).

Methods: The aged rats (12 and 24 months old) (n=8 for each group) were given subcutaneous injection of 17 β estradiol (0.1 μ g/g body weight) daily for one month. Learning was tested in a Morris water maze with expression of synaptic molecules synaptophysin and synapsin I and ultrastructural studies of brain region by Magnetic resonance imaging.

Results: The results obtained in the present work revealed that normal aging was associated with significant increases in the activity of monoamine oxidase and neurolipofuscin accumulation in aging rats, and a decrease in acetylcholinesterase activity, membrane polarization and GLUT3 expression. E2 treatments improved attention and memory functions of the aging rats with enhanced the levels of synaptic molecules synaptophysin and synapsin I. Ultrastructural studies revealed that the changes were more pronounced in the aged treated rats in terms of presence of lipofuscin and lysosomal degradation. Our data showed that exogenous administration of E2 brought these changes to near normalcy in aging female rats.

Conclusions: It can therefore be concluded that E2's beneficial effects seemed to arise from its, antioxidant and antilipidperoxidative effects, implying a therapeutic potential drug for age related changes. Based on our studies and others, we conclude that E2 have therapeutic potential for adjunctive therapy along with dopamine replacement in PD.

P02.09

Genetic disruption of Nr4a1 (Nur77) in rat reduces dopamine cell loss in experimental Parkinson's disease

Daniel Levesque¹, Joanie Baillargeon², Brigitte Paquet², Jérôme Maheux¹, Michel St-Hilaire², Noémie Darlix¹, Catherine Lévesque¹, Claude Rouillard²

¹ Faculté de Pharmacie, Université de Montréal, Montréal, Qc, Canada

² Axe Neuroscience, Centre de recherche du CHU de Québec, Québec, Qc, Canada

Parkinson's disease (PD) is the second most frequent neurodegenerative disorder after Alzheimer's disease. The pathological hallmark of PD is a striking loss of dopamine (DA)-producing neurons in the substantia nigra. This produces DA depletion in the striatum and generates the characteristic motor symptoms of the disease. Although oxidative stress and

mitochondrial dysfunction have been implicated in DA cell loss, the mechanism underlying the death of nigral DA neurons in PD is not established. We have previously shown that Nr4a1 (Nur77), a transcription factor of the nuclear receptor family, is closely associated with DA neurotransmission in the mature brain. However, the role of Nur77 in PD remains elusive. In basal conditions, Nur77 expression is not expressed or barely detectable in the substantia nigra. We report here that intra-striatal or intra-medial forebrain bundle 6-hydroxydopamine (6-OHDA) neurotoxin injections in rat lead to a rapid and transient ectopic up-regulation of Nur77 in the substantia nigra. A concomitant up-regulation of Nur77, and tyrosine hydroxylase (TH) and Nurr1 down-regulations, was also observed in organotypic cultures of midbrain sections exposed to 6-OHDA. To investigate the role of Nur77 in DA cell loss following 6-OHDA exposure, we used a unique rat strain originating from a N-ethyl-N-nitrosourea (ENU) mutagenesis program performed by the rat Knockout Consortium Program of the Medical College of Wisconsin. This rat strain (Nr4a1m1Mcwi) bears a unique point mutation that generates a stop codon at amino acid residue 130, leading to the production of a non functional truncated protein. This rat strain displayed similar behavioral and neurochemical phenotypes as previously described for the Nur77 knockout mouse. Using stereological counts of TH immunoreactive cells, we determined that genetic disruption of Nur77 in rat reduced 6-OHDA-induced DA cell loss. A similar observation was made in Nur77 knockout mice exposed to MPTP. Collectively, these results suggest that Nur77 is involved in DA cell loss in these experimental PD models.

P02.10

The neuroprotective action of UBP310 is dependent upon multiple kainate receptor subunits

Sandy Stayte, Aimee Lowth, Peggy Rentsch, Bryce Vissel
Garvan Institute, Darlinghurst, NSW, Australia

Objective: Excitotoxicity mediated by glutamate receptors as a result of aberrant BG signalling has been proposed to contribute to loss of dopaminergic neurons within the substantia nigra (SN). Antagonists directed against NMDA and AMPA receptors showed early promise as targets for PD treatment but their efficacy has fallen short due to side effects resulting from actions in multiple brain regions. Unlike NMDA and AMPA receptors, the ionotropic kainate receptor (KAR) is not critical to most fast excitatory synaptic transmission and instead is primarily a modulating influence. Furthermore, the KAR subunits GluK1-GluK3 are expressed in multiple PD-associated brain regions, suggesting a KAR antagonist may be neuroprotective against loss of dopaminergic neurons.

Methods: 12 week old male C57BL/6 mice were implanted subcutaneously with osmotic micro-pumps, filled with 2.5µM UBP310 or vehicle control, and connected to an infusion cannula placed in the right lateral ventricle (AP -0.26, ML -1.0). Pumps were also implanted into GluK1^{-/-}, GluK2^{-/-}, or GluK3^{-/-} mice (and their wild type littermate controls). The following day mice were administered MPTP subcutaneously (4 x 20mg/kg, 2 h interval) and brain tissue harvested 7 days later. Tissue was analyzed for dopaminergic and total neuron populations by immunolabelling for tyrosine hydroxylase (TH) and NeuN, respectively, and quantified in the SN pars compacta via stereology. In addition, quantification of striatal dopamine transporter (DAT) expression was performed by western blot.

Results: MPTP-injected animals that received UBP310 had significantly higher numbers of TH-positive cells compared to those that received vehicle. In addition, UBP310 significantly increased the survival of NeuN-positive cells, indicating that neuroprotection was not simply due to changes in TH expression. Interestingly, UBP310 did not alter striatal DAT expression following MPTP lesioning, suggesting that neuroprotection provided by UBP310 is

localized to the SN. Furthermore GluK1^{-/-}, GluK2^{-/-}, and GluK3^{-/-} animals that received UBP310 had similar numbers of surviving dopaminergic and total neurons following MPTP compared to their wild type controls that also received UBP310. Our study not only demonstrates a role of KARs in the MPTP mouse model of PD, but suggests that the neuroprotective action of UBP310 is dependent upon multiple KAR subunits and furthermore indicates its potential as a novel therapeutic target in the treatment of PD.

BASIC SCIENCE: PROTEIN MISFOLDING AND HANDLING

P03.01

Exosome-associated oligomeric alpha-synuclein transmission in vitro

Marion Delenclos, Teodora Trendafilova, Simon Moussaud, Ann Marie Baine, Pamela McLean
Mayo Clinic, Jacksonville, FL, USA

Pathogenic misfolding of the presynaptic protein, alpha-synuclein (αsyn), and its subsequent aggregation and accumulation is fundamental to the disease process of Parkinson's disease (PD) and related synucleinopathies. Recent data suggest that extracellular αsyn aggregates are implicated in interneuronal propagation of the pathology and drive the progression of neurodegenerative disorders in a prion-like manner. However, little is known about how the secretion or internalization of αsyn occurs in this process. A body of evidence indicates that αsyn can be released from neuronal cells by nonconventional exocytosis involving extracellular vesicles such as exosomes. The objectives of the present study are to elucidate the role of exosomes in the transmission of oligomeric form of αsyn and shed new light on the pathway leading to their internalization into recipient cells. Exosomes were purified from conditioned media of stable cells secreting αsyn oligomers. A novel bimolecular protein complementation assay was used to detect exosomes containing αsyn oligomers. Recipient cells were treated with exosomes containing αsyn oligomers or with supernatant devoid of exosomes and internalization were monitored. As a result, we demonstrate that cell-derived exosome-associated αsyn oligomers can be efficiently internalized by recipient cells. Interestingly exosome-free αsyn oligomers isolated from conditioned medium were not internalized but remained bound to the extracellular surface. In the second part of this study we attempt to investigate the endocytic pathway(s) required for the exosomes uptake. We first tested the hypothesis that heparin sulfate proteoglycans (HSPGs) act as internalizing receptors for exosome-associated oligomeric αsyn. However, manipulation of HSPG using genetically modified recipient cells (CHO-M1, CHO-745) did not attenuate internalization of exosome-associated αsyn oligomers. In conclusion, it appears that exosomes associated αsyn are internalized via alternative endocytic pathways that yet need to be elucidated and we are currently studying the possible involvement of others of clathrin- and caveolin-dependent mechanisms.

P03.02

Molecular underpinnings of neurodegeneration in PD and DLB, two synucleinopathy disorders.

Paola Montenegro
Medicinal Chemistry and Molecular Pharmacology, Purdue University, West Lafayette, IN, USA

Synucleinopathies, including Parkinson's disease (PD) and dementia with Lewy bodies (DLB), are characterized by the presence in neurons of Lewy bodies enriched with aggregated forms of the protein alpha-synuclein (α Syn). Pathogenic mechanisms underlying synucleinopathies are poorly understood, and therapies only temporarily relieve symptoms without slowing the underlying neurodegeneration. We are using a two-pronged approach in order to identify: (i) potential neuroprotective genes with deregulated expression in DLB, and (ii) mechanisms by which α Syn elicits neurodegeneration in PD and DLB. First, we examined the expression levels of candidate neuroprotective genes, including DJ-1, PGC1- α , MsrA, and ATP13A2, in post-mortem brains from DLB patients and age-matched controls via qRT-PCR and western blot analysis tissue. Additional studies showed that α Syn neurotoxicity in primary midbrain cultures varies with the expression levels of each of these proteins. Current efforts are aimed at characterizing the expression levels of the same panel of proteins in post-mortem PD brains. Our results suggest that differential expression of proteins involved in cellular neuroprotective responses contributes to neurotoxicity in DLB. As a second approach, we are examining mechanisms by which α Syn elicits neurotoxicity in an in vivo PD model. We hypothesize that membrane-induced α Syn aggregation coupled with membrane permeabilization plays a key role in nigral dopaminergic cell death in PD. To address this hypothesis, we are characterizing α Syn variants with different abilities to undergo membrane-induced self-assembly and trigger vesicle disruption in terms of their effects on the behavioral and dopaminergic phenotypes of rats receiving intranigral injections of α Syn-encoding viral vectors. Key experimental parameters to be examined include motor function, striatal DA terminal density, nigral DA neuron viability, α Syn inclusion levels, and levels of membrane-bound α Syn oligomers. Collectively, our results will shed light on cellular pathways disrupted by aberrant gene expression in DLB and PD, and how these aberrant pathways could enhance α Syn neurotoxicity via mechanisms involving membrane-induced α Syn aggregation and vesicle disruption. In turn, these insights will set the stage for developing new therapeutic strategies to slow neurodegeneration in synucleinopathies.

P03.03

Untangling the role of tau and alpha synuclein in Parkinson's disease pathology

Romina Vuono, Antonina Kouli, Caroline Williams-Gray, Roger Barker

John van Geest Cambridge Centre for Brain Repair, Department of Clinical Neuroscience, University of Cambridge, Cambridge, United Kingdom

Protein aggregation as a result of misfolding is a common feature underlying neurodegenerative diseases. In Parkinson's disease (PD), research on protein misfolding and aggregation has raised a lot of interest following the association of alpha-synuclein gene mutations with familial forms of the disease and the identification of the protein as a major component of Lewy bodies and Lewy neurites, a pathological hallmark of PD.

Previous data from our group have shown that tau protein, which forms aggregates in the form of neurofibrillary tangles (NFTs) in a number of neurodegenerative diseases, might be also critical to the development of PD.

Prior to the formation of stable aggregates, like NFTs or Lewy bodies, intermediate species of the respective proteins appear. Recent studies have shown that there is evidence that these intermediate forms, called oligomers, are the true toxic species as they can spread through the brain, possibly seeding disease in a prion-like manner and as such may be the best target for anti-tau/anti alpha-synuclein therapies. However, the relevance of these

early aggregates of alpha synuclein and tau in human PD and how they interact with each other is still not clear.

We are therefore investigating the presence and distribution of oligomeric species of tau and alpha synuclein in post-mortem PD brains and their relationship with clinical progression of the disease during life. The characterization of such intermediate oligomeric toxic species in the PD brains will aid the development of better therapies and diagnostic markers.

P03.04

Inhibition of membrane-induced aSyn aggregation: a strategy to interfere with alpha-synuclein neurotoxicity in Parkinson's disease

Daniel Ysselstein¹, Isabel Costantino², Benjamin Dehay³, George McCabe⁴, Erwan Bezar³, Matthew Frosch², Julia George⁵, Jean-Christophe Rochet¹

¹ Purdue University, West Lafayette, IN, USA

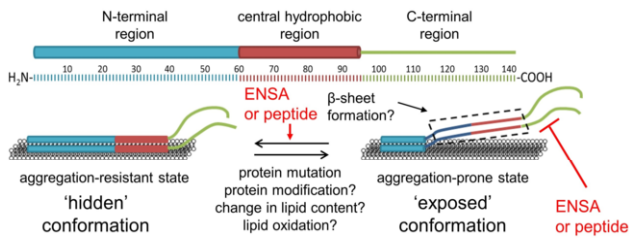
² Massachusetts General Hospital, Charlestown, MA, USA

³ University of Bordeaux, Bordeaux, France

⁴ Department of Statistics, Purdue University, West Lafayette, IN, USA

⁵ Queen Mary University of London, London, UK

Oligomerization of the presynaptic protein alpha-synuclein (aSyn) is thought to play a key role in the pathogenesis of Parkinson's disease (PD). aSyn exists in a number of conformations, including a membrane-bound state likely involved in regulating synaptic vesicle trafficking. aSyn interacts with anionic phospholipid vesicles by forming an amphipathic α -helix of various lengths. We hypothesize that disruption of interactions between aSyn and phospholipid membranes leads to a shift to a short-helix, lipid-bound form, which is more susceptible to the formation of toxic aSyn oligomers due to exposure of the protein's central hydrophobic region. Therefore, stabilization of the long-helix form of lipid-bound aSyn should prevent membrane-induced aggregation and alleviate aSyn neurotoxicity. We characterized two aSyn variants with disrupted aSyn-membrane interactions, A30P and G51D, in terms of their aggregation on synthetic phospholipid vesicles and their ability to permeabilize the membrane. aSyn neurotoxicity was assessed via adenoviral-mediated expression in a primary midbrain culture model. Endosulfine alpha (ENSA), a protein that interacts selectively with membrane-bound aSyn, and a series of peptides identified as interactors of lipid-bound aSyn via phage display screening were characterized in terms of their effects on membrane-induced aSyn aggregation, aSyn-mediated membrane permeabilization, and aSyn neurotoxicity. We found that A30P and G51D had an increased ability to form SDS-resistant aggregates at the membrane surface and to elicit neurotoxicity than WT aSyn, and both triggered the disruption of dye-loaded vesicles under conditions identical to those that promoted membrane-induced aggregation. WT ENSA, but not the non-aSyn-binding S109E variant, interfered with aSyn self-assembly at the membrane surface, vesicle disruption, and aSyn neurotoxicity. Intriguingly, ENSA was found to be down-regulated in the frontal cortex of patients with dementia with Lewy bodies versus non-diseased individuals. Finally, peptides that bound lipid-associated aSyn were found to inhibit membrane-induced aggregation and vesicle disruption, and peptidomimetic derivatives alleviated aSyn neurotoxicity in primary midbrain cultures. These results strongly support the idea that membrane-induced aSyn aggregation plays a critical role in aSyn neurotoxicity, and they suggest that targeting this process is a viable therapeutic strategy for PD and other synucleinopathy disorders.



BASIC SCIENCE: MITOCHONDRIA, OXIDATIVE STRESS, INFLAMMATION, PATHOGEN

P04.01

Glatiramer acetate (Copaxone) causes restoration of the nigrostriatal pathway in a progressive MPTP mouse model of Parkinson's disease.

Madeline Churchill¹, Charles Meshul²

¹ Portland VA Medical Center, Portland, OR, USA

² Portland VA Medical Center and Oregon Health and Sciences University, Portland, OR, USA

Patients with Parkinson's disease (PD) have been shown to have an increased inflammatory response as the disease progresses (Greer et al., 2008). This inflammatory response has an associated activation of the pro-inflammatory m1 subtypes of microglia, which are polarized by the pro-inflammatory interleukins secreted by macrophages. Just as there are two subtypes of macrophages, there are also m2 types of microglia that act as an anti-inflammatory which secrete growth and regenerative factors. A shift from the pro-inflammatory microglia (m1) to the anti-inflammatory (m2) subtypes could be therapeutically relevant in PD by allowing the m2 subtypes to promote recovery of dopamine (DA) neurons and terminals. Glatiramer acetate (GA) (Copaxone), a current therapy for MS, is a known microglial activator that polarizes the m1 into m2 subtypes. To test GA in a more clinically relevant neurorestoration model, we utilized a mouse model of PD in which the neurotoxin, MPTP, is injected over a 4-wk time period, resulting in a 50-70% loss of striatal DA (Goldberg et al., 2011). GA treatment (1.5mg/kg or 3.5 mg/kg i.p) was initiated following (i.e. restoration) 4 weeks of MPTP administration. Grip test analysis revealed that the MPTP only group had a 50% increase in grip strength vs the vehicle group ($p < 0.0001$). This was attenuated in the MPTP+GA group, resulting in only a 12% increase in grip strength vs the vehicle group ($p = 0.0004$). Optical density and protein analysis for tyrosine hydroxylase (TH) in both the striatum and substantia nigra (SN) revealed a 65% loss of TH in the MPTP only vs the vehicle group ($p < 0.0001^*$). There was only a 13% loss of TH in the MPTP+GA group vs the vehicle despite 4 weeks of previous MPTP administration. ($p = 0.0191^*$). IBA1, a structural protein of microglia, was increased in the SN by 163% in the MPTP only vs the vehicle group ($p < 0.0001^*$). This increase was reversed in the MPTP+GA groups and was 28% lower vs the vehicle group ($p = 0.4634$). Microglial markers typifying the two subtypes, nitric oxide synthase 2 and arginase 1, showed no changes compared to either the vehicle or MPTP groups. Our data suggests that GA treatment caused a recovery of TH within the remaining DA neurons in the SN, resulting in improved motor function and increased TH expression within the striatum. Interestingly, the microglial analysis suggests that GA is exerting the recovery through down-regulation of microglia rather than polarizing the m1 subtypes into m2.

P04.02

Neuroinflammation parallels α -synuclein accumulation and precedes nigral degeneration induced by intrastriatal injection of preformed α -synuclein fibrils

Megan Duffy¹, Timothy Collier¹, Katrina Paumier¹, Kelvin Luk², D. Luke Fischer¹, Nicole Polinski³, Christopher Kemp¹, Caryl Sortwell¹

¹ Department of Translational Science and Molecular Medicine, Michigan State University, Grand Rapids, Michigan, USA

² University of Pennsylvania, Philadelphia, PA, USA

³ USA

Neuroinflammatory markers are observed in post mortem Parkinson's disease (PD) brains, and longitudinal PET imaging reveals early microglial activation in the basal ganglia of PD patients. α -synuclein (α -syn) activates microglia in vitro, suggesting that α -syn may participate in PD neuroinflammation. However, it remains unclear whether inflammation contributes to nigral degeneration or is merely a secondary consequence of degenerating neurons. Historically, one difficulty in delineating this sequence of events is the lack of an animal model that displays both α -syn aggregation and nigral degeneration in a protracted time course. Our lab recently characterized the accumulation of phosphorylated α -syn (pSyn) intraneuronal inclusions and bilateral nigrostriatal degeneration following intrastriatal injection of mouse α -syn preformed fibrils (PFFs) into rats. α -syn PFFs are taken up by striatal terminals and seed endogenous α -syn conversion into a pathological hyperphosphorylated form resulting in widespread Lewy-body like pathology and ~40% substantia nigra (SN) dopamine neuron degeneration over 6 months. To examine the neuroinflammatory signature in this model male Fischer344 rats received unilateral intrastriatal injections of mouse α -syn PFFs or saline. Cohorts of rats (total $n = 96$) were euthanized at various times post-injection (0.5, 0.75, 1, 2, 3, 4, 5 & 6 months). Outcome measures at each time point included quantification of tyrosine hydroxylase positive (TH+) neurons, phosphorylated α -syn (pSYN+) aggregates, microglial density and major histocompatibility complex-II antigen-presenting microglia (MHC-II+) in the SN. Both intraneuronal pSYN+ inclusions and MHC-II+ microglia peaked between 1-2 months following PFF injection, and decreased over time in association with SN dopamine neuron loss. By month 4 significantly fewer MHC-II+ microglia were present in the ipsilateral SN ($p < 0.05$). Few to no MHC-II+ microglia were observed in the contralateral SN at any time point or in the ipsilateral SN of saline-injected control rats at 2 months and beyond. Additional analysis of MHC-II+ microglia in the striatum (ST) and microglial density and inflammatory cytokines in both the ST and SN are ongoing. These initial results demonstrate that neuroinflammation precedes the loss of SN dopamine neurons induced by α -syn aggregation and suggests that α -syn-mediated neuroinflammation may contribute to the degenerative process.

P04.03

Biochemical mechanisms of DJ-1-mediated neuroprotection in Parkinson's disease

Sayan Dutta¹, Daniel Ysselstein¹, Josephat M. Asiago¹, John D.

Hulleman², Lake N. Paul¹, Jean-Christophe Rochet¹

¹ Purdue University, West Lafayette, Indiana, USA

² UT Southwestern, Dallas, Texas, USA

Parkinson's disease (PD) is a neurodegenerative disorder that involves a loss of dopaminergic neurons from the substantia nigra. Evidence suggests that potentially toxic oligomers ('protofibrils') formed by the presynaptic protein α -synuclein (aSyn) play a central role in PD pathogenesis. Mutations in the gene encoding the homodimeric protein DJ-1 have been identified in patients with

familial PD, and wild-type (WT) DJ-1 undergoes a loss of function as a result of oxidative damage in sporadic PD. A variant of DJ-1 (referred to as the '2O' form) in which residue C106 is oxidized to the sulfinic acid, inhibits aSyn fibrillization via a molecular chaperone function, whereas a truncated variant lacking the C-terminal 15 residues ('DJ-1-Δ15C') exhibits proteolytic activity. This proteolytic activity is similar to that of PH1704, a hexameric thermophilic cysteine protease of the same family. A central objective of our research program is to understand the underlying biochemistry of how DJ-1 suppresses neurodegeneration in PD, in order to stimulate the development of new therapeutic strategies. Using a combination of analytical ultracentrifugation, gel filtration, and SDS-PAGE analysis, we have found that DJ-1 interacts with potentially neurotoxic aSyn protofibrils. Moreover, a DJ-1 variant in which cysteine 106 is substituted with alanine shows a significant reduction in the interaction with aSyn protofibrils. This result suggests that the oxidation of DJ-1 at cysteine 106 is involved in modulating the protein's affinity for oligomeric aSyn. In additional studies, we performed a computer modelling study of DJ-1Δ15C to identify the mutant protein's predicted quaternary structure. The results showed that (i) DJ-1Δ15C has the ability to form a hexamer stabilized by two distinct inter-subunit interfaces, and (ii) hexamer formation could potentially lead to the formation of a catalytic triad involving residues C106 and H126 from one subunit and E84 from another subunit. Current efforts are focused on determining experimentally whether DJ-1Δ15C can function as a cysteine protease involved in the degradation of aSyn aggregates, and whether it adopts a hexameric structure similar to that of PH1704 (and in contrast to homodimeric, full-length DJ-1). The insights gained from this project are expected to advance our understanding of the molecular mechanisms behind PD and thus lead to the development of disease-modifying treatments.

P04.05

Vascular function in Parkinson's Disease patients

Brandon Pollock, Keith Burns, Kylene Boka, Angela Ridgel, John McDaniel
Kent State University, Kent, Ohio, USA

Background: Oxidative stress likely contributes to the cascade leading to dopamine cell degeneration in Parkinson's disease (PD). It is possible that the exercise intolerance associated with PD partially results from oxidative stress induced vascular dysfunction and subsequent poor blood flow to the exercising muscles.

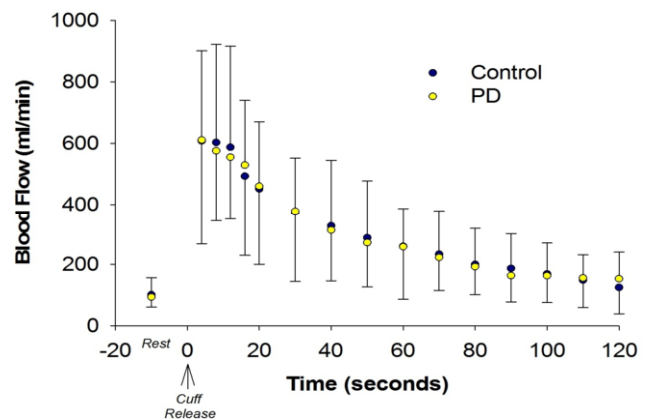
Purpose: The purpose of this research was to compare vascular function, using FMD and handgrip exercise, between those with PD and healthy age and gender matched individuals.

Methods: Ten individuals diagnosed with PD (66.8±6.1 years) and sixteen healthy controls (68.8±7.6 years) were recruited for this investigation. A Doppler ultrasound system was used to measure participant's brachial artery diameter and blood velocity at baseline and for the first 2 minutes immediately following 5 minutes of forearm blood flow occlusion (%FMD was calculated as: %FMD=(peak diameter – baseline diameter)/baseline diameter). After a 20 minute rest period, participants underwent a progressive handgrip protocol in which they were asked to squeeze an isometric handgrip dynamometer for four 3-minute intervals (30 N, 60 N, 90 N, and 120 N) at a rate of 60 contractions per minute with 2 minute rest periods between intervals. Blood pressure, brachial artery diameter and blood velocity were measured during the last minute of each interval.

Results: Independent samples t-test revealed no significant difference (p=0.55) in %FMD between PD (7.66±3.29%) and control (8.61±4.27%). When %FMD was expressed relative to shear, there was still no significant difference (p=0.81) observed between PD (.0002±.00008) and control (.0002±.00012). Independent samples t-

test showed no difference in the slope of average force produced per state to blood flow (p=0.349) and no difference in slope of percent change in shear to percent change in diameter dilation (p=0.404) across all four intensities between the groups.

Conclusions: PD patients did not appear to exhibit a reduced %FMD compared to healthy controls and there was also no difference when expressed relative to the stimulus of dilation, shear. Furthermore, no differences in vascular response during progressive handgrip exercise were observed between PD patients and healthy controls. These data indicate that vascular dysfunction may not be present in PD beyond what is expected with normal aging, and exercise intolerance associated with PD may not result from oxidative stress induced vascular dysfunction.



P04.06

Influenza vaccine or Oseltamivir (Tamiflu®) can protect against microglial activation and a subsequent increase in oxidative stress susceptibility of dopaminergic neurons in the substantia nigra following infection with the non-neurotropic H1N1 influenza virus.

Shankar Sadasivan, Bridgett Sharp, Stacey Schultz-Cherry, Richard Smeyne
St. Jude Children's Research Hospital, Memphis, TN, USA

According to the CDC (<http://www.cdc.gov/flu/about/qa/disease.htm>), between 5 and 20% of the US population contracts influenza each year, with H1N1 being the predominant flu strain in 2009 and 2014. Previous published research performed in our lab have shown that H1N1 is not neurotropic (does not enter the CNS, PNS or ENS). Despite this lack of neurotropism, H1N1 infection does induce microglial activation in the brain, including the substantia nigra. To determine if this inflammatory response had any downstream effects, we performed a stereological analysis of SNpc dopaminergic neurons. We found that H1N1 infection, alone, did not affect the number of SNpc dopaminergic neurons. Given that the majority of Parkinson's disease diagnoses have no identified etiology, we examined if prior infection with H1N1 influenza could increase the susceptibility of these neurons to a second insult (the multiple hit hypothesis). Mice were infected with H1N1 influenza and allowed to recover for 30 days. After this recovery period, they were injected with 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), an agent shown to cause parkinsonism in man by blockade of Complex I of the Electron transport chain. Mice treated with MPTP had a significantly greater loss of SNpc DA neurons that mice administered saline followed by MPTP. This suggests that even though H1N1 did not, in and of itself, induce dopaminergic neuron loss, prior infection with this virus did make the SNpc dopaminergic neurons more vulnerable to a second insult. We then treated mice

with monovalent H1N1 vaccine or Tamiflu®. We find that both vaccine or Tamiflu® prior to H1N1 protected against H1N1-induced neuroinflammation, and the Tamiflu® protected against the synergistic effects of H1N1 and MPTP. Studies are underway to examine if H1N1 vaccine can also protect against the synergistic effects of viral infection and oxidative stress (MPTP). Results of this study supports the "multiple-hit" hypothesis for Parkinson's disease and also provides a public health notice for prophylactic administration of seasonal influenza vaccine or Tamiflu® treatment of influenza infection following its diagnosis.

P04.07

Do PINK1 and Parkin influence the accumulation of mitochondrial DNA mutations in somatic tissues?

Colby Samstag¹, Jake Hoekstra¹, Scott Kennedy¹, Richard Youle², Leo Pallanck¹

¹ University of Washington, Seattle, WA, USA

² NIH, Bethesda, Maryland, USA

The accumulation of somatic mitochondrial DNA (mtDNA) mutations is implicated in aging and in common diseases of the elderly, including the neurodegenerative disease Parkinson's Disease (PD). There are typically thousands of copies of the mitochondrial genome in a single cell; when mtDNA mutations occur, they frequently share residence with wild-type mtDNA, a condition known as heteroplasmy. High levels of heteroplasmy have been correlated with the severity of maternally-inherited mitochondrial diseases as well as PD, yet we know little about the factors that influence mtDNA mutation frequency or the emergence of their associated phenotypes. Further, our knowledge of the pathways that influence the frequency and pathogenesis of mtDNA mutations has been hampered by technical limitations in DNA sequencing technologies and the lack of a genetically tractable model system. To address these matters, we created a mtDNA mutator *Drosophila* strain expressing a proofreading-deficient mitochondrial DNA polymerase. Mutator flies have a dramatically increased somatic mtDNA mutation frequency that correlates with the dosage of the proofreading-deficient polymerase. Mutator flies also exhibit characteristic hallmarks of PD, including mitochondrial dysfunction, shortened lifespan, a progressive locomotor deficit and dopaminergic neuron loss. To analyze the mutational spectrum of mutator flies, we employed Duplex Sequencing, a novel next-generation sequencing approach capable of accurately detecting a single mutation among $>10^7$ sequenced bases. Sequence analysis revealed that mutator flies exhibit an elevated ratio of nonsynonymous mtDNA mutations relative to synonymous mutations, greatly exceeding expectations under conditions of neutrality and suggesting positive selection for particular mtDNA variants. To investigate the nature of these variants, we analyzed evolutionary conservation across the mitochondrial genome. We discovered that mutator flies bear an increased prevalence of mutations in sites that are highly conserved, consistent with positive selection acting to preserve non-neutral variants. We now present data on the mutation frequency and signatures of selection in mutator flies following genetic perturbations of critical mitochondrial quality control genes, including PINK1 and Parkin. This work will provide critical insight into the mechanisms by which harmful mtDNA mutations rise in abundance and cause disease.

P04.08

Antiparkinson and antioxidant effect of phenylpyrazolinyl substituted heterosteroids in LPS induced neuroinflammation model of rat

Ranjit Singh, Ranju Bansal

Panjab University, Chandigarh, India

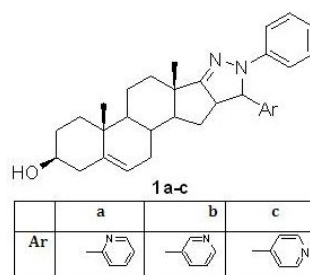
Objective: Neuroactive steroids include endogenous and synthetic steroidal compounds able to control the brain damage and promote the repair process such as inhibition of neuronal death, promotion of neurogenesis and myelination and reduction of neuroinflammation. The uncontrolled neuroinflammation contributes associated with several CNS disorders like Alzheimer's disease, Parkinson's disease. This study is aimed at design and synthesis of new therapeutically useful steroidal neuroprotective agents against neuroinflammation that involved in the progression of neurodegenerative disorders such as Parkinson's Disease, Alzheimer's Disease and Multiple Sclerosis. The new androstane derivative has been synthesized by fusing phenylpyrazoline moiety at 17 and 16 positions of steroid nucleus. These D ring modified heterosteroids were then explored for their antiparkinson and antioxidant effect.

Background: Parkinson's Disease (PD) is a progressive, disabling neurodegenerative disorder characterized by an insidious onset with variable expression of motor, vegetative, sensory and psychopathological symptoms. Recent literature reports indicated that neuroinflammation cause dopaminergic neuron death that involved in progression of PD.

Methods: Aldol condensation of dehydroepiandrosterone with requisite pyridine carboxaldehyde in basic medium gave corresponding 16-arylidene steroidal derivatives, treatment of which with phenyl hydrazine in refluxing glacial acetic acid afforded phenylpyrazoline substituted steroid 1a-c. Rats (male wistar) were anesthetized with thiopental sodium (45 mg/kg, i.p.), stereotaxic surgery has been done and intranigral injection of LPS (10µg in 2µl) was infused into left substantia nigra using the Hamilton microsyringe. Heterosteroids were evaluated against behavioral alternations using actophotometer, elevated plus maze at dose 2mg/kg after 7th, 14th and 21st day of LPS administration. Biochemical estimation of different makers for neuroinflammation, cholinergic activity and oxidative stress has also been carried out.

Results: The synthetic heterosteroids were characterized using IR, ¹H NMR. All heterosteroids 1a-c exhibited potent activity against PD. The pyridin-4-yl group substituted steroid 1c displayed activity comparable to that of standards dexamethasone and celecoxib.

Conclusion: Phenylpyrazolinyl substituted heterosteroids exhibit potent anti-neuroinflammatory activity and could be useful for the prevention of PD and oxidative stress.



P04.09

Identification of novel biologically active DJ-1 small molecule modulators with activity in cellular and in vivo models of oxidative stress relevant to Parkinson's disease

Gergely Toth¹, Thomas Neumann², Carlos Velez-Pardo³, Marlene Jimenez-Del-Rio³, Miguel Mendivil-Perez³, Manuela Kárpáti¹, Balázs Herberth¹, Vartika Mishra⁴, Jagadish Hindupur⁴, Max Zhu¹, András Czajlik⁵, Anasztázia Hetényi⁶, Róbert Kiss⁵, Balázs Főrizs¹, Lilla Tóth¹, Tamás Martinek⁷, Jean-Christophe Rochet⁴

¹ Cantabio Pharmaceuticals, Sunnyvale, California, USA

² Novalix SAS, France

³ Grupo de Neurociencias, Instituto de Investigaciones Médicas, Facultad de Medicina, Universidad de Antioquia, Medellín, Colombia

⁴ Department of Medicinal Chemistry and Molecular Pharmacology, Purdue University, West Lafayette, USA

⁵ MTA-TTK-NAP B – Drug Discovery Research Group – Neurodegenerative Diseases, Institute of Organic Chemistry, Research Center for Natural Sciences, Hungarian Academy of Sciences, Budapest, Hungary

⁶ Department of Medical Chemistry, University of Szeged, Szeged, Hungary

⁷ SZTE-MTA Lendület Foldamer Research Group, Institute of Pharmaceutical Analysis, University of Szeged, Szeged, Hungary

Familial mutations in the DJ-1 gene have been linked to the early-onset of Parkinson's disease (PD). Moreover, results from studies of neurotoxicant- and alpha synuclein-based in vivo PD models suggest a role for DJ-1 in sporadic PD. Loss of DJ-1 native tertiary structure and consequently its functions due to familial mutations and/or over-oxidation of the protein during disease conditions are linked to the onset and progression of PD. Herein, we describe a drug discovery approach to identify small molecule therapeutic candidates for the treatment of PD by targeting DJ-1. Our approach is based on the concept that specific binding of small molecules to wild-type native dimeric DJ-1 can result in enhancing DJ-1 function under oxidative stress conditions in PD. Our drug discovery approach involved the use of a high-throughput chemical microarray surface plasmon resonance imaging method to screen over 110,000 immobilized drug-like fragments and lead-like compounds to detect the binding between small molecules and the DJ-1 protein. This screen identified a novel set of drug-like fragments and lead-like compounds that bound to DJ-1 protein. We report herein on one selected hit compound, and its analogues, which had substantial biological activity in cellular and in vivo models of oxidative stress. The hit compound, and selected analogues, reduced neuroblastoma cell toxicity and dopaminergic neuronal loss mediated by paraquat treatment. The selected hit compound also rescued rotenone-treated neuronal differentiated mesenchymal stem cells from toxicity, reactive oxygen species accumulation, mitochondrial membrane potential dysfunction, and caspase-3 activation. Moreover, the hit compound increased significantly the life span of *Drosophila melanogaster* treated with paraquat, an in vivo oxidative stress model. 2D HSQC NMR was applied to identify the binding site of the hit compound on DJ-1. On the basis of this, structure based docking and molecular dynamics simulations determined a 3D model of the DJ-1 – hit compound interaction. These results suggest that CB-B1 regulates DJ-1 activity under oxidative stress conditions, thereby enhancing DJ-1 cytoprotective function. In conclusion, our studies show that the DJ-1 protein can be targeted by a variety of drug-like small molecules, and that the hit compound is a novel biologically active DJ-1 modulator that serves as a promising drug candidate for further optimization and development for the treatment of PD.

P04.10

Inhibition of the Parkin-antagonizing deubiquitinase USP8 corrects a *Drosophila* PINK1 mutant model of Parkinson's disease

Sophia von Stockum¹, Alvaro Sanchez-Martinez², Alice Nardin³, Joy Chakraborty³, Emilie Schrepfer⁴, Vanni Ferrari³, Caterina Da Rè⁵, Paola Cusumano⁵, Rodolfo Costa⁵, Luigi Bubacco³, Alexander J Whitworth², Luca Scorrano⁴, Elena Ziviani¹

¹ Department of Biology, University of Padova; Istituto IRCCS San Camillo, Lido di Venezia, Venezia, Italy

² MRC Centre for Developmental and Biomedical Genetics, Sheffield; Department of Biomedical Sciences, University of Sheffield, Sheffield, United Kingdom

³ Department of Biology, University of Padova, Padova, Italy

⁴ Department of Biology, University of Padova; Dulbecco-Telethon Institute, Venetian Institute of Molecular Medicine, Italy

⁵ Department of Biology, University of Padova; Neurogenetics and Behavior of *Drosophila* Lab, Department of Biology, University of Padova, Italy

During mitophagy, impaired in genetic Parkinson's disease (PD), the kinase PINK1 recruits the E3 ubiquitin ligase Parkin to damaged mitochondria. Increased Parkin levels correct PINK1-deficient *Drosophila melanogaster* PD models, suggesting that targeting the Parkin-opposing deubiquitination enzymes (DUBs) can yield the same result. Here we show that silencing and pharmacological inhibition of the Parkin-opposing DUB USP8 rescues a *D. melanogaster* PD model. A targeted RNA interference screening for DUBs antagonizing Parkin ubiquitination of its key mitochondrial target Mitofusin (MFN) identified five DUBs among which USP8 caught our attention. Biochemical and functional analyses indicated that USP8 impinges on the PINK1-Parkin pathway to regulate mitophagy. In vivo, silencing or pharmacological inhibition of USP8 corrected mitochondrial dysfunction, dopaminergic neuron loss and locomotor performance in a *D. melanogaster* PINK1 mutant model of PD. Our data identified a novel therapeutic target antagonizing mitochondrial dysfunction and clinical symptoms in a model of PD.

BASIC SCIENCE: PATHOLOGY

P05.01

Active release of dyskinetic energy through ancient and newer creative expressions

Frances Evans

B.C. Parkinsons Society, Canada

The one word I think that we can all relate to, as PwPs is lopsided. It is not a fancy, scientific or unusual word but it describes so many aspects of how we live. The inequality of strength, co-ordination and balance is more than an impairment! In my experience? A random, hurtful insult as I always enjoyed my physical self. Swimming and kayaking and motorcycling were my favorites...all fluid movement! 3 major events enlarged my perspective and contributed to my fascination with Anatomy: having children, being struck down on a sidewalk by a moving vehicle and completing training and teaching Power Vinyasa, it is the WORKING breath with movement form of the Practice. On the flipside, since my Dx 4 years ago and lately the stiffness and dyskinesia that follows, my physical strength waxes and wanes, and I've discovered a new surrendering style of movement and joy! More capable for "off" times! Forgiving, looser, childlike and relaxed. Mostly standing work for our motor functions and some silly and sad movements for our egos... some free but guided dance, breathwork, and self love for our souls.

BASIC SCIENCE: ANIMAL & CELLULAR MODELS OF PARKINSON'S DISEASE & PARKINSONISMS

P06.01

Intranasal stem cells treatment for Parkinson's disease model in mice.

Ahmed Abdalla, Mahmoud Imam, Mahmoud Sobh, Dina Sabry Mansoura, Dakahlyia, Egypt

Objective: We are evaluating intranasal delivery as an alternative route for cell based therapy administration in Parkinson's disease (PD).

Background: Parkinson's disease is the second commonest neurodegenerative disease. It affects locomotor system leading to a final severe disability through degeneration of dopaminergic neurons. Despite several therapeutic approaches, none proved its effectiveness. However, Cell therapy is a promising therapeutic measure. Deciding the ideal route for delivery to the brain is challenging. The use of intranasal (IN) route has been advocated for delivering different therapies inside the brain. In our work, we tested this route for administration of mesenchymal stem cells (MSCs) in mouse model of PD.

Methods: The PD model was developed in C57bl/6mice using rotenone administered intraperitoneally for 60 consecutive days. MSCs were isolated from mononuclear cell fraction of pooled bone marrow from C57bl/6 mice and incubated with MPIO (Micron sized iron oxide Particles). For intranasal application, we used a 20µl of 5x10⁵ cells suspension. Mice were tested neuro-behaviorally. After sacrifice, brain sections were stained with Prussian blue to detect MPIO-labeled MSCs. Immuno-histochemical evaluation was done to detect TH (Tyrosine Hydroxylase) antibodies in Corpus striatum and Dopaminergic neurons in substantia nigra pars compacta (SNpc).

Results: Neuro-behavioral assessment revealed progressive deterioration in the locomotor functions of the rotenone group however the MSCs group showed improvement. Histopathological evaluation of treated animals' brain sections revealed successful delivery evidenced by positive staining by Prussian blue. Rotenone treatment led to significant decrease in dopaminergic neurons number in SNpc, this was paralleled by a similar decrease in corpus striatum fiber density. Meanwhile, in the animals received IN stem cells, the degeneration caused by rotenone treatment was significantly counteracted.

Conclusions: In this study, we validate IN delivery of stem cells as a safe, easy and cheap alternative route for stem cell treatment in neurodegenerative disorders

P06.02

Characterization of dopaminergic neurodegeneration following very low doses of MPTP

Gelareh Alam, Jason R Richardson, Muhammad Hossain USA

Background: MPTP is a prototypical neurotoxicant used to study the mechanism(s) of Parkinson's disease (PD) pathogenesis. High doses of MPTP result in dopamine (DA) cell loss in the Substantia nigra (SN) and striatal DA depletion. Although multiple high doses (10–30 mg/kg) of MPTP are generally required to cause dopaminergic cell loss, Dovero and co-workers (2016) recently reported that a single administration of very low doses of MPTP (0.1–1 mg/kg) caused a loss of tyrosine hydroxylase positive (TH+) cells in young OF1 mice.

Methods: We sought to confirm and extend the Dovero study using young male C57BL/6J mice. Mice were injected once with saline or MPTP (0.1, 2 or 20 mg/kg, i.p) and sacrificed 7 days following dosing for determination of striatal DA neurochemistry and stereological counts of DA neurons in the SN.

Results: Significant striatal DA depletion was observed only in the group treated with 20mg/kg of MPTP. Levels of DA terminal markers, including the DA transporter (DAT), vesicular monoamine transporter (VMAT2) and TH were measured using western blot. A significant reduction in the expression of striatal DAT and TH was observed only in the group treated with 20 mg/kg MPTP. Unbiased stereological counts of TH+ cells in the SN showed a significant reduction in all the groups treated with MPTP compared to controls. Loss of neurons was confirmed by observation of a similar loss of NeuN+ neurons. The loss of TH+ neurons followed a typical dose-response curve rather than the inverted U-shaped dose-response curve observed in the Dovero study.

Conclusions: These data demonstrate that higher doses of MPTP (at least 2 mg/kg) are needed to alter striatal neurochemistry. However, loss of dopaminergic cells in the SN was observed in a dose-related manner in all the groups treated with MPTP. Although we did not replicate the U-shaped dose-response curve from the Dovero study, these data do demonstrate that very low doses of MPTP can kill DA neurons. Further, the OF1 mice used in the Dovero study may represent a particularly susceptible genetic background that could be used to identify genes contributing to sensitivity to MPTP-induced dopaminergic degeneration.

Supported in part by R01ES021800 and Michael J Fox Foundation

P06.03

Whole transcriptome analysis in the striatum and substantia nigra in mice with MPTP-induced earliest stages of the pathogenesis of Parkinson's disease

Anelya Alieva¹, Anna Kolacheva², Elena Filatova¹, Margarita Rudenok¹, Petr Slominsky¹, Michael Ugrumov², Maria Shadrina¹

¹ Institute of Molecular Genetics of Russian Academy of Sciences, Moscow, Russia

² Koltzov Institute of Developmental Biology of Russian Academy of Sciences, Moscow, Russia

To date it is clear that genetic factors play an important role in the pathogenesis of Parkinson's disease (PD). However, processes that trigger the development of PD remain unknown in the connection with the above. Whole transcriptome analysis of striatum and substantia nigra at the earliest stages of the PD pathogenesis was performed. Models of the earliest presymptomatic stages of PD were used in this study (decapitation 6 and 24 hours after the four-time MPTP administration).

As a result, it was revealed, that terminals of neurons located in the striatum are the first to be involved in the earliest stages of PD pathogenesis, because more genes change their expression in the striatum than in the substantia nigra, when compared to the control. Thus, expression of 77 and 212 gene was altered in the striatum (6 and 24 hours after MPTP administration, respectively), while expression changes of 26 and 22 genes were revealed in the substantia nigra (6 and 24 hours after MPTP administration respectively).

A statistical overrepresentation test by PANTHER resource was carried out for genes that changed their expression in the striatum. Three functional groups of genes associated with apoptosis, morphogenesis processes and the functioning of the immune system were revealed 6 hours after MPTP injections. Several functional groups, including the most of the genes that are associated with transport of substances, including vesicular transport, processes of the immune system and proteolysis were revealed 24 hours after MPTP administration.

No significant functional groups in substantia nigra were discovered. However, the most interesting differentially expressed genes that were identified in the substantia nigra were the following:

- 6 hours after administration of MPTP: Anxa2, Anxa3, Gabarap and Chac1.
- 24 hours after administration of MPTP: Ndufa9, Surf1, Laptm4a and Psma5.

Thus, the processes related to the functioning of the immune system and mitochondria, apoptosis, proteolysis, and vesicular transport are among the first to be activated at the earliest stages of pathogenesis of PD.

The work was supported by the Russian Foundation for Basic Research (Projects no. 15-04-05606 and 16-34-00200).

P06.04

Low-dose sub-anesthetic ketamine infusions reduce the development of L-DOPA-induced dyskinesias in a preclinical model.

Mitchell Bartlett¹, Mitchell Zehri², Andrew Flores³, Scott Sherman², Torsten Falk⁴

¹ Department of Neurology, University of Arizona College of Medicine; Medical Pharmacology Graduate Program, University of Arizona College of Medicine, Tucson, AZ, USA

² Department of Neurology, University of Arizona College of Medicine, Tucson, AZ, USA

³ Department of Neurology, University of Arizona College of Medicine; Graduate Interdisciplinary Program in Physiological Sciences, University of Arizona, Tucson, AZ, USA

⁴ Department of Neurology and Department of Pharmacology, University of Arizona College of Medicine; Graduate Interdisciplinary Program in Physiological Sciences, University of Arizona, Tucson, AZ, USA

Repurposing drugs proven safe in humans has the potential to offer new therapies in a fraction of the time required to develop new treatments. Ketamine is FDA-approved with a known safety profile. Low-dose, sub-anesthetic ketamine infusions have been shown to be an effective therapy for refractory depression, posttraumatic stress disorder (PTSD), and chronic pain. Ketamine is known to change oscillatory electric brain activity. Hypersynchronous electric activity in the brain, also seen in the basal ganglia, is a similarity shared between migraine headaches, depression, PTSD, Parkinson's disease (PD) and L-DOPA-induced dyskinesia (LID). Therefore, we have recently investigated the use of low-dose ketamine in PD case studies (Sherman SJ, et al., Case Reports in Neurology 2016; 8:53-58) and evaluated ketamine's ability to reduce established LID in a pre-clinical model (Bartlett MJ, et al., Neuroscience Letters 2016; 612:121-125). Here, we evaluated low-dose ketamine's ability to suppress the development of LID.

In the pre-clinical studies, 20 micrograms of 6-hydroxydopamine (6-OHDA) was injected unilaterally into the medial forebrain bundle (MFB) of male Sprague-Dawley rats to create a PD model. Rats (n=9 per group) were primed with escalating daily i.p. doses of L-DOPA (Days 0-13: 6 mg/kg; Days 14-28: 12 mg/kg). Rats were given vehicle or 20 mg/kg ketamine for 10 hours (5x i.p. injection, 2 hours apart; and co-injected with L-DOPA at the 5th injection). Treatment occurred on days 0, 7, 14 and 21. Abnormal involuntary movements (AIMs) were scored every 3-4 days to assess LID severity, and differences evaluated with ANOVAs and Tukey post hoc tests.

We recently showed a long-term therapeutic effect (reduced dyskinesia, improved on time, and reduced depression) of low-dose ketamine infusion in 5 PD patients. Additionally, in a pre-clinical LID model, a low-dose infusion of ketamine led to a long-term, dose-dependent decrease in AIMs. In this study, we show that after 28 days of L-DOPA-priming, PD rats treated once a week with low-dose ketamine for 10 hours had a 50% reduction in their total AIMs

as compared to vehicle treated rats ($p < 0.05$), indicating possible early utility for low-dose ketamine to prevent development of severe dyskinesia. This novel use of low-dose sub-anesthetic ketamine could lead to fast clinical translation, and since depression and pain states are critical problems for many PD patients could create a new dual therapy for patients with LID.

P06.05

Assessment of olfactory dysfunction in an inducible mouse model of α -synucleinopathy via multi-modality imaging

Elodie Brison¹, Simone P. Zehntner¹, Alex P. Zijdenbos¹, Kelvin Luk², Barry J. Bedell³

¹ Biospective Inc., Montreal, QC, Canada

² University of Pennsylvania, Philadelphia, PA, USA

³ Biospective Inc. and McGill University, Montreal, QC, Canada

Background: Parkinson's disease (PD) is currently diagnosed based on motor impairment and neuropsychiatric disturbances. However, non-motor deficits, such as olfactory impairment, typically precede the cardinal motor symptoms by several years. This prodromal period represents an ideal window for therapeutic intervention to prevent development of motor symptoms. In this study, we characterized pathological changes associated with the olfactory system in an inducible mouse model of α -synucleinopathy using state-of-the-art, multi-modality, imaging techniques in order to provide well-validated tools to accelerate the development of disease-modifying treatments for PD.

Methods: The mouse model of α -synucleinopathy was induced in Wild-type (Wt) B6/C3H and M83 Transgenic (Tg) mice by injection of preformed murine or human α -synuclein fibrils (PFFs) into the anterior olfactory nucleus (AON). Animals were tested for olfactory deficits at 15 weeks post-surgery using the buried pellet test. Anatomical MRI, manganese-enhanced MRI (MEMRI), and diffusion MRI (dMRI) scans were acquired at baseline and at follow-up (18 weeks post-surgery). All MR images were processed using Biospective's NIGHTWING™ software. Upon completion of MRI scanning, mouse brains were extracted and quantitative immunohistochemistry (qIHC) studies were performed to assess α -synucleinopathy, neuronal degeneration, and neuroinflammation using Biospective's PERMITS™ software.

Results: Injection of PFFs into the AON induced statistically significant olfactory deficits, measured by the latency in the buried pellet test, in Wt and Tg mice compared to control animals. Injection of PFFs into the AON led to α -synucleinopathy in the mitral cell layers of the olfactory bulb (OB) and other brain regions, indicating that propagation of the PFFs can induce pathology in anatomically connected olfactory regions. Analysis of the MRI data revealed both structural changes and functional alterations in the PFF-inoculated mice.

Conclusions: In conclusion, we have developed an inducible mouse model of α -synucleinopathy that demonstrates olfactory dysfunction. Our approach allows for a comprehensive understanding of the microstructural alterations underlying in vivo MRI-based imaging biomarkers. This inducible model can be used for preclinical assessment to accelerate the development of disease-modifying treatments for PD and other synucleinopathies.

P06.06

A novel VPS35 knock-in mouse model of Parkinson's disease: investigating pathophysiology for an improved understanding of prodromal PD

Stefano Cataldi¹, Igor Tatamikov², Chelsie Kadgien², Jaskaran Khinda², Jesse Fox², Austen Milnerwood², Matthew Farrer²

¹ Vancouver, BC, Canada

² Canada

Recently our lab linked a point mutation (D620N) in the VPS35 protein with autosomal-dominant, late-onset, clinically-typical parkinsonism (Vilariño-Güell, 2011). VPS35 is a core component of the retromer system, which regulates sorting of proteins from endosomes to lysosomes, the trans-Golgi network, or the plasma membrane. Cargos include CIM6PR, β_2 adrenergic and AMPA receptors (Bhalla, Harbour, Breusegem, & Seaman, 2012; Munsie, 2015).

The DN mutant has been reported to disrupt lysosomal delivery of Cathepsin D, an enzyme integral to degradation of aSyn (Follett, 2014) and thus increase aSyn burden. We have shown that wild-type and DN VPS35 overexpression alter glutamate synapse number and mEPSC in vitro (Munsie, 2015).

We engineered a mouse carrying the DN mutation within the endogenous mouse VPS35 gene (VPS35 knock-in:VKI). We have found that this mutation confers large increases in mEPSC frequency and amplitude in cultured cortical cells from VKI mice and alterations to VPS35 binding to several substrates.

To evaluate the behavioral consequences of this point mutation we have performed standardized testing on VKI mice at time points ranging from 3 to 18 months. Assessment of motor activity and cognition (open-field, rotarod, puzzle box, elevated plus maze) were conducted. Ex vivo fast scan cyclic voltammetry and immunohistochemistry (IHC) were also performed to assess nigrostriatal dopamine (DA) function and an intact nigrostriatal functional markers. At 3 months VKI mice exhibit increased anxiety-like behaviors and improved performance on the rotarod, and stimulated release of DA is significantly elevated. At 18 months of age, behavioral alterations are reversed, with transgenic animals presenting an anxiolytic-like behavior.

A biphasic phenotype is common in PD-related mouse models and reminiscent of recent data gathered in humans carrying PD-linked LRRK2 mutations prior to, and after, the onset of motor dysfunction (Lam, 2011; Sossi, 2010). We are currently evaluating DA transmission, behavioral correlates and IHC in old animals. Altered nigrostriatal function (prior to or in the absence of neuronal loss/pathology) will inform upon early disease mechanisms and improve our understanding prodromal PD. This study provides defined, clinically-relevant phenotypes in a genetically faithful mouse model, and will enable screening of small molecules for their potential to slow (or halt) disease progression in PD and related disorders.

P06.07

The overexpression of LRRK2 fragments containing the kinase domain increases the neurotoxicity of mutant A53T α -synuclein.

Noemie Cresto¹, Marie-Claude Gaillard¹, Charlene Joséphine¹, Liliane Kangue¹, Gwennaelle Aurégan¹, Martine Guillermier¹, Suéva Bernier¹, Caroline Jan¹, Fanny Petit¹, Pauline Gipchtein¹, Alain Joliot², Philippe Hantraye¹, Nicole Déglon¹, Karine Cambon¹, Alexis Bemelmans¹, Emmanuel Brouillet¹

¹ CEA, Direction des Sciences du Vivant, Institut d'Imagerie BioMédicale, Molecular Imaging Research Center (MIRcen), and The Neurodegenerative Diseases Laboratory, UMR 9199, CEA, CNRS, Fontenay aux roses, Paris, France

² Centre Interdisciplinaire de Recherche en Biologie (CIRB), Collège de France – CNRS/UMR 7241 – Inserme U1050, Paris, Fontenay aux roses, Paris, France

Alpha-synuclein (α -syn) and leucine-rich repeat kinase 2 (LRRK2) proteins are likely to play crucial roles in Parkinson's disease (PD). The most prevalent mutation in LRRK2 is the G2019S substitution which induces neurotoxicity through a marked increase of its kinase activity. A possible interplay between LRRK2 and α -syn may be

involved in the dysfunction and death of dopaminergic (DA) neurons in the substantia nigra (SNc) in PD.

Here, we aimed at studying the consequences of an increase in the kinase activity of G2019S-LRRK2 mutation on the neurotoxicity induced by a mutant form of α -syn (α -synA53T) in vivo in DA neurons using adeno-associated viral (AAV) approaches.

To address this question, we developed AAV vectors encoding the wild type (WT), G2019S or "dead kinase" forms of the C-terminal part of LRRK2 (dLRRK2) containing the kinase, the GTPase and the WD40 domains. We also generated an AAV encoding the mutant A53T α -syn (AAV- α -synA53T). AAVs (AAV-dLRRK2G2019S, AAV-dLRRK2WT, AAV-dLRRK2dead kinase or AAV- α -synA53T) were stereotactically injected into the rat SNc and their effects were characterized by histological evaluation at 15 weeks post-infection. The results indicated that the AAV-dLRRK2G2019S efficiently transduced SNc DA neurons. However, no major signs of neurotoxicity were observed as compared to AAV-GFP (control) and dLRRK2WT. In contrast, injection of an AAV- α -synA53T in the SNc produced the loss of DA neurons and motor deficits (cylinder test). Next, we asked whether dLRRK2G2019S could increase the neurotoxicity of α -synA53T using co-infection approaches. Unbiased stereological count showed that the loss of DA neurons produced by co-expression of dLRRK2G2019S with α -synA53T was significantly greater than that produced by overexpression of α -synA53T alone or with GFP. Moreover, rats co-infected with dLRRK2G2019S and α -synA53T exhibited less phospho- α -synS129-positive aggregates, consistent with increased neuronal death. We are currently assessing the behavioural correlates of these histological results. We are also currently testing whether the increased toxicity of α -syn in presence of dLRRK2G2019S selectively results from an increase in its kinase activity thanks to an AAV coding the "dead kinase" form of LRRK2 (dLRRK2dead kinase). The results of these experiments should contribute to a better understanding of the "functional" interaction that exists between α -syn and LRRK2 in vivo in the DA neurons of the SNc.

P06.08

F1 crossbreds of C57BL/6 and CD-1 mice demonstrate resistance to 1-Methyl-4-Phenyl-1,2,3,6-Tetrahydropyridine (MPTP) induced nigral neurodegeneration

Vidyadhara D J, Yarreiphang H, Raju T R, Phalguni Anand Alladi
National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore, Karnataka, India

Background: Asian-Indians are less vulnerable to Parkinson's disease (PD) than the Caucasians. Interestingly their admixed population is at much lesser risk. Here we study the molecular aspects governing this difference in populations using mice strains with differential resistance to MPTP-induced toxicity.

Objective: To establish the neural basis of varying susceptibility to MPTP in MPTP resistant CD-1 mice, susceptible C57BL/6 mice, and their crossbreds; simulating the variable incidence of PD in different ethnic populations.

Methods: The primary nigral dopaminergic (DA) phenotypes such as neuronal numbers, neuronal size, and tyrosine hydroxylase (TH) expression were studied using stereology, morphometry, and densitometry, respectively, on TH-immunostained midbrain sections in C57BL/6, CD-1 and their F1 crossbreds (n=6/group). Western blotting was performed to check the expression pattern of TH, Nurr1, and PITX3. Comparisons were made following four injections of 15 mg/kg MPTP-HCl, at 2hrs interval.

Results: The number of DA neurons in CD-1 and both the crossbreds were significantly higher compared to C57BL/6. DA neuronal morphology in crossbreds was comparable to CD-1, whereas the neurons of C57BL/6 were larger. TH expression in the crossbreds was significantly higher when compared to the parent

strains. MPTP administration resulted in approximately 60% loss of C57BL/6 DA neurons, whereas only 15% loss in CD-1 mice. Interestingly, crossbreeds did not show any loss of DA neurons. A significant neuronal shrinkage was noted only in C57BL/6, but not in CD-1 and the crossbreeds. The surviving neurons showed stable TH, Nurr1 and PITX3 expression upon MPTP in CD-1 and the crossbreeds, whereas, it was reduced in C57BL/6.

Conclusions: Our findings of higher basal numbers of DA neurons and relatively attenuated death of DA neurons in neurotoxic conditions in CD-1 mice provide anatomical evidence for its resistance to MPTP. The crossbreeds are even better protected against MPTP, which is reflected as supernumerary nigral neurons, an absence of neuronal death, stable TH, Nurr1 and PITX3 expression and unaltered morphology following MPTP injection. A similarity in anatomical substrates and molecular mechanisms of neuroprotection may be envisaged in the Anglo-Indians. This animal model of admixture provides an interesting experimental paradigm to study the molecular mechanisms pertinent to the human phenomenon of a differential prevalence of Parkinson's disease.

P06.09

Anti-Parkinsonian effects of Fluvoxamine maleate in maternally separated rats

Ernest Dalle, William Daniels, Mabandla Musa

University of KwaZulu-Natal, Durban, KwaZulu-Natal, South Africa

Exposure to early life stress has been shown to result in anxiety-like symptoms and exacerbates dopamine degeneration in a rat model for Parkinson's disease (PD). First line treatment for anxiety disorders include the use of Fluvoxamine maleate (FM). In this study, we investigated whether treating anxiety-like symptoms with FM has an effect in alleviating the neurotoxic effects of 6-OHDA in a parkinsonian rat model. Early maternal separation was used to create a rat model that depicts anxiety-like symptoms. Maternally separated adult Sprague-Dawley rats were treated with FM prior to and following lesion with 6-OHDA. The elevated plus-maze (EPM) and the forelimb akinesia tests were used to evaluate anxiety-like symptoms and motor impairment respectively. Blood plasma was used to measure corticosterone concentration and striatal tissue was collected for dopamine (DA) and serotonin analysis. Our results show that animals exposed to early life stress displayed increased anxiety-like symptoms and elevated basal plasma corticosterone concentration which were attenuated by treatment with FM. A 6-OHDA lesion effect was evidenced by impairment in the forelimb akinesia test as well as decreased DA and serotonin concentrations in the lesioned striatum. These effects were attenuated by FM treatment in the pre-lesion treated as opposed to the post-lesion treated rats. This study suggests that early treatment of anxiety-like behavior decreases the vulnerability of DA neurons to neurotoxic insults later in life thus slowing down DA degeneration in PD.

P06.10

Understanding the pathogenesis of Parkinson's Disease through genetic modifiers

Marie Davis

Seattle, WA, USA

PD is a common neurodegenerative disorder associated with aging, characterized by progressive motor symptoms and cognitive decline. Our understanding of its pathogenesis is limited, and currently no disease-modifying therapies exist. Mutations in GBA1 are the strongest genetic risk factor for PD, and GBA1 encodes glucocerebrosidase, an important enzyme in ceramide and lipid metabolism. However, most GBA1 carriers do not develop PD,

suggesting the presence of modifiers. To investigate how GBA1 influences PD pathogenesis, we created a *Drosophila* model of GBA1 deficiency (GBA1del) that has age-dependent phenotypes due to neurodegeneration and impaired lysosomal protein degradation.

A pilot screen using our GBA1del model was conducted to identify genetic modifiers. Fifty chromosomal deletions on chromosome 2, each containing 30-40 genes, were screened in heterozygous state for suppression or enhancement of the 5 day old climbing deficit present in GBA1del homozygotes compared to controls. The modifier locus within a deletion was identified by narrowing candidate regions using publicly available smaller overlapping deletions and mutation alleles. Modifiers were further characterized by enhancement/suppression of other GBA1del phenotypes, including impairment in autophagy.

Two candidate genes were identified: 1) Glucosylceramide transferase (GlcT-1) and 2) Brainwashing (bwa). A publicly available mutation of GlcT-1 suppressed accelerated insoluble protein aggregation in GBA1del homozygotes. Ectopic expression of GlcT-1 enhanced the climbing deficit, increased insoluble ubiquitinated protein aggregation, and shortened lifespan of GBA1del homozygotes. A publicly available mutation in the putative alkaline ceramidase bwa modified the GBA1 mutant climbing phenotype and accelerated ubiquitinated protein aggregation in GBA1 mutant flies. GlcT-1 and bwa are modifiers of GBA1-mediated pathogenesis in *Drosophila*. Since mutations in both of these genes suppressed GBA1 mutant phenotypes, and loss of function in both enzymes are predicted to increase ceramide levels, we hypothesize that decreased levels of ceramide may impair autophagy flux, leading to neurodegeneration in GBA1del homozygotes. Further studies using this model, including targeted lipidomics, will elucidate the pathogenic mechanisms causing PD and may reveal potential new targets for disease-modifying therapies in the most common neurodegenerative movement disorder.

P06.11

KH176 as a novel disease-modifying therapeutic for Parkinson's disease

Ria de Haas¹, Julien Beyrath², Frans Russel³, Bas Bloem⁴, Jan Smeitink⁵

¹ Departments of Pediatrics and Pharmacology and Toxicology at the Radboud Center for Mitochondrial Medicine, Radboud University Medical Center, Nijmegen, Netherlands

² Khondrion BV, Nijmegen, Netherlands

³ Department of Pharmacology and Toxicology at the Radboud Center for Mitochondrial Medicine, Radboud University Medical Center, Nijmegen, Netherlands

⁴ Department of Neurology, Donders Institute for Brain, Cognition, and Behavior, Radboud University Medical Center Nijmegen, Nijmegen, Netherlands

⁵ Department of Pediatrics at the Radboud Center for Mitochondrial Medicine, Radboud University Medical Center and Khondrion BV, Nijmegen, Netherlands

Parkinson's disease (PD) is a progressive neurological disorder that is increasingly prevalent with age, with the incidence rising from approximately 4 people per 10,000 in their forties to 2 in 100 over the age of eighty. Current evidence from postmortem human brain tissue, genetic and toxin-induced animal and cellular models indicate a central role of mitochondrial dysfunction and oxidative stress in the pathophysiology of PD. Mutation in at least 7 genes (ATP13A2, DJ-1, LRRK2, Parkin, PINK1, SNCA, VSP35) are known to underlie monogenic PD, most of them encode proteins that impact mitochondrial function and clearance, cellular oxidative stress and redox balance. In addition, biochemical evidence indicates that a subset of idiopathic PD is also associated with

detectable mitochondrial dysfunction. Recently, novel rat knockout (KO) models of DJ-1 and PINK1 genes were generated and characterized. In contrast to mice, the loss of either DJ-1 gene or PINK1 gene in rats result in a marked behavioral dysfunction and significant loss of dopaminergic neurons in the substantia nigra, a major characteristic of PD. These findings support the use of the DJ-1 and PINK1 KO rat models as relevant tools for the discovery of novel therapeutic strategies for PD.

This project is aimed to repurpose KH176, a new molecule currently under clinical development for the treatment of mitochondrial disease (MD), as a novel disease-modifying therapeutic for PD. Here we will show that KH176 has a proven pre-clinical efficacy in different models of MD (in vitro and in vivo) and PD (in vitro). Furthermore, pharmacokinetic properties of KH176 will be evaluated in wild type rats, necessary to determine the optimal dosing regimen leading to the targeted brain exposure. This optimal dosing regimen will then be used in the long-term therapeutic efficacy study in DJ-1 and PINK1 KO rats.

P06.12

Diffuse brain injury in swine causes plasmalemmal disruption and α -Synuclein over-expression in the substantia nigra

John E. Duda, Carolyn Keating, Marissa Kamarck, James P. Harris, Kevin D. Browne, John A. Wolf, D. Kacy Cullen

Corporal Michael J. Cresenz Veterans Affairs Medical Center and the Perelman School of Medicine at the University of Pennsylvania, Philadelphia, Pennsylvania, USA

Introduction: Studies suggest that traumatic brain injury (TBI) may increase the risk of developing Parkinson's disease (PD), but the mechanisms involved are unclear. Experimental models of TBI have suggested that biomechanical forces may transiently disrupt the plasma membrane of neural cells which can lead to delayed cellular injury. We hypothesize that this plasmalemmal disruption might engender cell-to-cell transmission of intracellular proteins, including pathologic forms of α -synuclein, thus contributing to the spread of PD pathology.

Methods: We utilized an established porcine model of closed-head rotational acceleration to investigate plasmalemmal integrity and α -synuclein expression following mild TBI. Yucatan minipigs were subjected to rotational head acceleration (100–300 radians/second), using a HYGE pneumatic actuator or a sham procedure. Different groups were exposed to a single acceleration or two accelerations done either on the same day or after a seven day delay. Two hours prior to final injury, the normally cell-impermeant dye Lucifer Yellow was injected into the interstitial space and allowed sufficient time to diffuse throughout the brain. Animals were sacrificed 15 minutes after the final injury and perfused to eliminate extracellular Lucifer Yellow. After characterizing the structure of the SN pars compacta (SNc), SN pars reticulata (SNr), and surrounding nuclei in naive animals, the integrity of these structures was assessed in injured animals. Disruption of plasmalemmal integrity was determined by intracellular Lucifer Yellow and α -synuclein immunohistochemistry was performed.

Results: Neurons containing Lucifer Yellow were observed in both divisions of the SN and related nuclei, suggesting transient disruption of plasmalemmal integrity. In addition, increased α -synuclein expression was observed in a subpopulation of these cells. Some permeabilized cells also expressed dopaminergic markers, although many did not. Ongoing studies are characterizing the phenotype of these non-dopaminergic cells as well as the emergence of pathological isoforms of α -synuclein.

Conclusions: These results suggest that diffuse brain injury induces transient disruption of neuronal plasmalemmal integrity and over-expression of α -synuclein, which may play a role in linking

physical injury at the cellular level to development of chronic neurodegenerative sequela like those found in PD.

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P06.13

Generation of human iPSC-derived midbrain organoids as a novel model to dissect pathological features of familial Parkinson's Disease

Emanuele Frattini, Giacomo Monzio Compagnoni, Sabrina Salani, Paola Rinchetti, Dario Ronchi, Massimo Aureli, Monica Nizzardo, Marco Baccarin, Nereo Bresolin, Giacomo Pietro Comi, Stefania Corti, Alessio Di Fonzo

Italy

Objective: To generate and characterize human induced pluripotent stem cell (iPSC) – derived midbrain organoids of patients with familial Parkinson's Disease (PD).

Background: PD is the second most common neurodegenerative disorder. Although advances have been made in the identification of genetic causes of PD, the molecular mechanisms that underlie the progressive loss of dopaminergic (DA) neurons in the substantia nigra of the midbrain remain largely unknown. In this project, we developed a human stem cell-based 3D model that recapitulates some aspects of PD pathology and may lead to novel insights in alpha-synuclein accumulation and DA neurons degeneration.

Methods: Fibroblasts derived from skin biopsies of two PD patients (one heterozygous for the L44P mutation in GBA, and one with SNCA duplication) and two healthy controls were reprogrammed into iPSCs via viral transduction of OSKM factors. Pluripotency was assessed by the expression of stem cell markers. Karyotype analysis excluded genetic rearrangements during reprogramming. Protocol for the generation of cerebral organoids by Lancaster et al. (2013) was adapted to generate 3D cultures of DA neurons exhibiting midbrain identity. To assess the region specificity and maturity of obtained midbrain organoids, RT-PCR and RNA-seq analyses were conducted. WB and IHC analyses were performed to fully characterize generated 3D cultures and evaluate differential expression of alpha-synuclein and tau protein. Chemiluminescent enzymatic assay of glucocerebrosidase (GCase) activity was performed. Lipid composition profile of neuronal membranes was analyzed to assess functional integrity of lipid raft organization.

Results: Midbrain organoids generated from iPSCs of controls and PD patients were densely populated by neurons (mainly DA) and other cell types. Gene expression profile and global transcriptome of obtained organoids reproduced embryological development and maturity of midbrain structures. Alpha-synuclein and tau protein were expressed in both control and PD 3D cultures. GCase enzymatic activity was significantly decreased in PD organoids compared to controls. Lipid content and lipid raft-dependent signalling were determined in PD and control organoids.

Conclusions: 3D cultures of DA neurons represent a comprehensive human platform that can be exploited for the elucidation of pathogenetic mechanisms involved in PD and for the screening of potential therapeutic strategies.

P06.14

Targeting soluble TNF with XPro1595 to ameliorate motor and non-motor symptoms in a progressive non-human primate model of Parkinson's disease

Valerie Joers, Gunasingh Jeyaraj, Alison Weiss, Jocelyne Bachevalier, Ronald Voll, Mark Goodman, Leonard Howell, Yoland Smith, Malú Tansey

Emory University, Atlanta, GA, USA

Parkinson's disease (PD) is now recognized as a multisystem disorder affecting the central and peripheral nervous systems giving rise to motor and non-motor symptoms. Numerous studies have highlighted a potential role for inflammation; specifically, tumor necrosis factor (TNF) levels are elevated in CSF and brain tissue of PD patients, suggesting that TNF is a good target for therapeutic intervention. Yet, current FDA-approved anti-TNF therapies target both transmembrane (tm)TNF and soluble (sol)TNF and are undesirable in view of their immunosuppressive effects and adverse findings including neurological deficits and demyelinating diseases in some patients. The novel TNF inhibitor XPro@1595 acts by a "dominant-negative" mechanism to eliminate only solTNF. Here, we report preliminary findings of the anti-inflammatory and neuroprotective effects of XPro1595 on motor and non-motor symptoms in a low-dose chronic MPTP monkey model of PD. Based on earlier work in rodents, we hypothesized that solTNF is a critical mediator of DA neuron loss and therefore predicted that XPro1595 would delay the development of motor and non-motor symptoms by reducing TNF-dependent inflammation and apoptosis. Five rhesus monkeys were given weekly doses of MPTP (0.2-0.8mg/kg, im) and evaluated weekly for clinical rating scores. Peripheral treatment of XPro1595 (10mg/kg, n=3) or vehicle (n=2) began 11 weeks after the start of MPTP and continued every 3 days. PET scans were performed using 18F-FEPPA to evaluate microglial activation and using 18F-FECNT to assess DA transporters at baseline and at 8, 16, 28 and 40 weeks after the start of MPTP. Animals were assessed for gastrointestinal function and cognitive flexibility/behavioral inhibition. Blood and CSF were collected monthly to measure levels of XPro1595 and pro-inflammatory cytokines. The study ended when an animal developed moderate parkinsonism as determined by a clinical rating. Preliminary analysis of in vivo measures reveal that chronic MPTP dosing produced deficits in cognitive performance after 6 weeks of MPTP and gastrointestinal motility after 10 weeks of MPTP, both occurring prior to the development of PD motor signs. Furthermore, increased systemic IL-6 levels correlated with the decrease in 18F-FECNT binding in the substantia nigra after 16 weeks of MPTP (R=0.995, p=0.0004). We are currently evaluating the disease-modifying properties of systemically administered XPro@1595 on the remaining outcome measures.

P06.15

The role of myeloid MHC-II in α -synuclein-induced degeneration and risk for PD

Elizabeth Kline, George Kannarkat, Jianjun Chang, Jeremy Boss, Malú Tansey

Emory University School of Medicine, Atlanta, GA, USA

The process of antigen presentation via major histocompatibility complex class II (MHC-II) proteins links the innate and adaptive immune systems and controls the duration and nature of the immune response to specific targets. In patients with Parkinson's disease (PD), substantia nigra dopamine neurons are burdened with proteinaceous intracellular aggregations of misfolded and post-translationally modified α -synuclein. Microglia expressing MHC-II have been identified within the post-mortem substantia nigra (SN) of PD patients often in juxtaposition to dopamine (DA) neurons and extracellular α -synuclein aggregates. One way that brain-resident microglia and peripheral monocytes may contribute to neuroinflammation is by presenting a neuron-derived antigen (possibly α -synuclein) to naïve CD4+ T cells via expression of MHC-II proteins, a process that initiates T-cell differentiation and maturation into T effector cells that secrete pro-inflammatory cytokines.

rs3129882, a common single nucleotide polymorphism (SNP) in the HLA-DRA gene in the MHC-II loci was found to be associated with

risk for PD, implicating antigen presentation in PD risk. Our group found that peripheral blood monocytes of healthy control (HC) human subjects with the high-risk genotype at rs3129882 (GG) display 30 times more MHC-II protein on their surface relative to HC (AA); and PD (GG) patients exhibit a 300-fold greater increase in MHC-II mRNA compared to PD (AA), suggesting that myeloid MHC-II expression levels may contribute to PD progression.

We hypothesize that myeloid MHC-II is required for CD4+ T cell-dependent vulnerability of DA neurons to α -synuclein-induced degeneration. To test this hypothesis, mice with myeloid deletion of the mouse MHC-II gene I-Ab in microglia and peripheral monocytes received a stereotaxic injection of rAAV2-human WT α -synuclein (or rAAV2-GFP as negative control) to the SN. We have performed immunohistological labeling of DA neurons (tyrosine hydroxylase, TH+ cells) and total neurons (Nissl counterstain). Unbiased stereology to estimate loss of DA neurons and total neurons in the SN is in progress and will be presented. Completion of these studies will enable us to establish the direct contribution of myeloid MHC-II in α -synuclein-induced degeneration and will aid in interpretation of the role of myeloid MHC-II in DA neuron loss within the context of PD.

P06.16

Functional interaction of the Parkinson's disease risk factor RIT2 with alpha-synuclein

Julia Obergasteiger, Corrado Corti, Alexandros Lavdas, Cristian Ascione, Christa Uberbacher, Peter Pramstaller, Andrew Hicks, Mattia Volta

Center for Biomedicine, EURAC Research, Bolzano, Italy

Parkinson's disease (PD) has a multifactorial etiology, hypothesized to be the result of a combination of genetic and environmental factors. Several gene mutations cause familial, albeit rare, PD cases. On the other hand, genome wide association studies (GWAS) have identified genetic risk factors in the general population that could participate in the onset of sporadic PD (most frequent). One of the current theories posits that this genetic variability can synergize and precipitate the effects of pathogenic gene abnormalities. In this light, we are investigating the convergence of alpha-synuclein (aSyn) and the novel GWAS hit RIT2 onto cellular mechanisms that might be altered in PD. While aSyn mutations are well established causes of rare forms of familial PD, that SNCA locus variability is the most reproducible susceptibility factor and that aSyn protein inclusions are the pathologic hallmark of the vast majority of PD cases, little is known about the RIT2 locus and its coded protein Rin. Importantly, RIT2 gene expression is enriched in the dopamine (DA) neurons of the substantia nigra (SN) and shows a reduction in PD brains. Rin belongs to the Rit subfamily of Ras-like small GTPases and mediates neuritogenesis through p38 MAPK and ERK pathways. Notably, Rin mediates the internalization of the DA transporter through direct interaction.

We used the human aSyn overexpressor Drosophila model and knocked down its ortholog Ric through RNA interference. We observe an attenuation of aSyn-induced motor deficits, indicating a functional genetic interaction. Consistently, we detected a strong trend for increased Rin protein expression in the cortex of Thy1-aSyn transgenic mice, while mRNA transcription in the same area was unchanged. Thus, we studied the expression of Rin in the mouse brain. Rin is expressed in the DA neurons of the SN and their striatal DA terminals. Lastly, we are using SK-N-SH neuroblastoma cell lines overexpressing aSyn or Rin to study their physical molecular interaction and consequent modulation of intracellular signaling.

Our data confirm that Rin is expressed in PD-relevant areas in the mouse brain and point towards a functional interaction with aSyn.

Modulation of this interaction in cell models of increasing complexity (cell lines, primary neurons, human iPSC-derived DA neurons) will indicate a possible pathologic mechanism that could be targeted for therapy.

P06.17

Development of a qualitative systems pharmacology model to support hypothesis generation and testing for Parkinson's disease.

Michael Reed
San Carlos, CA, USA

Aims: In order to improve the understanding of the alpha-synuclein system and its role in Parkinson's disease, Elan and Rosa collaborated in the development of a Synuclein PhysioMap®, a graphical model architecture to support hypothesis generation and testing. The objectives of the project were to provide insight into alpha-synuclein function in vesicle trafficking by creating a PhysioMap™, memorialize and communicate the current state of knowledge within Elan in a Synuclein Model Qualification Method Document (MQM), and to recommend experiments to test hypotheses, resolve uncertainties and identify and prioritize potential targets.

Methods: The PhysioMap was developed using both publically available literature and proprietary Elan data. The Synuclein PhysioMap was designed and curated by a multidisciplinary team to represent synuclein synthesis and distribution within a neuron, SNARE complex formation, phagocytosis, cytokine release, neurotrophic factor release, and mitochondrial function.

Results and Conclusion: Following the development of the PhysioMap, the team identified key biological uncertainties and hypotheses and recommended focused laboratory experiments to gain a better understanding of synuclein function in Parkinson's disease.

P06.18

Longitudinal live imaging of retinal α -synuclein:GFP deposits in a transgenic mouse model of Parkinson's disease/dementia with Lewy bodies

Edward Rockenstein¹, Diana Price², Michael Mante¹, Brian Spencer¹, Karen Doung-Polk¹, Douglas Bonhaus², James Lindsey¹, Eliezer Masliah¹

¹ University of California San Diego, La Jolla, CA, USA

² Neupore Therapies Inc., San Diego, CA, USA

Abnormal accumulation of α -synuclein (α -syn) in the CNS is proposed to underlie neuronal cell and synaptic dysfunction leading to motor and cognitive deficits in synucleinopathies such as Parkinson's Disease (PD), Dementia with Lewy Bodies (DLB), and Multiple Systems Atrophy (MSA). Multiple groups have demonstrated that α -syn also accumulates in accessory structures of the CNS such as the eyes and olfactory terminals and in peripheral organs such as the gut, skin, heart and salivary glands of Parkinsonian patients. In vivo longitudinal monitoring of α -syn levels in these accessory structures and peripheral organs could potentially be used to assess biomarkers for therapeutic evaluations. There is mounting evidence that ophthalmic pathology mirrors neuropathological processes of the brain. Retinal imaging methods such as fundal mapping and optical coherence tomography provide a non-invasive means to evaluate optical pathology in vasculature, changes in retinal layer morphology, and protein aggregates.

In an effort to evaluate the presence and progression of retinal pathology in transgenic mouse models of PD/DLB, we conducted longitudinal retinal imaging of mice overexpressing the α -syn:GFP fused protein under the PDGF-beta promoter (PDNG78 line).

Retinal maps were acquired at 1 month intervals for 3 months followed by fluorescent images in the same orientation for each eye for transgenic and non-transgenic mice. In vivo retinal imaging of transgenic mice revealed a progressive accumulation of GFP tagged α -syn in retinal cells and in the edges of arterial blood vessels. The accumulation of α -syn persisted in the same cells overtime and increased with age. No accumulation was observed in the non-transgenic mice. Ex vivo immunofluorescence evaluations confirmed that the α -syn:GFP-positive cells contained α -syn and that they were retinal ganglion cells.

This study demonstrates that longitudinal live imaging of the retina in the PDGF- α -syn:GFP mice, and other models of α -synucleinopathy, might represent a useful, non-invasive, tool to monitor the fate of α -syn accumulation in the CNS and to evaluate the therapeutic effects of compounds targeting α -syn.

P06.19

Lipid accumulation in Gaucher disease promotes α -synuclein pathology in Parkinson's disease

Yumiko Taguchi, Jun Liu, Pramod Mistry, Sreeganga Chandra
Yale University, New Haven, CT, USA

Parkinson's disease (PD) is a neurodegenerative disease characterized by α -synuclein aggregation into pathologic Lewy bodies. The most common risk factor for PD is mutation of GBA1, which encodes for a lysosomal glucocerebrosidase. Homozygous mutations in GBA1 also cause Gaucher disease (GD), a lysosomal storage disorder resulting in the mass accumulation of glyco- and sphingolipids (including glucosylceramide, glucosylsphingosine, sphingosine, and sphingosine-1-phosphate). Although the genetic connection between PD and GD is well established, the molecular mechanisms linking these two diseases is still unclear. In order to better understand the molecular connection between PD and GD, we investigated the role of accumulated lipids in GD on α -synuclein aggregation into pathologic species.

We initially determined whether GD lipids affected the rate of α -synuclein aggregation. We incubated α -synuclein with several GD lipids and tracked the aggregation state of the protein using circular dichroism. We found that, in the presence of GD lipids, α -synuclein aggregated significantly faster than with control lipids, suggesting that GD lipids interact with α -synuclein to accelerate development into pathologic species. Following these experiments, we turned to a mammalian cell culture model to further elucidate the effects of GD lipids on α -synuclein pathology. Our results suggested that GD lipids promote the production of α -synuclein fibrils capable of internalization and cell-to-cell transfer.

In order to further study the relationship between α -synuclein and GD lipids in vivo, we generated novel joint GD/PD mouse lines as a model for PD patients with GBA1 mutations. These studies revealed a shortened lifespan of GD/PD mouse lines as compared to a PD control line, suggesting that GBA1 mutations accelerate PD-related neurodegeneration. Current experiments involve expanding studies using our novel GD/PD mouse lines and further in vitro experiments using human neurons derived from induced pluripotent stem cells (iPSCs). Through our research, we hope to better understand the mechanism underlying GBA1-related PD, contributing to the advancement of the PD field as a whole.

P06.20**Reverse genetics screening reveals LRRK2 phosphorylation regulators**

Jean-Marc Taymans¹, Tina De Wit², Evy Lobbstaef², Marc Bölliger³, Matthieu Drouyer¹, Marie-Christine Chartier-Harlin¹, Veerle Baekelandt², Jeremy Nichols³

¹ Jean-Pierre Aubert Research Center, Inserm/Université de Lille/Lille University Hospital, Lille, France

² Laboratory for Neurobiology and Gene Therapy, KU Leuven, Leuven, Belgium

³ The Parkinson's Institute, Sunnyvale, CA, USA

Leucine rich repeat kinase 2 (LRRK2) exists physiologically as a highly phosphorylated protein. Phosphosite mapping studies have distinguished 2 notable clusters of phosphorylation sites, one in or near the ROC-GTPase domain and another in the ankyrin repeat (ANK) and leucine rich repeat (LRR) interdomain region. Evidence of a physiological role for LRRK2 phosphorylation has accumulated in recent years for those phosphosites of the ANK-LRR interdomain region, i.e. the S910/S935/S955/S973 sites. These phosphosites are dephosphorylated in several pathogenic mutants such as R1441G, Y1699C and I2020T. The shift of the phosphorylation equilibrium towards dephosphorylation of LRRK2 observed in disease indicates that phosphatases play an important role in LRRK2 cellular regulation. We have previously reported that protein phosphatase 1 (PP1) recruitment and PP1-mediated dephosphorylation underlie the reduced LRRK2 phosphorylation observed in the presence of several pathogenic mutations and upon LRRK2 kinase inhibitor treatment. Here, we aimed to identify PP1 partners and additional physiological phosphatases of LRRK2 via an RNAi screen using siRNAs directed against 298 phosphatase targets in U2OS cells expressing LRRK2. From this initial screen 39 proteins with the greatest effect on LRRK2 phosphorylation levels at its cellular phosphosite S935 were included in follow up secondary screens. This was achieved by lentiviral vector-mediated miRNA-based knock-down or overexpression in SH-SY5Y cells and HEK293 or HEK293T cells stably overexpressing LRRK2. With further validation experiments ongoing, these experiments confirm the importance of PP1 and reveal novel phosphatases responsible for regulating LRRK2 phosphorylation levels and may give insight in kinase inhibitor-mediated effects that potentially will lead to new therapies for PD.

P06.21**PD-like pathology triggered by α -synuclein overexpression in the dorsal motor nucleus of the vagus nerve**

Ayse Ulusoy, Michael Helwig, Raffaella Rusconi, Michael Klinkenberg, Ruth E. Musgrove, Donato A. Di Monte
German Center for Neurodegenerative Diseases (DZNE), Bonn, Germany

Multiplication mutations of the α -synuclein gene (SNCA) are causally associated with familial Parkinsonism. As importantly, a common feature of Parkinson's disease (PD) risk factors, such as aging, toxic insults and SNCA variations, is their ability to enhance intraneuronal levels of α -synuclein. We developed animal models of increased α -synuclein expression to study pathogenetic processes of likely relevance to PD. Data showed that one of the consequences of protein overexpression is that it triggers neuron-to-neuron α -synuclein transmission. It is conceivable that, through this mechanism, toxic species of the protein may diffuse throughout the brain and contribute to the progressive exacerbation of pathological and clinical disease manifestations. Experiments in models of enhanced α -synuclein expression also revealed unique features of cholinergic neurons in the dorsal motor nucleus of the vagus nerve (DMnX) that bear potential relevance to PD. The DMnX is highly

vulnerable to α -synuclein pathology in PD. It could also be the site from where initial α -synuclein lesions may diffuse toward more rostral brain regions during disease progression. Our experimental work is consistent with these observations in human brains. DMnX neurons were found to be preferential targets of α -synuclein toxicity, and the DMnX was identified as a key relay center for α -synuclein diffusion via anatomically interconnected pathways. In summary, important PD features can be mimicked by α -synuclein overexpression in animal models. These models therefore represent valuable tools for elucidating pathogenetic disease processes and testing new therapeutic strategies against synucleinopathies like PD.

P06.22**Increased power of sleep spindle oscillations in the LRRK2 mouse model of Parkinson's disease**

Jean-Paul Wiegand¹, Kathleen Gies², Mitchell Bartlett³, Torsten Falk³, Stephen Cowen⁴

¹ Evelyn F. McKnight Brain Institute, University of Arizona; Department of Neuroscience, University of Arizona, Tucson, AZ, USA

² Department of Psychology, University of Arizona, Tucson, AZ, USA

³ Department of Neurology, University of Arizona; Department of Pharmacology, University of Arizona, Tucson, AZ, USA

⁴ Evelyn F. McKnight Brain Institute, University of Arizona; Department of Psychology, University of Arizona, Tucson, AZ, USA

The LRRK2 mutation is the most common genetic cause of Parkinson's disease (PD). Despite this, no study to date has investigated its impact on network-level neural activity. Recent data from Beccano-Kelly et al. (2014) suggest that LRRK2 knock-in mice exhibit an increase in glutamatergic release in cortical neurons. Such changes could significantly alter cortico-thalamic networks and enhance oscillatory activity produced by cortico-thalamic interactions.

Objective: We hypothesized that sleep spindle oscillations are enhanced in LRRK2 knock-in mice. To investigate this question, we compared spindle activity recorded from LRRK2 knock-in and wild-type mice.

Methods: 5 LRRK2 G2019S and 9 WT C57bl/6 male mice (The Jackson Laboratory) were implanted with depth electrodes and surface EEG electrodes. Depth electrodes were implanted into the motor cortex (M1), anterior cingulate cortex (ACC), hippocampus and striatum. Surface electrodes were implanted above somatosensory (S1) and visual cortex (V1). We recorded neural activity during sleep periods preceding and following an open-field foraging task and novel object exposure. Activity was recorded at 20kHz, down-sampled to 2kHz, and filtered for spindle activity (9-16Hz) that exceeded 2.5 standard deviations above the mean power.

Results: LRRK2 mice expressed a significant increase in the power of both early and late peak spindle frequency (dB/Hz) relative to controls ($p < 0.05$, Student's t-test) in all cortical regions (M1, ACC, S1, and V1). In contrast, no difference in the distributions of peak spindle frequencies and durations was observed between LRRK2 and wild-type mice.

Conclusions: Our results support the conclusion that the LRRK2 G2019S mutation results in the lasting enhancement of cortico-thalamic interactions. Cortical sleep spindle oscillations are highly preserved across species suggesting that altered spindle activity could serve as a diagnostic biomarker for LRRK2 PD.

BASIC SCIENCE: BRAIN PHYSIOLOGY AND CIRCUITRY

P07.01

Role of direct pathway Gq- and Gs-signaling activation in L-DOPA-induced dyskinesia

Cristina Alcacer¹, Laura Andreoli¹, Irene Sebastianutto¹, Tim Fiebinger¹, Johan Jakobsson², M. Angela Cenci Nilsson¹

¹ Basal Ganglia Pathophysiology Unit, Department of Experimental Medical Science, Lund University, Lund, Sweden

² Laboratory of Molecular Neurogenetics, Wallenberg Neuroscience Center, Lund University, Lund, Sweden

L-DOPA is the reference treatment for Parkinson's disease (PD). However, this treatment is complicated by L-DOPA-induced dyskinesia (LID). Current theories assume that LID results from an imbalance in the activity of the direct and indirect pathway favoring an overactivity of the direct pathway. However the above theory has never been verified experimentally.

Aims: To selectively activate the striatal projection neurons of the direct pathway (dSPN) in a mouse model of PD and LID, we developed chemogenetic approaches based on expressing designer receptors exclusively activated by designer drugs (DREADD) selectively to dSPN. DREADD are only activated by administration of the inert compound, clozapine-N-oxide (CNO). Cre-inducible DREADD constructs were injected in the striatum of hemiparkinsonian D1-Cre transgenic mice to target dSPN. We aimed at comparing the behavioral effects of two activatory DREADDs: Gq- (hM3Dq) and Gs- (rM3Ds) coupled-DREADD whose stimulation by CNO triggers activation of Gq- and Gs-mediated signaling, respectively.

Results: CNO increased general motor activity to a similar extent in both hemiparkinsonian D1-Cre mice transfected with Gq and Gs-DREADD. However, hM3Dq-mediated activation of dSPN was unable to induce dyskinesia compared to rM3Ds, which induced moderate dyskinesia. We further observed that activating Gs-mediated signaling potentiated established dyskinesia in L-DOPA treated mice to a higher extent than Gq-mediated signaling dSPN activation.

Conclusions: This study shows that using Gs- versus Gq-DREADD to activate dSPN results in different behavioral outputs. We show that different behavioral responses depend not only on activating particular types of neurons, but also through which signaling mechanism these neurons become activated.

P07.02

Cortical disinhibition is neuroprotective in a progressive mouse model of Parkinson's disease

Rebecca Hood¹, Cynthia Moore², Patrick Fuller³, Charles Meshul⁴

¹ Oregon Health & Science University, Portland, OR, USA

² Portland VA Medical Center, Portland, OR, USA

³ Beth Israel Deaconess Medical Center, Boston, MA, USA

⁴ Portland VA Medical Center, Oregon Health & Science University, Portland, OR, USA

Objective: The progressive loss of dopaminergic cells that occurs in Parkinson's disease (PD) leads to a dysregulation in brain signaling. Imaging studies in PD patients have demonstrated an alteration in motor cortex (MC) activation when compared to control patients and repetitive transcranial magnetic stimulation targeting the MC temporarily attenuates motor impairments in PD patients. This suggests the MC is a viable therapeutic target, so we investigated

the neuroprotective potential of cortical disinhibition in a progressive mouse model of PD.

Methods: To disinhibit the motor cortex, Vgat (the gene for the vesicular GABA transporter, VGAT) was deleted in the MC of Vgatflox/flox mice through unilateral injections of AAV-Cre-GFP. Since VGAT is required for GABAergic function, we believe targeting GABAergic interneurons with focal AAV-Cre-GFP injections prevents inhibitory GABAergic signaling in the MC. Mice were then subjected to 4 wks of an increasing dose of 1-methyl-2-phenyl-1,2,3,6-tetrahydropyridine (MPTP), 5 d/wk injected i.p., at doses of 8, 16, 24, and 32 mg/kg/d. Protection was assessed by immunohistochemistry. Changes in the activity of brain region were assessed using cytochrome oxidase (CO) as a marker for cellular metabolism and post-embed immunogold labeling for glutamate in the striatum.

Results: Optical density of tyrosine hydroxylase-immunoreactive (TH-ir) nerve terminals in the striatum showed a 79% reduction in wild type (wt) mice after MPTP lesioning compared to the vehicle group that was completely prevented by cortical disinhibition in Vgatflox/flox mice. This protection was bilateral with no significant difference between injected and uninjected hemispheres. Surface counts of TH-ir cells of the substantia nigra pars compacta (SNpc) demonstrated that the 59% loss of TH-ir cells in wt/MPTP mice was completely prevented by cortical disinhibition. Though no significant difference in immuno-gold particle density was observed in striatal nerve terminals, suggesting no change in glutamate signaling in the corticostriatal pathway after cortical disinhibition, CO optical density analysis did show a decrease in activity of the SN after MPTP lesioning in wt mice that was partially attenuated by cortical disinhibition. Tracing studies revealed direct projections from the targeted region of the MC to the SNpc and subthalamic nucleus, indicating two regions of the basal ganglia that may mediate this neuroprotective effect.

P07.03

Striatal cholinergic interneurons expressing calretinin are numerically increased in Parkinsonian monkeys

Sarah Petryszyn, Thérèse Di Paolo, André Parent, Martin Parent
Université Laval, Quebec City, Quebec, Canada

The most abundant interneurons in the striatum of primates are those expressing the calcium-binding protein calretinin (CR). Yet, despite their prevalence, the function of these striatal elements is poorly known. The present immunohistochemical study provides detailed assessments of the morphological traits, number, and topographical distribution of these chemospecific striatal interneurons in normal monkeys (*Macaca fascicularis*) and in monkeys rendered parkinsonian (PD) by MPTP-intoxication. The population of CR-positive (+) striatal interneurons in cynomolgus monkeys comprises small (8-12 μm), medium (12-20 μm) and large-sized (20-45 μm) neurons, each with distinctive morphologies. The small CR+ neurons were about 2-3 times more abundant than the medium-sized CR+ neurons, which were themselves 20-40 times more numerous than the large CR+ neurons. In both normal and PD monkeys, the mean density of small and medium-sized CR+ neurons was twice as high in the caudate nucleus than in the putamen, whereas the inverse occurred for the large CR+ neurons. The density of all three types of CR+ neurons was relatively constant along the anteroposterior extent of the caudate nucleus, whereas in the putamen the small and medium-sized CR+ neurons displayed a decreasing gradient compared to an increasing gradient for the large CR+ neurons. Double immunostaining experiments revealed that none of the small and medium-sized CR+ neurons expressed choline acetyltransferase (ChAT), a marker of cholinergic neurons, while the majority of large CR+ neurons did so. The number of large CR+/ChAT+ neurons was found to increase

markedly (4–12 times) along the entire anteroposterior extent of both the caudate nucleus and putamen of PD monkeys compared to controls. A detailed quantitative comparison of the number of large CR+, ChAT+ and CR+/ChAT+ neurons together with experiments involving the use of bromo-deoxyuridine (BrdU) as a marker of newly generated cells in both normal and PD monkeys showed that it is the level of expression of CR by the large neurons – and not their absolute number – that is increased in the dopamine-depleted striatum of PD monkeys. These findings reveal the modulatory role of dopamine in the phenotypic expression of the large cholinergic striatal neurons, which are known to play a crucial role in PD pathophysiology.

BASIC SCIENCE: DOPAMINE, RECEPTORS AND OTHER NEUROTRANSMITTERS

P08.01

Role of β -arrestin 2/Akt/GSK 3 β survival pathway in cadmium induced dopamine D2 receptor mediated function: protective efficacy of quercetin

Richa Gupta¹, Rajendra Shukla¹, Raajev Gupta², Aditya B Pant¹, Vinay K Khanna¹

¹ CSIR- Indian Institute of Toxicology Research, Lucknow, Uttar Pradesh, India

² Babu Banarashi Das University, Lucknow, Uttar Pradesh, India

Earlier, we found that cadmium induced brain cholinergic and dopaminergic dysfunctions are protected in rats on simultaneous exposure to cadmium and quercetin, a bioflavonoid. Further, role of mitochondria and associated pathway in such dysfunctions are also established. In continuation to this, the present study is focused to investigate the involvement of β -arrestin 2/Akt/GSK 3 β survival pathways on cadmium induced Dopamine D2 receptor mediated behavioral functions and to assess the protective potential of quercetin. β -arrestin 2 a signaling intermediate that is implicated in the cAMP independent regulation of Akt and GSK-3 β by dopamine. Exposure to cadmium (5 mg/kg bw, p.o.) caused a significant alteration in the motor functions. A significant decrease in the locomotor activity and muscle co-ordination was observed following cadmium exposure. Further, a decrease in 3H-Spiperone was observed following cadmium exposure as compared to controls. Cadmium exposure caused an increase in the expression of AKT and ERK and decrease in the GSK-3 β and CREB proteins. Simultaneous exposure to cadmium and quercetin (25 mg/kg bw, p.o.) resulted to restore cadmium induced Dopamine D2 receptor mediated functions and cell survival proteins as compared to cadmium alone. The results of the present study exhibit a potential role of β -arrestin 2/Akt/GSK 3 β pathway survival cadmium induced dopaminergic dysfunction and also reveal the protective potential of quercetin.

P08.02

Gene therapy blockade of dorsal striatal p11 improves motor function and dyskinesia in Parkinsonian mice

Roberta Marongiu¹, Margarita Arango-Lievano², Veronica Francardo³, Peter Morgenstern¹, Xiaoqun Zhang⁴, M. Angela Cenci Nilsson³, Per Svenningsson⁴, Paul Greengard⁵, Michael Kaplitt¹

¹ Laboratory of Molecular Neurosurgery, Department of Neurological Surgery, Weill Cornell Medicine, New York, New York, USA

² Institute of Functional Genomic, Montpellier, France

³ Basal Ganglia Pathophysiology Unit, Dept. Experimental Medical Sciences, Lund, Sweden

⁴ Translational Neuropharmacology, Department of Clinical Neuroscience, Center for Molecular Medicine, Karolinska Institute, Stockholm, Sweden

⁵ Laboratory of Molecular and Cellular Neuroscience, The Rockefeller University, New York, New York, USA

Complications of dopamine replacement for Parkinson's disease (PD) can limit therapeutic options, leading to interest in identifying novel pathways that can be exploited to improve treatment. p11 (S100A10) is a cellular scaffold protein that binds to and potentiates the activity of various ion channels and neurotransmitter receptors. We have previously reported that p11 can influence ventral striatal function in models of depression and drug addiction, and thus we hypothesized that dorsal striatal p11 might mediate motor function and drug responses in parkinsonian mice. To focally inhibit p11 expression in the dorsal striatum, we injected an adeno-associated virus (AAV) vector producing a short hairpin RNA (AAV.sh.p11). This intervention reduced the impairment in motor function on forced tasks, such as rotarod and treadmill tests, caused by substantia nigra lesioning in mice. Measures of spontaneous movement and gait in an open-field test declined as expected in control lesioned mice, whereas AAV.sh.p11 mice remained at or near normal baseline. Mice with unilateral lesions were then challenged with l-dopa (levodopa) and various dopamine receptor agonists, and resulting rotational behaviors were significantly reduced after ipsilateral inhibition of dorsal striatal p11 expression. Finally, p11 knockdown in the dorsal striatum dramatically reduced l-dopa-induced abnormal involuntary movements compared with control mice. These data indicate that focal inhibition of p11 action in the dorsal striatum could be a promising PD therapeutic target to improve motor function while reducing l-dopa-induced dyskinesias.

P08.03

Striatal NMDA receptor signaling is related to abnormal SPN responses to dopamine in Parkinsonian monkeys

Arun Singh¹, Stella Papa²

¹ Atlanta, GA, USA

² Emory University, Atlanta, GA, USA

Objectives: Striatal glutamatergic hyperactivity is thought to play a crucial role in the mechanisms of LID in Parkinson's disease (PD). Striatal projection neurons (SPNs) are markedly hyperactive and often exhibit inverted (bidirectional) firing frequency changes following dopaminergic stimulation in the primate model of PD. We have previously shown that the abnormal SPN responses to dopamine can be reversed to stable, unidirectional responses by local microinjection of an NMDA receptor antagonist at the recording site. In addition, the systemic (s.c.) administration of NMDA antagonists reduces LID. However, the impact of NMDA receptor blockade localized to the striatum on the primate dyskinetic behavior remained unknown.

Methods: We determined the effects of blocking the striatal NMDA transmission in primates. The selective NMDA antagonist LY235959 (9 mM; 10 μ l total volume at 0.33 μ l/min) or vehicle (aCSF) was infused into the putamen in one side of the brain of advanced parkinsonian macaques exhibiting LID (n=3). Striatal injection sites were determined by electrophysiological mapping targeting the posterolateral region of the putamen (the sensory-motor territory). The infusion was followed by a systemic injection of L-DOPA at predetermined dyskinesigenic doses. Animals were then assessed for motor disability scores (MDS) and LID severity using standardized rating scales for primates.

Results: Striatal LY235959 significantly reduced LID (total and peak dyskinesia scores) on the contralateral side without compromising the antiparkinsonian action of L-DOPA, as shown by unchanged MDS. The striatal infusion of vehicle did not change LID scores. These findings confirm that the NMDA signaling in the dysfunctional striatum participates in the abnormal SPN response to dopamine and the generation of dyskinesias in the primate.

BASIC SCIENCE: NEUROPHARMACOLOGY

P09.01

Ameliorative effects of linagliptin in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine induced mouse model of Parkinson's disease

Jayasankar Kosaraju¹, Kin Yip Tam²

¹ Macau, Macau, Macau

² Taipa, Macau, Macau

Type 2 diabetes (T2D) is one of the risk factors associated with Parkinson's disease (PD). Recent studies have found similarities in molecular mechanisms that underlie the respective degenerative developments in the two diseases. Pharmacological agents, such as dipeptidyl peptidase-4 (DPP-4) inhibitors, which increase the level of glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP), ameliorate T2D, might be valuable candidates as disease modifying agents in the treatment of PD. In particular, endogenous GLP-1 and GIP shown neuroprotective properties in animal models. The present study examines the efficacy of linagliptin, a DPP-4 inhibitor in a 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) induced mouse model of Parkinson's disease. Ten week old mice were orally administered linagliptin (10, 20 and 30 mg/kg) for 21 days. Following treatment with linagliptin, mice were evaluated for their motor coordination test. The effect of the DPP-4 inhibitor on brain GLP-1 and GIP levels, tyrosine hydroxylase, apoptosis markers and inflammatory markers were evaluated. Linagliptin prevented the motor impairment, reduction in tyrosine hydroxylase levels present in MPTP mice. This remarkable therapeutic effect of linagliptin mediated through DPP-4 inhibition demonstrates a unique mechanism for preventing neurotoxicity by increasing GLP-1 levels and reverses the motor impairment and pathology observed in PD.

P09.02

Exploring neuroprotective efficacy of ginsenoside Rg3, the putative peroxisome proliferation receptor complex :PPARgamma agonist, in 1-methyl-4-phenyl-pyridinium (MPTP) model of Parkinson's disease

Hana Raheb¹, Simon Chiu¹, Jurui Hou¹, Kristen Terpstra¹, Yves Bureau¹, Zack Cernovsky¹, Autumn Carrie¹, Mujeeb Shad², Michel Woodbury-Farina³

¹ University of Western Ontario/Lawson Health Research Institute, London, ON, Canada

² Oregon Health Sciences University, Portland, OR, USA

³ University of Puerto Rico, San Juan, Puerto Rico

Despite biotechnology advances in our understanding of Parkinson disease (PD), current pharmacological treatments fail to substantially alter PD course. There is converging evidence in support of the emerging role of the Peroxisome-Proliferator-Receptor-complex (PPAR)gamma mediating neuroinflammation in

PD. In Oriental medicine, Panax Ginseng has been used for centuries for treatment and prevention of various neurological disorders: stroke syndrome, age-related cognitive impairment, and Parkinson disease (PD). The ginsenosides extracted from Panax Ginseng exert neuroprotective effects via PPARgamma signaling pathway. The objective of our study was twofold: 1) to examine the neuroprotective efficacy of the purified Rg3 ginsenoside extract:Rg3 in the in vitro and in vivo MPTP model of PD; and 2) to correlate the neuroprotective effects of ginsenoside Rg3 with the anti-inflammatory effects in regulating the panel of pro-inflammatory cytokines. In the primary rodent mesencephalic cultures, Rg3 rescued the dopamine neurons from decrease in Tyrosine hydroxylase (TH+)positive and the apoptosis index. In the subchronic MPTP model, Rg3 at daily oral dosage of 5 mg/g, 10 mg/kg, 20 mg/kg, significantly improved the impaired motor performance as measured with the climbing pole and rotarod test and general locomotor activity. At the end of the drug treatment period, we dissected various brain regions from the Rg3 treatment and placebo groups. Our results showed that Rg3 treatment significantly attenuated the reduction in the number of TH(+) neurons as measured with immunohistochemistry in the striatum and the substantia nigra and reversed the decline in dopaminergic indices: levels of dopamine and the metabolites DOPAC and Homovanillic acid (HVA) as estimated with high performance liquid chromatography. In the MPTP treated group, the pro-inflammatory cytokines: Tumor necrosis factor: TNF- α , and interleukins: IL-1 β , IL-6 were found to increase whereas Rg3 significantly antagonized the changes in the panel of inflammatory cytokines in the striatum as measured with Western blot and RT-PCR method. Furthermore, Rg3 significantly ($p < 0.05$) upregulated mRNA expression of the host of neurotrophic factors: PPAR γ and Brain-derived neurotrophic factor (BDNF). In conclusion, our findings that Rg3 exerts neuroprotection in the MPTP model through antagonizing cytokine-mediated neuroinflammation while up-regulating the PPAR and BDNF merit clinical trial of Rg3 in PD.

P09.03

Multi-modal recruitment strategies lead to expeditious enrollment in STEADY-PD III

Tanya Sumini

Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA

Introduction: Timely recruitment in disease modification trials for Parkinson's disease (PD) has been challenging. STEADY-PD III is a 56 sites NINDS funded 36 month, Phase 3, parallel group, placebo-controlled study of the efficacy of isradipine 10mg daily versus placebo on the progression of disability in early PD.

Objective: To review recruitment strategies in a clinical trial of early untreated PD patients.

Methods: Prior to initiating recruitment, we developed a comprehensive recruitment strategy including 1) development of a Recruitment Committee of relevant stake holders including principal investigators, project managers, patient advocates, representatives from the sites, NINDS and the Michael J. Fox Foundation (MJFF); 2) Early and consistent involvement of advocacy organizations, including the Parkinson's Disease Foundation, MJFF, the National Parkinson Foundation, and the Muhammad Ali Foundation; 3) Presence at local, national and international meetings and patient events; 4) Recruitment tools including a toll-free number to connect patients with a study site, dedicated study website and study specific email address, Fox Trial Finder, advocacy training webinars, study specific printed recruitment brochures, posters, and newsletters; 5) National and local press releases; 6) Monthly coordinator teleconference calls to review and modify recruitment strategies; 7) Targeted minority recruitment strategies including

additional funding of selected sites; and 8) Involvement in the NIH sub-study RECRUIT to increase the racial/ethnic diversity of study participants.

Results: A total of 413 patients were screened with 336 participants including 34 minority subjects enrolled between November 3, 2014 and October 28, 2015. This was 6 months ahead of schedule with over 20 potential participants on reserve. Referral sources included: Site personnel (n=222), Neurologist (n=99), Fox Trial Finder (n=42), MJFF communication (n=16), Website or Web Ad (n=10), Self (n=9), Primary Care Physician (n=3), Family or friend (n=3), Event (n=3), Specialist (n=2), other (n=4).

Conclusions: A multi-modal recruitment approach involving relevant stake holders can expedite enrollment in PD clinical trials and can be utilized for future PD research studies. Involvement of the patient advocacy organizations is essential. Further efforts should be made to increase minority recruitment.

P09.04

Atypical antipsychotic therapy in Parkinson's disease psychosis: a retrospective study

Mei Yuan¹, Laura Sperry², Norika Malhado-Chang², Alexandra Duffy², Vicki Wheelock², Sarah Farias², Kevin O'Connor², John Olichney², Kiarash Shahlaie², Lin Zhang²

¹ Neurology, Hengyang, Hunan, China, People's Republic of,

² Neurology, Sacramento, CA, USA

Background: Parkinson's disease psychosis (PDP) is a frequent complication of idiopathic Parkinson's disease (iPD) with significant impact on quality of life and association with poorer outcomes. Atypical anti-psychotic drugs (APDs) are often used for the treatment of PDP, however, their use is often complicated by adverse drug reactions (ADRs). In this study, we present patients with PDP who were treated with the most commonly used atypical antipsychotic agents and review their respective ADRs. **Methods:** A retrospective chart review of electronic medical records (EMRs) was carried out to include a total of 45 patients with iPD who visited the movement disorders clinic between 2006 and 2015. After reviewing each patient's EMR, patients with incomplete records and/or with psychotic symptoms attributable to other conditions were excluded. All PDP patients treated with atypical APDs were included in the analysis for their specific ADRs. **Results:** Forty-five iPD patients (mean age of onset: 62.67±9.86 years) were included, of those 10 patients had psychosis (mean age of onset: 76.80±4.61 years). Out of the 45 patients, 22.2% were found to have psychotic symptoms, of whom 70% had hallucinations, 20% had delusions and 10% illusions. There were 46.7% iPD patients exposed to L-dopa monotherapy and 23.8% of these patients were reported to develop PDP. While 28.6% had their onset of psychosis when they were taking L-dopa and dopamine agonist therapy together, 25% reported onset during dopamine agonist therapy alone. Seventy percent of psychotic symptoms occurred after ten or more years from diagnosis of iPD. PDP patients were treated with quetiapine, olanzapine and risperidone separately or in combination, all of which were found to have certain ADRs (including sedation, sialorrhea, motor worsening and agitation). **Conclusions:** The prevalence of PDP is relatively high in older patients with iPD. The uses of the currently available atypical APDs in this patient population are often complicated by ADRs. The selective 5-HT_{2A} inverse agonist, pimavanserin, could be a better alternative in the treatment of PDP.

BASIC SCIENCE: ELECTROPHYSIOLOGY & FUNCTIONAL IMAGING, OPTOGENETICS

P10.01

The change of activation pattern in different stages of PD – importance of proximal muscle exercise

Chang-Hwan Kim¹, Bee-Oh Lim², Mi-Young Kim³, Jeheon Moon⁴, Jihyeon Kim⁴, Wooyoung Yang⁴

¹ Department of Physical & Rehabilitation Medicine, InHa University Hospital, Incheon, South Korea

² Physical Education, Chung-Ang University, Seoul, South Korea

³ Medical Science Res., InHa University, Incheon, South Korea

⁴ Biomechanics Laboratory, Korea Institute of Sport Science, Seoul, South Korea

Background: In the progression of Parkinson disease (PD), gradual derangement of the usage of lower extremity muscles are disabling. Therapeutic exercises has been effective on the mobility and balance. But the change of muscle activation pattern with progression of PD might give important information for therapeutic exercise implementation.

Objective: The purpose of this study was to investigate the activation of lower-extremity muscles according to Hoehn-Yahr scale during gait.

Patients and methods: Thirty six PD patients (Hoehn and Yahr stage 1; 13, 63.1±7.8, stage 2; 15, 67.1±6.4, stage 3; 8, 63.7±8.7) participated in this study.

Gait analysis was done with GAITRite system. We recorded EMG signals in tibialis anterior (TA), medial gastrocnemius (MG), soleus (SOL), rectus femoris (RF), and biceps femoris (BF) muscles using Noraxon 16 channels EMG system during walking at preferred speed. Rectified EMG signals were normalized to reference voluntary contractions (RVC) over a gait cycle at the preferred speed.

Results: In whole gait cycle, distal muscle group (TA, MG, SOL) showed similar patterns between H&Y stages. But in proximal muscle group (RF and BF) showed gradual changes without significance ($p>0.05$). And in specific gait cycle analysis, TA showed gradual attenuation throughout H&Y stages, but MG showed gradual increment in preswing phase ($p<0.05$).

The side to side difference in whole gait cycle showed difference in proximal muscles and SOL ($p<0.05$). The proximal muscles (RF, BF) showed significant changes of activity in swing phase.

Conclusion: The side to side difference of muscle activity were greater in proximal muscles (RF, BF) with progression of PD stages. The inter-limb co-ordination reduction might cause increment of risk of falling. The proximal muscle intervention might be more useful for exercise rehabilitation for the efficient gait and prevention of falling.

P10.02

Stimulation dependent, widespread cortical effects of galvanic vestibular stimulation in Parkinson's disease

Soojin Lee¹, Diana J. Kim², Jiayue Cai², Z. Jane Wang², Martin J. McKeown¹

¹ Pacific Parkinson's Research Centre, University of British Columbia, Vancouver, BC, Canada

² University of British Columbia, Vancouver, BC, Canada

Objective: With growing recognition of the roles of abnormal neural dynamics involved in PD and the success of deep brain stimulation (DBS) therapy, non-invasive brain stimulation has been actively investigated. Galvanic vestibular stimulation (GVS) is one such

approach that stimulates the vestibular nerves non-invasively and results in cortical changes via thalamocortical projections. Recent fMRI work examining brain connectivity has suggested that static/slowly-varying connectivity may be on the basis of anatomical considerations, but more fluid, flexible connectivity may result from functional interactions mediated with oscillations. The goal of this study was to determine if different GVS stimuli had influence on the functional interactions beyond classic vestibular cortices in the parietoinsular and temporal regions using fMRI and electroencephalography (EEG).

Methods: A total of 15 mild-moderately affected PD subjects (3 females; mean age: 65.7 ± 8.8 years; off medication) participated in the fMRI. We applied either noisy (nGVS: 0.1–10 Hz; 1/f-type power spectrum; 90% of individual threshold) or sinusoidal (sGVS: 1 Hz; 500 μ A) stimulus during resting-state fMRI. We performed a statistical analysis on BOLD signal amplitude changes to investigate significant brain regions affected by either GVS stimulus compared to rest. For the EEG study, a total of 11 PD subjects (4 females; mean age: 62.1 ± 7.7 years; off medication) and 11 age-matched healthy controls (5 females; mean age: 59.8 ± 8.7 years) participated. We investigated the effects of nGVS on EEG interhemispheric coherence in PD subjects and compared that to the baseline coherence in healthy controls.

Results: sGVS affected the BOLD signals near the parietoinsular region, whereas the areas affected by nGVS were found broadly distributed in the brain compared to rest condition. nGVS also induced widespread changes in the cortical interhemispheric connectivity and normalized connectivity altered in PD compared to the controls in the frontal, parietal and motor cortex areas.

Conclusions: Functional GVS effects are not merely restricted to brain regions with fixed anatomical relation to the vestibular system but can be modulation by stimulation parameters. This warrants developing fundamental methodologies to optimize stimuli waveforms in order to enhance previously-shown potential therapeutic effects of GVS by modulating disease-affected functional networks and/or potentially augmenting compensatory regions.

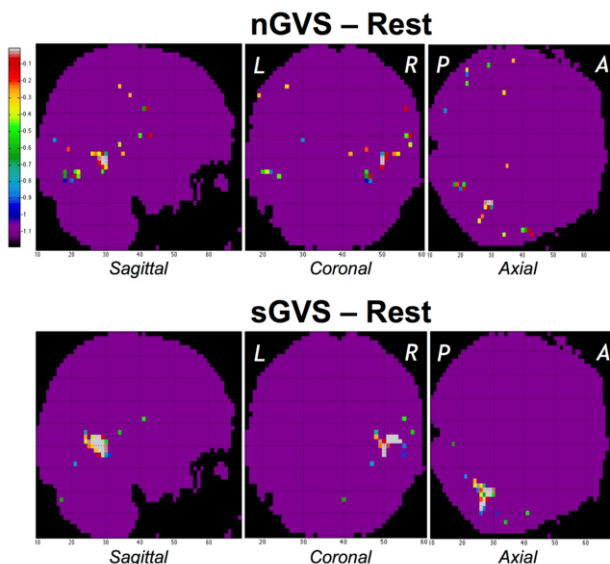


Figure: BOLD signal amplitude changes by different stimuli. p-value (FDR corrected) map (note: the colorbar shows p-value as multiplied by -1 for visual purpose)

P10.03

A novel somatostatinergic – cholinergic interneuronal circuit in the dorsal striatum

Alexandria Melendez-Zaidi, Austin Lim, Dalton James Surmeier
Northwestern University Feinberg School of Medicine, Chicago, IL, USA

Striatal interneurons are a diverse group of cells whose activity shapes overall striatal functioning and output. Interneurons exert their influence through diverse measures ranging from canonical inhibition via GABA release to excitation of pre- and postsynaptic muscarinic and nicotinic receptors to synthesis and release of the gaseous neuromodulator nitric oxide (NO). Recently, we have shown NO releasing plateau and low threshold spike interneurons (PLTSIs) exert powerful regulatory influences over excitatory inputs onto striatal projection neurons (SPNs). Because PLTSIs are autonomously active cells, their activity pattern likely dictates what their primary function is at any given time. However, what controls the activity of PLTSIs is not known. Given the robust expression of mAChRs in the striatum, we asked whether acetylcholine modulated PLTSI activity. Activation of postsynaptic mAChRs was found to induce a profound change in PLTSIs firing. Specifically, mAChR stimulation induced bursting in PLTSIs. mAChR stimulation also elevated PLTSI firing. Furthermore, this shift in firing could be recapitulated by a large burst of acetylcholine generated by optogenetic activation of ChIs. Because ChI activity is heavily influenced by glutamatergic afferents from the parafascicular nucleus (PFN), we asked whether these same afferents had any influence over PLTSIs. Retrograde tracing using a monosynaptic rabies virus revealed that, like ChIs, PLTSIs received robust inputs from both PFN. Recordings from mice in which PFN axons had been labeled with channelrhodopsin revealed that, as previously published, a burst/pause firing pattern could be induced in ChIs. Stimulating these inputs also induced a similar pattern in PLTSIs that was dependent on intact intrastriatal circuitry. The PFN-mediated burst/pause response in tonically active neurons (TANs) has been previously shown to be tied to learning. This work reveals that those TANs are actually a heterogeneous population composed of two distinct interneurons. Because bursting in PLTSIs is likely tied to periods of elevated nitric oxide (NO) or somatostatin (SST) release, thalamic stimulation of these cells may contribute to learning and plasticity through a coordinated flux of neuromodulators from both ChIs and PLTSIs. This new data suggests a reevaluation of our models of striatal learning with a greater emphasis on the modulatory properties of PLTSIs.

P10.04

The relationship among clinical features, DAT scintigraphy, and MIBG cardiac scintigraphy in patients with Parkinson's disease

Satoshi Orimo¹, Junya Ebina², Takehumi Sato², Teruhiko Sekiguchi², Makoto Takahashi², Akira Inaba²

¹ Kanto Central Hospital, Tokyo, Japan

² Japan

Objective: The aim of this study is to evaluate correlations among clinical features of Parkinson's disease (PD), odor stick identification test for Japanese (OSIT-J) score, nigro-striatal FP-CIT uptake, and cardiac MIBG uptake.

Background: Olfactory loss and cardiac sympathetic denervation on MIBG cardiac scintigraphy are in the supportive criteria and normal functional neuroimaging of the presynaptic dopaminergic system is in the absolute exclusion criteria in the new MDS Clinical Diagnostic Criteria for PD (Mov Disord 2015). However, the

relationship among clinical feature of PD, olfactory function, striatal FP-CIT uptake, and cardiac MIBG uptake remains to be elucidated.

Methods: One hundred patients with PD (average age: 70 years old, 33 men and 67 women) were enrolled in this study. Dopamine transporter (DAT) scintigraphy was performed in all the patients from April 2014 to November 2015. We evaluated correlations among the clinical features including age, duration of illness, MDS-UPDRS scores, OSIT-J score, the specific binding ratio (SBR) of DAT scintigraphy, and heart to mediastinum (H/M) ratio of MIBG cardiac scintigraphy. The clinical features, OSIT-J test, and MIBG cardiac scintigraphy were checked before and after three months from the time of DAT scintigraphy.

Results: FP-CIT uptake was decreased in all the patients. We found correlations between SBR and the age, the durations of illness, Hoehn-Yahr stage, MDS-UPDRS part2, part2+3, part4, and delayed phase of H/M ratio together with a tendency of correlation to MDS-UPDRS part 3 and delayed phase of H/M ratio. On the other hand, we found no correlations between SBR and MDS-UPDRS part1 as well as OSIT-J score.

Conclusion: We conclude that there is a correlation between the nigro-striatal dopaminergic function and motor symptoms together with cardiac sympathetic nervous system, but not olfactory system in PD.

P10.05

Maladaptive neuroplasticity in Parkinson's Disease?

Caroline Paquette, Jennifer Beer, Alexander Thiel
Canada

L-DOPA induced dyskinesias (LID), are a severely disabling long-term side effect of chronic L-DOPA therapy in Parkinson's disease (PD) causing a major impairment in the quality of life of these patients and their caregivers. There is evidence that the pathologically altered output from the basal ganglia toward the premotor and motor cortices may be a significant factor in the pathogenesis of LID symptoms (Brotchie 2000; Obeso et al. 2000). The premotor cortex is of special interest since it has been shown that corticospinal neurons, originating from the pre-motor cortex can directly be stimulated using TMS and Motor Evoked Potentials (MEPs) can be recorded from upper-extremity muscles (Teitti et al. 2008). In contrast to the primary motor cortex, this "secondary" motor area in the premotor cortex is less somatotopically organized and simultaneous activation of proximal and distal muscles has been described, producing a movement pattern in normal subjects which resembles dyskinesias.

We mapped, using single pulse TMS, the premotor cortex to directly measure cortical excitability in dyskinetic versus non-dyskinetic patients with PD. Our goal was to investigate a possible relationship between LID and cortical excitability in the premotor cortex.

Fifteen subjects with PD (aged 60±5 yrs) of which eight had LID. The premotor cortex was mapped bilaterally with single pulse transcranial magnetic stimulation (Neuronavigated Nexstim System) at 110% of the resting motor threshold (first dorsal interosseous (FDI) muscle) using a 1cm² grid centered at the dorsal premotor cortex. Motor evoked potentials of the FDI, extensor carpi radialis, and biceps brachii muscles were recorded. Excitability of the premotor cortex was quantified with muscle responses.

Responsiveness of each subject was characterized by total responses per total stimuli. Responsiveness in the dominant side of the dyskinetic group was smaller and less variable (LID Left Hemisphere 12±3%, LID Right Hemisphere 27±13%, non-LID Left Hemisphere 25±11%, non-LID Right Hemisphere 28±12%).

A symmetry difference in premotor excitability in subjects with LID compared to controls may indicate an asymmetry in synaptic plasticity in the premotor cortex, which may be related to the movement disorder.

P10.06

Optogenetic activation of striatal cholinergic interneurons or D1 medium spiny neurons regulates L-dopa-induced dyskinesias

Maryka Quirk¹, Xiomara Perez², Danhui Zhang¹, Tanuja Bordia¹

¹ USA

² SRI, USA

Dyskinesias are a disabling motor complication that arises with prolonged L-dopa treatment. Numerous studies indicate that multiple neurotransmitter systems play a role in L-dopa-induced dyskinesias (LIDs), although the pathways and mechanisms are poorly understood. Here we used optogenetics to investigate the role of striatal cholinergic interneurons and D1 GABAergic medium spiny neurons (MSNs) in LIDs. Choline acetyltransferase (ChAT)-Cre mice were lesioned by unilateral injection of 6-hydroxydopamine. After stable expression of AAV5-ChR2-eYFP or AAV5-control-eYFP in striatal cholinergic interneurons, mice were treated with L-dopa until dyskinetic. Continuous stimulation with short duration optical pulses (1-5 ms) enhanced LIDs, while longer duration optical pulses (20 ms to 1 s) reduced LIDs, with no effect in control-eYFP mice. This latter response was nicotinic receptor-mediated, suggesting that, similar to nicotine treatment, prolonged acetylcholine release reduces dyskinesias by desensitizing nicotinic receptors and dampening excessive cholinergic transmission. Studies were subsequently done to evaluate a role for D1 MSNs of the direct pathway. For this work, we used 6-hydroxydopamine-lesioned D1-Cre mice expressing AAV5-ChR2-eYFP or AAV5-control-eYFP selectively in striatal D1 MSNs. Both single pulse (100 ms to 30 s) and burst D1 MSN stimulation paradigms led to dyskinesias in L-dopa-naïve mice, with no effect of stimulation on dyskinesias in control-eYFP mice. Chronic L-dopa treatment alone induced dyskinesias to a similar extent as optical stimulation. Unexpectedly, combined L-dopa administration and stimulation resulted in an additive increase in dyskinesias. These data indicate that complex adaptive responses extending beyond activation of D1 and/or D2 receptors contribute to the expression of dyskinesias. Parkinsonism, as assessed via forepaw use, was not affected by optical activation of either cholinergic interneurons or D1 MSNs, suggesting that stimulation selectively regulates LIDs. Molecular studies indicate that changes in c-Fos and ERK are involved. This work directly demonstrates that both striatal cholinergic interneurons and the D1 MSN pathway play a critical role in regulating LIDs.

P10.07

Regulation of abnormal striatal oscillatory activity by glutamate receptor blockade in Parkinsonian monkeys

Arun Singh¹, Stella Papa²

¹ Atlanta, Georgia, USA

² Emory University, Atlanta, GA, USA

Objectives: Dopamine depletion in Parkinson's disease (PD) has been associated with abnormal oscillatory activities in the cortico-basal ganglia network (i.e. cortex, globus pallidus, and subthalamic nucleus). However, oscillatory activity in the striatum following dopamine loss and chronic replacement therapy remains poorly defined. Here, we studied striatal oscillations during "off", "on" and "on-with-dyskinesia" states in advanced Parkinsonian primates. Additionally, glutamate receptor antagonists known to stabilize neuronal firing changes after L-dopa administration were used to regulate the abnormalities in striatal activity.

Methods: Striatal local field potentials (LFPs) were recorded in MPTP-treated monkeys with standard techniques. The NMDA receptor antagonist LY235959 was injected into the striatum at the recording site before the systemic injection of levodopa. Striatal

LFPs were analyzed during “off”, “on” (after local artificial CSF or NMDA antagonist and systemic levodopa administration), and subsequently during “on”-with-dyskinesia states.

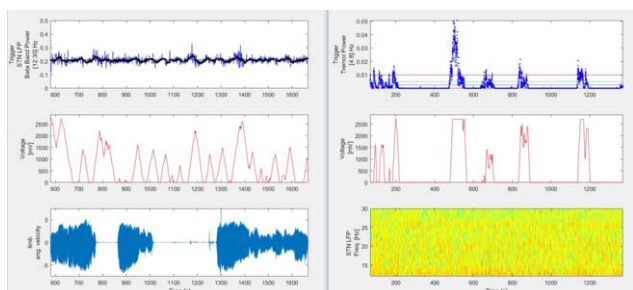
Results: A peak with the higher amplitude (relative power) in the 8-13 Hz (alpha frequency band) was recorded in the “off” state. This peak significantly decreased in the “on” state (local aCSF). However, a peak with higher amplitude in the 13-20 Hz (low-beta frequency band) was observed during “on” state. The NMDA antagonist reduced the peak amplitude in 13-20 Hz during the “on” state. No clear peak was observed in relation to dyskinesia. Therefore, reduced peak in 8-13 Hz and increased peak in 13-20 Hz could be associated with the dopamine response in chronically treated severe Parkinsonian animals. These results also indicate that the reduction of glutamatergic transmission regulates abnormal striatal oscillations in response to levodopa in the advanced stage of PD.

P10.08

Kinematic versus neural triggered adaptive DBS in a tremor dominant Parkinson’s disease patient

Anca Velisar, Judy Syrkin-Nikolau, Talora Martin, Megan Trager, Zack Blumenfeld, Helen Bronte-Stewart
Stanford University, Palo Alto, CA, USA

Adaptive Deep Brain Stimulation (aDBS) delivers neurostimulation only when and in doses that are necessary, compared to continuous (c)DBS for Parkinson’s disease (PD). For aDBS to be realized, it will be important to understand its safety and tolerability and to determine optimal control variables to drive changes in neurostimulation. We compared the efficacy of a kinematic (angular velocity of a tremoring limb) versus a neural variable to control a DBS in a tremor dominant PD patient. The patient was implanted with Activa PC+S Medtronic Neurostimulator that can sense local field potentials (LFPs) from subthalamic nucleus DBS leads. The system was updated with Nexus D3 firmware that allowed stimulation voltage to be externally controlled. The tremor was measured using a tri-axial gyroscope of a LG smart watch placed on the hand contralateral to the stimulated STN. For the kinematic triggered aDBS, the stimulator was off (0V) for long periods (several seconds), followed by periods when it was on at maximum voltage. In contrast for neural triggered aDBS, the stimulator was rarely off but the maximum voltage was also rarely achieved. Average kinematic triggered aDBS and average neural triggered aDBS voltage were 15.85% and 25.77% the voltage that was clinically set for the same period of cDBS (2.7V). In both aDBS cases the patient tolerated the stimulation changes and there were no adverse effects reported. Tremor resolved 64.44% of the time during kinematic aDBS and 31.37% during neural aDBS. In conclusion, during both kinematic and neural triggered aDBS, tremor improved using lower average voltages than cDBS, and aDBS was safe and tolerable.



P10.09

Gamma-band oscillatory activity in the motor cortex is progressively enhanced following repeated ketamine administration in 6-OHDA-lesioned rats.

Tony Ye¹, Mitchell Bartlett², Matthew Schmit¹, Scott Sherman², Torsten Falk², Stephen Cowen³

¹ Department of Psychology, University of Arizona, Tucson, AZ, USA

² Department of Neurology, University of Arizona, Tucson, AZ; Department of Pharmacology, University of Arizona, Tucson, AZ, USA

³ Evelyn F. McKnight Brain Institute, University of Arizona, Tucson, AZ; ARL Division of Neural System, Memory & Aging, University of Arizona, Tucson, AZ; Department of Psychology, University of Arizona, Tucson, AZ, USA

⁴ Department of Neuroscience, University of Arizona, Tucson, AZ, USA

Sub-anesthetic administration of ketamine has been used to successfully treat a variety of disorders such as treatment-resistant depression, post-traumatic stress disorder, and chronic pain. Recent clinical case studies from our group now indicate that low-dose ketamine infusion (0.15–0.3 mg/kg/hr for up to 72 hrs) acutely reduces motor impairments in Parkinson’s disease (PD) patients and ameliorates levodopa-induced dyskinesias (LID) for up to one month. Abnormal patterns of hypersynchronous oscillatory activity have been reported in all of the disorders treated successfully with ketamine, suggesting that it may act to disrupt network-level pathological oscillations. In PD, hyper-synchronous beta (β) oscillations (13–30 Hz) in the cortex and striatum may contribute to increased immobility, and is reduced with deep-brain stimulation (DBS) or levodopa treatment. Furthermore, gamma (γ) oscillations (30–70 Hz) in the motor cortex (M1) are associated with motor execution in healthy subjects. Administration of ketamine has been shown to increase high-frequency oscillations (HFOs) in rats and -band activity in humans. As such, it is proposed that ketamine-induced HFOs suppresses low-frequency activity associated with PD.

Using the unilateral 6-OHDA animal model of PD, we examined if ketamine administration reduces low-frequency oscillations associated with the pathology and enhances HFOs associated with motor execution.

Electrode arrays were implanted in the striatum, hippocampus, and M1 of naïve and 6-OHDA-lesioned rodents. To reflect human infusion protocols, repeated administration (i.p.) of sub-anesthetic doses of ketamine (20 mg/kg every 2 hrs) were used. Neural activity was recorded from awake and freely behaving animals for an 11-hr period.

Preliminary findings suggest that a single ketamine injection triggers HFO and oscillations in the dorsolateral striatum (DLS) and M1. We also observed that repeated injections increased activity in the M1 ($p=0.02$, $n=15$ sessions in 3 rats) in 6-OHDA rats. This is consistent with the idea that ketamine enhances motor function by altering the activities of networks of interneurons in the M1. We also observed that ketamine injections decoupled and oscillations in the M1. Given the role of oscillations in PD pathology, this decoupling may also contribute to ketamine’s capacity to mitigate motor impairments. Ongoing experiments aim to incorporate more 6-OHDA animals and the examination of effects in treating LID.

BASIC SCIENCE: PREVENTION, NEUROPROTECTION, NEUROPLASTICITY

P11.01

Transcranial magnetic stimulation over motor cortex in Parkinson's disease patients – which motor symptoms does it help?

Shashank Agarwal¹, Milton Biagioni¹, Miroslaw Brys², Michael D. Fox³, Andre Son¹, Geraldine Dacapano¹, Pawan Kumar¹, Elizabeth Pirraglia⁴, Robert Chen⁵, Allan Wu⁶, Hubert Fernandez⁷, Apama Wagle Shukla⁸, Jau-Shin Lou⁹, David K Simon¹⁰, Alessandro Di Rocco¹, Alvaro Pascual-Leone³

¹ Marlene and Paolo Fresco Institute for Parkinson's and Movement Disorders, Department of Neurology, New York University School of Medicine, New York, NY, USA

² Biogen, Boston, MA, USA

³ Berenson-Allen Center for Noninvasive Brain Stimulation, Division of Cognitive Neurology, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, USA

⁴ New York University School of Medicine, New York, NY, USA

⁵ Toronto Western Research Institute, University of Toronto, Toronto, ON, Canada

⁶ Ahmanson-Lovelace Brain Mapping Center, University of California School of Medicine, Los Angeles, CA, USA

⁷ Department of Neurology, Cleveland Clinic, Cleveland, OH, USA

⁸ Department of Neurology, University of Florida, Gainesville, FL, USA

⁹ Department of Neurology, University of North Dakota School of Medicine, Grand Forks, ND, USA

¹⁰ Parkinson's Disease and Movement Disorders Center, Department of Neurology, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, USA

Objective: The objective of this report was to perform secondary subset analysis in the MASTER-PD study exploring which specific motor symptom within UPDRS III improved with high frequency rTMS over motor cortex (M1) among Parkinson's disease (PD) patients.

Background: TMS has shown to improve motor symptoms in PD particularly high frequency stimulation over the M1. The primary results of the MASTER-PD study confirmed that bilateral M1 stimulation is better than sham for motor symptoms in PD. However, there are only a few reports that mention which specific motor symptoms improve.

Methods: 29 PD subjects were included in this subset analysis of the MASTER-PD study which was a multicenter, double-blind, sham-controlled, parallel-group trial. TMS protocol consisted of daily sessions of 2000 stimuli (50 x 4-sec trains of 40 stimuli at 10Hz) for 10 days, Monday to Friday for two consecutive weeks over bilateral M1 vs. placebo. Patients were evaluated OFF PD medications at baseline and 1 month post treatment. Sub-scores were calculated using aggregates of different items in UPDRS III. Outcome sub-scores were bradykinesia, rigidity, axial symptoms and tremor.

Results: Baseline demographic and clinical variables were comparable between the 2 groups. Total UPDRS III score decreased more in the M1 group than the sham group (-4.9 points vs. -0.3 points; $t=-2.1$, $p<0.05$). Post-hoc analysis revealed that only bradykinesia (-0.29 points vs. -0.01 points; $t=-2.099$, $p=0.045$) and rigidity (-0.2 points vs. 0.24 points; $t=-2.955$, $p=0.006$) decreased more in the M1 group than sham group.

Conclusion: The results of our study demonstrate that high frequency rTMS over bilateral M1 in PD is effective for improving bradykinesia and rigidity. This may reflect the potential for

developing targeted rehabilitation for specific motor symptoms based on rTMS frequency and specific cortical regions.

References:

[1] Chou Y-H, Hickey PT, Sundman M, et al. Effects of Repetitive Transcranial Magnetic Stimulation on Motor Symptoms in Parkinson Disease: A Systematic Review and Meta-analysis. *JAMA Neurol.* 2015;277(10):1-9.

P11.02

Neuroprotective effect of a new withanolide analogue of withaferin-A in mouse models of Parkinson's disease

Guillaume Brisson¹, Catherine Gilbert¹, Marcos Schan Profes¹, Jean-Pierre Julien², Martin Lévesque²

¹ Centre de Recherche de l'Institut universitaire en santé mentale de Québec, Québec, Québec, Canada

² Centre de Recherche de l'Institut universitaire en santé mentale de Québec/Département de Psychiatrie & Neuroscience, Université Laval, Québec, Québec, Canada

Withaferin (WA) is a withanolide extracted from the leaf of *Withania somnifera* a plant used in traditional Indian medicine. WA has been associated with various biological properties including anti-inflammatory, anti-tumor, anti-angiogenic and immune-regulating activities. WA is a known inhibitor of the Nuclear Factor-kappa B (NF-kB), a key transcription factor involved in the microglial cells proinflammatory response. Inactivation of NF-kB has been shown to reduce the production of inflammatory mediators by the microglia and to prevent dopaminergic neuronal loss in mice models of Parkinson's disease (PD). Here we tested a new withanolide from ImStar Therapeutics, IMS-088, that has improved pharmacological properties compared to WA. The inhibiting effect of IMS-088 on the NF-kB-mediated proinflammatory response and its incidence on dopaminergic neuron function and motor recovery was tested in a 6-hydroxydopamine (6-OHDA) animal model. Unilateral intrastriatal injection of 6-OHDA were performed on adult male C57BL/6 mice. Mice were administered IMS-088 during 4 weeks by oral gavage (25 mg/kg body weight) twice a day starting at 5 days prior to unilateral intrastriatal stereotaxic injection of the toxin. The animal rotational behavior, paw preference, and pole test coordination were performed every two weeks post-surgery to assess the effect of the drug on the motor behavior. Immunohistological analysis was performed to verify sign of axonopathy and neuron degeneration by staining the dopamine markers tyrosine hydroxylase and stereological analysis was used to quantify the effect of IMS-088 treatment on cell survival at midbrain level. Level of inflammatory markers and NF-kB activation were determined by a cytokine array and immunoblot, respectively. Behavioral analysis showed encouraging motor improvements. No significant change in dopaminergic neuron survival or axon density was observed in the 6-OHDA model despite the drug being efficient in reducing NF-kB activation and glial activation. Cytokines profile in the striatum suggested an inhibiting effect of IMS-088 on several pro-inflammatory cytokines and a beneficial increase in anti-inflammatory cytokines (IL-10 and IL-13). These results suggest that IMS-088 was effective reducing inflammation in our toxin model of PD. Work is on the way to increase the bioavailability of the compound in the brain. Results from this study could lead to the development of an efficient neuroprotective therapy for PD.

P11.03

Improving Parkinson's Disease outcomes with mobile software and wearables therapy

Jeff Broderick¹, Shelley Batts², Jeff Law², Ken Kubota², Eric Nelson²

¹ Benefit, Inc., Kentfield, CA, USA

² USA

Rapid advancements in mobile and sensor technology are providing new opportunities to improve population health cost-effectively. There are currently no pharmacological solutions that cure neurological disease, and few interventions have been shown to slow disease progression or improve quality of life (QOL). However, simple changes to lifestyle, diet, or co-morbidity risk reduction may delay disease onset, slow disease progression, and improve QOL. Specifically, there is growing evidence that exercise, and cycling in particular, may positively impact the symptoms and disease progression of Parkinson's disease by stabilizing essential tremor and muscle weakness.

Benefit is a digital health company that combines disease-specific software with mobile devices, wearable technology and data analytics to monitor and change behavior in a manner that improves patient outcomes. Our Parkinson's disease-specific application, pdFIT™, has been improving outcomes for participants with Parkinson's disease for almost two years as measured by our circleTap™ finger tapping test (a measurement of manual dexterity). Benefit features exercise protocols derived from high-cadence cycling benefits discovered by Dr. Jay Alberts of the Cleveland Clinic.*

Benefit has advanced the Albert protocol by creating a suite of personalized protocols driven by a user-friendly graphical interface suitable to patients of all fitness levels. In a 2-year longitudinal pilot study of four participants with Parkinson's disease who used pdFIT™ in conjunction with personalized high-cadence cycling routines, we found that individual and cohort-level circleTap™ scores improved significantly over baseline levels among all participants ($p < 0.05$). In addition, fitFactor scores (a measure of overall physical fitness) improved significantly for two of the four participants ($p < 0.05$), and all participants' fitFactor scores improved numerically.

We propose a new study that will validate this device-enabled, patient-driven therapy, potentially capable of positively impacting the course of Parkinson's disease. We will expand the scope of the user base of pdFIT™ and track self-reported UPDRS scores along with Benefit's circleTap™, fitFactor™ and walk360™ outcome measures.

* Alberts, J.L., Linder, S.M., Penko, A.L., Lowe, M.J. & Phillips, M. It is not about the bike, it is about the pedaling: forced exercise and Parkinson's disease. *Exercise and sport sciences reviews* 39, 177-186 (2011).



P11.04

Investigating the potential neurorestorative effects of a clinical Sigma-1 receptor agonist in a mouse model of Parkinson's disease.

Veronica Francardo¹, Francesco Bez¹, Jeffrey Sprouse², Christopher Missling², M. Angela Cenci Nilsson¹

¹ Basal Ganglia Pathophysiology Unit, Department of Experimental Medical Science, Lund University, Lund, Sweden

² Anavex Life Sciences, New York, New York, USA

Background: Sigma-1 receptor is an endoplasmic reticulum-chaperone protein promoting mechanisms that protect cells under stress. We have recently demonstrated, for the first time in an animal model of Parkinson's disease (PD), that a compound known to enhance the activity of Sig-1R promotes recovery of motor functions and activates neuroplasticity mechanisms in the nigrostriatal system (Francardo et al Brain 2014).

Objective: Using the same animal model of PD as in our previous study, we aim to investigate the potential neurorestorative effects of ANAVEX 2-73, a compound with activity at both Sigma-1 and muscarinic receptors that is currently being tested in people affected by Alzheimer's disease. In addition, we aim to study the Sigma-1 receptor occupancy of different doses of ANAVEX 2-73 in the brain.

Methods: The following experiments are now ongoing: (i) dose-response effects of ANAVEX 2-73 on the behavior of intact mice, (ii) setting up a radiographic method to assess brain Sigma-1 receptor occupancy by ANAVEX 2-73 in the mouse, (iii) behavioral-pharmacological evaluation of the effects of the compound in mice sustaining intrastriatal 6-hydroxydopamine (6-OHDA) lesions. Treatment is given daily for 5 weeks.

Results: In intact mice, ANAVEX 2-73 reduced novelty/stress-induced horizontal activity (a potential anxiolytic effect), although basal activity levels were not significantly reduced. Behavioral patterns were completely normal (no signs of either dystonia or stereotypic behaviors). Ongoing experiments on mice sustaining 6-OHDA lesions show trends towards an amelioration of parkinsonian motor symptoms in tests assessing spontaneous rotational activity and forelimb use asymmetry.

Significance: If successful, this study will accelerate the clinical development of ANAVEX 2-73 as a potential disease-modifying therapy for PD. We are in the fortunate situation that safety, bioavailability, tolerability of this compound have already been proven in human subjects, and that preliminary indications of a cognitive benefit have been obtained in a Phase 2a clinical trial for Alzheimer's disease (ANAVEX™ Life Science Corp).

P11.06

Laughter benefits – what would Robin Williams say?

Dwight Roth

Wichita, KS, USA

Laughter has many health benefits including

- Increase vascular blood flow and oxygenation of the blood
- Give a workout to the diaphragm and abdominal, respiratory, facial, leg, and back muscles
- Reduce certain stress hormones such as cortisol and adrenaline
- Increase the response of tumor- and disease-killing cells such as Gamma-interferon and T-cells
- Defend against respiratory infections—even reducing the frequency of colds—by immunoglobulin in saliva.
- Increase memory and learning; in a study at Johns Hopkins University Medical School, humor during instruction led to increased test scores
- Improve alertness, creativity, and memory

<http://www.care2.com/greenliving/8-health-benefits-of-laughter.html>

Before his death Robin Williams developed Parkinson's. What might he have said in his humor about PD? This session, while noting the negatives of PD, also notes humorous aspects about my own Parkinson's. An assumption is that if we can laugh at a challenge we are in control of it.

P11.07

Search for correlations of cycling and neuro genesis response in recruitment of new brain regions to support lost function in patients with Parkinson's disease

Joe Williams
USA

This submittal is based on the work of a small team of professionals working together to help one of their clients. The client (Joe R. Williams) was diagnosed in 2010 with Parkinson's disease and made a deliberate decision to forge new pathways to maintaining his health and concurrently to use his engineering background as a tool in establishing new pathways for lost neurological connections. The use of a bicycle outfitted with specialized measuring devices provided insight into providing a quantifiable base line for ability to perform basic as well as advanced motor tasks. To date, data gathered over five years has not been subjected to deep analysis. However, clear indications exist that our proposed study will provide movement disorder specialists with information that can provide an alternative and non-pharmaceutical treatment for those suffering from the effects of early to mid-stage Parkinson's disease.

Study overview: test study groups for improvement in neurological function through development of multi stage fitness and cycling programs. This study will utilize existing PD specific exercise routines and bring into this program a secondary cycling exercise regimen that is based on recent explorations in the improved neuro function in PD patients through cycling.

Our program objective is to document improvements in neuro function "neurogenesis".

CARE DELIVERY & QUALITY OF LIFE: CAREGIVING, RELATIONSHIPS, RESPIRE CARE, FAMILIES

P12.01

Through the eyes of the care partner: a balancing act

Sue Berger¹, Tiffany Chen², Jenna Eldridge², Linda Tickle-Degnen²

¹ Boston University, Boston, MA, USA

² Tufts University, Medford, MA, USA

Background: Previous research has focused on the activities and outcomes of caregiving for people with PD. Rarely has this research addressed the activities of care partners beyond the role of caregiving. The purpose of this study was to understand the variety of frustrating and satisfying activities experienced by care partners. Understanding this experience will guide rehabilitation therapy practice that includes both the person with PD and their care partners.

Methods: This qualitative study, using grounded theory and content analysis methods, analyzed transcripts of interviews with care partners describing recent satisfying and frustrating activities. Transcripts were a subset of data from a larger mixed methods longitudinal study, Emergence and Evolution of Social Self-Management of Parkinson's Disease (Tickle-Degnen et al., 2014,

BMC Neurology). Participants were the primary family care partners (all spouses) who were co-enrolled with qualifying community-living, English-speaking participants with idiopathic PD (Hoehn & Yahr Stages 2-4, 60-80 years old, scoring =26 on Mini-Mental State Exam). Care partners were interviewed in-person at baseline, 6-months, and one-year and these transcripts from twenty care partners were analyzed. Two researchers analyzed each transcript using NVivo 10, a qualitative data management program. During data analysis, initial codes were generated from current literature while additional codes arose from the data. A coding manual provided consistency between researchers. When new codes emerged, the coding manual was updated and changes were recorded in a process log. Researchers then reviewed and recoded previously coded transcripts as needed. Finally, the coding was analyzed to understand emerging themes.

Results: When talking about frustrating and satisfying experiences, care partners described a variety of activities, strategies, and attitudes. Major themes that emerged included 1) Activities: Caregiving and Beyond; 2) A Balancing Act: Caring for Self and Caring for Partner; and 3) Emotional Impact

Discussion: Findings provide a snapshot of the lives of care partners of people with PD. By understanding care partners' activities, strategies, and attitudes, rehabilitation therapists will have the tools to facilitate care partner engagement in meaningful activities. Supporting care partner health and well-being will benefit the person with PD.

P12.02

Parkinson's disease and parenting: the impact on children, teens and young adults

Elaine Book

Pacific Parkinson's Research Centre, Vancouver, BC, Canada

According to the World Health Organization, the management of chronic diseases should incorporate the well being of the patient's whole family. For a number of reasons, more children are growing up today affected by various parental chronic medical conditions. With respect to Parkinson's Disease (PD) more specifically, approximately 10% of patients are diagnosed with PD before the age of 50. Early onset diagnosis, postponement of childbearing and second marriages with younger families increase the likelihood of children/teens being impacted by Parkinson's Disease. As a parent of children/adolescents/young adults or as a professional working with families with PD, it is important to consider how PD specifically impacts children and family life. With appropriately timed support and resources, children and parents may experience a more positive family environment helping them live well with PD.

The poster content is the result of clinical experience, informal qualitative interviews with children/teens and a review of previous research on the impact of PD on the family. Key issues and practical suggestions for patients/families and health care professionals will be presented as well as detailing current resources.

P12.03

Perception gap for the motor and non-motor symptom between patients with Parkinson's disease and caregivers

Masaaki Hirayama¹, Tommi Minato², Tetsuya Made³, Kenichi Kashiwara⁴

¹ Nagoya Graduate University, Nagoya, Aichi, Japan

² Nagoya Graduate University, Nagoya, Aichi, Japan

³ Research Institute for Brain and Blood Vessels-Akita, Akita, Akita, Japan

⁴ Japan Okayama Kyokuto Hospital, Okayama, Japan

Objectives: To estimate the perception gap for social and living backgrounds between patients with Parkinson's disease and their caregivers.

Methods: Pairs of PD patients and their caregivers who were able to answer the question were enrolled to the study. We recruited patient-caregiver pairs using local Parkinson's family network at Aichi in Japan. All of them answered our original questionnaires. The questionnaire for patients constituted of three parts; 1) clinical symptoms, 2) social and medication-associating issues and 3) care-associating issues. Part 2 and 3 were summarized by the frequency in this study. We mailed a questionnaire to their families of Parkinson's disease patients. Reply was agreed in the survey.

Results: We could recruit 50 male and 69 female patients. Their mean age (standard deviation) was 70.3 (7.3). They had 9.3 (5.7) years of mean disease duration. Mean Hoehn and Yahr stage was 3.0 (1.2). Almost patients were not working. Among motor symptoms, freezing gait (41.2%), postural instability (39.5%), bradykinesia (31.9%), frequent falls (32.8%), and tremor (21.8%) were the main symptoms for PD patients to feel distress. Among non-motor symptoms, constipation (38.7%), low back pain (28.6%) and frequent micturition (21.0%) easy fatigue (21.8%) and dribbling saliva (22.7%) was complained frequently to feel distress by patients. The distressing symptoms for caregivers were frequent falls (32.3%), postural instability (24.2%) and freezing (34.3%) as motor symptoms, and constipation (32.3%), easy fatigue (10.2%), drowsiness (11.1%) as non-motor symptoms. Feelings when diagnosed were hopeless in 21.8%, blue in 45.4%, unchanged in 5% and optimistic in 26.6%. In caregiver burden, Persons responsible for their care were wife or husband in 57.1%, children in 15.1%, nursing care staffs in 14.3%, brothers or sisters in 4.2%. According to perception gap for the motor and non-motor symptom, easy fatigue, low back pain and urinary incontinence were significantly different between patients with Parkinson's disease and caregivers ($P < 0.05$).

Conclusion: Almost motor symptoms were shared the notion with patients and caregivers, while non-motor symptoms could not be detected even by caregivers. Especially, pain is most frequent complication but not detectable by caregivers.

P12.04

REFRESH!™ – online support groups: reducing the strain and isolation experienced by people with Parkinson disease and care partners through video based online support groups.

Sarah Jones, Judy Talley

Parkinson & Movement Disorder Alliance, Tucson, AZ, USA

32,000 people in Arizona are diagnosed with Parkinson disease. As the disease progresses, these individuals either now have or will have a caregiver, usually a family member. The complexity and progression of PD can result in increased isolation in people with PD and their care partners, particularly in rural areas and when the disease makes leaving home increasingly difficult.

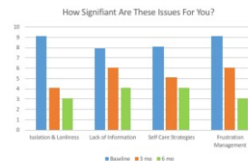
Refresh™, is a program of twice monthly, one-hour web-based support group meetings for people with PD and their care partners. Well suited to meet an increasing number of people with PD and caregivers within our aging population, Refresh!™ expands support once out of reach for people living in rural areas, small towns and isolated at home. It also readily allows for specialized groups – young onset, men, women, etc. Volunteer meeting leaders are recruited, trained, supervised and supported by PMDAAlliance staff. While online support groups are not new, after extensive research of more than 50 articles, evaluation at national and international conferences, and discussion with leaders in the caregiving and PD field, it is clear that no existing model performs or reaches underserved populations like Refresh!™. Current telephonic and online models, do not use the best features of web-based real-time

technology as it relates to reducing isolation and improving wellness. Refresh!™ capitalizes on the best of technology and human-centered design.

Program results include: 1. Reduced isolation for people with PD and care partners who live in rural communities and/or cannot attend live support group meetings. 2. The program increases knowledge of the disease and symptom management, eases stressors through association with others, and an improves the sense of wellbeing. 3. The interests and concerns of subgroups of underserved populations within the PD population, such as young onset, women with PD, male care partners and seasonal residents are effectively and conveniently addressed.

Refresh!™ fosters emotional improvement and enhances support to participants as measured using validated instruments. In addition to tracking number of participants/groups, results are measured using the Zarit Burden Interview, PDQ-Carer Inventory (complimentary license through Isis Innovation, UK) and UCLA Loneliness scale for care partners. PDQ-8 captures quality of life improvement for people with PD. All inventories are completed prior to joining the group, then again at 12-weeks and 6 months.

REFRESH! Online Support Group



JANE, 39, MOM HAS PARKINSON'S, DIAGNOSED 9 YEARS AGO.

"Living in rural Arizona is not easy. My dad recently died, he had Parkinson's and Alzheimer's. Now my mom has Parkinson's. I can't help but wonder what my future has in store for me. I feel so alone and had no one to talk with who understood what I was going through."



LILLY, 68, HUSBAND HAS PARKINSON'S, DIAGNOSED 7 YEARS AGO.

"People call us snowbirds. We live in Arizona during the winter and Minnesota during the summer. In Minnesota I miss my primary support. My support group in Arizona has about 50 Parkinson's care partners. It is a lifeline for me, now I can stay connected."

CHUCK, 71, WIFE HAS PARKINSON'S, DIAGNOSED 12 YEARS AGO.

"I am not used to care giving. I was an engineer all my life. I needed a small group to really talk through things. I just don't feel comfortable in large groups, and as my wife's disease progresses it is hard for me to get out."

SANDY, 52, HUSBAND HAS PARKINSON'S, DIAGNOSED 3 YEARS AGO.

"It is tough to be able to juggle helping him with PD and my work. Having a group that I can do from home and yet still connect with people who understand, help give me ideas and support is priceless."

P12.05

The journey from a draggin' daughter to a dragon daughter

Lily Liu

Family Caregiver for Mother who has Parkinson's Disease, Washington, DC, USA

The voice of the family caregiver for a relative who is living with Parkinson's Disease must be present and, most important, heard at The 4th World Parkinson Congress. The life of one individual living with Parkinson's has a tremendous impact on the lives of others, especially of the family caregiver.

My Mother has had Parkinson's for more than twenty-five years. I have been her sole family caregiver for the past five years, following the sudden passing of my Father. It has been a difficult journey, with many challenges, especially because my Mother suffers from severe biphasic dyskinesia. But, with the help and support of excellent physicians (Dr. Eric Ahlskog of Mayo Clinic and Dr. Stephen Reich of the University of Maryland), I have been able to help her enjoy a relatively good quality of life.

This presentation will highlight:

1. the importance of family caregivers serving as advocates for their family member living with Parkinson's Disease;
2. the lessons learned by applying The Scientific Method to caring for my Mother – experimenting with the dosage/frequency of her medications, making observations, testing my hypotheses, analyzing the data, and drawing conclusions about the best medication regimens; and
3. the unique situations faced by diverse/multi-cultural (in my case, Asian-American) family caregivers.

I wish to share my experiences so that other family caregivers feel empowered to help their relatives living with Parkinson's Disease. I have written essays about my family caregiving situation that have been printed and also published online. The theme I have focused on is the opportunity for family caregivers to transition from being a "draggin" (with exhaustion, worry, etc.) daughter to a "dragon" daughter, who is empowered by having knowledge, access to good neurologists and useful resources, and courage.

P12.06

Enhanced wellness for the Parkinson's care partner through group support

Virgen Luce¹, Trudy B. Festinger², Amy C. Lemen³

¹ New York University Silver School of Social Work, NYC, NY, USA

² Professor of Research, New York University-Silver School of Social Work, NYC, NY, USA

³ Fresco Institute for Parkinson's and Movement Disorders. NYU Langone Medical Center/NYU School of Medicine, NYC, NY, USA

Background: Parkinson's disease (PD) has been identified as a chronic progressive illness that can present many challenges to the caregivers. As such, the therapeutic group process can be effective in supporting caregivers to manage the perceived burden and stress. It can also explore options and creative ways of caring for their spouse with PD.

Aims: This study is an assessment of caregivers' perception in caring for their spouse with PD in the same household.

Methods: The anonymous survey was completed by participants in a Parkinson's Care Partners' Support Group in an urban community based wellness program in the northeastern USA during 2012 – 2015. The purpose of the research was to identify the caregivers' perception of self-efficacy for self-management of their caregiver's responsibilities.

Results: Survey data was obtained electronically via Qualtrics, from group participants. The sample includes 27 caregivers. Measurement scales showed good reliability. For ex., 6 items addressing thoughts and feelings experienced by caregivers showed a reliability of .855 and yielded a mean of 3.34 on a 5-point scale that ranged from Strongly Disagree to Strongly Agree (n=27). On another item, caregivers indicated that they often do not have the help they need in caring for the person with PD during anytime of the day or night or even in a crisis situation, with an average mean score of 2.09 on a 5-point scale that ranged from Never to Nearly Always.

Discussion: Findings from the study include 1) an analysis of caregivers' perceptions of the types of care the person with PD required based on physical, cognitive and emotional functioning; 2) the type of care the caregivers felt they provided and their experience with care-giving; 3) aspects of life changes as a result of care-giving responsibilities; and 4) how caregivers thought the support group experience was helpful in increasing confidence in managing the care-giving responsibilities.

Conclusion: This study indicated that the therapeutic group process is an effective intervention in supporting caregivers to manage the associated burden and stress in caring for their spouse with PD. The valuable intervention of mutual support helps caregivers (in their role) gain insight aimed at self-preservation, adaptation and self-efficacy. Future evaluations will assess the impact of experience on self-efficacy for self-management; participant satisfaction; and further replication of the program will be considered.

P12.07

C.O.P.E. – care optimally Parkinson education for caregivers, a small group education and support group for new caregivers and care partners

Anissa Mitchell

Florida Hospital Neuroscience Institute Parkinson Outreach Center, Winter Park, FL, USA

Objective: Many caregivers are unprepared for the demands of long-term caregiving in Parkinson's disease (PD) and have difficulty adjusting. Failure to make preparations and poor coping skills add to the burden resulting in significant caregiver strain causing health decline in both caregiver and patient. Available education resources are either written materials or online and lack the supportive component. Conversely, support meetings offer the supportive component but often lack clear, defined education. COPE small group programs seek to offer both.

Methods: COPE groups offer caregivers four-module education and support sessions. Maximum attendance per session is ten people allowing for an intimate small group experience. Education modules address disease progression and accessing resources, behavioral aspects of PD, caregiver support/stress management and relationship concerns, including intimacy. Sessions provide presentation, discussion and utilize cognitive behavioral therapy techniques pertaining to stress and coping. Individual sessions are additionally offered with the social worker. Caregivers are asked to complete a caregiver burden screen and questionnaire at the start of program, survey at completion and a six month follow up survey and burden screen.

Results: 58 caregivers attended COPE in the first year. The majority of caregivers were women (86%), most were spouses (66.07%) or other family/friend (14.28%) followed by children (12.5%) and hired caregivers (7.14%). Ages varied from under 40 to over age 70. Most had loved ones diagnosed between one and five years (73%). Attendees were surveyed on content significance and practical assistance at the end of the session and at six months. Caregiver burden was screened at beginning and at six months. 84.7% (n=46) rated the content as extremely practical, offered opportunity to address concerns and provided needed support. Mean burden scores on the Zarit Caregiver Burden Screen were 7.0 at the beginning (n=44 completed) (score of 8 and higher indicating risk) and an average of 6.38 (n=21 completed) at six months. At six month follow up 80% (n=25) indicate they have referred back to material, 90% felt material continued to be useful and practical, and 88% felt like they were better managing their stress. Ongoing support offered in caregiver support groups.

P12.08

Decreased burden among caregivers of patients with Parkinson's disease psychosis (PDP) treated with pimavanserin, a selective 5-HT_{2A} inverse agonist

James Norton¹, Doral Fredericks², Dag Aarsland³, Kathy Chi-Burris², Michaela Karstedt⁴, Clive Ballard⁵, Randy Owen²

¹ San Diego, CA, USA

² ACADIA Pharmaceuticals Inc., San Diego, CA, USA

³ Stavanger, Norway

⁴ Stockholm, Sweden

⁵ Newcastle, United Kingdom

Objective: To determine the effect of pimavanserin, a selective 5-HT_{2A} inverse-agonist, on caregiver burden.

Background: Parkinson's disease Psychosis (PDP) is associated with functional and cognitive decline, significant morbidity and mortality, and increased caregiver burden, which often leads to early institutionalization. Pimavanserin (NUPLAZID™) is a potent 5-HT_{2A}

inverse-agonist being developed for PDP. Unlike other antipsychotics, it has no dopaminergic, histaminergic, adrenergic or muscarinic activity. In two randomized, 6-week controlled trials of pimavanserin 34 mg, PDP patients demonstrated improvements in symptoms of psychosis (hallucinations and delusions), as well as improvements in the clinical global impression of severity and improvement, nighttime sleep, daytime wakefulness, and caregiver burden.

Methods: A consented caregiver who attended all clinic visits with the patient completed the Zarit 22-item caregiver burden scale (CBS), which assesses the impact of the patient's disabilities on the caregiver's life. The goal of this exploratory endpoint was to gauge how treatment of the patient's PDP affected the caregiver's sense of burden. Most caregivers were spouses or other family members.

Results: Mean baseline (pretreatment) CBS scores were 30.6 for placebo (N=133) and 28.8 for pimavanserin 34mg (N=135). Significant improvement in burden was observed for the pimavanserin group (-4.8 points) over placebo (-1.1 points) at 6 weeks ($p < 0.001$) (LSM difference of 3.7 points [95% CI -5.6, -1.5]; Effect size: 0.43). Although no single item drove the CBS effect, the item with the strongest response was Item 16 (Responsibility subscale), which asked about any inability to take care of the relative for much longer (LSM difference of -0.43 points [95% CI: -0.63 to -0.22; $p < 0.001$]).

Conclusions: While the CBS score was an exploratory endpoint in these studies, the trend in improvement does provide further support that caregivers are impacted by the severity of psychosis in the PD patient. Stressors may cause them to make decisions around care for the patient, such as placement into a nursing home, due to their perceived inability to care for the patient. Additional study in this area is warranted.

Previously presented at AAN 2015 in Washington, DC

P12.09

Coping with dual-care challenges: managing personal Parkinson's care needs while caring for a spouse with dementia

Kaitlyn Roland, Neena Chappell

University of Victoria, Victoria, British Columbia, Canada

Spouses comprise a large proportion of dementia caregivers and are often faced with their own health concerns, in addition to care stressors. The increasing prevalence and extended survival of persons with neurodegenerative disease may increase dual-diagnoses in couples. No one has yet examined the lived experience of caregivers coping with dual-care challenges. Interpretive phenomenological analysis was used to describe the lived experience of adults diagnosed with Parkinson's (PD) who care for a spouse with Alzheimer's disease (AD).

Semi-structured interviews captured rich descriptions of the dynamic process of integrating care for self and other. Content and thematic analysis identified themes using an emerging strategy. Statements that highlighted essential aspects and context of the lived experience were extracted. The analysis was mainly concerned with the meaning of the simultaneous experiences of caring/receiving, lived spousal relationship, and interpretations of quality of the lived experience. Units of meaning were grouped together into sub-themes and themes. Resultant themes were incorporated into a narrative description of the experience.

Participants were two persons with PD (65-69years) who were caring for a spouse at home with moderate-severe AD for 3-6years. Three themes emerged. (1) 'Role Tension' captured the internal conflict around prioritizing care and the need to conserve energy. (2) 'Changing Expectations' described the subtleties of daily losses and continual re-acceptance of the current situation as if "caught in the current". (3) 'Meaning' was expressed through (a) 'choosing

positivity' and being grateful that "our heads are above water, even though my feet aren't on the ground. That's all I can ask for"; and (b) 'time limit on future goals' brought a sense of motivation to accomplish something significant while there is still the opportunity: "S/he'll go into care while I'm still standing. There's no point in losing him/her if I can't create a life for me."

Understanding the process of caring for a spouse with AD while simultaneously managing personal PD care needs is important for future interventions aimed at developing self-care skills needed to manage role strain, disability, and disengagement. This knowledge may be applied to healthcare interactions in providing supportive care for persons with dual roles.

P12.10

Synergistic quality of life for people with Parkinson's disease and their caregivers

Pennie Seibert¹, Nichole Whitener², Colleen Poulton²

¹ Research Institute at Saint Alphonsus Regional Medical Center, Boise, ID, USA

² USA

Parkinson's disease (PD) progression increases responsibility for the individual's spouse and immediate family members who are likely to assume the role of caregiver (CG). This interpersonal blending of responsibilities as a spouse and family member with the role of CG creates a cyclical relationship that impacts overall quality of life (QoL), well-being, and family dynamic.

We constructed two questionnaires specified for PD (84 items) and their CG (81 items). Both were either mailed or emailed to 256 people from a PD association list and we conducted in person interviews with 8 pairs of individuals with PD and their CG. The questionnaires and interviews included a wide range of topics such as health history and change, physiological health, social engagement, support availability, stressors, emotional health, sleep, financial concerns, and overall QoL. Data were analyzed using Chi-square, regression, and T-tests to evaluate the sleep similarities and differences of individuals with PD and CGs.

Fifty-nine participants responded to the questionnaire (PD: 20 males, mean age 73.42; 11 females, mean age 77.73); (CG: 4 males, mean age 85.25; 24 females, mean age 69.13). We analyzed data specific to CG then compared the CG and PD groups. Analyses revealed numerous differences between groups. For example, the PD group expressed greater overall support satisfaction while CG reported a lack of support from family and close friends, 72% of CG reported an increase in stress levels versus 51.6% of those with PD. Both groups reported a decline in QoL with increases in sleep disturbance, health issues, depression, feelings of isolation, fatigue, anger, and tearfulness.

PD creates multifaceted challenges to QoL for both those with PD and their CG. The need for accessible support systems within the caregiving community has grown substantially and contemporary research suggests that few therapeutic methods or treatments have been developed to correct this shortcoming. CG frequently being ignored by medical professionals despite their essential role intensifies challenges to their QoL. New medical policies and protocols need to be implemented to better address the critical role of CGs and the impact PD has on the development and/or exacerbation of psychological and physiological health factors.

CARE DELIVERY & QUALITY OF LIFE: FITNESS, WELLNESS, NUTRITION

P13.01

Enteral feeding using Duopa PEG-J – a case report

Andréane Bernier

CHUM (Centre hospitalier de l'Université de Montréal), Montreal, Québec, Canada

Introduction and objective: In Parkinson's disease, as in many other diseases, malnutrition is associated with a decreased quality of life. When dysphagia occurs, it can induce malnutrition that can be resistant to oral feeding. Enteral nutrition is an option to increase nutritional status and lower the risk of aspiration pneumonia. Patients treated with Duopa already have a percutaneous endoscopic gastrojejunostomy (PEG-J) in place for their treatment. We hypothesized that this could be a viable route to nourish them through. Enteral nutrition using Duopa PEG-J has never been reported in the literature before.

Case report: A 71-year-old man treated with Duopa was referred to our clinical nutrition service with repeated aspiration pneumonias incurring frequent hospitalisations and antibiotic treatments. His pneumologist recommended enteral feeding. His Parkinson's motor symptoms were well managed by his medication. At that time the patient suffered from moderate to severe malnutrition and moderate dysphagia. Enteral nutrition was begun using his Duopa PEG-J through the gastric port. The nutrition was administered with a feeding pump during the night. An adaptor had to be crafted to fit the enteral feeding and PEG-J ports that were not compatible. This modification reduced the size of opening to 8 or 9 Fr which did not allow for medication administration on elevated obstruction risks. Therefore, the patient's PEG-J was changed for a larger caliber (20 Fr) which made medication administration possible. To eliminate night feedings for the patient's comfort, both enteral nutrition and Duopa were provided simultaneously during the day. This did not have a significant impact upon the effectiveness of Duopa. After a few months, enteral feeding had to be stopped due to a severe gastrointestinal condition that was not related to the use of the Duopa PEG-J.

Discussion and conclusion: This case illustrates that it is possible to use the Duopa PEG-J to administer enteral nutrition. The 20 Fr PEG-J is more useful as it can also be used for medication administration. The Duopa PEG-J is not currently designed to fit with enteral feeding tubes but it could be an interesting avenue for Parkinson's patients presenting malnutrition and dysphagia.

P13.02

The impact of a 6-month Dance for Parkinson's® program on physical function and well-being: a mixed methods pilot study

Sandra Brauer¹, Erica-Rose Jeffrey², Robyn Lamont¹, Graham Kerr³, Gene Moyle⁴

¹ School of Health & Rehabilitation Sciences, The University of Queensland, Brisbane, Qld, Australia

² Dance for Parkinson's, and Dance, Creative Industries Faculty, Queensland University of Technology, Brisbane, Qld, Australia

³ Institute of Health & Biomedical Innovation, Queensland University of Technology, Brisbane, Qld, Australia

⁴ Dance, Creative Industries Faculty, Queensland University of Technology, Brisbane, Qld, Australia

Background: A recent systematic review of a wide variety of dance interventions for people with Parkinson's disease (PD) has reported that dance may improve balance, endurance and reduce

impairments in some people with PD. The Dance for Parkinson's® program, developed by the Mark Morris Dance Company NY, has been adopted by dance studios internationally, but little research has been undertaken to understand its effects, particularly from the perspective of the person with PD.

Aim: To evaluate the impact of a 6-month pilot Dance for Parkinson's program on physical function and wellbeing in an Australian sample of people with PD.

Methods: Twelve people with PD volunteered to participate in this mixed-methods research project. All attended up to 30 ability-appropriate Dance for Parkinson's classes that were conducted in the Queensland Ballet Dance Studios between October 2013 and July 2014, using live music and choreographic material from five ballets. Clinical measures of physical function including gait and balance, and in-depth interviews were performed the week before and after the 6-month program.

Results: Eleven research participants (7 female, 4 male) aged 38-80, completed the Dance for Parkinson's program and both pre and post assessments. On average participants attended 82.7% of classes. Quantitative analysis revealed significant improvements in functional mobility under single ($p=0.027$), and dual-task ($p=0.001$) conditions. Gait velocity also increased significantly under single and dual task conditions ($p<0.05$). There was a trend towards improvement in functional balance ($p=0.052$). Qualitative analysis revealed that Dance for Parkinson's positively contributed to the physical, emotional and cognitive health of participants, in addition to providing a vehicle for social engagement and creative expression. With respect to their physical health, participants reported that participation in the classes helped improve their daily mobility, co-ordination and fluency of movement. Participants reported that the dance class acted as a 'gateway activity' to participation in additional exercise, social activities and other new dance experiences.

Conclusion: Dance for Parkinson's provided a community-based, creative opportunity for people with PD to participate in exercise that was beneficial to walking and balance, emotional and cognitive health, and social and artistic participation.

P13.03

Feasibility of peer coaching to increase physical activity in people with Parkinson's disease

Cristina Colon-Semenza¹, Nancy Latham², Lisa Quintiliani³, Nicole Sullivan¹, Terry Ellis¹

¹ Boston University, College of Health & Rehabilitation Sciences: Sargent College, Center for Neurorehabilitation, Boston, MA, USA

² Boston University, School of Public Health, Health & Disability Research Institute, Boston, MA, USA

³ Boston University School of Medicine, Boston, MA, USA

Background: The great majority of individuals with Parkinson's disease (PD) are sedentary. Long-term engagement in exercise and physical activity increase quality of life and function and may mitigate the progression of the disease. Prior research reveals that common barriers to exercise are primarily psychosocial factors (ie: self-efficacy, outcome expectations), as opposed to physical factors (ie: motor impairments). Peer support may positively affect the behavioral factors that are crucial for the adoption of physical activity. There is a critical need for a safe, feasible, and effective method to assist those with PD to consistently participate in active lifestyles.

Objective: To determine the safety, feasibility, acceptability and initial efficacy of a peer coaching model to increase physical activity (ie: walking activity) in people with PD.

Method: A peer coaching training program was developed and pilot tested with 10 individuals with PD (5 peer coaches, 5 peer mentees). The five peer coaches were trained in basic knowledge of

PD and exercise, active listening and motivational interviewing during online and in-person training. All ten participants were given FitBit Zip activity monitors. Peer pairs interacted via the FitBit application and via weekly telephone calls for a period of 8 weeks.

Results: There were no adverse events over the course of the study. All participants would recommend this program to others with PD. All peer coaches and mentees were satisfied/very satisfied with either the peer coach training program or the peer coaching experience. All peer coaches and mentees would recommend this program to others. Four of the five peer pairs completed all eight recommended phone conversations and the remaining pair completed six of the eight phone conversations. The peer mentees increased their average steps per day by 31% from 5428 steps (SD 2440) to 7115 steps per day (SD 1291). Four of the five peer mentees increased their average steps/day above the minimally clinically important difference.

Conclusions: Peer coaching is safe, feasible and acceptable in people with PD. Peer coaching may be an effective method to increase physical activity in people with PD. Further research is needed to understand the factors that mediate this relationship.

P13.04

Parkinson's specific HI-FIT group exercise class: developing and maintaining a successful class

Amanda Elliott, Rachel Kaufenberg

Struthers Parkinson's Center, Golden Valley, MN, USA

Objective: Develop an innovative high intensity group exercise class (HI-FIT: High Intensity Functional Interval Training) designed to address impairments secondary to Parkinson Disease (PD) while maintaining regular class attendance.

Background: High intensity exercise is recognized as an important evidence based treatment for PD. Group exercise yields improved compliance compared to individual. Developing a class that meets the needs of individuals of varied ages, disease states, and physical abilities as well as maintaining attendance can be challenging.

Methods: A 60 minute HI-FIT class has been offered 2 days/week for 2 years at Struthers Parkinson's Center, developed and taught by 2 physical therapists with PD expertise. Instructors incorporate evidence based activities including PWR! and large amplitude movements, boxing principles, and TABATA intervals, as well as low intensity stretching. Activities are varied each class. In addition, fun/up-tempo music, cognitive challenges, verbalizations, group exercises, and participant feedback is integrated. A survey was given to participants within a 2 week period at the 2 year mark, posing questions regarding reasons for attendance and benefits received.

Results: Monthly attendance was taken over 2 years; 35 participants attended 2 or more classes with the highest class size being 18. Percent attendance was calculated; 17 participants attended >50% of available classes since their start date. Surveys were distributed to 20 participants and 18 were returned. The 3 variables considered very important were the instructor, PD-specific training, and a fun atmosphere; the 3 variables considered not important were time of class, music selection, and cost. Camaraderie was frequently stated as a reason for attendance. All participants reported benefit in areas commonly affected by PD (i.e. balance, posture, strength). 72% reported they would attend more often if additional classes were offered.

Conclusions: Attendance rates and survey responses indicate a high degree of value and participant satisfaction. Instructors will continue to place emphasis on variables considered very important by participants. Consideration will be given to offering the class at a greater frequency.

P13.05

Nordic walking improves postural stability and gait spatial-temporal characteristics in people with Parkinson's Disease.

Marie-Anne Gougeon¹, Lei Zhou², Julie Nantel³

¹ Applicant

² Faculty of Health Sciences, University of Ottawa, Ottawa, Canada

Background: Postural instability, gait deficits and mild cognitive impairments increase risk of falling in individuals with Parkinson's disease (PD). Evidence showed that a six-week Nordic Walking (NW) training could improve postural stability and some aspects of locomotion in older adults. However, it is not known if a self-directed NW training program could improve postural stability and gait spatial-temporal characteristics in individuals with PD.

Purpose: The purpose of this study is to assess the effect of a NW training program on postural stability, gait spatial-temporal characteristics and arm symmetry in individuals with PD and to determine the attentional demands associated with NW compared to normal walking.

Methods: Twelve individuals with PD (age: 61.6±11.7yo) participated in a 6-week independent NW training (12 to 16 sessions x 30 minutes). Following the training, we assessed gait spatial-temporal characteristics, upper and lower limb asymmetry and trunk postural stability when walking without poles (NP) and with NW poles. Participants were asked to perform four 25m walking trials; with/without poles and with/without cognitive task. The cognitive task consisted of naming as many words as they could within a given category. Data were collected with APDM accelerometry system. Two-way ANOVA were used to assess the effect of the poles and of the cognitive task on gait pattern. Mild Cognitive Impairments were assessed using the Montreal Cognitive Assessment (MoCA).

Results: NW reduced arm symmetry index, trunk frontal range of motion and peak velocity when walking with and without performing a cognitive task ($p<0.05$). The addition of the cognitive task when walking with and without poles decreased cadence and gait speed and increased gait cycle time ($p<0.05$).

Conclusions: The reduced range of motion and velocity of the trunk in the frontal plane of motion suggest that NW can improve postural stability independently of the addition of a cognitive task. However, dividing attention affected gait spatial-temporal characteristics. This shows that an independent 6-week NW training program can improve postural stability and some aspects of gait in individuals with PD. It also suggests that NW is a suitable practice for gait rehabilitation protocols.

P13.06

Dance and Parkinson's disease: exploring the physical and psychological effects of a dance programme in people with Parkinson's disease

Katherine Grosset¹, Miriam Early², Catherine Cassidy³, Jenny Langlands³, Angela O'Donnell¹, Gordon Duncan⁴, Donald Grosset¹

¹ Institute of Neurological Sciences, Glasgow, United Kingdom

² Dance Base, National Centre for Dance, Glasgow, United Kingdom

³ Dance Base, National Centre for Dance, Edinburgh, United Kingdom

⁴ Western General Hospital, Edinburgh, United Kingdom

Background: Exercise has benefits for people with Parkinson's (1) and dance in particular has physical, social and psychological benefits. The majority of studies of dance in Parkinson's have focused on tango, and used balance outcome measures (2), but other forms of dance may have broader appeal (2) and other outcome measures such as life satisfaction, quality of and fluidity of

movement may be more meaningful. Contemporary dance has been studied in older people (3) but not specifically in people with Parkinson's. There may be a wider impact on caregivers, family member and friends of people with Parkinson's.

Objective: To explore the effect of a combined approach of ballet and creative contemporary dance combined with live music on life satisfaction, and quality of life in people with Parkinson's disease and their caregivers, family member and friends, and on fluidity of movement.

Methods: 70 people with Parkinson's, and 70 people without Parkinson's (caregivers, spouses or friends) will attend weekly one-hour dance classes run by Scottish Ballet and Dance Base. A control group of 70 age, sex matched Parkinson's cases will be recruited from a movement disorder clinic. Comparative assessments will include demographics, and questionnaires on satisfaction with life and quality of life using the PDQ39. Fluidity of movement will be assessed using videos.

Results: We will compare life satisfaction and quality of life between dance class participants and matched controls.

Conclusions: Our hypothesis is that dance will have positive effects on life satisfaction, quality of life and fluidity of movement.

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P13.07

Parkinson's fitness-community based programs

Linda Hall¹, Keith Hall²

¹ Salem, MA, USA

² Parkinson's Fitness, Salem, MA, USA

Objective: A Parkinson's diagnosis delivers the challenge-try to take flight or enter the fight!

Methods: Our non-profit foundation has expanded its mission of providing locally based goal-oriented exercise programs to include participation in specialized art, drumming, boxing, dance and movement, and upcoming chorus instruction. Designed by ability levels, individualized balance, stability, and strength training exercises help participants concentrate on "competing" against their Parkinson's symptoms- similar to an athlete in training. They challenge themselves and fellow members to consistently increase their physical goals, while sharpening cognitive and social relationship skills through participation in an eclectic series of art programs.

Results: Following an initial Parkinson's diagnosis, eventually everyone asks: "So, what do I/we do now?" Concerned about future physical and emotional challenges, many people will diligently seek out physicians who will best listen and guide, join clinical trials, research the Internet, read the newest articles, consider joining a support group, and participate in Parkinson's assessment programs, where they learn the importance of regular exercise to increase endurance, improve balance and mobility, and help avoid injury.

Our vision for presenting inventive multi-faceted Parkinson's exercise and arts programs in our previously underserved local area is to educate otherwise healthy individuals and families that they can continue to create confident, proactive, resilient lives by establishing empowering physical and cognitive goals. Parkinson's Fitness classes offer welcoming, non-intimidating opportunities for sharing interactive resourcing and social interaction with others who

understand the questions, fears, frustrations, limitations and triumphs associated with the effects of a life changing physical condition.

P13.08

Use it or lose it: a comparison of forms of exercise in progression of Parkinson's disease

Kasey Holland

Bastyr University neurology research with Dr. Laurie Mischley, Kirkland, WA, USA

Objective: To determine which form of exercise is associated with the lowest symptom severity score in a cohort of patients with Parkinson's Disease (PD).

Background: Exercise is a key component of lifestyle modification in delaying the progression of Parkinson disease. Exercise seems to have a dose – dependent effect on disease modification in PD. Determining what type of exercise is the most effective is vital for effectively counseling patients and empowering them to take control of the modifiable factors that can influence their health and quality of life.

Methods: An internet-based natural history study was designed to generate information useful to patients and providers. An assessment tool, the Patient-Reported Outcomes in PD (PRO-PD) scale, was designed to assess PD severity and was validated against the existing measures of disease severity. Disease severity was defined as PRO-PD, adjusted for age, years since diagnosis, and income. Baseline survey data was used to identify individuals who claimed to have done the said activity consistently over the past 6 months. 844 participants asked subjects how many days a week they exercised. Patients were then asked what kind of exercise they were performing in categories including swimming, running, biking, hiking, dance, walking, climbing, tai chi, yoga and other.

Results: 844 participants participated in the study, with a mean age of 62.8 years and an average 5 years since diagnosis. The most common forms of activity were walking (74%), biking (25%), and yoga (22%). After adjusting for age and years since diagnosis of Parkinson disease, all three forms of exercise were associated with statistically significant improvements in PROPD scores when compared to subjects not doing those activities. Individuals who did yoga had an average 174 point lower PD symptom score, with the biking cohort 89 points lower than non-cyclists, and walking only being associated with a 63 point lower score.

Conclusion: Individuals who report doing yoga conceitedly over the previous six months reported less severe PD symptoms in this cohort of patients, followed by biking and walking. This study gives additional evidence to develop further studies of yoga in modifying disease progression in Parkinson Disease.

P13.09

MOVE IT!™ exercise club – real time streaming exercise program: maximizing technology to deliver an online Parkinson specific exercise program provided by Parkinson trained exercise professionals.

Sarah Jones, Judy Talley

Parkinson & Movement Disorder Alliance, Tucson, AZ, USA

Exercising is vital for those with Parkinson's disease, but to obtain optimum results, it must be done right. Many people in Arizona lack access to qualified interactive instruction. This grant enables PMDAAlliance to establish 5 new Move It!™ exercise clubs for people with PD living in underserved communities to join disease specific exercise classes – regardless of where they live.

Move It! clubs utilize a streaming service called Zoom that gives participants access to video-based, real-time participation. Participants log onto the designated Zoom link for the class they enroll in via a single click of a weblink on any computer, tablet or smart phone. They are then placed in the live class via camera streaming. Everyone is able to see everyone in the class. The teacher can talk with and see the participants as the class is happening. Classes are conducted by professionals trained in PD. Unlike a DVD, which requires a high level of self-motivation and does not offer community engagement, socialization or feedback, the Move It! Exercise Club enables people to engage with each other, develop a sense of community and participate in an exercise program that is specific to their needs.

Program results include: 1. People with Parkinson disease will report improved physical outcomes, including but not limited to balance, range of movement, flexibility and strength. 2. Self reported improvement in overall sense of wellness and engagement in community for people with Parkinson disease who live in rural, underserved or home bound locations. As a result of this program individuals who have become isolated and marginalized build connection to a community through real-time streaming and engagement with an active exercise class and the class leader. 3. Improved understanding of the physical, mental, social and motor issues that impact people with PD. We will provide helpful and essential information to people with PD while educating them about the various ways they can improve their physical, mental and social health.

In addition to tracking demographic information – number of people served, sex, age, and zip code (to ensure we are reaching target areas) – we capture measurable impact by using the Parkinson Disease Questionnaire (PDQ8) when the individual joins a club, at 3 months and at 6 months. The PDQ-8 is a disease specific measure of health status in which the participant rates him/herself in eight dimensions of health.

MOVE IT!™ Online Exercise Club

Online Streaming Exercise Club Outcomes:

- Improved physical outcomes (balance, range of movement, flexibility and strength).
- Improved overall wellness and engagement for people living in rural, underserved and homebound locations.
- Strengthened sense of social connection
- Improved understanding of the physical, mental, social and motor issues of PD.

Class originates from a location and is led by a fitness professional trained in PD specific exercise. Club members log on the computer using a specialized link for Move It! members and join the class in real time allowing people to be part of an exercise class and community regardless of where they live.

P13.10

A program evaluation of a patient to participant, rehab to wellness program for persons with Parkinson's Disease: bridging the gap between illness and wellness.

Erin Keefer¹, Lindsay Holloman¹, Elizabeth Woolley¹, Matthew Ford²

¹ Southeast Alabama Medical Center, Dothan, AL, USA

² Samford University, Birmingham, AL, USA

Objective: The purpose of the program evaluation was to assess the implementation of a patient to participant, rehab to wellness program for PWP in a 3 year period.

Methods: Southeast Alabama Medical Center identified the need for a program evaluation of a patient to participant, rehab to wellness program for PWP in an outpatient community hospital setting. The program has been providing services for PWP in Dothan, AL, USA, since January 2013. The program evaluators

developed the program's evaluation of strategy, quality, delivery and effectiveness of services for PWP using the Centers for Disease Control's program evaluation toolkit. 1 Outcome indicators included functional outcome data, balance and self-report measures, dropout rates, participant surveys (SERVQUAL), staff surveys (Jefferson Scale of Empathy), focus groups and 1 on 1 interviews with staff and participants. Outcome indicator data were organized using the U.S. Army ADRP 5-0 Design Methodology 2 for strategic planning and complex problem solving. SAMC receives assistance from SAMC Foundation, APDA – Birmingham and Department of Physical Therapy at Samford University.

Results: Since January 2013, 112 PWP have participated in the patient to participant, rehab to wellness program. In 3 years, 42 PWP transitioned from rehabilitation to the wellness program. Program evaluation results suggest improved strategic planning, modification to the "Therapist to Trainer" model 3 and modified protocols may improve care for a PWP along the illness-wellness continuum⁴. Program effectiveness results demonstrate improved functional outcomes, balance measures and self-report measures with rehabilitation, continued improvement at 6 months and a plateau of gains at 1 year. Results from quality indicators suggest improved education of wellness staff, improved staff confidence in use of outcome measures, increased professional development opportunities and incentivizing for wellness staff may improve the quality of services for PWP. Results from the SERVQUAL and the Jefferson Scale of Empathy, assessments of service quality, demonstrated the center has exceeded service quality with providing modern facilities but has only slightly exceeded service quality with reliability, responsiveness, assurance and empathy. Results of the program evaluation were analyzed in the context of the illness-wellness continuum⁴, the "Therapist to Trainer" model³ and Transformative Exercise Framework⁵.

References available upon request

P13.11

Face yoga

Renee Le Verrier
Washington, USA

Objective: Portray how applying a yoga approach to the rigid, frozen, dystonic muscles of the face improves overall relaxation, increases facial movement and has a positive impact on social interaction.

Methods: A yoga instructor living with Parkinson's gives step-by-step instructions for a number of exercises and tools (such as mirrors and working with partners) that target various areas of facial movement. Photographs support the text for clarity. Includes sidebar on how to practice at home.

Results: To show how yoga can help manage motor symptoms of Parkinson's that affect the face.

P13.12

Wellness Boot Camp: a successful and cost effective implementation of exercise, education and empowerment for individuals with Parkinson's disease.

Claire McLean

USC, CSULB, Parkinson Wellness Recovery, San Pedro, CA, USA

This Wellness Boot Camp (WBC) is designed to include exercise, education and empowerment in a cost effective manner, for individuals with Parkinson disease (PD). There is mounting evidence that exercise is beneficial, not only for the symptoms of PD, but also for other aspects of health. Exercise has been shown to help with both motor and non-motor symptoms of PD, with great

potential to improve overall quality of life. Research in motor learning indicates, frequent, intense practice may be ideal for learning and skill acquisition. To decrease cost, this exercise is administered in a group setting. The beneficial effects of group exercise include improved physical function, comradery and the potential for improved cognitive and gait measures compared to individual exercise/therapy.

Designed and administered by a Physical Therapist (PT), there is also an understanding that success with an exercise program is determined by many factors. Education about overall wellness, with appropriate lifestyle changes is critical to achieve success.

The WBC is designed to include 1 hour of exercise and 1 hour of education/discussion (2 hours total) each day, 5 days consecutively. Exercise is led by a PT and education/discussion is facilitated by the PT through use of a wellness manual, videos and discussion among the group. There is a specific challenge related to each day's topic. Exercise includes the PWR! Moves and Circuit Exercises.

Education and discussion cover a different topic each day. Day 1: Exercise, Activity, Intentional Medicine. Day 2: Sleep. Day 3: Happiness, how to train optimism. Day 4: Nutrition. Day 5: Putting it all together and maintaining social connectedness.

In the first WBC, which included a population who was already exercising regularly, physical assessments were not performed, but self-reported success included: Improved mood/optimism, improved sleep, healthy changes to diet and improved quality of life. For future WBC, more objective pre and post assessments will be completed.

There are many potentially successful ways to begin an exercise program. Clinical experience indicates a commitment to a program and experiencing improvement in a short amount of time increase the motivation for an individual to continue with exercise. This WBC is designed to be a cost effective (\$150 per person), intense introduction to exercise and wellness. A 5 day, short term commitment may be more reasonable for some individuals compared to a lengthier program.

P13.13

Transforming people with Parkinson's physically, emotionally and socially through free Parkinson's focused fitness program

Nina Mosier¹, Susan Stahl²

¹ Power for Parkinson's, Austin, TX, USA

² Co-director/founder, Power for Parkinson's, Austin, TX, USA

Objective: To engage and transform the quality of life for a broad community of people with Parkinson's and their care partners through Parkinson's group fitness classes, dance classes, singing groups and multiple social activities while improving physical, emotional and social well-being.

Methods: Two women whose fathers had Parkinson's disease (PD) began group fitness & dance classes for people with Parkinson's in the Austin area in January, 2013. By collaborating with the existing local Parkinson's organization that provided support groups & monthly speakers, they were able to initially spread the word. They aimed to make classes easily accessible in multiple areas in the sprawling community to minimize drive time, to offer all classes for free, to be inclusive of all degrees of PD and their care partners. They trained highly experienced group fitness and dance instructors about the complex symptoms of PD. Using this knowledge, they taught with a focus on balance, coordination, sequencing, strength training, cardio, and vocal power in a fun energetic environment. Chairs were available in every class and instructors modified exercises for those who could not stand. All spaces were donated for the classes. They began with 8-10 participants in each of 3 locations.

Results: In less than three years they became an independent non-profit organization offering 11 free classes weekly at 8 different locations with more on the horizon. They serve over 200 people

weekly with class sizes ranging from 12-15 in newer classes to 32-50 in more established classes. Through social media they've reached a national and international audience providing multiple free opportunities for home exercise through their full-length and 10 minute exercise videos. Power for Parkinson's has developed a tight knit community of people with Parkinson's and their care partners.

By engaging talented enthusiastic group instructors who can accommodate varying degrees of physical abilities, the organization has a 90% retention rate. With participants claiming the exercise classes are as important as their medication, many participants have improved balance, coordination, overall mobility and most importantly have made invaluable social connections which have helped combat the the isolation and depression so common in PD. The organization hopes other communities can use a similar model to help even more people with Parkinson's alleviate many of their symptoms & delay the progression of PD.

P13.14

Rhythmic exercise: A 5 year follow up study in Norway

Audun Myskja

Norwegian Parkinson Union, Ski, Norway

Rhythmic exercise: A 5 year followup study in Norway

- 2011-16
- n=43 2011 Levanger n=20; Oslo region n=23);
- n=40 2015 Levanger n=23; Oslo region n=17)
- Age 69.2 yrs (53-83), M/F 63/37%, 5,7 yrs since diagnosis (0-26 yrs), H & Y 2.2 mean
- 1 x/w; 1 hr duration

Exercise principles

- Flexible approach to exercise plan: Fixed initial exercise program; dialogic evolution of program:
- 45 min movements continually less effect, compliance and motivation than movements, voice exercises and relaxation
- Rhythmic movements (RAS principles) involving large joints, diagonal, sagittal/frontal/transversal plane
- Series of 14 vertical, 12 horizontal, DVD and instructor

Design

- Planned controlled study; attrition of control group
- Mixed evaluation methods, quantitative and qualitative, 1/yr
- Quantitative: H & Y, UPDRS (cognitive, motor, ADL), PDQ-39, FES-1, TUG, Senior fitness, MADRS, Herth Hope Index, Motivation self-rating, thorax excursion
- Qualitative: Interviews (EPICURE; Malterud et al.), video analysis, peer group, professional group
- Results (preliminary)
- General mobility stable (TUG, PDQ-39, 2 min knee elevation), UPDRS decrease (statistically non-significant)
- Discrepancy between objective tests and subjective evaluation: Increased fear of falling
- Reduced pain and fatigue
- Depression low; improved mental state (MADRS, PDQ-39, Herth; interviews)
- Voice exercise program stabilizes voice function

Points to notice

- Attrition prevented when program individually adjusted, avoiding rigid structure and lack of structure
- FES1 increased, but not incidence of falls
- Individually adjusted exercises prevent falls
- Group participation improves wellbeing, activity and motivation
- Non-participants rapid progression of symptoms
- Individual variations in progression linked to degree of home training

Conclusion

- Rhythmic exercise stabilizes gait (stride length, cadence, symmetry), mobility, and flexibility

- Rhythmic exercise may decrease pain, fatigue and prevent falls
- A flexible and dialogic evolution of exercise programs prevents attrition and improves long-term exercise motivation
- Group training improves long-term exercise motivation and may contribute to coping with long term disease
- A low incidence of depression and other mental/emotional complaints may be linked to group exercise program

P13.15

Laughter as exercise for strengthening communication skills: verbal and non-verbal. Improve attitude, voice production/diaphragm breathing, and facial movement.

Laura Lou Pape-McCarthy

Parkinson's Resources of Oregon, Portland, OR, USA

People with PD symptoms often experience loss of facial mobility, precise movements of speaking mechanisms of the mouth (lips, teeth, tongue & jaw) and reduced volume & projection of speech. Muscle movements we think of as automatic are affected, include facial expressions indicating attention, level of interest/understanding, the sense one is "in" on humor & much more. However you describe it losing communication skills can radically affect how we interact with ourselves, with loved ones & with society.

Laughter recruits muscles in the face & throat & throughout the body. Practicing laughter as exercise promotes diaphragmic breathing & extended exhalations. Often laughter triggers more laughter just as laughter shared after a joke is often funnier than the punch line. Remember you can laugh without waiting for humor or jokes or even "feeling like laughing".

How can I get started right now? Where can I find group laughter? Watch a funny show, or see stand up comics. There are several systems developed in the last 25-30 years to make great group or solo activities: World Laughter Tour, Laughter Yoga, Laughter Wellness & more are found online.

The intensity of laughter can be carefully paced through an exercise system like Laughter Yoga® making it possible to:

- Maintain a specific heart rate range for a set amount of time, fulfilling the requirements for cardiovascular conditioning.
- Complete sufficient sets of percussive contractions to achieve strength & endurance training for the diaphragm & all the "core" musculature.
- Complete production of "natural" vocalizations of varying volume & pitch.
- Complete slow deep breaths to ensure full inhalation after full exhalation.
- Benefits digestion (effectively "internal jogging") & waste elimination systems (Lymph production & movement through the body).
- Boosts self-confidence & self-efficacy, promotes compassion, deepens creativity, & creates ease of generosity for ourselves & others.

Follow basic exercise principles: be hydrated, warm up for the first 1/5th of the workout including your voice, pay attention to posture & alignment, return to neutral posture in between repetitions of movement. Reaching out or up & relaxing back to neutral as you laugh, shifting weight side to side, raising & lowering shoulders all work as movement focuses to create a trigger for laughing. Let yourself laugh! Smiling big counts!

P13.16

Early results on preservation of motor performance in a community-based exercise program

David Riley, Benjamin Rossi, Elizabeth Stiles

InMotion, Warrensville Heights, Ohio, USA

Objective: To present 6-month results of motor performance assessments of participants in a physical activity program at a new community center, InMotion (IM), for persons with movement disorders.

Background: Numerous studies in the past decade have demonstrated the value of physical activity for Parkinson's disease (PD). IM is a destination in suburban Cleveland for persons with movement disorders offering open classes with certified instructors in a variety of physical activities free of charge. Disciplines include traditional exercise (3 levels), tai chi, yoga, cycling, boxing, modern dance and ballroom dance.

Methods: Participants all carried a diagnosis of PD. Motor performance assessments were conducted at baseline and after 6 months. Assessments (with data endpoints) included a 2-minute walking test (distance), 60-second sit-to-stand and lateral stepping tests (# repetitions), and 30-second bilateral single-limb balance (# corrective floor touches with contralateral foot), single-arm clean-and-press (C&P), and rotational body turn tests (# repetitions). Participants also completed an extended Timed-Up-and-Go (ETUG) test in alternate directions (time). Mean figures of all data endpoints were derived. Statistical significance was determined using a paired t test.

Results: 28 participants completed the assessments. Mean 2-minute walking distance improved from 186 to 214 meters (NS). Sit-to-stand repetitions improved from 27.2 to 31.0 (p=.05). Lateral stepping increased from 49.6 to 53 cycles (NS). Right arm C&P increased from 12.9 to 15.4 (p=.001), left arm 12.8 to 14.5 (NS). Balance corrections on single-leg stance were virtually unchanged before/after (4.2/4.1 left, NS; 4.3/4.2 right, NS). Rotational turns increased (19.9/23.7 left, p=.001; 20.2/24.3 right, p=.001). ETUG time decreased from 12.2 to 10.4 (NS) seconds with a left turn and 11.5 to 9.8 (NS) with a right turn.

Conclusions: Motor performance in this cohort was stable or improved over a 6-month period, as measured by mobility and balance tests. We cannot claim an intervention effect because we could not control for other contributory factors such as changes in medication and outside levels of physical activity. However, given the progressive nature of PD, our results suggest we may be contributing to stabilization of the clinical course of these participants. In that respect, the data are consistent with a large body of literature documenting the value of physical activity for persons with PD.

P13.17

A clinical trial of a ketogenic diet as treatment of Parkinson's disease

Richard Rosenbaum¹, Shaban Demirel², Angela Senders³, Andy Erlandsen³, Amy Reiter², Kathy Dodson⁵, Heather Zwickey⁵, Alar Mirka²

¹ The Portland Parkinson's Program of the Oregon Clinic and Legacy Health, Portland, OR, USA

² Legacy Health, Portland, OR, USA

³ National College of Naturopathic Medicine, Portland, OR, USA

⁴ The Oregon Clinic, Portland, OR, USA

⁵ National College of Naturopathic Medicine, Portland, OR, USA

Background: People with Parkinson's disease have decreased levels of CNS adenosine. Ketosis can increase adenosine levels.

Methods: 13 people with moderate Parkinson's disease ate a ketogenic diet (intended fat content 80%) for 12 weeks. They received weekly dietary counseling at the National College of Naturopathic Medicine. Dietary adherence was confirmed by monitoring beta-hydroxybutyrate levels. Outcomes measures included the UPDRS, PDQ 39, Mini Best, TImed Up and Go, and Freezing of Gait score. Patient symptoms and lab tests were used to monitor toxicity.

Results: 1 patient worsened and terminated the trial after 4 weeks; re-challenge confirmed his intolerance of the diet. 12 patients completed the trial. For these 12 patients UPDRS showed a trend to improvement; the sum of UPDRS tremor items showed a significant improvement (baseline – 4.6, week 12 – 2.8, $p=0.04$); and 6 patients had clinically significant improvements in UPDRS. For a 360 degree turn, turn time and total steps were significantly improved. Adverse symptoms, if present, were mild. Mean weight loss was 12.3 lbs; mean increase in LDL cholesterol was 33 mg/dl.

Discussion: This was a short, small, and uncontrolled trial of ketogenic diet treatment of Parkinson's disease but is the longest and largest such trial reported to date. With one exception, patients were able to adhere to the diet and complete the trial. One half of those completing the diet had a clinically significant improvement in UPDRS with a suggestion that tremor was the most responsive motor symptom. We plan a longer and larger treatment trial of fat-rich diet for people with Parkinson's disease, first screening for responders with one month of a ketogenic diet and then maintaining responders long term on a modified Atkins Diet.

P13.18

Forging neuronal circuitry through the practice of yoga, meditation and Dance for Parkinson's®.

Elizabeth Ruinard

Parkinson's Queensland, Brisbane, Queensland, Australia

Keywords: neuronal circuitry, neuroplasticity, neuro-rehabilitation, yoga, dance, mindfulness

Background: In recent years there has been a consistent message about the value of exercise for PWP. This message expresses: "the notion that exercise ... might enhance neuroplasticity, which is important for driving motor and cognitive behavioural improvement" (Petzinger et al, 2013, 716). This poster attests to the benefits of yoga and dance and those ensuing from the practice of meditation.

Aims and objectives: The poster aims to demonstrate to fellow PWP the way in which relief from the physical symptoms of Parkinson's and an improved outlook has been achieved through the practice of postures and asanas from yoga and exercises and a suite of movements from Dance for Parkinson's (over a period of three years). This has been connected with developing a state of mindfulness. The opening of the heart space, the rotation of the shoulders, the articulation of the feet and toes, the stretching of the arms, hands and fingers, the bending in plies through the legs and the growth in strength and flexibility through the practice of the warrior pose, along with the movement of the breath associated with the above, have provided much physical and emotional relief for this PWP; it is however acknowledged that, owing to the idiopathic nature of P.D. the set of optimal asanas and movements will be a personal one.

Results and benefits: Results reveal improvement in the flow and smoothness of the movements of the afflicted body parts. This includes enhanced mobility, gait, posture and balance, the reduction of stiffness and pain, the decrease of tremor, improved strength in the centre of gravity or core, an enhanced sense of well-being, the reduction of anxiety about falling as well as a reduction in the number of actual falls. It has coincided with the maintenance and improvement of score on the Unified Parkinson Disease Rating Scale (UPDRS) and the non-progression to a higher dose of medication over three years.

The poster covers the topics of neuroplasticity, mindfulness and the idea of a personalised program of neuro-rehabilitation for PWP. It features images of certain of the asanas and postures and will explain the key role of the breath and mindfulness in yoga and meditation.

References

Petzinger, GM, Fisher BE, McEwen, S, Beeler, JA & Jakowec, MW. 2013 Exercise enhanced neuroplasticity targeting motor and cognitive circuitry in Parkinson's Disease. *The Lancet* 2, 715-726.

P13.19

The benefits of racquetball for PwP (People with Parkinson's)

Jacques Séguin

Ottawa, Ontario, Canada

Little is known about the benefits that racquetball activities can provide to PwP. This topic is not based on scientific or medical research. It is based on the wellness factor. Of all sports and exercise programs that I have tried, racquetball has the fastest, the strongest and the longest lasting positive effects on my Parkinson symptoms. A racquetball session consist of four phases: warm up – hitting a soft ball on a wall – racquetball activities (or game) – cool down and stretching. For PwP who have never played a racket sport just hitting the ball on the wall is beneficiary on its own. Within 10 minutes most PwP will feel balance issues and coordination problems diminish considerably or practically disappear. There is something inexplicable about the sound of the ball hitting the wall over and over again. The fluidity of movement becomes evident after 5 to 10 minutes.

In the Ottawa, Orleans and Gatineau area 19 PwP have been introduced to racquetball in the last 4 years; 2 others the Maritimes and we have communicated with 2 PwP in Washington who play racquetball and also with a couple in Australia. In the 3 communities of Ottawa, Orleans and Gatineau of the 19 PwP 9 still actively play racquetball; 2 have an area in their basement to hit a ball on the wall and several play badminton; 3 occasionally play racquetball but also play badminton on a regular basis (for whom badminton is 20 minutes closer to their home) 1 (one) has passed away; and the age combined with Parkinson's and other health issue are preventing 2 other PwP from participating. Racquetball Canada provides sports kits with racket, ball and eye protectors

Difficulties related to our program:

- transportation; the Gatineau community racquetball courts have been converted to other athletic activities Travel distance from Gatineau to Ottawa and Orleans becomes an issue
- motivation: to convince PwP to come and try

Unforeseen benefits

4 non-PwP play with us on a regular basis. Of our initial group (six) 6 PwP can now play (non-adapted racquetball) by themselves or (more fun) with regular non-PwP at top speed. Examples can be seen on my web page at jseguin.ca.

P13.20

Nutrition in Parkinson's Disease: a closer look from the patient's perspective

Jeffrey Wertheimer¹, Ann Gottuso¹, Carol Walton², Aurore Duboille², Margaret Tuchman², Kathrynne Holden³

¹ Cedars-Sinai Medical Center, Los Angeles, CA, USA

² The Parkinson Alliance, Kingston, New Jersey, USA

³ USA

Objective: Given the complex and bidirectional relationship of nutrition habits/management and symptoms of PD, the current objective was to improve understanding about the patient's perspective about nutrition and related experiences. This study (1) investigated important eating/dietary habits for individuals with PD with and without DBS, and (2) provided empirically-based recommendations.

Methods: Using cross-sectional design, 1492 participants, including 402 participants with PD who underwent DBS and 1,090 individuals with PD without DBS, completed a diet/nutrition questionnaire regarding clinical characteristics, nutrition habits, and eating behaviors.

Results: Most participants (93%) believe diet/nutrition is important in managing PD symptoms, but almost half of the participants perceive themselves as not following a healthy diet most of the time, and few have received recommendation to follow a specific diet. 80% of the participants take vitamins/supplements. Non-motor symptoms were prevalent for Younger (50-69 years) and Older Groups (>70 years), and Early Advanced (disease duration of 6-10 years) and Late Advanced Stage Groups (disease duration of >10 years). As age and disease duration increase, motor symptoms (i.e., tremor, slowness of movement, swallowing difficulties, etc.) and non-motor symptoms (i.e., constipation, changes in smell and taste, depression, etc.) appear to be barriers to optimal nutrition and diet management for many individuals with PD, and increased assistance from others often becomes necessary. After accounting for age and disease duration, the DBS group did not differ in nutritional habits and eating experiences, with exception to higher incidence of choking.

Conclusions: Good nutritional management can positively impact well-being for individuals with PD. Current results reinforce the need for an interdisciplinary approach to address the needs of individuals with PD. It is recommended that individuals with PD speak to a movement disorder specialist, a registered dietician, and a speech language pathologist regarding food/nutrition and the relationship with symptoms of PD and medications. Recommendations pertaining to nutrition habits/management for individuals with PD are discussed.

P13.21

Determinants of physical activity in persons with Parkinson's disease

Andrew Zaman

Iowa State University, Ames, IA, USA

Objectives: Physical activity (PA) interventions have proven to have positive effects on Parkinson's disease (PD) symptoms and quality of life. This study's goal is to identify the determinants of physical activity in PD. We also want to know what PD interventions are most appealing. Finally we want to use this information to identify an appropriate behavioral theory to aid exercise intervention development.

Methods: In a sample of 20 persons diagnosed with mild to moderate PD, we conducted a semi-structured interview to determine how their current physical activity level compares to 1) their previous PA history; 2) the motivations and barriers to PA; 3) their knowledge about PA benefits; 4) social and environmental influences; 6) and their concerns about PD and other health related issues. Finally we asked what exercise interventions were most appealing and likely to be beneficial. Determinants were coded and compared between exercisers and non-exercisers.

Results: We found that a large majority of our participants exercised regularly. We also found that those with active lifestyles prior to being diagnosed continued to be active. The main factors associated with PA were the social atmosphere group classes provided and a belief that PA helped delay PD. Most participants said that their symptoms and a being afraid of falling made it hard for them to exercise but there were no differences between exercisers and non-exercisers. Common barriers such as accessibility, time, and financial were not present. Most participants said they were not motivated to exercise by friends and family. Those who exercised regularly displayed less concern regarding health compared to inactive individuals. Most participants seemed to

be unaware of the emotional and cognitive benefits of exercise. Participants said they would have tried a variety of the activities including boxing, dancing, and yoga. Most participants who were in exercise programs had been participating regularly and had no intentions of changing their PA routines.

Conclusions: The Theory of Planned Behavior and Theory of Reasoned Action appear to be inappropriate behavioral theories for people with Parkinson's because influence by "close others" and health concerns were not strong predictors of PA behavior. Instead the Social Cognitive Theory may be more appropriate theory because social aspects and knowledge factors were the strongest motivators.

P13.22

Nordic walking enhances gait power profiles at the knee joint in Parkinson's disease

Lei Zhou, Marie-Anne Gougeon, Julie Nantel

School of Human Kinetics, Faculty of Health Sciences, University of Ottawa, Ottawa, Ontario, Canada

Background: Gait impairment and postural deficits are very common in people with Parkinson's Disease (PD). Some evidence showed that in older adults, Nordic Walking (NW) could improve some gait characteristics. However, it is not known if NW could be beneficial to improve gait stability and power generation pattern in individuals with PD.

Purpose: This study aims at investigating whether NW can improve trunk stability, gait spatial-temporal characteristics and kinetics in individual with PD following an independent 6-week training.

Methods: Following a 6-week training (16 sessions x 45min), gait spatial-temporal characteristics, and kinetics data were collected with NW poles and without poles (NP) in 12 adults with PD (age: 61.58±11.7 years) and 12 healthy older adults (mean age: 68±6.4 year). Participants performed six 5m walking trials; 3 with / 3 without poles. Data were collected with a motion capture system (Vicon, Oxford, UK) and 2 force platforms (Kistler, Winterthur, Switzerland). Two-way ANOVAs were used to compare gait pattern PD and older adults. Adjustments for multiple comparisons were performed when necessary.

Results: PD participants had significantly larger knee power absorption during pre-swing (K3) compared to older adults in both NP and WP. Moreover, during the NW condition, individuals with PD had significantly larger hip power absorption with hip flexor (H2) and generation with hip extensor (H3) compared to older adults. No differences were seen between or within the groups for trunk stability or spatial-temporal characteristics. Longer stride length, lower cadence, and larger single support time were found in PD in NW compared to NP. NW in PD also led to larger knee power generation during mid-stance by knee extensor concentric activity (K2) as well as decreased power absorption by knee extensor (K3).

Conclusions: Walking with poles after an independent 6-week NW training can improve certain spatial-temporal aspects of gait as well as power generation and absorption at the knee in individuals with PD. The increased time spent in the single support phase when walking with the poles, suggests that postural stability could be enhanced and therefore improves gait kinetics in PD. As the poles improve gait stability, NW training could be used to improve specific aspects of gait such as gait speed and power generation at the ankle joint.

CARE DELIVERY & QUALITY OF LIFE: CREATIVITY & ALTERNATIVE OR COMPLEMENTARY THERAPIES

P14.01

Dance and Parkinson's disease: a research dissemination project

Rachel J. Bar¹, Jennifer L. Lapum², Michelle Dionne³, Lorraine V. Kalia⁴, Joseph F.X. DeSouza⁵

¹ Canada's National Ballet School & Department of Psychology, Ryerson University, Toronto, ON, Canada

² Department of Nursing, Ryerson University, Toronto, ON, Canada

³ Department of Psychology, Ryerson University, Toronto, ON, Canada

⁴ Movement Disorder Clinic, Toronto Western Hospital, Toronto, ON, Canada

⁵ Centre for Vision Research, Department of Psychology, Biology and Interdisciplinary Studies, York University, Toronto, ON, Canada

Background: Recent research, including primary studies, systematic reviews, and a meta-analysis, has established the therapeutic benefit of dance as an intervention for people with Parkinson's disease (PD). Despite this evidence, healthcare professionals rarely refer clients to dance programs and thus dance programs remain relatively underused.

Objectives: In this presentation, we review current research on dance for PD and discuss our arts-informed knowledge translation (KT) initiative. Specifically, the initiative aims to: (1) broaden healthcare professionals' and the community's concepts of integrative care and understanding of dance as a therapeutic intervention in the PD population; (2) enhance healthcare providers' referral frequency of dance and PD patients' uptake of dance; and (3) catalyze new initiatives for future research on dance and PD.

Methods: We are organizing two dissemination events at Toronto Western Hospital and Canada's National Ballet School in Toronto, Canada in April 2017, which will be open to healthcare providers and the community. These events will include visual displays highlighting research as well as a dance class designed for people with PD. The latter event will be live-streamed online to allow for international participation. To evaluate outcomes of the events, questionnaires will be sent to health professionals who work with people with PD one month before and after the events. We aim to recruit fifty health professionals who participate in the events (in-person or virtually). We hypothesize that participation will increase rate of referral to dance for PD patients. Twenty patients who participated in the events (in-person or virtually) will be recruited for qualitatively-informed, semi-structured interviews. Descriptive content analysis of interviews will provide insight into the accessibility and informative utility of such events for patients.

Results/Discussion: We anticipate these events will increase awareness of the benefits of dance for people with PD. Thus this project could result in more healthcare professionals recommending dance to their PD patients, ultimately increasing the number of people with PD benefiting from dance programs. Additionally, we expect our findings will demonstrate that integrative, interactive arts-based methods can be an effective method of KT to the PD community.

Funding: This KT initiative is funded by a Canadian Institutes of Health Research dissemination grant.

P14.03

Mucuna pruriens product standardization and Indian ethnobotanical analysis

Tanya Denne¹, Amala Soumyanath², Veni Krishnaveni³, Santhosh Reddy³, Soundara Rajan⁴

¹ previous OHSU volunteer research assistant, at time of conger I will be current medical student at Bastyr University fall16, Kirkland, WA, USA

² Oregon Health and Science University, Portland, WA, USA

³ JSS College of Pharmacy, Ooty, Tamil Nadu, India

⁴ Center Council of Research in Homeopathy, Emerald, Tamil Nadu, India

(Phase I) Lab work conducted at Oregon Health and Science University, Oregon, USA Previously presented at IRCIM 2012. Not published

(Phase II) Field work conducted at JSS College of Pharmacy, Ooty, India No affiliation to OHSU

(Phase I)

Purpose: Mucuna pruriens (MP) seeds contain 3-6% levodopa (L-DOPA), and have been used in traditional Ayurvedic medicine to treat diseases resembling Parkinson's disease (PD). Pilot studies in PD show that MP seed powder has similar effects to conventional levodopa/carbidopa medication. Formulations of MP seed are readily available through the internet, and are used by some PD patients as an alternative to conventional levodopa/carbidopa medication. The purpose of this study was to examine the L-DOPA content of a range of popular MP products, in order to assess the veracity of label claims.

Methods: Six different brands of MP product were ordered through the internet. Certificates of analysis were obtained where possible. A standard amount of each product was extracted using methanol:formic acid, for analysis using reversed-phase high performance liquid chromatography (HPLC) with ultraviolet and fluorescence detection. L-DOPA content was calculated using a standard curve prepared using L-DOPA as reference.

Results: The claimed L-DOPA content ranged from 25 to 250 mg per dose for the six products. HPLC analysis revealed that only two of the products had L-DOPA values close to the value claimed. The remaining products contained considerably less L-DOPA, <10% in two cases, than implied on the label. Certificates of analysis suggested that not all manufacturers routinely measure L-DOPA content of their MP product.

Conclusions: Four of six products examined showed a large discrepancy between label claim and L-DOPA content, independently measured by HPLC. This finding warrants further investigation as these deficiencies could impact both patients, and the outcome of clinical studies using these products.

(Phase II)

India yielded ethnobotanical observable data on MP native growing conditions. Three varieties of mucuna seeds were collected. The 'silent Valley,' 'Paniya Village' in Kerala and the 'Irulea Village' in Tamil Nadu, India these field sites offered undisturbed native growing conditions and specimens for observation.

Greenhouse starts and horticulture research is being carried out at Eastern Oregon University on collected Indian MP seeds. Germination is underway with the goal being seed reproduction for future crop planting.

Product #	Label claim for L-DOPA content/ dose 1 dose = 1 serving	Single dose (Serving size)	L-DOPA CLAIMED mg/dose	L-DOPA FOUND mg/dose	L-DOPA % OF CLAIM
1	Mucuna Pruriens 60% L-Dopa 100mg	1 capsule	60	3.6	6 %
2	Mucuna (Mucuna Pruriens) (Kaunch) seeds 25% L-DOPA 135mg per capsule	1 capsule	33.8	11.6	34 %
3	Cowhage extract (standardized to contain 15% L-DOPA) (mucuna pruriens) (seed) 200mg	1 capsule	30	12.0	40 %
4	Velvet Bean (Mucuna pruriens) (seed extract) 333mg; (Guaranteed 66mg [20%] catecholamines including 50mg [15%] L-dopa)	1 capsule	50.0	55.6	111 %
5	Mucuna pruriens Seed extract 166 mg Yielding 100mg L-DOPA	1 capsule	100	120.2	120 %
6*	Each 7.5g contains: standardized processed seed powder of Mucuna pruriens Bak..6.525g in a flavored base	*As directed by the physician*	250	357.2	143 %*

*Label does not state L-DOPA content, serving size or dosage but 7.5g scoop provided. Internet sites indicate 7.5g has 250mg L-DOPA.

P14.04

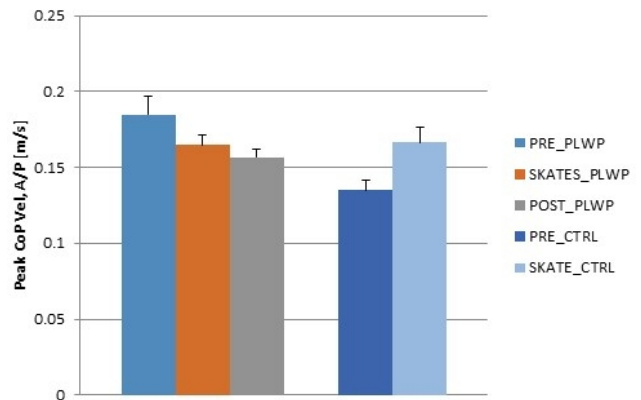
Skating improves balance amongst people living with Parkinson disease

Jon Doan, Brittany Mercier, Elani Bykowski, Claudia Steinke, Natalie de Bruin, Lesley Brown
University of Lethbridge, Lethbridge, Alberta, Canada

Objective: Paradoxically persistent skills provide a most appropriate exercise intervention modality – the preserved high skill level should allow for increase enjoyment, adherence, and vigor. Ice skating is paradoxically preserved amongst many Canadians living with Parkinson disease, and the nature and place of hockey in Canada could make it a particularly available neurotherapy for many. As with any proposed exercise intervention, it is important to maintain the safety of participants, by measuring the feasibility of the proposed exercises. In the current study, we measured the balance of people living with Parkinson disease in shoes and skates.

Methods: 14 people (59.0±6.1 years in age, 2 female; PLWP) previously diagnosed with Parkinson disease (5.5±3.4 years of diagnosed disease duration) and self-identified as capable of ice skating attended a single testing session. 9 neurotypical participants (CTRL) also attended the same sessions. All participants performed 3 quiet standing balance trials in their skates (60 seconds per trial, 200 Hz sampling rate, Bertec force plate). Participants performed these same balance trials pre- and post-skating, in their chosen footwear. Conventional postural control measures were calculated for each trial, and averaged within condition (PRE, SKATE, POST). A factorial ANOVA [FOOTWEAR, 2 levels (SHOES, SKATES) x GROUP, 2 levels (PLWP, CTRL)] was conducted to examine group differences, and interactions. A within subjects repeated measures ANOVA was performed on the mean values for the PLWP group, and significant differences were isolated with follow-up t-tests (PRE:POST, PRE:SKATE, SKATE:POST).

Results: All participants were able to stand for all trials in either footwear conditions. A significant interaction existed for minimum, maximum, and peak (average) posture centre of pressure velocity in the anteroposterior direction. While CTRL subjects used significantly smaller velocities to control postures in the PRE (shod) condition, groups were equal in the SKATES condition (Figure 1). More excitingly, t-tests revealed that a single session of ice skating significantly reduced postural disturbances amongst PLWP, including smaller velocities and increased stability. While the duration of this improvement is unknown, it does suggest possible postural benefits from a regular skating exercise intervention.



P14.05

Singing with Parkinson's: a unique approach to maximize participation and performance

Samantha Elandary

Parkinson Voice Project, Richardson, Texas, USA

Speech deficits associated with Parkinson's disease (PD) are treatable through speech therapy; however, long term maintenance remains challenging. Research suggests singing may improve loudness, speech clarity, respiratory support, and prosody. One of six singing groups reviewed has designed its program as a maintenance activity to follow individual speech therapy. This presentation describes this unique approach.

A review of six singing groups for people with Parkinson's (PWP) was conducted, noting participant criteria, group size, professionals involved, therapeutic approach, and repertoire. Additional details regarding Parkinson Voice Project's approach was obtained by reviewing clinic protocols and interviewing participants (n=37) to analyze age, diagnosis, time since diagnosis, and musical training/experience.

Parkinson Voice Project's program was found to be distinctive. Of the six singing programs reviewed, five groups include non-PD adults; whereas, Parkinson Voice Project's chorus of nearly one hundred singers only includes people diagnosed with Parkinson's or atypical Parkinson's. Another difference that singles out the program provided at Parkinson Voice Project is that each participant completes individual speech therapy prior to joining the singing program. In addition, the group is led by a music director and a speech-language pathologist, uses a singular focus of "intent", and performs more complex repertoire.

All six groups reviewed had no criterion for musical background for participants. The survey of Parkinson Voice Project's participants (mean age=73) revealed 43% read sheet music; 43% previously performed with another singing group; and 22% have had formal music training; no comparative data available.

At Parkinson Voice Project, modifications to address cognitive and physical limitations of participants are implemented, including: specially formatted lyrics (preferred by 62% of participants), and use of sheet protectors (for page turning), music stands, small water bottles, seated risers, headset microphones for soloists, and strategic rest breaks. Many rehearsal and performance videos are available to feature during this presentation.

Conclusions: The musical and environmental modifications used in the singing group at Parkinson Voice Project enable PWP to perform challenging repertoire with minimal direct assistance. This approach can be a valuable tool for speech therapy maintenance and can be easily replicated.

P14.06

Improvisational dance and Parkinson's

Maura Fisher¹, Dr Ian Gold², Alba Kane², Joanabbey Sack³

¹ Montreal Neurological Institute, Montreal, Quebec, Canada

² McGill University, Montreal, Quebec, Canada

³ Concordia University, CAHD, Montreal, Quebec, Canada

Objective: This poster presents the research on the effects of Dance Movement Therapy (DMT) on motor and cognitive domains in a cohort of individuals diagnosed with Parkinson's (PD). Dance for Parkinson's patients is an increasingly explored strategy for addressing the motor and non-motor symptoms of PD. DMT addresses the total person and also offers the time and space for expression of ideas, responses to the experience of PD and improvisation in dance and communication. The improvisational component of this form of therapy is potentially useful in focusing on the clinically important feature of spontaneity in movement. The vast majority of motor behaviour is not pre-planned but arises as an immediate adaptation of a motor goal and the circumstances afforded by the environment (including other people) which require both motor behavior and cognition (deciding, planning, and the like); in short, real-world movement is improvisational. Improvisation in movement is also essential to the communicative character of movement. This in turn plays a role in the emotional component of cognition. Homann (2010:91) notes, for example, that "movement synchrony and affective attunement, can create a profound experience of being emotionally connected." (Batson et al 2014/ Ribeiro & Fonseca 2011) Further, improvisational movement is central to adapting to the movements of others, and thus in engaging in collaborative behaviours. Improvisational movement is therefore closely related to social cognition. Improvisational movement within the DMT session thus facilitates the capacity to engage meaningfully with other people and with the environment. The potential benefits of DMT with an emphasis on improvisation, however, have not been explored in a systematic way. The present pilot study, therefore, sets out to examine whether DMT leads to improvements in both the motor and cognitive domains in a cohort of individuals diagnosed with PD. We will employ a basic paradigm in which participants will be given a battery of motor and cognitive tests prior to being given a twelve-week DMT intervention. Results on the same tests administered after the intervention will allow us to test the hypothesis that motor behaviour as well as cognition can be improved by DMT.

P14.07

Dancing with Parkinson's YYC: a community-based dance program improves functional daily activities in people with Parkinson's disease.

Afra Foroud¹, Anne Flynn²

¹ The University of Lethbridge, Lethbridge, Alberta, Canada

² The University of Calgary, Calgary, Alberta, Canada

Background: In recent years, studies have begun to demonstrate that dance may be beneficial for people with Parkinson's disease (PD). In particular, people with PD who participate in weekly dance classes improve in standardized tests of balance, gait, mobility, and quality of life (QOL) (Hackney et al., 2010; Heiberger et al., 2011). Interestingly, outcomes on qualitative measures from interviews are positive even in groups with marginal improvement on the standardized tests (Houston 2011; Westheimer et al., 2015). Thus, it is likely experiences gained from a dance program may have a greater impact on PD than what can be quantified by standardized measures. For example, it is not yet known how the effects of dance translate into day-to-day living.

Objective: The purpose of this study is to evaluate how participation in the community-based dance program, Dancing Parkinson's YYC, influences daily activities essential for maintaining independent living.

Methods: Thirty participants (18 PD and 12 healthy controls) were video-recorded while performing a novel series of tasks that reflect functional behaviour in a natural setting, such as pouring a drink, carrying a drink, getting dressed, and moving about in a room. Five months later, participants repeated the tasks after having completed the weekly Dancing Parkinson's YYC program offered at Decidedly Jazz Danceworks.

Results: Preliminary results (data from the first 9 PD and 9 control participants) differences in how the tasks are performed between the PD and control groups prior to the dance program. Further, both groups improved after completing the dance program. For e.g., in a task involving buttons, both groups improved in orienting their arms and hands in relation to the fabric and in grasping the buttons. The PD group also improved in articulation of the digits, wrists, elbows and shoulders.

Discussion: Findings from this study suggest participation in a weekly dance program may help improve fine motor skills and indicate how dance may be beneficial for daily functional activities. This work is part of a larger project currently in progress on emotional expression and social communication, QOL, and performance in the dance class thus bridging quantitative and qualitative research so as to increase our understanding on how dance influences people with PD.

Acknowledgement. SSHRC, Rozsa Foundation, Parkinson Alberta

P14.08

"Artisans with Parkinson's: the power of art and creativity in managing Parkinson's disease"

Joellyn Fox, Heather Cianci

Dan Aaron Parkinsons Rehabilitation Center/Penn Therapy and Fitness, Philadelphia, PA, USA

Objective: To gain insight in to the phenomenon of enhanced artistic creativity in Parkinson's disease (PD) and it's application to physical and occupational therapy. This information was used to develop a framework for therapists to use in guiding their patients toward using creativity and art during and after their therapy.

Methods: A scientific literature review was performed to learn about the connection between creativity and PD, and creativity and dopaminergic therapy. Art from 10 patient subjects of the Dan Aaron Parkinson's Rehabilitation Center was showcased in the clinic through the "Artisans with Parkinson's" program. Artists provided statements for others to read about how PD affected their art. Artists were also interviewed about their art, when their interest in art began, the time they dedicate to the art, how PD impacts their art, and if/how art assists in coping with, and managing PD. While in therapy, patient subjects engaged in exercises and therapeutic activities to combat motor symptoms like bradykinesia, hypokinesia, and flexed posture, as well as non-motor symptoms like depression and fatigue – which all can challenge artistic performance.

Results: Findings from the review and interviews suggest that those with PD can develop new artistic creativity, a change in their art style and technique, and that the act of being creative leads to feelings of control, empowerment, and independence. Subjects viewed therapy as a tool to help stay active with their artwork. Therapists viewed art as a way to help keep subjects motivated in therapy, and stay socially and physically active outside of therapy.

P14.09**Massage, bodywork and mind-body interventions for Parkinson's disease: a case report**Rosi Goldsmith¹, Martha Menard, LMT²¹ Portland, OR, USA² Crocker Institute, Kiawah Island, SC, USA

Introduction: Parkinson's Disease (PD) is usually characterized by motor symptoms. Non-motor symptoms (NMS) include sleep disorders, fatigue, emotional issues, and cognitive changes. All symptoms negatively impact quality of life (QoL).

Objective: Research conducted largely in other populations using massage, focused exercise, mind-body practices, and imagined movement have shown benefits to several brain areas implicated in PD, improvements in emotional issues and/or PD motor symptoms. This study asks whether these combined therapies could affect PD symptoms and QoL, in a patient-centered research design.

Case Presentation: A 63 year old male on Sinemet had been diagnosed with PD five years earlier. He identified goals of pain relief, improved mobility, slowing PD progression, and symptom control. Initial assessment showed moderately stooped posture; mild to moderate rigidity of neck and major joints; bilateral pain at shoulders; erratic vertical eye saccades; significant olfactory impairment and impaired balance.

Methods: Fifty-six bodywork sessions over eight months included: massage; Ortho-Bionomy; posture, mindfulness, interceptive awareness training; and functional neurological exercises. A daily home program of adapted yoga, meditation, and mental rehearsal of exercises was developed from clinical practices. Assessments of presenting symptoms and Visual Analog Scales (VAS) of pain were noted weekly. Clinical assessment and self-report of validated instruments were measured five times: Non-Motor Symptom Scale (NMSS), PD Quality of Life-39 (PDQ-39), Modified PDQoL (PDQoL), and Unified Parkinson's Disease Rating Scale (UPDRS).

Results: All scales showed overall improvements: VAS pain (35%); NMSS (26%); PDQ-39 (8%); PDQoL (12%); and UPDRS (17%). Notable subscale improvements were: Parkinsonian Symptoms (21.6%); Motor Examination (15%); Sleep/Fatigue (10%). Patient self-report indicated novel findings: improved olfactory perception and that he could sometimes control "off" symptoms of fatigue, tremor and restless legs, by meditation and exercise/yoga mental rehearsal alone.

Conclusions: Multiple therapies and medication changes may have introduced confounding variables; and variations in Parkinson's symptoms and massage clinical practice make it hard to reproduce. The possibility of QoL and NMS benefits suggests a controlled study using bodywork and evidence-based mind-body therapies in a patient-centered design might be worthwhile.

P14.10**Experimental theater program integrating people living with Parkinson's and able-bodied performers in Carolinas Healthcare Systems Neurosciences Institute community-based RENEW Carolinas program**Monika Gross¹, Anna Kapousizi²¹ At-A-Site Theater, Asheville NC; The Poise Project, Asheville NC, Asheville, NC, USA² MDA HELLAS, Drama Program Director, Athens Greece; Resident Fulbright Artist Scholar, RENEW Carolinas, Charlotte NC, USA, Athens, Greece

Objective: To design an experimental theater program for people with Parkinson's and able-bodied performers to train together in equality. To form an ongoing theater ensemble led by the newly trained participants.

Background: Since 2011, Anna Kapousizi has run an experimental theater program for people with neurological disorders through MDA HELLAS in Athens. She is the 2016-17 Fulbright Artist Scholar for Greece and will be resident at the RENEW Carolinas program in Charlotte NC from 10/16-03/17. RENEW (Research and Education in Neuro Wellness) is a joint initiative by CHS Neurosciences Institute, Carolinas Rehabilitation, LiveWELL Health Center and the YMCA to promote a community based neuro wellness program for people with Parkinson's disease and other neurological conditions, improving quality of life by promoting a culture of active lifestyle to maintain or increase independence, safety and well-being. These programs have been singled out for recognition in the field of participatory medicine for utilizing an innovative "patients-as-partners" approach that develops programs through collaboration with patients, partners and community leaders.

Methods: People with Parkinson's from the Charlotte NC metropolitan area will participate in Kapousizi's actor training classes alongside able-bodied actors. Co-trainer Monika Gross will teach Butoh dance and Alexander Technique. Butoh, a post-WWII Japanese avant garde form, uses poetic scripts as a method of imagining bodily transformation. In contrast to traditional dance relying on choreography, Butoh is improvisatory and offers a liberating expressive activity for people with Parkinson's. Alexander Technique (AT) is a training method enhancing the connection of thought and movement through improved proprioception, spatial awareness and more accurate body schema applied to specific activities of daily living (ADLs).

Results: People with neurological diseases often suffer from psycho-social factors related to isolation. Their vivid emotional lives are not given spaces to be made visible and physicalized. Kapousizi's program provides them with an adaptive form to openly express themselves and create connections to their larger community through the medium of professional-quality public performances. This presentation will define useful experimental theater techniques for the PD population and will display images from past performances as well as subjective responses by participants in Kapousizi's productions.

P14.11**Use of music attention control training to improve gait**

Sandra Holten

Struthers Parkinson's Center, Golden Valley, MN, USA

Background: Research demonstrates that patients with Parkinson's disease (PD) have difficulty walking while multi-tasking, navigating obstacles, and with auditory or cognitive distractions. Neurologic Music Therapy (NMT) includes techniques that address attention deficits. Following sessions in which a music therapist used a NMT intervention, Musical Attention Control Training (MACT), patients displayed improved gait. This emerging idea was explored further in sessions with a 71 year old PD patient for strategies to improve gait and decrease freezing episodes.

Objective: Develop and implement a MACT protocol to explore the impact of MACT on attention and gait, and use MACT to improve patient's function and quality of life.

Methods: 8 individual sessions were conducted using MACT to improve the patient's attention. The protocol integrated foot movements for real-life application with additional NMT Auditory Perception Training (APT). Improvement was measured with Timed Up and Go (TUG) at beginning and end of sessions. Adjustments were made during most sessions due to patient's motor fluctuations, presence of dyskinesia and barriers to movement.

Results: Using Timed Up and Go as a measurement, patient displayed a 26% improvement in his time from his initial session to his last session with fewer freezing episodes. In addition to this, what began as an attempt to document MACT protocol with standardized pre to post measurement, turned into a dynamic story

of a couple's journey with Parkinson's. Although variability in Parkinson's made adhering to protocol difficult, it also presents NMT's ability to adapt to patient needs. Results also show that even through the variability of client's functioning between and within sessions, overall improvement was made in the TUG results. Anecdotal results from patient and his wife included transfer and generalization of learning and colleagues/friends reported improved ability to attend and contribute to discussions.

Conclusions: MACT appears to be a viable intervention to improve attention. Further, NMT techniques can address attention deficits found in Parkinson's, the connection between improved attention and improved gait, as well as the emotional challenges that result when living with a movement disorder.

P14.12

The benefits of animal-assisted therapy (AAT) in people with Parkinson's disease

Kristin Johnson¹, Richard VandenDolder¹, Sherry Eddy², Catherine Wielinski¹

¹ Struthers Parkinson's Center, Golden Valley, MN, USA

² Animal Inspirations, LLC, Glencoe, MN, USA

Background: Living with advanced Parkinson's Disease can limit opportunities for activities previously enjoyed. Interaction with gentle animals is known to have therapeutic benefits. Individuals with Parkinson's were offered an innovative therapy dog program designed to promote voice, attention, range of motion and strength.

Objective: To measure the impact of AAT on adult day program participants who choose to interact with registered therapy dogs, with therapist guidance.

Methods: Clients in a therapeutic day program were offered interaction with therapy dogs for one of their hourly scheduled activities. This was offered on three separate 4-week sessions over the course of one year. Sessions consisted of individual and small group interaction with two trained therapy dogs under the guidance of their handler, and with the specific direction of either a Physical or Occupational Therapist in each session. Activities consisted of grooming the dogs, tossing balls, reaching, holding hoops, pulling a wagon, and/or walking with the dog, all while giving adequately audible verbal commands. Clients were asked to rate their energy level immediately prior to and after each session, with the use of a visual analog scale of 0–10 (with 0 indicating no energy and 10 indicating very high energy). Participation was for one hour weekly, for 4 weeks. Sessions were limited to 5 to 6 clients per session. Those present for a majority of the sessions were included in the data. Participants were also asked to rate their enjoyment level, using a similar visual analog scale.

Results: Self-rated improvement in energy level was an average of 1.34 points. The self-rated enjoyment level was 9.13 (out of 10) respectively. Several care-partners reported that clients demonstrated improved communication, attention and engagement. A calming effect was noted in anxious clients.

Conclusions: Directed interaction with animals is an innovative and successful program to increase pleasure and perceived energy level in people with advanced Parkinson's Disease.

P14.13

Development and testing of a yoga intervention program for subjects with Parkinson's disease

Catherine Justice¹, Corjena Cheung², Amy Samson-Burke³

¹ Hennepin County Medical Center and University of St. Catherine, Minneapolis, MN, USA

² University of Minnesota, Minneapolis, MN, USA

³ USA

Objective: To develop and test a biweekly, 12-week yoga program and determine its safety and feasibility for people with Parkinson's Disease (PD).

Methods: Yoga for PD literature reviews were performed by the lead yoga teacher who designed and developed a draft of a yoga for PD intervention program. The program was reviewed by a group of yoga experts (n=6) that was made up of physical therapists, registered/certified yoga teachers, a yoga therapist, a yoga researcher, and a PD patient. The yoga expert panel meeting was held at a community center that lasted for 1.5 hours. At the meeting, certain precautions were discussed such as avoiding sequences of poses that would trigger orthostatic hypotension or retropulsion episodes and the importance of teaching careful transitions to and from the poses. The therapeutic value of balancing and standing postures, poses to correct slumped forward posture, and poses encouraging thoracic and hip mobility were also emphasized by the panel. The intervention program was implemented to 10 individuals with PD, mean age 63±8 (49–75).

Results: Through this comprehensive development process, a series of 24 individual hour-long yoga sequences were created. The initial classes focused on foundational yoga postures, basic breathing techniques, and yogic principles of mindfulness, body awareness, and self-compassion. Each class built upon the previous, adding 1–4 new poses each session. The yoga postures gradually increased in difficulty from week to week, progressing to balancing postures, advanced breathing techniques, and poses that encourage thoracic extension and rotation, deep relaxation, and fluidity of movement. The specific yoga postures were chosen in order to address concerns unique to the PD population, such as thorax/ spine/ hip flexibility, balance, movement initiation, respiratory capacity, relaxation, etc. The sequence encouraged the use of yoga props (bolsters, blankets, blocks, chairs, etc.) to help improve stability, safety, and comfort within the poses. To accommodate a wide variety of physical abilities within the subject pool, modifications to the traditional yoga postures (such as seated versions of standing poses) were also included in order to address the specific needs of each individual student. The yoga for PD intervention program began in April, 2016, results on safety and feasibility will be analyzed in June, 2016.

P14.14

Moving through glass: exploring augmented reality technology for people with Parkinson's

David Leventhal¹, Craig von Wiederhold²

¹ Mark Morris Dance Group, Brooklyn, NY, USA

² SS+K, New York, NY, USA

People with Parkinson's often benefit from external visual and auditory cues to compensate for the loss or disturbance of internal cueing related to walking and other automatic movements. Preliminary research indicates that dance provides an established system of external aesthetic, rhythmic and physical cues that may help people with Parkinson's initiate and maintain certain kinds of sequential movement. But even if people with Parkinson's benefit from movement classes or see a therapist regularly, they spend most of their time outside of an organized session and need to navigate the world outside on their own.

Using technology to extend the reach of a dance-based approach, a team of dance professionals, design specialists and programmers created a new app, built on the Google Glass platform, that is designed to provide movement cueing and initiation through a portable, private augmented reality tool. The app, called Moving Through Glass, aims to enable people with Parkinson's to harness the cueing and rhythmic strategies of professional dancers wherever they are, providing an on-demand movement toolkit and fostering sense of agency and independence. In one module, the app

delivers visual and musical examples of a march, waltz and tango on demand to help people initiate a first step and keep a steady, rhythmic walking cadence; in another, a set of short dance phrases encourage fluidity and stability.

Using Moving Through Glass as a current case study, this presentation will explore how the intersection of arts, technology and patient-centered design yields important discoveries and compelling questions about the future and promise of wearable technology for people living with Parkinson's. Drawing on preliminary data from testing groups at Stanford Medical Center, Syracuse University and Weill Cornell Medical Center, the session will take a critical look at the app's benefits and challenges, revealing a set of best practices and lessons learned that can serve as a template for future wearables. Video examples and a live demo of the app will round out the presentation and spark questions: Is augmented reality safe for people with Parkinson's? What technological advances are needed to create a perfect system? What kind of flexibility do systems need to provide a user-friendly experience to the broadest range of users? Does a group-oriented, aesthetically-motivated movement form like dance have measurable benefits when adapted for a private, high-tech device?

P14.15

Complementary therapies in Parkinson's disease

Sadie McGregor, Sarah Donley

Struthers Parkinson's Center, Golden Valley, Minnesota, USA

Background: There is little research on the use of complementary therapies in Parkinson's Disease (PD). This study determined if people with Parkinson's Disease (PWP) use complementary therapies and, if used, were these therapies effective and on what symptoms.

Methods: Patients with Parkinson's Disease or related movement disorders were mailed a survey with their clinic paperwork. Surveys were returned at their clinic appointment. The following complementary therapies were included in the survey: Tai Chi, Yoga, Aromatherapy (Aroma), Essential oils (Oils), Acupuncture (Acupx), Acupressure (Acupress), Massage, Meditation (Med), Visualization (Visual), Reiki, and Homeopathy (Homeop). Results of each therapy include the use (percent 'yes' expressed as 'U: %') and effectiveness (percent 'yes' expressed as 'E: %'). Reasons for not using complementary therapies was also asked as was interest in participating in non-medication treatment research. Results are reported for PD respondents.

Results: To date, 168 surveys have been returned (46.3% response rate) with 150 by PWP. 50.7% of respondents reported using 1 or more therapies. Therapies reported: Tai Chi (U: 16.8%; E: 70.6%), Yoga (U: 25.8%; E: 83.3%), Aroma (U: 8.8%; E: 80.0%), Oils (U: 12.8%; E: 78.6%), Acupx (U: 17.8%; E: 52.4%), Acupress (U: 5.3%; E: 83.3%), Massage (U: 41.7%; E: 87.5%), Med (U: 21.2%; E: 95.7%), Visual (U: 8.0%; E: 100.0%), Reiki (U: 0.9%; E: 100.0%), and Homeop (U: 7.1%; E: 66.7%). For those that used therapies, an average of 2.6 different therapies were used (range 1-8 therapies). Reasons for not using therapies were: Don't know them (58.7%), Doctor didn't tell me to try (33.3%), Don't know where to find them (25.4%), Don't believe they will work (22.2%), Lack of research (20.6%), Don't need them (15.9%), Too expensive (12.7%). 74.2% indicated they would be willing to participate in a non-medication research study.

Conclusion: Our results indicate that despite a number of effective treatments for Parkinson's Disease, many patients are trying complementary therapies to help treat their symptoms. Further, many of the therapies used were felt to be effective by the PWP. There is clear interest in the PWP population to explore research in these non-medication therapies.

P14.16

Improvement in quality of life for people affected by Parkinson's through personalized yoga: a pilot project by Parivarthan, community support group for Parkinson's, Chennai, India

Sudha Meiyappan¹, Saraswati Vasudevan²

¹ Parivarthan for Parkinson's, Chennai, Tamil Nadu, India

² YogaVahini, Chennai, Tamil Nadu, India

Objective: This pilot project presents the improvements in the quality of life for people affected by Parkinson's Disorder (PD) through personalized yoga therapy. Studies have shown effectiveness of yoga on people with Parkinson's (Colgrove YS, Sharma N, Kluding P, Potter D, Imming K, et al. (2012). There has been no published research on personalized yoga with breath as the main driving force.

Background: The principles of the therapy are drawn from the teachings of Sri T. Krishnamacharya. He taught that anyone who can breathe can practice yoga. The yoga practice has to be customized based on the physical and mental condition of that person. Hence in this therapy along with breath and asanas, emphasis is also on personalizing diet, lifestyle habits and practicing meditation.

Method: The therapy was a customized 40-minute yoga practice for 12 weekly guided sessions at the center, along with the requirement of daily home practice. The group consisted of twelve male members, and six therapists. Members were in various stages of PD, with the number of years with PD ranging from two to eleven years. Most members also had other pre-existing health ailments. Each therapist was assigned two members. During each session the therapist would review and monitor the members' condition and modify the practice accordingly. Typically, a family member of the individual with PD would be trained along with the member to ensure consistent daily practice at home.

Results: The benefits of this therapy varied on motivation, regularity and accuracy their daily home practice. Specific results:

- Improved quality of sleep with reduced bathroom breaks at night.
- Reduction in constipation without laxatives.
- Mild decrease in tremors and rigidity.
- Discernable drop in off-time intensity, particularly if the yoga routine was practiced during off-time.
- Reduced weight loss
- Increased appetite and energy levels.
- Improvement in clarity of speech.
- Significant decrease in involuntary movements due to dyskinesia.
- Fewer symptoms of depression and an improved sense of well-being.
- Increased frequency of social interactions.

Currently phase II of yoga therapy for new members is underway along with standardization of evaluation and assessment tools.

P14.17

Utilization of entrainment to develop novel complementary therapy for Parkinsonian patients through a mobile application – NeuroNote.

Ayush Noori

USA

According to the World Health Organization, there are approximately 1 billion people around the world with neurological conditions, which span from Parkinson's to Progressive Supranuclear Palsy (World Health Organization, 2006). While the clinical symptoms of these conditions are varied, they share a

common thread – a spectrum of motor, speech and cognitive impairment, resulting in significant morbidity and mortality rates (Levi-Montalcini, 2007). While various modalities of rehabilitation exist for support of neurological conditions, rehab is often expensive, time consuming and difficult to access (Aarli, 2007; Chan, 2007). Neurologic music therapy has rapidly emerged and been accepted as an effective method for motor, speech/language, and cognitive rehabilitation in patients with Parkinsonian conditions. More specifically, the discovery that auditory rhythmic patterns and cueing could improve movement patterns in patients with neurological disorders in the early 1990s has led to the development of a strong body of research to support this technique, called entrainment (Thaut et al., 1993, 1997; Thaut et al., 1996; McIntosh et al., 1997; Hurt et al., 1998; Thaut et al., 1998; Thaut, 2010; Thaut and Hoemberg, 2014). Entrainment primes the speech, cognitive, and motor systems in the subcortical and prefrontal brain areas to increase response and execution quality. Such a powerful technique has yet to be implemented into a mobile app, until today. Using this technique, the concept behind NeuroNote was developed. NeuroNote is an app which will encourage users to complete simple movements and exercises, including strengthening, flexibility, focus, breathing, and vocal exercises while listening to rhythmic music. This will, through the subconscious and clinically-proven process of entrainment, improve the motor, speech/language, and cognitive function of users. Extensive market research demonstrated no app currently available provides all the features that NeuroNote does, nor in the manner in which they are presented. NeuroNote utilizes mobile sensors including the accelerometer, gyrometer, microphone, and user feedback for personalization, as familiar music better facilitates music therapy (Tomaino, 2002). NeuroNote does not aim to replace a therapist, rather it offers the best currently available solution to those that cannot access personal therapy, and presents an invaluable complementary tool for use by music therapists.

The developed wireframe is attached.



P14.18

Complementary and alternative medicine (CAM) use in people with Parkinson’s disease (PD)

Ju Young Shin¹, Ryan Pohlig², Barbara Habermann¹

¹ University of Delaware, College of Health Sciences, School of Nursing, Newark, Delaware, USA

² University of Delaware, College of Health Sciences, Newark, Delaware, USA

PD is affecting at least one million people in the U.S. and requiring ongoing treatment. CAM has been used both alone and in adjunct to pharmacological therapy to manage PD symptoms in some people with PD. While CAM use in several countries has received attention, this area has not been systematically studied in the U.S. in over a decade. A better understanding of CAM use would provide a foundation to help both people with PD and providers have a dialogue about CAM use.

The purpose of this study was two-fold: a) to describe the prevalence, types, and associated factors of CAM use in people with PD and b) to explore reasons for CAM use.

A self-administered, cross-sectional survey was utilized. The CAM section included previous and current use of CAM therapies (e.g., 25 supplements and 29 modalities/therapies). Institutional Review Board approval was obtained and data were collected from community-dwelling individuals with PD between March and December 2015. Descriptive statistics, t-tests, chi-square tests, and a logistic regression were utilized.

The response rate was 61.9% (N=135), and 74.1% of participants used CAM for either PD or general health. The mean of CAM use for PD symptoms was 2.56 (range 0 – 32) and for general health was 4.10 (range 0 – 32). Specifically, 23% of CAM users responded that they had used more than 10 CAM supplements or modalities/therapies. The most widely used CAM included exercise, yoga, massage, vitamins, coenzyme Q10, and coconut oil. The recommendations for CAM usage from health care providers were higher than the findings of previous studies. Higher level of education and treatment by a movement disorder specialist were significantly related to CAM use. Participants used CAM for general health and to delay the progress of PD.

Findings of this study suggested CAM usage in the U.S. has grown. Health care professionals have a role in providing a coordinated and safe care for people with PD. Further studies on effectiveness and safety of commonly used CAM therapies are warranted.

P14.19

Investigating behavioural and EEG effects of dance on people with Parkinson's disease (PwPD)

Stephanie Simone¹, Karolina Bearss², Sophia Maquire³, Kaili-Larissa Martin⁴, Gaëlle Nsamba Luabeya⁴, Brenda Owe⁴, Prabhjot Dhani⁵, Kelsi Smith⁶, Rachel Bar⁷, Joseph DeSouza⁸

¹ Department of Psychology, Toronto, ON, Canada

² Department of Psychology, Graduate Program in Neuroscience, Centre for Vision Research, York University, Toronto, ON, Canada

³ Department of Psychology, University of Toronto, Toronto, ON, Canada

⁴ Department of Psychology, York University, Toronto, ON, Canada

⁵ Department of Biology, Centre for Vision Research, York University, Toronto, ON, Canada

⁶ Department of Biology, York University, Toronto, ON, Canada

⁷ Canada's National Ballet School, Department of Psychology, Ryerson University, Toronto, ON, Canada

⁸ Centre for Vision Research, Department of Psychology, Biology and Graduate Programs in Neuroscience & Interdisciplinary Studies, York University, Toronto, ON, Canada

Objective: This behavioural and EEG study examined the effects of one dance class on PwPD.

Background: Dance has been shown to have a positive effect on motor functioning in PwPD, but less well understood are the effects of dance on mood and cognition anecdotally observed within PwPD. Our aim was to examine the effects of dance on both motor and non-motor functioning and correlate these potential effects to onsite recordings of resting state EEG, collected immediately before and after the dance class.

Methods: 17 individuals with PwPD (M=68.82, SD=8.95) and 19 healthy controls (HC) (M=52.78, SD=17.30) participated in a single 1.25-hr dance class with the Dance with Parkinson's program at the Canada's National Ballet School (NBS). The effectiveness of dance was tested both before (PRE) and after (POST) a dance class using the standardized MDS-UPDRS (III), H&Y, PANAS-X, MMSE, PD-NMS and rsEEG (described in Levkov et al 2014).

Results: PANAS-X negative affect was higher before dance class compared to after for both PwPD and HC, $F(1,30)=30.30$, $p<.01$, large effect $\eta^2=.503$. Positive affect was higher after dance class compared to before, $F(1,30)=10.27$, $p<.01$, $\eta^2=.255$. In addition, an interaction in positive affect scores was found between Condition (PRE vs POST) and Group (PwPD vs HC), where HC positive affect increased after the dance class compared to before $F(1,30)=6.53$, $p<.025$, $\eta^2=.179$. PD group had significantly more non-motor symptoms in comparison to HC, $t(19)=3.781$, $p<.01$. For MDS-UPDRS III, PD showed greater motor impairment in comparison to HC, $F(1,34)=84.80$, $p<.001$, $\eta^2=.714$. Most significantly for our study was that motor impairments improved after a single dance intervention, $F(1,34)=31.21$, $p<.001$, large effect $\eta^2=.479$. A significant interaction was also found between Condition and Group, where there was motor improvement in PwPD following the dance class, $F(1,34)=22.85$, $p<.01$.

Conclusions: We are in the continual process of data collection and correlating these behavioural effects with the rsEEG recordings. As expected, motor impairment improved after a single dance class in PwPD. We also found differential effects of dance on negative and positive mood for both PwPD and HC.

P14.20

Have you tried holistic healing? It may change your life!!!

Anish Suri

Plano, TX, USA

Have Faith & give Holistic Healing a chance – IT MAY CHANGE YOUR LIFE for the better!!!

Our body is vibrating energy, so it RESPONDS TO ENERGY HEALING. It is made up of atoms with 95+% empty space. Modern science (Einstein, Bohr, Tesla) is endorsing (what ancient practitioners & realized beings said) about sub-atomic particles vibrating millions of times/second makes us solid objects.

Our body responds to traditional PD meds (Sinemet, Mirapex, and DBS) & also to many other healing modalities (Yoga, Meditation, Reiki, Tai Chi & Qi-Gong, Chakra Healing, Polarity Therapy, Pranic Healing, Quantum Touch, Music Therapy, Theta Healing, Acupressure & Acupuncture, Emotional Freedom Technique, Sound Therapy, Ayurveda, Traditional Chinese Medicine, Homeopathy, Naturopathy, Magnetotherapy, and many more) – we just haven't tried them all yet. Acupuncture can reduce need for meds; Reiki, Meditation, Tai Chi, & Yoga can reduce stiffness & tremors & eliminate sleep meds & anti-depressants. These modalities HAVE NO SIDE EFFECTS.

It has been 199 years!!! PD was discovered in 1817. While we've made huge medical progress (PD meds, DBS, stem cells research, etc.) to slow down the disease & improve life quality we haven't yet found a cure. Medical Science finds cures focusing on physical symptoms & bodies as solid objects (not vibrating energy) – and forgetting that the body is set up to Heal Itself.

HAVE FAITH IN THE CREATOR & PRACTICE ACCEPTANCE:

CREATOR'S PERFECTION: We are a tiny spec in this cosmos living on Earth, which is part of the Solar System, which is one of million galaxies. The Creator ensures cosmos runs perfectly; Sun and Moon rise & set every day; and we don't fall off our round moving planet. 8.4M different life forms live in harmony on Earth with each other & the environment. Animals use O₂ & throw CO₂; while plants use CO₂ & expel O₂. All life forms are designed to survive & thrive in their environment. Look around you for an endless list of PERFECTIONS!!!

Creator has a plan. Every moment is planned & inevitable. Have FAITH, practice ACCEPTANCE and BE POSITIVE. There must be a reason for everything – maybe there's a hidden blessing – we are not able to comprehend it.

Conclusion: Holistic healing focuses on the energy field to clear the energy blocks at the root of the imbalance that we call dis-ease, symptoms and pain. See your body as energy; accept your situation with faith in Creator's plan; and GIVE HOLISTIC HEALING A FAIR CHANCE – IT MAY CHANGE YOUR LIFE!!!

P14.21

Development of a Parkinson's exercise training program for community-based fitness trainers

Maria Walde-Douglas

Struthers Parkinson's Center, Golden Valley, MN, USA

Objective: To present a framework of a Parkinson's-specific exercise education program for community-based fitness trainers and group exercise instructors.

Background: Research has shown exercise to be beneficial for those living with Parkinson's disease (PD). It is an important component for maintaining balance, mobility and the ability to perform activities of daily living. People with PD who exercise a minimum of 2.5 hours a week were found to experience a slowed decline in quality of life. Establishing early exercise habits is an essential part of overall disease management. Traditionally, physical therapists provide short-term, episodic bouts of treatment.

Afterward, persons with PD often try and re-integrate into community-based exercise classes, fitness centers or work with personal trainers. The knowledge base of community-based fitness professionals often does not include basic PD knowledge or specific exercise methods or precautions. Providing education on PD and evidence-based exercise methods can benefit individuals with PD and ensure a safe and more effective exercise environment.

Methods: A physical therapist specializing in PD developed a curriculum for fitness professionals working in community-based settings. The program contained basic information on PD, evidence-based exercise techniques and safety precautions specific to PD. Case studies were also included for group discussion.

Results: A total of 94 professionals were trained in 8 locations. Six-month follow-up surveys were sent out to determine knowledge retention and to ascertain if the training resulted in changes in practice. The importance of emphasizing big movements ranked highest on the most important concept learned. One of the group exercise instructors went on to become certified in teaching a Parkinson's exercise class which was offered at a local YMCA. A personal trainer cultivated several clients with PD and requested additional training. A boxing gym developed classes for persons with PD in 3 locations. This PD education program offers a "train the trainer" approach to allow fitness professionals to provide more specialized care for their clients with PD.

P14.22

Creating a nature based environment at a National Parkinson Foundation Center of Excellence

Rose Wichmann

Struthers Parkinson's Center, Golden Valley, MN, USA

Objective: Design a comprehensive center for Parkinson's disease (PD) care incorporating a multipurpose nature-based therapeutic environment.

Methods: Throughout its 20 year history, Struthers Parkinson's Center (SPC) has continued to develop a comprehensive array of clinical, research, education and support programs for individuals/families living with Parkinson's disease (PD) SPC's first use of nature based activity started in 1996 through a collaborative relationship with the University of MN Landscape Arboretum. At that time, construction of accessible garden beds for SPC's adult day program offered initial opportunities for client exercise, social interaction, and creative expression in a nature-based setting. A water garden was added to the property in 2002, offering space for relaxation/quiet reflection. In 2015, a significant expansion project included development of new indoor and outdoor gardens. The indoor space provides a 4 season therapeutic path filled with live green plants, a water wall, and a bridge allowing stair climbing practice during Rehab therapy sessions. Outdoor garden spaces incorporate paved surfaces including ramps, curbs and, inclines. The south garden path has a crushed marble surface ideal for Nordic walking practice – this path includes activities for therapy/balance practice such as mailboxes, birdfeeders and outdoor seating.

Results: A nature based environment at SPC contains space for activity and rest, both important in the overall care plan of individuals living with PD. Clients have reported feeling reduced stress and a sense of community as they gather with others before/after exercise and support groups at the center. Those who enjoy gardening continue this leisure interest in an accessible environment, achieving physical exercise, social interaction and a creative outlet through their endeavors. Gardens also provide sensory enhancement and opportunity for other activities including harvesting, cooking, floral arranging, and artwork created from natural materials. Rehab therapists successfully incorporate

indoor/outdoor garden spaces into their care plan and goals for treatment.

Conclusions: Incorporation of a nature based environment at SPC offers a wide variety of benefits for individuals living with PD. Benefits include opportunities for physical exercise/rehabilitation, stress reduction, creative expression, feelings of support and enhanced well-being.

P14.23

"I am the guitar hero!" Psychosocial modulators of motor sequence learning in Parkinson's disease – behavioral pilot study using rhythmical computer game.

Petra Zemankova^{1,3}, Ovidiu Lungu^{3,4,5}, Martin Bares^{1,6}

¹ First Department of Neurology, St. Anne's University Hospital and Medical Faculty of Masaryk University, Brno, Czech Republic

² Behavioral and Social Neuroscience Research Group, CEITEC (Central European Institute of Technology), Masaryk University, Brno, Czech Republic, Brno, Czech Republic

³ Department of Psychiatry, University of Montreal, Montreal, QC, Canada

⁴ Functional Neuroimaging Unit, Research Center of the Geriatric Institute Affiliated with the University of Montreal, Montreal, QC, Canada

⁵ Department of Research, Donald Berman Maimonides Geriatric Center, Montreal, QC, Canada, Montreal, Canada

⁶ Department of Neurology, School of Medicine, University of Minnesota, Minneapolis, MN, USA

Introduction: There is a remarkable overlap between brain circuits affected in Parkinson's disease (PD) and neuronal correlates of motor sequence learning. Despite the fact that people with PD perform worse on some motor learning tasks, there is evidence indicating that motor learning can be improved in PD. Most studies investigating motor learning in PD used laboratory-specific tasks and equipment, with little resemblance to real life situations. Thus, it is unknown whether optimal stimulation and task cueing can be achieved in more ecological setups. In our study we aim to demonstrate that increased task engagement and motivation through music, ecological goals and social interaction can significantly improve procedural learning capacity in people with PD, most likely through increased activity in basal ganglia and the cortico-striatal motivational circuit, which seems to be spared in PD.

Method: 3 people with PD (age between 50-60) performed an implicit sequence learning task using computer game (similar to Guitar Hero). The goal is to hit the stimuli presented on a screen by pressing according buttons on a guitar like controller. Three conditions will be contrasted. First variant of the game does not involve music and rhythmical cues, in other two conditions the same game with music is used, once with and once without social interaction. This pilot study was to test the feasibility of the controlled experiment, more people with PD and age and gender-matched controls are now being recruited.

Results: In our pilot sample we did not find any significant differences in accuracy between random blocks and blocks with repetitive sequences (repeated measures ANOVA; $F=1.85$, $p<0.2$), very likely due to small sample. Participants managed to control the guitar controller in quite short time, the task was challenging, but still joyful. They were not aware of the repetitive sequences implemented in the game, which is a sign the learning process was implicit. With larger sample we will be able to test the effects of music and social interaction on learning rates (currently recruiting subsequent subjects).

Conclusions: This research is a step in further expanding the range of low-cost, non-pharmacological interventions aimed to preserve or restore motor function in PD, which can easily be implemented outside the clinical setting (i.e. at home) and tailored to one's needs.

CARE DELIVERY & QUALITY OF LIFE: LAY/PROFESSIONAL HEALTH LITERACY & PUBLIC THOUGHT

P15.01

Enhancing care for the hospitalized patient with Parkinson's disease: development of a formal educational program for nursing staff

Mary DiBartolo

Salisbury University, Salisbury, MD, USA

When persons with Parkinson's disease (PD) require hospitalization, they can experience higher rates of complications and lengthier hospital stays. Reasons for suboptimal outcomes can range from the nursing staff's general lack of understanding of the disease process and misconceptions about the motor versus non-motor symptoms, the inappropriate administration of contraindicated anti-dopaminergic medications for related symptoms, as well as the mismanagement of anti-Parkinson's medications (including missed or late doses) which can lead to significant motor fluctuations and impaired function. To address this knowledge gap, a formal educational presentation was developed. Key components of this two-hour educational offering are: 1) a PowerPoint presentation with an unfolding case study to provide an overview of the disease, symptoms, medications, mobility management, diet considerations, and critical timing of carbidopa/levodopa therapy; 2) a one-page handout of information condensed from the National Parkinson's Foundation (NPF) delineating key motor and non-motor symptoms, typical PD medications, as well as dopamine-blocking agents that are contraindicated; 3) a succinct and engaging one-page handout outlining the "10 Commandments for Parkinson's Care" for easy reference; and, 4) a review of the Aware in Care kit available from the NPF to enhance both self-advocacy for persons with PD and awareness on the part of hospital staff regarding evidence-based modifications in care. The instructional initiative also entailed the use of a pre- and post- knowledge assessment to determine program effectiveness and the extent of new learning among participants. These efforts to more formally and systematically educate staff about care for persons with Parkinson's disease can serve to increase both staff competence and confidence when working with this population in all domains of care. Any subsequent improvements in quality of care could also ease patient anxiety and potentially create a more positive experience during the hospital stay.

P15.02

Health literacy in Parkinson's disease caregivers

Jori Fleisher¹, Steven Bondi¹, Jamika Singleton-Garvin, CCRP¹, Marissa Lanoff¹, Sharon Xie², Judy Shea³, Joshua Chodosh⁴, Nabila Dahodwala⁵

¹ Marlene and Paolo Fresco Institute for Parkinson's and Movement Disorders, New York University School of Medicine, New York, NY, USA

² Department of Biostatistics and Epidemiology, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, USA

³ Department of Medicine, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, USA

⁴ Department of Medicine, New York University School of Medicine, New York, NY, USA

⁵ Department of Neurology, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, USA

Objective: To determine the prevalence of low health literacy among caregivers of community-dwelling individuals with Parkinson's Disease (PD).

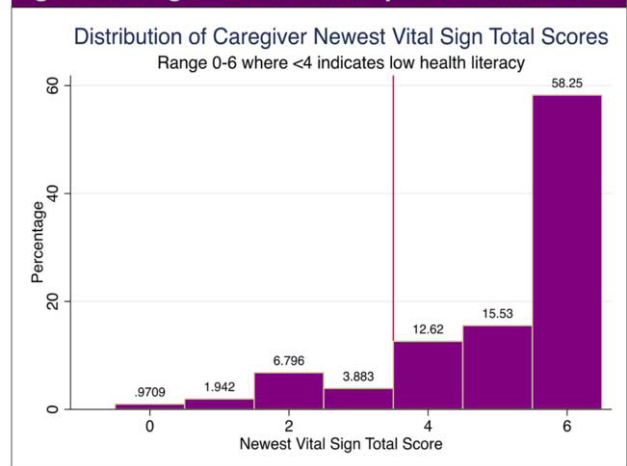
Background: Low health literacy (HL) indicates a limited ability to understand and apply basic information to make appropriate healthcare decisions. Previously, we reported that nearly 30% of non-demented, community-dwelling individuals with PD had low HL, which was associated with both increased caregiver burden and hospitalization rates. The HL of caregivers, however, has only begun to be explored in other, non-PD cohorts, and is disheartening. In PD particularly, caregivers with adequate HL may serve as a safety net for vulnerable patients, assisting with medication adherence and health-related activities.

Design/Methods: Cross-sectional study of caregivers of community-dwelling individuals with PD at two urban, academic referral centers. Individuals presenting for a clinical visit for PD were asked to participate in a study of HL and medication beliefs, and if available, self-identifying caregivers were asked to participate. Both patients and caregivers completed brief demographic questionnaires as well as the Newest Vital Sign, a validated 6-item screening instrument for HL, where 0-3 points indicates low HL and 4-6 points indicates adequate HL.

Results: 103 patient-caregiver dyads participated. Caregivers had a mean age of 65 (SD 9), 72% had a college degree or higher, and 72% were women. Paid caregivers constituted less than 2% of our sample. Low HL was detected in 23% of patients and 14% of caregivers, respectively, with low concordance between pairs (agreement 73%, kappa=0.1, p=0.1). There was no significant association between level of education and HL in either patients or caregivers. Among patients with low HL (n=24), 21% also had a caregiver with low HL.

Conclusion: Low HL is common in this sample of PD caregivers and patients despite high levels of education. In order to best educate and address the concerns of PD patients and families, we must recognize the prevalence and consequences of low HL.

Figure 2: Caregiver Health Literacy Score Distribution



P15.03

Conversation mapping as a technique to train student nurses in the care of Parkinson's disease patients and family members

Marjorie Getz

Methodist College, Peoria, Illinois, USA

In 2009, The Edmond J. Safra Foundation began funding a program to educate nursing faculty working in undergraduate nursing

programs to guide and encourage instructors as they trained (through knowledge acquisition and skills development) new nurses to be better prepared to care for patients with Parkinson's disease (PD) and their family members. This faculty training—hands-on experience with patients with PD, cultivation of interest in learning about PD, assistance with developing teaching materials suitable to an academic setting, and careful follow-up and guidance after a return to campus—led to the implementation of a novel project, Conversation Mapping and Parkinson's Disease, in PSY401 Health Psychology, an upper level elective on our campus. The purpose of a conversation map is to engage small groups of people—e.g., patients and family members—in open discussions about PD. The primary goal is to better educate a person about their disease in order to promote treatment follow-through and self-efficacy for better control over symptoms (including psychological symptoms). Although the conversation mapping process is structured and guided, the sessions using this resource allow a nurse to focus on specific areas of PD education and, concomitantly, allow patients/family members to ask about what they are most interested in learning. The sessions provide a background to allow patients and family members to learn from the experiences of one another. A nurse also can learn how patients verbally conceptualize their disorder which can enhance care when the healthcare provider has greater insights into the lived experience of having PD or being close to a person with PD. Appreciating this context allowed students to construct a conversation map session for a patient with PD and family members. Conceptualization, design and completion of the map followed a detailed rubric that began with the student nurses acquiring knowledge about PD using evidence-based resources (and preparing an annotated bibliography) and developing a hypothetical case. Students were encouraged to attend at least one meeting of the local PD support group while involved in developing their conversation maps. Examples of the posters will be shown. Research has demonstrated that increased preparation and knowledge of nurses can have a marked impact on the well-being of patients with Parkinson's disease and their family members.

P15.04

Parkinson's Inpatient Quality Initiative (PIQI): a retrospective review.

Deepak Gupta¹, Junaid Siddiqui², Curtis Tatsuoaka³, Benjamin Walter⁴

¹ Cleveland, OH, USA

² Neurology, University Hospitals Case Medical Center, Cleveland, OH, USA

³ Neurology & Biostatistics, Case Western Reserve University, Cleveland, OH, USA

⁴ Neurology & Movement Disorders, University Hospitals Case Medical Center, Cleveland, OH, USA

Background: Patients with Parkinsonian disorders, including Parkinson's Disease (PD), have multiple disease complications, cognitive/behavioral problems and co-morbid medical conditions, which make them prone to frequent hospitalizations. Studies show that PD patients have higher rates of ER visits and hospitalization than non-PD patients. As much 3 out of 4 people with PD do not receive medications on time in the hospital. In another study, 61% of PD patients who did not get their medications on time, had serious complications from it.

Methods: We aimed to assess the status of PD inpatient treatment quality in our academic medical center, which serves a large number of Parkinson's patients owing to huge volumes of inpatient services and a dedicated Movement Disorders Center. We first developed an algorithm (Figure 1) to identify patients with Parkinsonian disorders from hospital's Allscripts Sunrise EMR. We

then conducted a retrospective chart review study of patients admitted over 6months period from July 1st to December 31st 2015. Data were managed using using REDCap and SPSS software.

Results: Total 105 eligible admissions (excluding DBS/medication management), with valid outpatient medication reconciliation, were included. Of these, 48.6% were males and 51.4% females; 75% admission were admitted to medical service and 25% to surgical service; 43.8% patients were discharged to home while 56.2% were not discharged to home (56 rehab discharges, 3 deaths). Hospital admission duration ranged from 0 to 25 days. None of the patients were prescribed contraindicated (per APDA list) antipsychotics, antihypertensives and antidepressants in outpatient or inpatient while 1%, vs 6.7%, were prescribed contraindicated antiemetics (Promethazine/Reglan) in outpatient vs inpatient respectively. For 50.5% (52) of patients, who got levodopa as inpatients and were admitted for greater than 2 days, we found that levodopa was administered in suboptimal manner (missed doses or aberrant times) for 63.5% (33) cases and the average variability in daily levodopa equivalent dose (LED), compared to outpatient daily LED, was 62.63mg (range 0 to 513.64)

Conclusions: There exist important gaps in optimal management of PD medications on non-neurological services in hospitals. Prospective studies are needed to investigate contribution of specific factors and inform development of targeted interventions, such as Parkinson's Nurse (similar to Diabetes Nurse), for this preventable problem.

1. Any of following diagnosis (in any of the different categories of diagnosis):

Diagnosis Name	ICD-9 Code	ICD-10 Code
Idiopathic Parkinson's Disease	332.0	G20
Secondary parkinsonism	332.1	G21
Dementia with parkinsonism	331.83	G31.83
Progressive Supranuclear Palsy	333.0	G23.1
Multisystem Atrophy	333.0	G90.3
Corticobasal Degeneration	331.6	G31.85
Lewy Body Disease	331.82	G31.83

OR

2. Any of following medication (in any of the different categories of drugs e.g. home or inpatient or discharge medications):

- LEVODOPA-CARBIDOPA (Duopa; Dopar; Larodopa; Stalevo; Parcopa; Rytary; Sinemet; Sinemet CR)
- Dopamine Agonists [for dopamine agonists, exclude the subject if the subject has no diagnosis from criterion 1 AND has diagnosis of "Restless Legs Syndrome (ICD-9: 333.94, ICD-10: G25.81)" in any of the different diagnostic category]
 - a. PRAMIPEXOLE (Mirapex; Mirapex ER)
 - b. ROPINIROLE (Requip; Requip XL)
 - c. ROTIGOTINE (Neupro)
 - d. APOMORPHINE (Apokyn, APO-Go Pen, Uprima, APO-Go)
- COMT inhibitor
 - a. ENTACAPONE (Comtan)
 - b. TOLCAPONE (Tasmar)
- MAO-B inhibitor
 - a. RASAGILINE (Azilect)
 - b. SELEGILINE (Eldepryl; Emsam; Zelapar; Carbex)

P15.05

The impact Parkinson's New Zealand's Parkinsonian magazine has on individual health literacy in our community

Deirdre O'Sullivan, Natasha McDougall

Parkinson's New Zealand, Wellington, New Zealand

Objective: To utilize the Parkinson's New Zealand quarterly magazine 'The Parkinsonian' to improve levels of individual health

literacy in the Parkinson's New Zealand community. 56.2% of adult New Zealanders have poor health literacy skills¹. Lower levels of health literacy are associated with higher use of health services, lower levels of knowledge among consumers, and poorer health outcomes².

Methods: In New Zealand health literacy has been defined as:

"the degree to which individuals have the capacity to obtain, process and understand basic health information and services in order to make informed and appropriate health decisions"

Implicit in this definition is the need for the health system to not just present information in accessible ways, but also to engage with individuals to make sure they can access, understand and act on the information they receive².

A combination of telephone interviews and electronic and paper based surveys will be used to gather responses from people with Parkinson's, care partners and health professionals. Participants are invited to self-report on what part the Parkinsonian plays in their individual Parkinson's Health Literacy, the quality of the information received, the appropriateness of the information received, the appropriateness of the language, design and layout and the impact the information has on decision making and actions.

Results: Results will be analysed and conclusions presented once participation rates are <100.

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[1] Berkman ND, Sheridan SL, Donahue KE, Halpern DJ, Viera A, Crotty K, et al. Health Literacy Interventions and Outcomes: An Updated Systematic Review. EvidenceReport/Technology Assessment No. 199. (Prepared by RTI International–University of North Carolina Evidence-based Practice Center under contract No. 290-2007-10056-I) AHRQ Publication Number 11-E006. Rockville, MD. Agency for Healthcare Research and Quality, 2011.

[2] Ministry of Health. 2010. Korero Marama: Health Literacy and Maori Results from the 2006 Adult Literacy and Life Skills Survey. Wellington: Ministry of Health.

P15.06

Meet Val and Holly: An experiential tour through the lives of a PD family

Laura Kelly, Cheryl Leiningen

Monmouth University, West Long Branch, NJ, USA

Val, a vibrant 60 year old school teacher is diagnosed with PD and forced to retire early from her teaching job. Her partner Holly and she are struggling with learning to define the "new normal" which changes as the disease progresses. This case study follows the couple as they learn to live life and is presented to first semester nursing/health professional students in weekly vignettes that address key areas of functioning that affect PD clients and their loved ones.

This case study is utilized in a freshman course over a 14 week semester. The course "Becoming a Home Health Aide" introduces beginning practitioners to the fundamental ADL skills that often can be a struggle for PD clients. The course also addresses the psychological needs and challenges of living with a chronic disease. The utilization of a particular family allows the students to "get to know" Val and Holly and allows for the facilitation of empathy. The culmination of the course project requires that the students create an educational tool that will assist others (consumers and professionals) in developing a better understanding of PD and the resources available to them.

This project fulfills the requirement for the Edmond J. Safra Visiting Nurse Faculty Program and is the work of two faculty alums dedicated to integrating the needs those impacted by PD into health curriculum in a way that is truly meaningful to students.

CARE DELIVERY & QUALITY OF LIFE: DISABILITY AND QUALITY OF LIFE OUTCOME MEASURES

P16.01

Association between QOL and the sense of coherence in patients with Parkinson's disease

Yukako Ando¹, Akemi Abe², Yoshino Ueki³, Takemori Yamawaki⁴, Itsuko Ozaki⁵, Akira Inukai⁵, Ikuko Aiba⁵, Yufuko Saito⁵, Noriyuki Matsukawa³, Toshio Kobayashi⁶

¹ Nagano College of Nursing, Komagane, Japan

² Hatsuokaichi City Health Center, Japan

³ Nagoya City University, Japan

⁴ Hiroshima City Hospital, Japan

⁵ Higashi Nagoya National Hospital, Japan

⁶ Hiroshima University, Japan

Objectives: Parkinson's disease (PD) is characterized by motor symptoms, including resting tremor and bradykinesia, which often merge non-motor symptoms such as depression and dementia. Curative treatment for PD is difficult, and when the disease progresses, the burden for the patient and the family is extremely large. Therefore, maintaining the QOL of PD patients is an important issue. Attention has been paid to sense of coherence (SOC) as one of the prominent factors for promoting health. The higher score of SOC means higher stress coping ability, and those having high SOC have less health problems. Thus, the purpose of this study is to clarify the association between QOL and SOC in PD patients.

Methods: Self-reporting questionnaires were distributed to the outpatients of PD (n=185) who visited a hospital in Japan. QOL was measured by a scale for subjective QOL common to patients with intractable diseases, which consist of the "acceptance" and "morale". SOC (Antonovsky) is composed of three elements of the "comprehensibility", "manageability" and "meaningfulness". The shortened 13 items Japanese version of SOC scale (Yamazaki et al, 2005) was used in this study. In order to reveal the association between QOL and SOC, Spearman correlation analysis and covariance structure analysis were performed.

Results: The valid response rate was 95.7% (177 of 185). The results of the correlation analysis indicated that the age (p<0.05) and Barthel Index (BI) (p<0.01) had significant associations with QOL. By the covariance structure analysis, the SOC subscale of "meaningfulness" (p<0.001) and BI (p<0.001) showed a significant correlation with QOL. The goodness-of-fit of the model was GFI=0.95, AGFI=0.92 and RMSEA=0.06. These findings suggest that giving support to PD patients focusing on "meaningfulness" of SOC is important for increasing the PD patients' QOL.

P16.02

Conflicting and non-conflicting visual cues lead to error in gait initiation and gait inhibition in individuals with freezing of gait.

Zacharie Beaulne-Seguin, Julie Nantel

School of Human Kinetics, Faculty of Health Sciences, Ottawa University, Canada, Ottawa, Ontario, Canada

Introduction: Movement processes are affected in Parkinson's disease (PD) and are known to induce loss of postural reflexes, less flexible postural mechanisms and episodes of freezing of gait. Gait initiation is known as one of the main triggers of freezing of gait and can therefore lead to higher risks of postural instability and falls. However the effect of conflicting visual signals on postural control during gait initiation remains to be determined.

The objective of the study was to determine the effect of conflicting visual signals on gait initiation and gait inhibition in freezers, non-freezers and healthy older adults.

Methods: Twenty-five subjects with PD and 17 healthy older adults participated to the study. Participants were required to initiate gait (green stimulus) or stand still (red stimulus) independently of the written instructions (Go or Stop) inducing conflicting signals in some of the conditions. Conditions were as follow: Non-conflicting: Green Go (GG), Red Stop (RS), conflicting: Green Stop (GS) and Red Go (RG). Center of pressure (CoP) displacement, variability and mean velocity (VCoP) in the anterior-posterior (AP) and medial-lateral (ML) directions and movement time (MT) were measured.

Results: Gait initiation: Both freezers and non-freezers were different from controls in GG and GS. In GS, freezers had smaller CoP displacement and velocity in both directions ($p < 0.01$), while non-freezers had smaller VCoP in AP and ML ($p < 0.01$). AP CoP displacement in GS was smaller in freezers compared to non-freezers ($p < 0.05$). Freezers had longer MT compared to controls in GG and compared to both groups in GS ($p < 0.01$).

Gait inhibition: Controls and freezers had larger CoP displacement variability ($p < 0.05$) and velocity ($p < 0.01$) in both directions in RG compared to RS. No differences were seen in non-freezers. Three freezers initiated walking during the RG or RS conditions.

Discussion: Freezers were in general slower at initiating gait, displayed a more restrictive postural strategy and were more affected by the conflicting conditions compared to both controls and non-freezers. In freezers, the conflicting visual cues may have increased the cognitive load enough to provoke delays in processing the visual information as well as implementing the appropriate motor program.

P16.04

Characteristics associated with voice handicap in Parkinson's disease

Carrie Crino¹, Andrew D Palmer², Linda A Bryans², Donna J Graville²

¹ Oregon Health and Science University, Beaverton, OR, USA

² Oregon Health and Science University, Portland, Oregon, USA

Individuals with Parkinson's Disease (PD) often present with a variety of communication symptoms that are characterized within the domain of hypokinetic dysarthria, frequently resulting in voice handicap. Voice handicap is defined as the self-perceived impact of a voice disorder on an individual's ability to interact with others and perform everyday activities. The Voice Handicap Index (VHI) has been shown to be a reliable assessment of an individual's self-perceived handicap and to be valid for a wide range of voice disorders. Researchers have attempted to investigate the relationship between PD severity and voice symptoms. In some studies, associations have been reported between PD severity and voice handicap, but others have found no relationship at all. Using the World Health Organization's International Classification of Functioning, Disability and Health (ICF) as a framework, this study was conducted to better understand the relationship between voice handicap and other characteristics in individuals with PD; including, demographic characteristics, disease-related characteristics, acoustic voice measures, clinician-rated perceptual voice measures, and self-perceived communication disability. Records of eligible individuals with PD seen for a voice evaluation at Oregon Health and Science University over a 2-year period were reviewed. Higher voice handicap was found in women and those who were unmarried. These findings are consistent with research on gender differences and also may reflect the role of a partner in facilitating communication. Longer duration since PD onset and having undergone deep brain stimulation (DBS) was also associated with higher levels of voice handicap. Both of these finding may reflect the

progressive nature of PD since DBS is typically performed in later stage disease. Only one acoustic variable was found to be associated with VHI, namely maximum phonation time (MPT). This is a novel finding and may reflect the fact that MPT is a test of both the phonatory and respiratory systems. Like other global health measures, the VHI appears to be influenced by disease-related as well as demographic factors. Further research is merited with regard to its sensitivity to change as a treatment outcome measure in PD.

P16.05

Improvements in activities of daily living and quality of life measures in Hoehn & Yahr subgroups of advanced Parkinson's disease patients following treatment with IPX066, extended-release carbidopa-levodopa

Rohit Dhall¹, Ramon Gil², Elizabeth Lindemulder³, Robert Rubens³, Suneel Gupta³

¹ Parkinson's Institute and Clinical Center, Sunnyvale, CA, USA

² Parkinson's Disease Treatment Center of Southwest Florida, Port Charlotte, FL, USA

³ Impax Laboratories, Inc., Hayward, CA, USA

Background: IPX066 [RYTARY®, NUMIENT(TM)] is an extended-release capsule formulation of carbidopa-levodopa (CD-LD). Following an initial peak at about one hour, plasma levodopa concentrations are maintained for about 4–5 hours. In clinical trials, IPX066 significantly improved motor function and activities of daily living in early and advanced Parkinson's disease (PD) patients.

Objective: Describe the effects of IPX066 on the activities of daily living (ADL) and quality of life (QoL) in subgroups of advanced PD patients based on Hoehn & Yahr (H&Y) stage.

Methods: ADVANCE-PD examined the efficacy and safety of IPX066 vs. immediate-release (IR) CD-LD in patients with advanced PD. Patients (n=393) received 13 weeks of double-blind treatment with either IR or IPX066. The changes from baseline in the Unified Parkinson Disease Rating Scale (UPDRS) Part II (ADL) scores and the 39-item Parkinson's Disease Questionnaire (PDQ-39) were examined by treatment for each H&Y stage (I–II vs. III–IV) subgroup.

Results: In the study, UPDRS ADL ($P < 0.01$) and PDQ-39 total scores ($P < 0.05$) were significantly improved with IPX066 treatment vs. IR overall. On the UPDRS ADL scale, IPX066 also produced a numerically greater improvement from baseline compared to IR within both H&Y I–II and III–IV subgroups. IPX066 tended to improve individual items within the UPDRS ADL scale more than IR in both the H&Y I–II and III–IV subgroups, with the exception of tremor, which was improved as much (H&Y I–II) or more (H&Y III–IV) by IR. Although the PDQ-39 total score improved numerically, there was no statistically significant difference between treatment groups for either H&Y I–II [mean (SD) change from baseline of -2.6 (12.7) for IPX066 vs. +0.1 (9.7) for IR] or H&Y III–IV [-5.3 (11.4) for IPX066 and -4.4 (11.5) for IR] subgroup. For the H&Y III–IV subgroup, PDQ-39 mobility scores were significantly better for IPX066 vs. IR ($P < 0.04$); this improvement was not statistically significant in the H&Y I–II subgroup.

Conclusions: As compared to IR, treatment with IPX066 tended to produce greater improvements in the UPDRS ADL and the PDQ-39 scale in both H&Y I–II and H&Y III–IV subgroups.

Supported by Impax Laboratories, Inc.

P16.06

Depression and its related factors in patients with Parkinson's disease

Toshio Kobayashi¹, Akemi Abe², Yoshino Ueki³, Takemori Yamawaki⁴, Itsuko Ozaki³, Akira Inukai⁵, Ikuko Aiba⁵, Yufuko Saito⁵, Noriyuki Matsukawa³, Yukako Ando⁶

¹ Hiroshima University, Hiroshima, Japan

² Hatsukaichi City Health Center, Hiroshima, Japan

³ Nagoya City University, Nagoya, Japan

⁴ Hiroshima City Hospital, Hiroshima, Japan

⁵ Higashi Nagoya National Hospital, Nagoya, Japan

⁶ Nagano College of Nursing, Nagano, Japan

Objectives: In the rapidly rising aging population in Japan, it is predicted that the number of Parkinson's disease (PD) patients will increase more and more. When the disease condition progresses, not only the movement disorders, but also non-motor complications such as depression and sleep disorders will be increased. In addition, depression has been pointed out as one of the factors lowering the QOL of PD patients, taking the prevention measures for depression is important. In this study, we examined the relationship between depression and the psychosocial factors, including disease self-management behaviors, Sense of coherence (SOC) and Social capital (SC) in PD patients.

Methods: Self-reporting questionnaires were distributed to the outpatients of PD (n=185) who visited a hospital in Japan. For the measurement of the depression, Japanese version of K6 (6 items) was used. For the measurement of self-management behaviors, a total of 29 items (medication management, symptom management, etc.) was extracted from the literature and scored. The 13 items Japanese version of SOC (Yamazaki et al. 2005) was used, which is one of the stresses coping ability. The concept of SC is the resources for social connections or networks, so "reciprocity" and "trust" were measured in this study. In order to reveal the association between depression and psychosocial factors, Spearman correlation analysis and multiple regression analysis were performed.

Results: The valid response rate was 95.7% (177 of 185). The results of the multiple regression analysis indicated that depression showed significant association with SOC ($\beta=-0.61$, $p<0.001$) and Barthel Index (BI) ($\beta=-0.20$, $p<0.01$). There was no significant association between depression and self-management behaviors nor SC. Therefore, it is suggested that increasing SOC is important for preventing depression in PD patients.

P16.07

Motor complications and health related quality of life in Parkinson's disease: a literature review

Connie Marras¹, Alexander Niyazov², Amy Guo², Harald Murck²

¹ Morton and Gloria Shulman Movement Disorders Centre and the Edmond J Safra Program in Parkinson's disease, Toronto Western Hospital, University of Toronto, Canada

² Acorda Therapeutics, Inc., Ardsley, NY, USA

Objective: Motor complications including motor fluctuations (MF) and dyskinesias can have a negative impact on health related quality of life (HRQOL). HRQOL has been increasingly recognized as an important outcome measure for patients with Parkinson's disease (PD). A literature review was conducted to understand the associations of motor complications with HRQOL in PD patients. Understanding these associations may help clinicians optimize the management of motor complications.

Methods: Medline (from 1960) and Ovid BIOSIS previews (from 1993) were searched for studies on PD and HRQOL. Targeted search of reference lists from retrieved studies were also

undertaken. Inclusion criteria were original articles; studies that assessed the impact of MF or dyskinesias on HRQOL; randomized controlled trials or observational studies; use of a HRQOL instrument; English literature.

Results: A total of 1474 abstracts were identified in the initial text search. Of those, review of abstracts identified 159 potential articles and 24 full-text articles that met the inclusion criteria. Review of the 24 articles showed a wide heterogeneity in patient characteristics (H & Y stage varied from 1–5; disease duration ranged from 1.7–12 years), HRQOL instruments (EQ-5D, 15D, PDQL, PIMS, EQ-VAS, SF36, PDQ, NPH; PDQ was the most frequently used in 14/24), and assessments (19 assessed MF and 18 assessed dyskinesia). Within the MF articles, 74% reported that MF was associated with reduced HRQOL. 3 articles reported a negative association with one instrument but not another. Within the dyskinesia articles, 33% reported that dyskinesia was associated with reduced HRQOL. Of these, half reported a negative association with one instrument but not another.

Conclusions: In this review, there was a lack of uniformity in patient characteristics, HRQOL instruments, study design, and method of assessment. Although a causal relationship cannot be established in observational studies, in this review the majority of the articles showed that MF was more frequently associated with reduced HRQOL than was dyskinesia. These findings suggest that managing MF may be of particular importance in preventing HRQOL decline in patients with PD.

Supported by Acorda Therapeutics.

CARE DELIVERY & QUALITY OF LIFE: SHARED DECISION-MAKING: PWP – CAREGIVER – DOCTOR

P17.01

To DBS or not to DBS: sources of influence in the decision making process

Carol Clupny

Person with Parkinsons, Hermiston, OR, USA

Deep Brain Stimulation Surgery (DBS) is increasing in use as a therapy for Parkinson's Disease. Patients may be frightened to pursue this option as it is considered "brain surgery", and they perceive the risk factor to be high. Other patients may be willing to take any risk to relieve their symptoms of the disease. This small study looks at 20 People with Parkinson's Disease who have been exposed to the option of Deep Brain Stimulation as one of the therapies to mitigate their symptoms. Ten of these patients completed the surgical process for DBS and 10 did not. All subjects completed a short electronic survey designed to reveal individuals or factors which influenced their decision "To DBS or Not to DBS". The results of this survey may provide health care professionals, family and care providers information on how best to approach various medical therapies, especially DBS therapy with patients in a manner which leads to the best treatment option.

P17.02

Neurologists' perspectives on improving care for Parkinson's disease patients: current challenges and innovative care strategies

Rachel Schwartz, Meghan C. Halley

Palo Alto Medical Foundation Research Institute, Palo Alto, CA, USA

Studies have repeatedly documented how gaps in effective doctor-patient communication in neurology visits contribute to unmet Parkinson's disease (PD) patient needs, however little research to date has included neurologists as partners in identifying how to improve healthcare delivery. The goal of this study is to identify the challenges neurologists experience in providing effective care for patients with PD. Drawing on in-depth interviews with 15 neurologists across four institutions in the San Francisco Bay Area, we identify (1) neurologist-perceived communication and patient-education barriers that interfere with effective treatment and (2) strategies physicians have devised to improve care outcomes. Neurologist-identified clinical communication challenges include: patient misattribution of symptoms to causes other than PD, and an underreporting of non-motor symptoms, many of which are treatable; the need for communication strategies tailored to the different needs of men and women with PD, as well as those from different cultural backgrounds; and the need for an identified local network of specialists who provide high-quality PD-tailored support services. Neurologists cited significant unmet need in the area of PD psychosocial services, and voiced a desire for more palliative care interactions to facilitate discussions about how to maximize PD patient quality of life. Neurologists' innovations for improved physician-patient communication and patient education are discussed, with an emphasis on a partnership model of care delivery. This study seeks to provide neurologists, PD patients, and caregivers with an increased awareness of how to successfully manage the clinical encounter to achieve optimal care outcomes.

P17.03

Parkinson's Inside Out: a think tank of healthcare professionals and neuroscientists with Parkinson's

Jon Stamford¹, Dieter Scheller², Peter Jenner², Georg Stenberg², Cathy Oas², Stephen Shea², Sheila Roy², Jill Carson², Soania Mathur², Michele Bell², Stefan Strahle²

¹ Parkinson's Movement, London, United Kingdom

² Parkinson's Inside Out group, London, United Kingdom

Over the last decade, perception of Parkinson's disease (PD) has shifted radically. PD is no longer regarded simply as a movement disorder caused by dopaminergic deficit in the nigrostriatal pathway. Increased understanding of the importance of nonmotor symptoms has led to a reconceptualisation of PD as a complex, progressive, multifactorial neuropsychopathological condition of varying presentation. The prevalence and importance of nonmotor symptoms has also shifted the balance of understanding from the healthcare professionals, whose interests were primarily motor symptoms, to patients, whose interests placed more emphasis on nonmotor symptoms. This has produced a disparity between the objective assessment of PD (largely motor scales) and the subjective experience of PD (largely nonmotor and less readily quantifiable). This separation between patient experience and clinical assessment means that both facets present only partial pictures of PD. Both are intrinsically incomplete and, on their own, can give rise to separate parallel misunderstandings of the nature of PD. During the course of PD, patients will be exposed to many healthcare practitioners from a range of disciplines – general medicine, neurology, neurosurgery, pain management, nursing,

physiotherapy, speech therapy, psychology, and dietetics. Each separate specialty sees a different picture of the patient albeit, in each case, an objective outside view. And with each different specialty, a PD patient will share a portion of the subjective experience of PD, the inside view. A complete picture of PD is essential for healthcare practitioners and patients to jointly determine the best treatment for each individual. It follows therefore that this can best be achieved by individuals who are both patients and healthcare practitioners. A similar case can be made for those individuals who are both patients and neuroscientists. Responding to this need, Parkinson's Inside Out (PIO) is a novel think tank of healthcare practitioners and neuroscientists who have all been diagnosed with PD. PIO was assembled in September 2014 with the rationale that the group will be able to speak with authority on both the subjective and objective facets of PD and that this information would be of value to the wider clinical community, perhaps assisting in diagnosis and management. PIO has met twice, discussing mainly nonmotor symptoms. The first reports from PIO are now published.

PIO thanks UCB for support of its meetings



P17.04

The patient's perspective: the effect of dopamine on Parkinson symptoms

Heidemarie Zach¹, Michiel Dirkx², Jaco Pasman², Bastiaan Bloem², Rick Helmich²

¹ Department of Neurology, Radboud University Medical Centre, Donders Institute for Brain, Cognition and Behaviour, Netherlands & Department of Neurology, Medical University of Vienna, Vienna, Austria

² Department of Neurology, Radboud University Medical Centre, Donders Institute for Brain, Cognition and Behaviour, Nijmegen, Netherlands

Objective: To investigate the correlation between patient-based vs. clinician-based L-Dopa effects on PD symptoms in tremor-dominant patients.

Background: Medication adjustments are often solely based on patient reports. Therefore, it is crucial to know how well clinical ratings and patient ratings correlate, and which factors influence the patient's judgments about medication effectiveness. A better understanding has impact on clinical practice, but also on the use of subjective assessment scales in scientific research.

Methods: A standardized L-Dopa challenge test was performed in 42 tremor-dominant PD patients. Clinical scores (MDS-UPDRS part III) were collected OFF and ON dopamine (200/50 mg levodopa-benserazide). In both sessions, resting tremor intensity was quantified at REST and during cognitive co-activation (COCO), using accelerometry. Patients rated L-Dopa effect separately for tremor and for bradykinesia/rigidity, after the standardized L-Dopa challenge-test, using visual analogue scales (VAS). We tested whether the correlations between patient ratings (VAS) and clinical ratings (UPDRS, accelerometry) differed between symptoms, and whether (for resting tremor) the correlations differed between contexts (REST vs. COCO).

Results: Patients had a clear effect of L-Dopa, both for bradykinesia/rigidity (49% improvement) and for tremor (40%). L-Dopa reduced tremor power ($p<0.001$), while COCO increased it ($p<0.01$). We found similar patient-clinical correlations for bradykinesia/rigidity ($R=0.46$, $p<0.01$) and tremor ($R=0.60$, $p<0.001$; no significant difference; $p=0.32$). For tremor, patients' rating correlated better with accelerometry improvements during COCO ($R=0.46$; $p<0.01$) than during REST ($R=0.23$, $p=0.069$; difference between correlations coefficients: $z=-1.69$, $p<0.05$).

Conclusion: The patients' subjective experience of L-Dopa effectiveness on tremor is largely based on the ability of L-Dopa to reduce tremor during stress (COCO). This underlines the importance of using a cognitive co-activation task during clinical evaluation of tremor. It also implies that future therapies should focus on reducing Parkinson's tremor during stressful situations.

CARE DELIVERY & QUALITY OF LIFE: PALLIATIVE CARE/END OF LIFE CARE/ LONG-TERM CARE

P18.01

Using the RACE nursing toolkit in avoiding failure-to-rescue in Parkinson's care

Heintje Calara

Capella University, Rutherford, NJ, USA

Hospital admission time is a crucial time as this is the moment when patients need momentous rescuing. The turn of events at this time can impact the trajectory outcome whether such care would result to a rescue or failure of it. Hospital admissions for the Parkinson's disease (PD) patients rate higher than that of the general patient population (Oguh & Videnovic, 2012). The rate of deterioration for PD patients upon hospital admissions is of very high risk (Gerlach, Broen, van Domburg, Vermeij, & Weber, 2012). Nurses are always at the initial care touch point. The quality of nursing care the patient receives during this first contact is detrimental because nurses are the ones who lead, summon, and navigate the patient's needs, before any other clinicians see them, thus making the nurses the initial rescuers. However, the disease knowledge and awareness of nurses dictate their readiness and competency. PD is a particular entity that is notorious in presenting many variations of complicated symptomatology, making it very difficult for non-PD expert clinicians to misread or misdiagnose the patient needs (Ahlskog, 2014). It may not be feasible that all nurses are made into PD experts but if nurses are given the proper supportive resources in caring for PD patients, then they could arrest the deterioration of the admitted PD patients, because not being able to do so is a failure to rescue. In light of PD patient rescue during admission time, nurses could benefit from a systematic PD nursing care toolkit that would serve as their navigation tool from PD patient assessment, to planning, intervention, and then evaluation. The RACE toolkit could be utilized to support PD nursing care and sustain high quality PD patient care management. R is for PD nursing recognition, A is for nursing alert, C is for capacity, and E is for elevation of the situation (see figure). This concept is even supported by the Institute of Medicine (IOM) in their 2000, 2001, and 2011 publications. PD is the second most common neurodegenerative disorder, second only to dementia, and this number is just predicted to increase (Haahr, Kirkevold, Hall, & Ostegaard, 2010), and as this number rises so does the rate of hospital admissions. As the focus of health care is on patient safety and outcome, then not employing a PD nursing toolkit such as the RACE toolkit could just simply be a form of healthcare let down.

The RACE Nursing Toolkit

Nursing Measure (steps)	Center of Action	Elements in this nursing step
R - Recognition	Assessment	Nursing diagnosis, identifying PD patient needs
A - Alert	Planning	Strict medication reconciliation and adherence, prompt notification/communication made to PD or movement disorders team in the center, alerting the PD-DNP resource.
C - Capacity	Intervention	Safety measures, mobility, speech, swallowing, dietary, social work, etc. This is centered on multidisciplinary approach.
E - Elevation	Evaluation	Education (neuroscience nurses educating each other by sharing PD experiences, educate the patient and families/caregivers), appraise and survey the previous PD experience as compared to the new one, make use of this newly modified experience and training to support/uplift the potential next encounter).

P18.02

Feasibility and preliminary outcomes of an interdisciplinary home visit program for patients with advanced Parkinson's disease

Jori Fleisher, Meghan Sweeney, Sarah Oyler, Amy Lemen, Arash Fazl, Geraldine Dacpano, Rebecca Gilbert, Joshua Chodosh, Alessandro Di Rocco

Marlene and Paolo Fresco Institute for Parkinson's and Movement Disorders, New York University School of Medicine, New York, NY, USA

Objective: 1) To demonstrate the feasibility of an interdisciplinary home visit program (HVP) for advanced Parkinson's Disease (PD) providing expert, interdisciplinary care directly to homebound patients; 2) to test whether the HVP improves patient quality of life despite disease progression.

Background: As PD progresses, symptoms increase, quality of life declines, and individuals may lose access to neurologic care, becoming homebound. This leads to a surge in emergency department visits and hospitalizations. Improving access to expert in-home care may improve quality of life and minimize acute healthcare utilization.

Methods: PD patients treated at The Fresco Institute for Parkinson's and Movement Disorders who meet Medicare criteria for homebound status are eligible to receive four quarterly home visits over 12 months. Each visit entails an evaluation by a movement disorders specialist, social worker, and nurse, including detailed history of symptoms, falls, and healthcare utilization; physical examination including the UPDRS; medication reconciliation; psychosocial evaluation and follow-up; and referral to in-home services. Quality of life (Neuro-QoL) is measured at Visits 1 and 4.

Results: We have enrolled 26 subjects to date; 65% have completed 3 and 38% have completed 4 visits. At baseline, subjects' mean age is 81 years (SD 8); mean PD duration is 10 years (SD 6); mean UPDRS total score is 65 (SD 20, range 35-107). In the 12 months prior to enrollment, 48% had been hospitalized; 40% had visited an ED. Of the 10 subjects completing Visit 4, total UPDRS increased by a mean of 13 (SD 9), yet quality of life improved in 9/9 Neuro-QoL domains. Preliminary analysis of the first 74 visits shows no change in the rate of acute healthcare utilization between the 12 months preceding and time since HVP entry ($p=0.59$).

Conclusions: Despite the expected progression of functional and motor disability over one year, subjects report improved quality of life since entering the HVP. No difference in acute healthcare

utilization has yet been observed. We are in the process of assessing medication errors, adherence, and caregiver strain in this understudied population, with the aim of expanding the HVP as a novel model of care in the future.

Previously Presented: The design and interim analysis of the HVP model was previously presented at the International Congress of Parkinson's and Movement Disorders 2015 and 2016, respectively.

CARE DELIVERY & QUALITY OF LIFE: HEALTH ACCESSIBILITY/ UNDERSERVED POPULATIONS

P19.01

Pay it forward: creating a donation-based funding model where no patient is denied therapy services based on insurance or financial limitations

Samantha Elandary

Parkinson Voice Project, Richardson, TX, USA

Parkinson Voice Project is a 501(c)(3) nonprofit organization in Texas that runs a speech therapy clinic for individuals with Parkinson's disease and also trains speech-language pathologists from around the world in its SPEAK OUT!® and LOUD Crowd® therapy programs. What makes this clinic unique is that since 2008, all of its speech therapy services have been provided through donations and a Pay It Forward initiative. In other words, Parkinson Voice Project does not charge patients for speech therapy and does not bill insurance. Patients receive all the speech therapy they need and deserve, and then at the end of treatment, patients are provided an opportunity to make a donation to help the next patient receive treatment. As a result, no patient has been denied treatment due to insurance restrictions or financial limitations.

Each new patient receives an initial speech evaluation, and then if appropriate, receives a month of intensive speech therapy. Patients then transition to a maintenance program which consists of weekly speech groups, a singing program, and six-month re-evaluations. Parkinson's patients stay in this program for life, enabling them to not only regain their speaking abilities, but receive ongoing, continuous therapy which insurance will not reimburse.

All speech therapy services at Parkinson Voice Project are provided by licensed and certified speech-language pathologists. The organization's annual budget is 1.3 million, and its staff is paid comparable salaries for this medical profession. The clinic is housed in a free-standing 6,800 square foot facility which was remodeled and furnished entirely through donations.

In this presentation, Elandary will review how Parkinson Voice Project's "Pay It Forward" system works and review the pros and cons of funding a therapy clinic using this model. Sample donations cards will be shared, and comparison charts will demonstrate the difference between billing insurance and collecting donations. This type of funding model could be replicated in university rehabilitation clinics and nonprofit organizations and would enable people with Parkinson's to receive quality treatment. The challenges of funding a therapy program solely on donations will also be reviewed, based on the organization's eight-year history of using this type of funding model.

P19.02

Description of a novel early access clinic for Parkinson's disease patients: the navigator model

Priti Gros¹, Lucie Lachance², Jennifer Doran², Doulia Hamad¹, Marie Corbeil¹, Anne-Louise Lafontaine²

¹ Movement Disorders Unit, McGill University Health Centre, Montreal, Quebec, Canada

² Movement Disorders Unit, McGill University Health Centre and Montreal Neurological Hospital, McGill University Health Centre, Montreal, Quebec, Canada

Objective: Improve accessibility and quality of care for Parkinson's disease (PD) outpatients.

Background: In Canada, the time to access a movement disorders clinic (MDC) can be up to one year for PD patients. The navigation model is a new paradigm of care based on pivot nurses acting as point of entry and main contact persons for the patient. This model, developed for oncology patients, has shown better accessibility, survival and satisfaction. To our knowledge, no such program exists for PD patients.

Design/Methods: A navigator based MDC has been created at the MUHC and consists of two PD-trained nurses, 5 MD neurologists, a secretary, physiotherapist, occupational and speech therapists. The nurses call and assist in the triage of all referred patients within a few weeks. On first visit, they initiate information collection with a bio-psycho-social perspective prior to the neurologist consultation. Between visits, the patients can call the pivot nurses for any inquiry. Nurses may also make referrals to allied health teams and community resources. Seventy new patients with suspected PD from January 2013 to September 2014 were randomly chosen and included in this review.

Results: Patients waited 4.0±3.7 weeks between referral and triage, and 15.4±7.1 weeks between referral and first visit. 40.0% were referred to physiotherapy, 41.7% to occupational therapy and 25.0% to speech therapy. The main issues reported were non-motor symptoms (28.8% of all calls) followed by PD medication side effects (22.0% of all calls). 30.5% of the patients used 2.2±1.6 phone calls (or emails) for follow-ups with the nurses. 67.8% of the phone calls were managed by nurses alone. A satisfaction survey to evaluate the novel model is in process.

Conclusions: This review describes for the first time a navigation program for PD patients. This model helps improve accessibility to a MDC for PD-suspected patients and offers a proactive approach to provide early intervention for PD daily issues and better access to the inter-disciplinary team.

This abstract was accepted as a poster presentation at the 2015 American Academy of Neurology annual meeting. The poster was presented on April 23rd 2015.

P19.04

Multidisciplinary capacity building module for rehabilitation and care of Parkinson's in India

Navaz Irani¹, Maria Barretto², Nishaat Mukadam², Jagruti Wandrekar², Nicole Dsouza², Anjali Sivaramkrishnan²

¹ Parkinson's Disease and Movement Disorder Society, India, Neurology Foundation, India, Mumbai, Maharashtra, India

² Parkinson's Disease and Movement Disorder Society, Mumbai, Maharashtra, India

Rationale: Parkinson's (PD) affects multiple facets of one's life and its management demands a multidisciplinary approach to be adopted through pharmacological and paramedical therapies. In India, reliance on pharmacology is high and socio-cultural factors govern the use of paramedical therapy.

Aim: To create a standardized multidisciplinary model (MDM) of care which is cost effective, replicable and generic in order to overcome limited accessibility and acceptability of paramedical healthcare for PD in India.

Methodology: The MDM was developed, validated and applied over 3 phases.

Phase I: Based on a needs analysis and in consultation with Movement Disorder Specialists, the need for the MDM to be educative and rehabilitative was inferred. The services of experts in Physiotherapy, Speech and Occupational Therapy, Psychology, Nutrition and alternative therapies were mobilized to author sessions. Scrutiny at several checkpoints led to modifications.

Phase II: To evaluate its efficacy and establish it as a capacity training manual, a study was done by independent consultants with 15 people with Parkinson's (PwP) and 12 caregivers (CG) who were not previously exposed to paramedical therapies for PD. Qualitative and quantitative data was obtained on its effectiveness, concept, design, mode of delivery, relevance, acceptability, applicability.

Results: Paired t-test values between pre and post test data showed no significant differences on QoL, ADL and caregiver burden scores; however the mean values of each showed improvements in post-test scores in PwP and CG. Qualitative analysis revealed positive trends – perceived improved QoL and mobility, regained independence in ADL and skilled tasks, higher self-efficacy, improvement in emotional well-being and social support, and informed decision making.

The MDM itself, was found to be clear and novel in content; easily deliverable by lay facilitators; comprehensible and relevant to PwP and CG; adaptable to different groups; time – effective; interest generating; logical in flow and sequencing of sessions; practical and beneficial; and effective in a group – format.

Implications (Phase III): Thus, the MDM was established as a capacity training manual and its current applications in India are:

- Education and rehabilitation of PwP and CG in 33 locations
- Replication of group rehabilitation centres in 19 locations based on local language translations
- Training of Parkinson's care personnel in 11 cities and 1 Union Territory.

P19.05

Preliminary results of a multi-center case series of virtual visits for Parkinson's disease

Ryan Korn¹, Henry Tait Keenan¹, William Zhu¹, Steven Goldenthal¹, Tim Felong¹, Anna Stevenson¹, Michael Dodge², Kyle Rizer³, Nicholas Galifianakis², Maya Katz², Erica Byrd², Caroline M. Tanner², Gail Kang⁴, Kelly L. Andrzejewski¹, Richard Barbano¹, Kevin Biglan¹, Saluda Kanchana¹, Saloni Sharma¹, Ramon Rodriguez⁵, Aparna Shukla⁶, Ray Dorsey⁷

¹ University of Rochester Medical Center, Rochester, New York, USA

² University of California San Francisco Medical Center, San Francisco, California, USA

³ University of Florida Medical Center, Gainesville, Florida, USA

⁴ Berkeley, California, USA

⁵ University of Central Florida College of Medicine, Orlando, Florida, USA

⁶ University of Florida Medical Center, Gainesville, Florida, University of Central Florida College of Medicine

⁷ University of Rochester Medical Center, Rochester, New York, USA

Background: Current Parkinson's disease (PD) care delivers suboptimal and limited coverage. The use of video-conferencing to conduct virtual visits holds promise, but large scale studies are limited.

Objective: RACE-PD is a case series assessing feasibility, impact on quality of life, and acceptability of one-time remote consultations in the homes of people with Parkinson disease.

Methods: We conducted a six month, multi-center observational study of remote clinical evaluations with individuals from five states to assess the feasibility, the impact of remote care on participants' quality of life, and the long-term acceptability to patients in receiving ongoing telemedicine for their PD. Participants received a one-time virtual visit with a Parkinson disease specialist and completed remote assessments at baseline and at 6 months. Specialists provided recommendations during the visit and then sent a consultation note to patients and their physicians. All study activities, including recruitment and enrollment, were conducted remotely.

Results: As of February 2016, 552 individuals expressed interest, 287 participants enrolled, and 252 participants completed virtual visits with 13 different investigators. Ninety eight percent of visits were completed as scheduled with an average visit length of 42 minutes. Three-quarters of participants reported they would be interested in receiving care via virtual visits in the future. Participants were satisfied or very satisfied with the technical quality (86%), convenience (95%), comfort (96%), and overall care (93%) received during their virtual visit. Additionally, physicians were satisfied or very satisfied with the technical quality (81%), the convenience (95%), the care they provided (96%), and the overall virtual visit (94%).

Conclusion: Driven by a large latent demand, patient interest in receiving care via virtual visits is high. While the long-term impact of a one-time virtual visit on quality of life remains to be determined, delivering remote care to large numbers of individuals with Parkinson disease is feasible and well-received.

P19.06

A state-wide multi-disciplinary telemedicine care network for Parkinson's disease: PDCNY

Jill Lowell¹, Steven Goldenthal², Michael Bull¹, E. Ray Dorsey², Kevin Biglan¹

¹ Department of Neurology, University of Rochester, Rochester, NY, USA

² Center for Human Experimental Therapeutics, University of Rochester, Rochester, NY, USA

Background: Care for chronic conditions, like Parkinson disease (PD), in the USA is costly, ineffectual and often leads to poor outcomes. Individuals with PD benefit greatly from ongoing care from PD specialists and a multidisciplinary care team. However, over 40% of older adults with PD in the US have not seen a neurologist and have a higher risk of hip fracture, placement in skilled nursing facilities, and death. Telemedicine represents a convenient, efficient way to address geographic and disease-specific barriers to specialty and multidisciplinary care and has demonstrated feasibility and value in PD.

Objective: To implement a state-wide multidisciplinary telemedicine care network to improve access and outcomes in underserved individuals with PD. **Methods:** We will enroll approximately 500 individuals with PD in New York state who have difficulty accessing specialty care. Individuals will undergo evaluation by a PD specialist via telemedicine in their home. A comprehensive multidisciplinary care plan developed by the team will be implemented by a PD nurse specialist who will have ongoing follow up with participants via telemedicine. To evaluate the value of this novel program, we will measure (1) the ability to increase access to care, (2) clinical efficacy including satisfaction with care, quality of life, function and caregiver burden, (3) and economic value. In addition, we will evaluate the ongoing implementation of the program through process outcomes organized around (1) Outreach, (2) Enrollment

and (3) Feasibility. A subset of patients with iPhones may join the PD research smartphone study, "mPower", to explore the ability of remote monitoring of motor function to inform care.

Results: The program was funded by the Greater Rochester Health Foundation and the Edmond J. Safra Foundation beginning in December 2015. Efforts to date include website development (www.pdcny.org), regional outreach to community groups and community health organizations, and the development of an evaluation database.

Conclusions: The proposed care model, merging telemedicine and multidisciplinary care to manage PD may improve access for underserved individuals with PD and improve clinical outcomes at lower cost. Outreach to identify and enroll underserved individuals is ongoing.

P19.07

Art as a vehicle to represent the Spanish-speaking Parkinson's community in the Americas

Claudia Martinez¹, Gregory Pearce¹, Julio Angulo²

¹ Muhammad Ali Parkinson Center, Phoenix, AZ, USA

² Portland, Oregon, USA

Objective: To implement a participative art project to give Spanish-speaking undeserved PD communities in North, Central and South America the opportunity to be represented at the 4th WPC.

Methods: The Muhammad Ali Parkinson Center (MAPC) has a comprehensive Hispanic outreach program in Phoenix, USA. In the last three years services were expanded to create a network for people with Parkinson's disease (PWP), support groups and PD organizations in several Latin American countries. The network has stayed active through participation in online conferences offered by the MAPC and social media pages. These PD communities have shown great interest and appreciation for receiving education and resources to improve the quality of life of PWPs and their caregivers. Resources are scarce or non-existent within these communities.

The MAPC strongly promoted attendance to WPC 2016. Many network members wished to represent their countries at the congress, but found the language barrier and cost to be prohibitive; impeding them from attending and adding their voices to the PD global gathering. In response, with the help of art instructor Gregory Pearce we developed a mosaic-style poster to represent the Spanish-speaking PD community living in the Americas. PWPs and caregivers were invited to color the same drawing: Three calla-lilies with a tulip at its center representing Spanish-speaking PD communities in North, Central and South America. They are surrounded by other flowers and foliage signifying the international PD community convened by the WPC. Drawings were distributed locally at PD related events and by mail, email and social media to outlying communities. Participants were invited to color their drawings with a variety of materials and to add words, logos or collage pictures using their own creativity. They were then encouraged to return cellphone photos of their finished drawings via email.

Results: The poster on display, created with all the drawings is named "The Spanish PD Garden of the Americas". It will be available to all participants to use as an awareness tool in their local communities. A total of 104 drawings representing 36 cities/states from 14 countries were received. We hope this map will illustrate that the Spanish-speaking PD community in the Americas is indeed large, committed, and also in need of resources and outreach. It is a community that strongly wishes to be a contributing part of the WPC's vision for the future.



P19.08

A Promotores model for Parkinson disease (PD) outreach and education in the Hispanic community in Phoenix, Arizona

Claudia Martinez, Darolyn O'Donnell

Muhammad Ali Parkinson Center, Phoenix, AZ, USA

Methods: The use of promotores or Community Health Workers (CHW) to provide outreach and health education to minorities has shown positive results for chronic diseases. Promotores / CHWs are trained lay people who belong to the target population, share culture and language, and are able to establish a bridge between minority groups and health providers. Five years ago a group of 7 volunteers were trained at the Muhammad Ali Parkinson Center (MAPC) to start the Parkinson's Promotores Program. All volunteers had a close family member with PD or worked as a caregiver for a client with PD. They helped develop a PD-specific flipchart along with a successful 12-week home visit program to educate Hispanics with PD and their caregivers who were isolated due to a variety of barriers. To date, the program has served 45 families and has shown statistically significant improvement in the areas of social support and communication. A poster with these findings was presented at the WPC 2103.

Part of the continuing education of MAPC volunteer promotores includes attending local and national trainings for CHWs. By staying active in various CHWs networks, MAPC promotores identified the lack of information about PD among community health workers and in the general public. With the support of the MAPC, they received leadership and public speaking training, and worked with the MAPC Hispanic outreach coordinator to develop strategies to provide basic information about PD to peer promotores and to raise PD awareness in the general public.

MAPC promotores identified local organizations that use CHWs to provide services to the Hispanic population, and strategically selected community events and locations to raise PD awareness. They used a variety of creative approaches and utilized Spanish materials available from the NPF and PDF national organizations.

Results: Since fall of 2015, MAPC promotores conducted a total of 7 presentations to different promotores groups belonging to a variety of community organizations. They also participated in 12 different community events at a variety of locations such as libraries, consulates, churches and parks. The feedback received from community agencies has been positive, and other promotores groups in the community have expressed interest in receiving PD-specific education.

P19.09

The role of the advanced practice nurse in the management of Parkinson's disease

Kathleen McCoy
USA

Parkinson's disease uniquely crosses the bounds of both family and psychiatric spectrums of care. Often one side of care is neglected or overlooked due to scope of practice (SOP) limitations. This presentation blends both the physiological and psychiatric mental health aspects unique to persons with PD. The Review of Literature reveals SOPs for PMH Advance Practice Registered Nurses (APRNs) and Family Nurse Practitioners (FNP) cross over neurological areas of concern. The Advance Practice Consensus Model, addressing concerns related to Legislation, Accreditation, Certification and Education, defines roles of APRNs, relating appropriate roles of APRNs in such entities, bridging populations to APRN care. The author defines common physiological needs/PMH needs while describing/recommending evidence based strategies integrating needs without compromising SOP as defined by APRN role delineations of certifying bodies/National Organization of Nurse Practitioner Faculties (NONPF) guidelines. Inter professional team approaches as defined by the Institute of medicine (IOM) are encouraged. Additionally, persons with PD are best served in practices supporting inter professional team based comprehensive care. Considering the paucity of neurologists and psychiatrists; the APRN fills access to care gaps beautifully, especially when dual prepared for somatic and psychiatric overlapping areas of concern. Depression and anxiety are also a very palpable aspect of PD for persons with PD & their family members/caregivers. Successful physiological and PMH management begins with good planning and an ongoing integrative approach. The PD spectrum of care needs is appropriate for the APRN to manage: PMH APRNs are able to manage the PMH aspects; facilitating psychotherapies, medication management, crisis intervention, etc., integrating the Chronic Care Model, bridging of 2 specialties to care for persons with PD. State Nurse Practice Acts defines SOP for all APRNs. Certain settings can better facilitate services of an integrated PMH/FNP Role. This care approach can be the wave of the future, especially in the medical home model in states with APRN unrestricted licenses.

P19.10

Wellness Boot Camp: adapted for Korean American Parkinson support network

Claire McLean
USC, CSULB, Parkinson Wellness Recovery, San Pedro, CA, USA

This Wellness Boot Camp (WBC) is designed by a physical therapist to include exercise, education and empowerment in a cost effective manner, for individuals with Parkinson disease (PD). The

program is 2 hours per day, 5 days in a row. Goal is approximately 10 participants. The cost is \$150/person. This hourly rate with 10 participants is similar to insurance reimbursement for many US insurers and therefore may also be feasible as a cash based program from a clinic/rehab perspective.

After initiating the WBC, I was approached by the founder of the Korean-American Parkinson Support Network. She indicated that many of her members had not had access to these services available in the area due to multiple barriers. These included feeling uncomfortable, language difficulty and lack of education about potential benefits. She stated that most of her members were not exercising because they did not understand how helpful it could be, and that they also did not know what to do.

The WBC is designed to include 1 hour of exercise and 1 hour of education/discussion (2 hours total) each day, 5 days consecutively. Exercise is led by a PT and education/discussion was facilitated by the PT through use of a wellness manual, videos and discussion amongst the group. There is a specific challenge related to each day's topic.

Exercise as focused on the PWR! Moves. There is mounting evidence that exercise is beneficial, not only for the symptoms of PD, but also for other aspects of health. Exercise has been shown to help with both motor and non-motor symptoms of PD and; therefore, there is great potential to improve the overall quality of life. Evidence in motor learning and sports training indicates that frequent, intense practice may be ideal for learning and skill acquisition. The beneficial effects of group exercise include comradery, shared experience, and the potential for improved cognitive and gait measures compared to individual exercise/therapy.

Education and discussion covered a different topic each day. Day 1: Exercise, Activity, Intentional Medicine. Day 2: Sleep. Day 3: Happiness, how to train optimism. Day 4: Nutrition. Day 5: Putting it all together and maintaining social connectedness.

Modifications for this group include: an interpreter being present during exercise, videos with Korean subtitles, and an interpreter being present to assist with group discussions.

Participants completed assessments pre and post WBC. All participants experienced improvement.

P19.11

Nurse-managed telehealth clinic for Parkinson's disease: a case series

Ingrid Pretzer-Aboff¹, William Zhu², Tanya Heggans³, Jenny Hughes³, Carolyn Haines³, Susan Cross-Skinner³, Jill Lowell², Ray Dorsey²

¹ University of Delaware, Hockessin, Delaware, USA

² University of Rochester, Rochester, New York, USA

³ University of Delaware, Newark, Delaware, USA

Introduction: One of the many challenges facing individuals with Parkinson's disease (PD) and their caregivers in the USA is the burden of traveling to clinics to see qualified movement disorder specialists. The state of Delaware currently has no movement disorder specialists, forcing residents with PD to travel long distances to receive specialized care.

Methods: We established a multidisciplinary PD telehealth clinic at the University of Delaware Nurse Managed Health Center in Newark, DE that enabled Delaware residents with PD to receive a telehealth consultation from a movement disorder specialist in Rochester, NY using video conferencing technology. Recruitment was by advertisements and by word-of-mouth. A nurse practitioner collaborated with the specialist and was present at each remote visit. The specialist provided recommendations during the visit and sent a consultation note to patients and their physicians. At the

conclusion of the visits, patients filled out a 5-point Likert scale survey.

Results: From April 2014 through November 2015, 90 PD patients received a telehealth visit, 77% returned surveys, mean age=71.2, 70% were male, and 80% visit the center for the first time. Eighty-five percent of patients agreed/strongly agreed that the location of the clinic was convenient. On average, patients traveled 9.2 miles to the clinic, compared to 26.2 miles to see their usual PD provider. For the visit, 100% of respondents agreed or strongly agreed that they received good care and were able to communicate easily with the movement disorder specialist. Additionally, 97% of participants were comfortable with the video conferencing equipment, while 100% felt they had enough technical assistance for the remote visit. Eighty-two percent agreed/strongly agreed that they would rather use telehealth than travel long distances to see their usual provider, and 100% would recommend telehealth to others.

Conclusion: PD patients in Delaware were highly satisfied with the care and convenience provided at a nurse-managed telehealth clinic, and generally preferred it to receiving care from their local PD provider. The program demonstrates the feasibility of using remote clinics to connect patients with PD to movement disorder specialists, demonstrating another model for increasing access to specialized care for those with PD.

P19.12

Telemedicine clinic improves access to mental health care for people with Parkinson's disease

Ingrid Pretzer-Abhoff¹, Tanya Heggans², Roseanne Dobkin³

¹ University of Delaware, Hockessin, Delaware, USA

² University of Delaware, Newark, Delaware, USA

³ RUTGERS, The State University of New Jersey Robert Wood Johnson Medical School, Piscataway, New Jersey, USA

Introduction: Access to expert and appropriate mental healthcare for people living with Parkinson's disease (PWP) is essential to their function and quality of life. Approximately half of people diagnosed with PD will suffer from depression and it is important to recognize and provide appropriate treatment. There is currently a dearth of specialized mental health services available to PWP in the state of Delaware (USA).

Methods: Once per month, using video conferencing technology we are able to connect our PD patients at our multidisciplinary PD telehealth Clinic at the University of Delaware Nurse Managed Health Primary Care Center (NMPCC) to a clinical psychologist (RDD), with PD expertise, at Rutgers–Robert Wood Johnson Medical School in New Jersey (USA). Nurse practitioners used the Geriatric Depression Scale (GDS) and clinical interview to identify patients in need of a mental health consultation. During the initial visit with RDD, a comprehensive treatment plan was formulated. Consult letters with recommendations were shared with the patient, the clinic practitioners, and patient's healthcare providers. This paper will describe the baseline demographics, disease stage (H&Y), Part I–III of the MDS Unified Parkinson Disease Rating Scale (UPDRS), GDS, Timed Up and Go (TUG) scores, and recommendations of patients attending the Telepsych component of our multidisciplinary clinic.

Results: From August 2014 through February 2016, 28 unique individuals were evaluated at least once. Demographics were as follows: mean (m) age: 69.5 (SD=10.73); gender: 68% male; H&Y m: 2.48 (SD=0.64); GDS m: 6.67 (SD=3.74); UPDRS-I m: 13.96 (SD=7.71); UPDRS-II m: 17.57 (SD=9.19); UPDRS-III m: 33.5 (SD=15.87); TUG m: 12.5seconds (SD=4.61). Treatment recommendations were diverse and included: 1) referral to a local community-based psychotherapist working in consultation with RDD; 2) BIG and LOUD; 3) exercise; 4) caregiver support; 5) psychiatrist referral; 6) medication consultation with treating

neurologist or PCP for depression, anxiety, cognition, and/or psychosis; 7) quarterly telepsych follow-up.

Conclusion: Individuals with PD in Delaware were able to access expert mental health care using telehealth technology. This treatment model may be generalizable to other health care systems and has great potential to reduce mental health care disparities in PD worldwide.

P19.13

The PDF Women and PD Initiative: identifying and addressing unmet needs

Veronica Todaro¹, Lori Katz², Susan Foster², Robin Morgan², Karen Smith², Megan Feeney²

¹ USA

² Parkinson's Disease Foundation, New York, NY, USA

Objective: To demonstrate the impact of the Parkinson's Disease Foundation (PDF) Women and PD Initiative in identifying and addressing the unmet needs of women living with Parkinson's disease.

Introduction: There are significant unanswered questions and unmet needs when it comes to women living with PD and their disease experience, participation in research, medical care and support services yet there is no coordinated national effort to identify and address their needs. In September 2015, the PDF held a three-day conference launching the PDF Women and PD Initiative. The conference brought together 25 women leaders to learn about gender differences in PD and to gain the tools and leadership skills they need to advocate for the specific needs of women with Parkinson's disease in their communities.

Methods: Review and report on the post-conference engagement of the 25 women who participated in the September 2015 PDF Women and PD conference. Engagement includes organizing at least one women and PD event or a series of events in their communities to help other women live well and better manage their disease, and to be an advocate for the needs of women with PD.

Results: Reports provided by Advocates on their work within their communities will be analyzed and summarized. Other outcomes, such as research generated on women with Parkinson's that can be associated to the PDF initiative as well as increased general issue awareness will be reported.

Conclusion: Preliminary findings since September 2015 indicate that the majority of women who participated in the PDF Women and PD conference have begun to plan, have planned or have completed an awareness and education event in their communities. PDF, as well as Advocates have been successful in attaining media opportunities to increase awareness about the unmet needs of women with PD.

P19.14

Struthers Parkinson's Center Network (SPCN): improving PD care through growth and development of sustainable partnerships

Rose Wichmann, Joan Gardner, Ruth Hagestuen

Struthers Parkinson's Center, Golden Valley, MN, USA

Objective: Expand a collaborative network of home care agencies and senior residential communities dedicated to delivery of high quality care of persons with PD and related movement disorders.

Methods: Struthers Parkinson's Center (SPC) staff train "site champions" from each new member in a 4 day training course using the TULIPS curriculum developed at SPC. Site champions obtain tools to perform onsite training for their organization, and receive ongoing support through regular updates with SPC staff. Allied

health professionals at these sites are invited to attend discipline specific conferences at SPC. Staff surveys assessing PD understanding and confidence levels are distributed prior to and after staff training. Patient/ family surveys are routinely distributed to obtain feedback regarding PD care. SPC staff make periodic site visits to answer questions, provide resources and make suggestions for ongoing improvements.

Results: 100% of members have chosen to maintain annual membership after their first year in the program. The network is currently comprised of 21 residences offering assisted living and/or long term care options in the states of Minnesota, North Dakota, and South Dakota as well as 4 home care agencies representing 18 regional branch satellite offices around the state of Minnesota. To date, members have provided on-site training to over 4500 employees, sent over 325 health care professionals to SPC for full day training, and helped to start/maintain 18 new PD support groups in their respective communities. Reports from member sites indicate the network has provided improved care and service to over 750 individuals with PD and their family caregivers. Staff and resident/family survey results show significant improvements at network member sites.

Conclusions: Over the past 4 years, SPCN has continued to demonstrate growth. Periodic evaluation of staff knowledge and resident/client satisfaction is critical in measuring program outcomes. Addition of experiential toolkits used during training have met with positive feedback from participating site champions. SPCN staff are currently working on creating online training resources to be used in network training, with future plans for regional/national expansion of the care network.

CARE DELIVERY & QUALITY OF LIFE: DAILY LIFE ACTIVITIES INCLUDING WORKING & DRIVING

P20.01

Parkinson's disease affects mechanics and motivation for tooth brushing behaviour

Elani Bykowski, Jon Doan

Supervisor, Lethbridge, Alberta, Canada

Objective: Effective dental self-care is critical to maintenance of oral and whole-body health. Unfortunately, Parkinson's disease may place dental self-care in double jeopardy- motor deficits typical amongst people living with PD may compromise handling of a brush or floss; non-motor challenges, namely apathy & depression, might discourage habitual oral care. Inadequate oral health affects the way a person eats, speaks, and socializes, a connection that could exacerbate motor and non-motor symptoms in the long term through increased isolation and inactivity. The primary purpose of the present study was to analyze the reach to brush behaviour of people living with PD, in comparison to the reach to eat behaviour. The secondary purpose was to examine participants' attitudes toward oral self-care. The results of this study might inform both examinations and instructions from clinicians to people living with PD with respect to general health, oral health, & neural health status. **Methods:** Subjects were invited to engage in two different reaching tasks; reach to eat for a cereal piece and reach to brush. The trials were video-recorded from the frontal view and scored to characterize behaviour throughout the grasp. The Whishaw reach to eat scale, a 21 point rating scale, was used to score motor function based on 7 sequential reach to grasp behavioural phases: orient, lift, aim, pronate, grasp, supinate & return. A modified version of the

same scale was used to evaluate reach to brush. Both authors completed the scoring independently and then the score for every trial was averaged. Controls and Parkinson participants were also required to complete a Dental Status Questionnaire using a visual analogue scale. This scale measured self-efficacy at maintaining oral health, assessing pertinence of information from dental health clinicians, perceptions of ability for oral self-care, and motivation. **Results:** People living with PD experienced functional deficits during reach to brush and reach to eat, with scores lower than both the old & young adult controls. Exaggerated for the reach to brush task, PD subjects had a tendency to reach along a curvilinear path, likely to maintain an unobstructed view of the target (a toothbrush). PD would rotate head during the brushing action to compensate for restricted arm mobility and limited brush control (figure 1). Visual analogue scale data reinforced that people with PD experience deficits at floss and brush handling.

CARE DELIVERY & QUALITY OF LIFE: SELF-MANAGEMENT, EMPOWERMENT, COPING STRATEGIES

P21.01

Hispanics living with PD: perceptions on self-management

Julio Angulo¹, Claudia Martinez²

¹ Portland, Oregon, USA

² Muhammad Ali Parkinson's Center, Hispanic Outreach Services, Phoenix, AR, USA

Objectives: Anecdotal and research findings indicate that Hispanic patients tend to seek care late in the course of their disease and when they do consult with a doctor or health team they do so cautiously. These behaviors are generally interpreted as the result of a variety of "barriers".

Our purpose is to explore the perceptions and beliefs about self-management and partnership with health care teams that Hispanics living Parkinson's disease (PD) have. The support groups were based at the Muhammad Ali Parkinson Center (MAPC) Hispanic outreach program in Phoenix, USA.

Methodology: We chose the focus group method, where the main investigative goal is to gain an understanding of an issue from the perspective or subjectivity of the participants; namely their perceptions, sentiments, behaviors and opinions. In a focus group, participants are encouraged to interact, talk to each other and address the topic at hand. Moderators (in this case the authors) assumed the role of facilitators, assisting with the exploration of selected topics rather than direct or control the process.

The two existing support groups run by the MAPC were optimal places to conduct the focus groups. Their members already shared a trusting and empathic relationship and were comfortable to speak candidly, without fear of being judged. A total of 28 participants were gathered, and a total of 8 sessions were conducted. Each session lasted approximately 2 hours. All members spoke Spanish. All participants were born in Latin America and resided in the US for several years. Group members had various levels of education (see chart).

Results: Overall, participants agreed that when they meet with their health care teams they see themselves primarily as reporters of their felt symptoms and course of treatments. The notion of voicing personal opinions, sentiments, partnering with their attending professionals was known to exist, but was deemed to be largely unfamiliar or far from practiced. They believed that partnering stance could be learned and acquired and that it would be beneficial

to all involved but that several “barriers” stood in the way. Among those barriers they mentioned: Diverse cultural/subcultural beliefs, economics, social class membership, age, nation of origin, among others.

Conclusions: The obtained findings are discussed with reference to their impact on fostering Hispanic involvement in their own care as well as impact on future Hispanic outreach programming.

P21.02

Parkinson’s Disease: support groups use of PhotoVoice to share experiences

Joyce Bredesen

Metropolitan State University, St. Paul, MN, USA

Objective: The goal of this research was to utilize PhotoVoice as a therapeutic intervention for Parkinson’s disease (PD) that could assist in bringing about a deeper discussion, self-reflection, and a creative coping strategy to members within PD support groups. The PhotoVoice project brought the perspective of individuals who live with PD and attend a support group to share their life experiences within a safe environment through their pictures and stories.

Methods: Through PhotoVoice, a qualitative participatory research methodology, the lived experiences were exhibited through photographs and told through stories. The pictures and stories were shared within PD support groups to empower the participant and bring about a deeper discussion within a safe and trusted environment.

Results: PhotoVoice was found to be an effective tool within PD Support Groups to bring about more discussion and explore feelings about how Parkinson’s affects the individual and those around them. Eight support groups completed the project. A total of 82 surveys were filled out. Of the completed surveys, 88 percent stated that they found PhotoVoice to be helpful in bringing about more discussion within the support groups. Eighty percent stated they felt taking the pictures and writing down their feelings about the pictures helped them to explore more about PD and how it affects them. Ninety four percent stated that it was helpful to have others share their pictures and stories and to talk about their experiences.

P21.03

Gait, balance and mobility in Parkinson’s disease: Improvements after use of a DVD providing training in Alexander Technique

Bill Connington

Lecturer, Yale University, New Haven CT; Former Faculty, The Edmond J. Safra Parkinson’s Wellness Program, New York NY; The Poise Project, Asheville NC, New York, New York, USA

Objective: To measure effectiveness of an Alexander Technique (AT) educational DVD designed to train Parkinson’s patients to practice and reinforce skills for improved alignment, mobility, balance and gait so as to increase ease and confidence in activities of daily living (ADLs).

Background: AT is a method of mind-body education to improve ease, efficiency and confidence in ADLs. Studies indicate that AT can help people living with Parkinson’s in ADLs. Participants in one AT study reported “subjective improvements in balance, posture and walking, as well as increased coping ability and reduced stress. (Stallibrass C, 2002) A study of an AT-like intervention reported improved postural alignment, reduced postural sway, improved torso mobility, and smoother movement during step initiation, likely indicating better movement efficiency. (Cohen RG, 2015) Developing literature indicates positive potential results for retention. (Stallibrass C, 2005)

Methods: Protocols used in this DVD are based on over 6 years of practice with 50+ Parkinson’s patients in mid-stage of severity at the Jewish Community Center (JCC) in Manhattan, through the Edmond J. Safra Wellness Program, in partnership with The Marlene and Paolo Fresco Institute for Parkinson’s and Movement Disorders at NYU Langone Medical Center—a National Parkinson Foundation Center of Excellence. Protocols were developed to provide training in fall prevention and to help patients improve balance and gait, learn how to “unfreeze,” speak more loudly and clearly, move more easily, increase confidence and reduce anxiety. Of primary importance is learning simple, effective mental instructions to positively impact patients’ self-organization for movement. AT principles were delivered by group classes with hands-on and verbal instruction in a series of gentle movement sequences. This DVD is designed so the Parkinson’s patient can practice these protocols at home with the objective of long-term retention of improvements in ADLs. The DVD’s effectiveness will be measured through patient and partner surveys.

Results: All patients who took classes at the JCC reported subjective improvements, such as: less falling, less “freezing,” reduction in anxiety, more ease in motion, and improved gait and speech. Effectiveness is enhanced by cues taught to care partners for support during patients’ ADLs. The Alexander DVD will be released in the fall of 2016. Follow-up surveys of patients and partners will be analyzed in early 2017.

P21.04

Long-term effects of self-efficacy enhancing program for newly-diagnosed persons with Parkinson’s disease

Diane Cook¹, Cynthia McRae², Rajeev Kumar¹

¹ Colorado Neurological Institute, Englewood, CO, USA

² University of Denver, Denver, CO, USA

Objective: To determine whether the Parkinson’s Self-Efficacy Learning Forum (PD SELF) program improves physical and psychosocial functioning in newly diagnosed persons with Parkinson’s disease (PWP) over the 12-month period of the intervention and 1 year follow-up. This program used self-efficacy principles to assist individuals to adopt the healthcare behaviors that positively influence effective disease management and QoL.

Methods: Led by two trained lay facilitators (one with PD), 13 participants and their care partners attended 12 monthly 2-hour meetings designed specifically to introduce and reinforce self-efficacy behaviors. PWPs were assessed at baseline using the MDS-UPDRS and self-report psychosocial measures. The same measures were repeated at 12 months; psychosocial measures were completed at 1 year follow-up. Due to small sample size, significance level was set at $p < .10$.

Results: Scores on UPDRS Parts III and IV and 2 self-report physical functioning measures worsened from baseline to post-intervention ($p < .10$) while scores on the PDQ-39 Emotional Well-Being scale improved ($p = .07$). There were also trends toward improvement on self-efficacy, perceived support, and stress from baseline to post-intervention. From 12 months to follow-up, self-reported physical functioning worsened while hope, anxiety, sleep, and aspects of self-efficacy (e.g., ability to manage disease) improved (all $p < .05$).

Conclusions: These results suggest that introducing, modeling and supporting self-efficacy enhancing skills appear to contribute to improved psychosocial functioning despite a decline in physical functioning. Maintaining emotional stability in the face of declining health is an important outcome. Results show that participants’ psychosocial functioning continued to improve from the end of the program through 1 year follow-up, suggesting a change in behavioral patterns and expectations. After completion of the program, the group has continued their program of education

through guest speakers and guided discussions. The group has expanded to include other newly diagnosed PWP's and many have assumed active roles in the PD community. PWP's report feeling better and more fit now than they have in years. Future research may focus on determining whether enhancing self-efficacy helps participants in the future as they adjust to new challenges of this progressive disease; e.g., does this intervention have long-term protective benefits in managing PD in the future?

P21.05

Thinking in action: Alexander technique for Parkinson's disease

Candace Cox¹, Daniel Kral², Monika Gross³, Rajal Cohen²

¹ Big Sky Alexander Technique Studio, The Poise Project, Castleton, Ontario, Canada

² University of Idaho, Moscow, Idaho, USA

³ Form, Fitness & Function, The Poise Project, Asheville, North Carolina, USA

Background & Purpose: Alexander Technique (AT) is a holistic educational approach that uses attention and inhibition to change functional patterns, reduce rigidity, and improve balance and efficiency in activities of daily living. A randomized controlled trial found that 24 AT lessons reduced PD disability and depression (Stallibrass et al 2002), and benefits were retained at 6 months (Stallibrass et al 2005). A laboratory study found that even brief exposure to AT concepts led to immediate improvements in torso mobility, postural alignment, and postural control (Cohen et al 2015). We aim to develop a standard protocol for delivering AT lessons and assessing effects, to lay groundwork for a large multi-site study.

Method: Six PD patients (Hoehn and Yahr stages 1-4) received intensive AT training over 7 days. Patients were encouraged to follow their regular exercise and medication routines throughout the week. We performed assessments at the beginning and end of the week at the same time of day: Neck Disability Index (NDI), Berg Balance Scale (Berg), Mini-Balance Evaluation Systems Test (mBEST), Timed Up and Go (TUG), Stroop color-word naming (to test inhibitory control), height, and self-reported symptoms.

Intervention: Patients received one 90-minute group class and 4-6 private 45-minute lessons, including functional and anatomical instruction as well as hands-on guidance in upright and semi-supine positions. The main focus was on allowing movement through the neck, torso and legs to reduce co-contraction, improve stability, and to facilitate lengthening and maintain upwards intention. Where possible, a care-giver was included in lessons and taught a protocol for continuing at home.

Results: After AT lessons, NDI improved for 4/6 patients (clinically important), Berg for 5/6, mBEST for 3/5, TUG for 3/6, Stroop for 6/6, and height for 4/5. All patients reported improvement in symptoms, with the greatest changes in anxiety, balance, and posture. Improvements in Stroop correlated with improvement in NDI and mini-BEST, emphasizing the importance of inhibition.

Conclusion: Hybrid delivery of AT (individual and group sessions) shows promise as a cost-effective intervention for PD. Based on effect sizes for Berg ($d=3.7$) and height ($d=1.1$), 20 and 38 participants respectively are needed to achieve 90% power. Future studies will include matched control groups and will examine dose-response relationships, compliance at longer doses, and retention of benefits.

P21.06

Nursing advocacy in assessment of the Parkinson's patient in acute and outpatient urgent care: impact on health and quality of life

Mary Lou De Natale¹, Jolene Warford²

¹ University of San Francisco School of Nursing and Health Professions, San Francisco, California, USA

² Modesto Medical Center, Pittsburgh, California, USA

Introduction: This clinical project identified a need for health professionals, especially the nurses in the Emergency Room (ER) or Outpatient Urgent Care settings to be aware of the importance of the initial intake assessment on the symptoms and chronic care issues and support related to Parkinson's disease. The overall assessment and recognition of the health care issues and communication among the health team regarding medication management is important in the initial intake, triage, and patient-centered plan of care. The nurse's ability to support and recognize the patient's current presentation, reason for the admission, and further anticipate health care issues related to: current presenting symptoms, medications, medication management with compliance, nutrition, changes in cognitive thinking or speech, falls, sleep, or communication and follow-up or appointments with the health care team to support activities of daily living (ADL) and quality of life (QOL)

Background: Parkinson's disease is known to health professionals as a chronic, progressive neuro-degenerative disorder characterized by tremors, weakness, muscle rigidity, decreased or slowed movements that can influence daily life and their emergent health care concerns. Furthermore, it is the signs and symptoms of Parkinson's disease that are important markers for nurses and health care professionals in assessment in health care areas.

Findings: Health care providers and nurses need to take into consideration patient-centered care with the Parkinson's patients. Education is one of the best primary interventions to teach individual about health and promotion of the person with knowledge and understanding for a plan of care.

Outcomes, Conclusion, and Implications: Initially, this project did support a potential for the nurses and health care professionals to better understand the importance of human presence and listening to the patient in the ER and /or Outpatient Care setting and recognition of the overall issues related to the disease and activities of daily living as they are influenced by the: progression of the disease, changing in gait, medications, or discharge teaching and communication related to caregiving. This project could provide a foundation for nursing students, nurses in acute care or community clinics / agencies to better manage and give anticipatory guidance for the person and family living with Parkinson's disease.

P21.07

Does gender influence the types of questions asked by people living with Parkinson's?

Christiana Evers¹, Linda Pituch¹, Jill McClure¹, Jeanne Kirby¹, Casey Gallagher¹, Nancy Ralph²

¹ Parkinson's Disease Foundation, New York, NY, USA

² New York, NY, USA

Objective: To analyze the type of questions asked by women and men to Parkinson's disease HelpLine in the USA from August 2010 to January 2016.

Background: The Parkinson's Disease Foundation (PDF) is a non-profit organization located in the US that supports the research and ideas that improve the lives and futures of people affected by Parkinson's disease. PDF works to achieve this goal through three distinct yet complementary mechanisms: supporting Parkinson's

disease research, providing educational resources and advocating on behalf of those with Parkinson's. Our educational resources include a national toll-free HelpLine, staffed by trained information specialists, and established over 30 years ago. The HelpLine staff answers questions about Parkinson's disease, symptoms, treatments, complementary and alternative therapies and the latest scientific studies reported by the media; provides referrals to support groups and Parkinson's specialists and identifies financial, legal and other resources. The HelpLine provides access to an interpreter for non-English speaking callers. We now seek to ascertain the impact of gender on the types of questions asked by our callers over a 66-month period.

Methods: From August 2010 to January 2016, the Parkinson's Disease Foundation HelpLine responded to 21,521 calls from the Parkinson's community. Demographic and healthcare access data, call characteristics, referrals provided and categories of call content were recorded by HelpLine staff based on information provided by callers.

Results: Of the HelpLine callers, 66 percent were women and 34 percent were men. Analysis will include the distribution of the types of questions asked (e.g., clinical trials, diagnosis and treatment, financial assistance, caregiving, etc.) and referrals provided by gender. We will also explore gender differences broken out by caller type (e.g., a person with Parkinson's; spouse or family member or healthcare professional or other). By utilizing these metrics, it is PDF's goal to better understand the needs of women and men living with Parkinson's and develop programs to meet these needs.

P21.08

Alexander technique for Parkinson's: an initiative of the Poise Project

Monika Gross¹, Candace Cox²

¹ The Poise Project, Asheville NC, Asheville, North Carolina, USA

² Big Sky Alexander Technique Studio, Castleton Canada; The Poise Project, Asheville NC, Castleton, Ontario, Canada

Objectives:

- To design and deliver continuing education courses (CECs) for medical professionals, such as physical, occupational and speech therapists, nurses and social workers, to incorporate Alexander Technique (AT) strategies in their work with Parkinson's disease (PD) patients
- To design and deliver AT classes for people with Parkinson's and their partners in community-based settings
- To have specialized teams of AT teachers available to deliver intensive programs of group and private lessons for people with Parkinson's and their partners where need and interest is identified
- To identify alternative funding sources to make programs affordable across socio-economic groups
- To design protocols for research in the field of AT for Parkinson's and to facilitate large-scale, multi-site trials

Background: AT is a method of mind-body education to improve ease, efficiency and confidence in activities of daily living (ADLs). Parkinson's patients in one AT research study reported "subjective improvements in balance, posture and walking, as well as increased coping ability and reduced stress. (Stallibrass C, 2002) A study of an AT-like intervention reported reduced postural sway, improved torso mobility, and smoother movement during step initiation, likely indicating better movement efficiency. (Cohen RG, 2015) Developing literature indicates positive potential results for long term retention. (Stallibrass C, 2005)

Methods: The Poise Project is an international initiative to expand access to the benefits of AT by creating and delivering programs adapted for specific populations and industries and supporting research in the field. Our coordinated team approach unites AT

professionals, individuals who have benefited from AT, and industry experts to create targeted programs that will work within existing care delivery systems. For this initiative, we have identified AT teachers with experience teaching clients with Parkinson's and their partners; people with PD who are AT teachers; people with PD and their partners who have benefitted from AT lessons; medical professionals in the field who have studied AT; and we have reached out to experts in the field to test our models for effective service delivery.

Results: We will share examples of our programming at our exhibition booth during the World Parkinson Congress (WPC) and we will offer CECs for medical professionals and group classes for people with PD and their partners in Portland the weekend following the WPC.

P21.09

Balancing medication with self analysis

Jari Hämäläinen

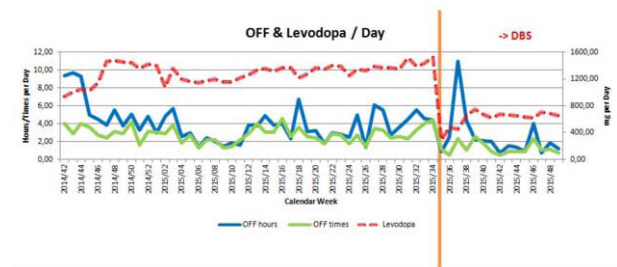
Nummela, Finland

The method of collecting data on daily actions including Medication, Exercise, Sleep and Off modes occurred. Symptoms are in three categories and measured by length and accuracy. Analyzing the data has been a tool for myself to balance the Medication and reduce the doses to feel better. It has also been welcomed by neurologists as it does provide more accurate information of patient's overall situation than what can be observed within the biannual meetings. Also the Finnish medical society has found the analysis useful and the head of neurology department of Helsinki University Hospital has asked permission to use the analysis for tutorial purposes.

The data is collected into MS Excel datasheet and utilized pivots and charts to analyse. The result are reported with MS Powerpoint into which the charts and tables are linked to.

There are a couple of occasions where the data analysis has been beneficial personally: 1) decrease the medication without negative effect to condition 2) identified change in the pattern that turned out to be malfunction in DBS device.

Weekly Average / long term



P21.10

Staying connected to veterans with deep brain stimulation

Miriam Hirsch

Department of Veterans Affairs, Richmond, VA, USA

Background: Deep brain stimulation (DBS) is an effective surgical intervention for medically refractory Parkinson's disease (PD). Since Food and Drug Administration (FDA) approval in 2002, we have seen remarkable results with DBS controlling symptoms and masking disease progression. Unfortunately, DBS does not cure PD

nor slow its progression. Keeping close contact with patients after surgery and preventing disruption of the DBS therapy is critical to overall wellbeing and long-term outcome. Careful monitoring of the DBS system minimizes the potential for catastrophic consequences that may occur without follow-up care and support. We must educate our patients about DBS and promote self-management strategies. Southeast Parkinson's Disease Research Education and Clinical Center (PADRECC), is located at Hunter Holmes McGuire Veterans Affairs Medical Center (VAMC) in Richmond, VA. This specialty care center for veterans with movement disorders hosts an interdisciplinary DBS clinic offering evaluation, surgical treatment, follow-up care, and programming. Visits can be in-person or remote via telehealth.

Objective: To demonstrate how a systematic approach to case management improves follow-up care, enhances two-way communication, educates patients and caregivers to maximize the potential of DBS therapy, and to minimize adverse events.

Methods: Case management strategies will be presented, including: regular follow up visits; databases for tracking demographics and patient outcomes; secure messaging – a web-based portal for patients to communicate non-urgent information; and telephone education support groups for veterans with DBS.

Results: Since 2001, over 200 veterans have had DBS surgery at the Southeast PADRECC. Data will be presented about this patient population and how the PADRECC is staying connected to them.

P21.11

Inside Scoop!™ – sharing collective wisdom: use of an online searchable database of tips that maximize self-efficacy and reduce isolation for people with PD and care partners

Sarah Jones, Judy Talley

Parkinson & Movement Disorder Alliance, Tucson, AZ, USA

We believe that information is power and that programs and services that facilitate information sharing are essential to improving quality of life for people with Parkinson disease who face the numerous daily challenges and obstacles caused by the disease. The usual outlet for people who live with PD and their care partners to share their hard won wisdom, experiences, tips and hints is in support groups; however, many people do not attend a support group, or simply may have missed the meeting where a useful tip was shared. Inside Scoop!™ solves this access problem by offering a searchable online data base of tips, tools and hints that make everyday life easier for people with Parkinson disease.

Here is an example: if a person is having difficulty getting in and out of car, they might enter "Mobility" in the database. Among the tips, they would see a picture of the Handybar Vehicle Support Handle and a review by one of their peers. All submissions will be reviewed by our coordinator to ensure they are appropriate for posting and not medical in nature.

Currently there is no centralized online or published resource offering this information. While some websites exist, such as Patients Like Me, they tend to be cumbersome and challenging to navigate and locate meaningful, high quality information. Inside Scoop!™, designed with the end-user in mind, focuses specifically on Parkinson disease.

Inside Scoop!™ empowers all who use it. Created by people with Parkinson disease and care partners, they welcome the opportunity to share their wisdom and tips about living optimally despite the disease. With contributions both practical and personal, contributors and users alike develop a sense of pride, ownership and empowerment for a difficult disease that rarely generates such feelings.

Program outcomes are geared at increasing quality of life. They include: 1. Provide meaningful tips and tools to people with PD and their care partners that results in self-reported increased self-

sufficiency. 2. Engage underserved, rural and homebound individuals, thereby reducing isolation and improving quality of life.

To evaluate effectiveness, we measure utilization and repeat use by people throughout Arizona. Participants are asked to evaluate the impact of the information they find on the database as it improves their quality of life. Finally, we also track the number of new ideas submitted each month to measure engagement and growth.

INSIDE SCOOP!™ Searchable Tips Database

INSIDE SCOOP!™ Outcomes:

- Provide meaningful tips and tools to people with PD and their care partners that results in self-reported increased self-sufficiency.
- Engage underserved, rural and homebound individuals, thereby reducing isolation and improving quality of life.

Searching Sunday 10am
Search Term: Incontinence

Searching Wednesday 6am
Search Term: Mobility

Tip: Handybar by Stander

Searching Monday 11pm
Search Term: Medication

Inside Scoop!™ empowers all who use it. It can be used by anyone, anywhere, anytime. Created by people with Parkinson disease and care partners, they welcome the opportunity to share their wisdom and tips about living optimally despite the disease. With contributions both practical and personal, contributors and users alike develop a sense of pride, ownership and empowerment despite a difficult disease.

P21.12

Reversing symptoms of Parkinson's disease by Parkinson's patient, Cape Town, South Africa

John Pepper

Cape Town, Western Province, South Africa

Up until 2002 there was nothing we could do about Parkinson's disease other than treat the symptoms.

That has now changed! I, and many other patients, have adopted a positive attitude towards the management of PD, with great success. Through FAST WALKING and an MAO-b inhibitor, I was able to reverse many of my movement symptoms. This was mentioned by Dr Norman Doidge in his book, "The Brain's Way of Healing" in 2015.

After 8 years of taking Selegiline and doing fast walking, I was able to permanently come off all PD medication. I have continued the FAST WALKING ever since. I am now 81 years old. In 2011, others started to follow this exercise regimen with good results. Many more are doing so without my involvement.

Dr Beth Fisher, at the 1st WPC held in Washington DC in 2006, announced the results of a study to find the effect of exercise on PD. Those results showed that the lab rats, monkeys and Pd patients all got measurably better after doing exercise, some of them more than others, compared with the control groups which did no exercise.

The rats who all received an injection of MPTP before exercising showed that those which did the high intensity exercise fared the best. The monkeys were injected with MPTP after exercising. The monkeys that did the high intensity exercise did not succumb to the injection. All the other monkeys got varying degrees of PD. The PD patients all showed significant improvements and those that did high intensity walking did by far the best.

I have found that PD only appears to affect movements controlled by my SUBCONSCIOUS brain, such as walking, writing and bringing food to my mouth. My CONSCIOUS BRAIN appears to still be able to control all my movements normally and I now lead a 'normal' life as if I no longer had Pd, which I still do. I have been able to show all but one patient, who could not stand up, how to walk normally after a maximum of 2 minutes instruction.

P21.14

Baseline characteristics of a longitudinal study of the social self-management of Parkinson's disease (SocM-PD)

Linda Tickle-Degnen¹, Michael T. Stevenson¹, Marie Saint-Hilaire², Barbara Habermann², Linda S. Sprague Martinez⁴, Cathi A. Thomas⁵, Elena N. Naumova¹

¹ Tufts University, Medford, Massachusetts, USA

² Boston University Medical Center, USA

³ University of Delaware, USA

⁴ Boston University, USA

⁵ Boston University Medical Center, Tufts University, USA

Background: Social activity has been found to be an important determinant of health trajectories in older adults, yet rarely is this studied in people with Parkinson's disease (PD) and their care partners. The Emergence and Evolution of Social Self-Management of Parkinson's Disease is a 3-year prospective cohort study of people with PD and co-enrolled care partners. In this in-progress study, participants are interviewed quantitatively and qualitatively at baseline and every 3 months (14 waves of data collection). This presentation defines social self-management and its measurement and reports baseline characteristics of the participants with PD.

Methods: Eligible participants were diagnosed with idiopathic PD, Hoehn & Yahr Stages 1–4, scoring ≥ 26 on Mini-Mental State Exam, community living, and English-speaking. A care partner was enrolled if eligible and available. Variables were based on our definition of social self-management: one's practices and experiences that ensure personal social comfort while supporting one's mental and physical well-being. Key variables and measures include: 1) social participation and management of social activities (e.g., Baum and Edward's Activity Card Sort, ACS); 2) social networks (e.g. Litwin's social network scales; 3) social comfort (e.g. Medical Outcome Study Social Support Survey items); and 4) health and well-being (e.g. PDQ-39, MDS-UPDRS).

Results: Of the 95 participants with PD who were screened, 90 were eligible for, and completed, baseline, 56 (62%) of whom enrolled with a care partner. The average participant was White (99%) and 65.5 years old. Thirty-four (38%) were women. In general, participants' quality of life and symptom severity were in early stages –H&Y mode score was 2 (73%), and the average UPDRS Total Score and PDQ-39 Summary Index Score were 58.6 and 26.7, respectively. Participants retained 86.2% of their activities (ACS), reported regular contact with partners, children, and friends, and gave and received similar amounts of daily activity, emotional and financial support as the members of their households.

Discussion: The project will provide evidence to guide the development of interventions for supporting social integration and health and well-being while aging with PD. The repeated measures design detects triggers of rapid changes in social and health outcomes.

much has been written on the role of social work as part of the team. This descriptive study describes the role of a social worker at a Center of Excellence of the National Parkinson's Foundation.

Methods: Observation of job duties and responsibilities can best be broken down into 3 main areas of care. The first is coordination of care, which is introducing new patients to the center and to other specific programs, such as the newly diagnosed program and the adult day program. The second area is clinical care, which covers the gamut from emotional support and education, to community resources to future planning of health care and finances. The third area is support group facilitation for groups conducted at the center, which are part of a network of over 90 group in a 5 state area. Support groups are offered for early, mid- and late-stages, for caregivers, and for those with atypical Parkinson's diagnoses. Data collected throughout the year on social worker tasks was analyzed. In addition, a survey to support group attendees was given over one-month period. Survey respondents scored the importance of the group in his or her emotional coping and the effectiveness of the leader on a 5.0 scale, with higher scores indicating greater importance or effectiveness.

Results: In one year, the social worker coordinated 450 new patients to the center, conducted 511 individual or family sessions and facilitated monthly support groups attended by 1050 patients and family members. Activities for new patients focused on understanding center services, ensuring optimal scheduling based on patient needs, and directing entry into the FOCUS program for newly diagnosed patients. 53 support group attendees scored coping at 4.3, indicating a high level of importance of the support group. Respondents scored leader effectiveness at 4.5, indicating a high level of effectiveness.

Conclusions: Characterized as a multi-faceted disease impacting each person and family in a different way, it is not surprising that to care for people with PD one needs a team of professionals. The social worker is trained and skilled at supporting patients and family with the complex and multidimensional aspects of PD; including those new to the diagnosis of PD, those struggling with the transitions throughout the disease, and those coping with the impact of PD.

P22.02

Redefining social work for Parkinson's: the development of a new model of care for specialized, comprehensive support in the clinic, community and home

Amy Lemen¹, Meghan Sweeney¹, Virgen Luce², Deanna Rayment¹, Alessandro Di Rocco¹

¹ Fresco Institute for Parkinson's and Movement Disorders at New York University Langone Medical Center/New York University School of Medicine, New York, NY, USA

² New York University Silver School of Social Work, New York, NY, USA

Objective: The development of a dynamic, multimodal social work program for individuals, care partners and families living with Parkinson's disease

Background: "They were talking a lot about symptoms—my tremor and my trouble walking—and what pills I could take. But no one was talking to me about how I felt. I felt like my world had fallen apart." – John S, Parkinson's patient

Patients living with Parkinson's disease (PD) face a constantly evolving array of psychosocial impacts throughout the disease process. There is a need for dynamic resources that support emotional health and ongoing adaptation for patients and families to improve quality of life and outcomes. PD expert social workers are in a unique position to address ongoing psychosocial need with a multi-modal intervention model.

CARE DELIVERY & QUALITY OF LIFE: PHARMACY AND/OR SOCIAL WORK

P22.01

Understanding the integral role of the social worker in multi-disciplinary team care for Parkinson's disease

Joan Hlas

Struthers Parkinson's Center, Golden Valley, MN, USA

Purpose: Over many decades the benefit of multi-disciplinary care in Parkinson's disease has been researched and proven, yet not

Methods: This program was launched in a PD expert clinic with traditional social work service provision including assessment, counseling, education and resource referral for patients, care partners, couples and families. The program was expanded to include a community partnership to provide a robust Parkinson's wellness program with group based exercise, support and education opportunities. The program then developed a one-year training program for master of social work level students. The latest phase of expansion includes coordination of an interdisciplinary home visit program for advanced Parkinson's. Specialized therapeutic support groups for patients and for care partners are also provided. Within this program paradigm, social workers are valued members of the expert, interdisciplinary team and act as a communication hub for multimodal continuity of care.

Results: The multimodal social work program has expanded from the clinical setting to encompass community partnerships, educational training and service provision to the homes of our most vulnerable patients. The program has been in high demand since its inception and has proven popular with patients, families and providers. Plans for expansion and evaluation include continued needs assessment, as well as program impact on quality of life, self-efficacy and ongoing adaptation to the disease process.

Discussion: The multimodal model of social work care offers potential benefit in multiple domains of individual and systemic psychosocial need that affect quality of life and outcomes. This poster will demonstrate in graphics and narrative the development and growth of the social work multimodal program model.

P22.03

Medication errors: the role of the nurse in an interdisciplinary home visit program for advanced Parkinson's disease patients

Sarah Oyler, Jori Fleisher, Meghan Sweeney, Amy Lemen, Arash Fazl, Geraldine Dacpano, Rebecca Gilbert, Alessandro Di Rocco, Joshua Chodosh

New York University School of Medicine, New York City, NY, USA

Background: Medication errors including non-adherence are independently associated with increased morbidity and mortality in the elderly population. In the USA, medication errors are estimated to increase healthcare costs by over \$170 billion annually. In Parkinson's disease (PD) specifically, medication non-adherence directly increases disability and healthcare costs. When PD progresses and patients become homebound, office-based medication reconciliation is not possible and errors may go undetected.

Objectives: To examine the number and types of medication errors detected by a registered nurse during interdisciplinary home visits for patients with advanced PD.

Methods: We defined medication discrepancy errors as errors of dose, frequency, strength, omission, and commission. We compared provider-documented prescriptions with the patient- or caregiver- administered regimen for 26 subjects completing at least one home visit (and up to 4) during a one-year period of quarterly home visits.

Results: Among 26 subjects, 11 subjects (42.3%) had completed four visits. In total, 54 errors were detected across 78 visits (0.69 detected errors per visit), with a median of 1 error per subject (range 0–9). The most common types of detected errors were errors of commission (35%) in which the subject was taking a medication not known to the provider or which they were instructed to discontinue, followed by errors of frequency (28%) and omission (24%).

Conclusion: Medication errors are frequent among advanced PD patients and are ongoing even with medication reconciliation efforts. To our knowledge, this is the first study documenting the prevalence of medication errors in homebound patients with advanced PD and supports the value of a home visit program in advanced PD.

This abstract has previously been presented at the 20th International Congress of Parkinson's and Movement Disorders on June 20th, 2016.

P22.04

Assessment and connection to care: the vital role of the social worker in an interdisciplinary home visit program for advanced Parkinson's disease patients

Meghan Sweeney¹, Amy Lemen¹, Sarah Oyler¹, Rebecca Gilbert¹, Arash Fazl¹, Joshua Chodosh², Alessandro Di Rocco¹, Jori Fleisher¹

¹ Fresco Institute for Parkinson's and Movement Disorders at NYU Langone Medical Center, New York, NY, USA

² NYU School of Medicine, New York, NY, USA

Objective: 1) To describe the role of social workers in managing the care coordination of homebound patients with advanced Parkinson's disease (PD); 2) to demonstrate whether social workers increase access to needed services and 3); to determine whether multiple visits have added value.

Background: As PD progresses, the burden of motor and non-motor symptoms as well as other comorbidities increases, eventually leading to a homebound state. Patients lose access to many essential services, resulting in reduced quality of life, hospitalization, and greater care partner burden. Homebound patients are eligible to participate in the Interdisciplinary Home Visit Program (HVP) at the Fresco Institute for Parkinson's and Movement Disorders. Visits include cross-discipline evaluations. The social worker's role is to identify unmet needs, provide diagnosis-specific education, counsel the patient and care partner, provide crucial resource referral, and coordinate care following each visit to ensure patients are connected to services. The value of multiple visits is unknown.

Methods: We examined social work effort and dyad need by the number and type of referrals delivered through the HVP caring for the first 26 enrolled patients. We collected data across multiple visits to determine the value of repeat visits. "Referrals" here are defined as a successful connection to a referred service.

Results: We observed a mean referral rate of 2.69 for the first visit. Although referral numbers decreased at each visit, the need for new referrals continued to be identified (0.5 referrals at the fourth visit). Referrals were diverse in type but specific types were frequent across patients: physical therapy – 73%; speech therapy – 58%; psychotherapy – 54%; home safety assessment – 27%; and psychiatry – 15%. Other referrals included support group, visiting primary care physician, medical alert system, home health care, elder care attorneys, and assistive devices.

Conclusions: Homebound patients with advanced PD are in need of a variety of referrals to improve care. Through repeated social work assessments, new needs continue to be identified. Follow up home visits provide the social worker with the opportunity to facilitate continued assessment, connections to new resources, reinforce previously identified unmet needs, and provide supportive counseling that adapts to the patient and family's evolving circumstances as PD progresses.

CLINICAL SCIENCES: SYMPTOMS, SIGNS, FEATURES & NON-MOTOR MANIFESTATIONS

P23.01

A targeted web-based approach to support staff nurse learning in the care of Parkinson's disease patients in acute care settings

Michael Clark

Rutgers School of Nursing-Camden, Camden, NJ, USA

Research indicates the need for improved outcomes for hospitalized patients with Parkinson Disease. Acute care nurses must have the knowledge and skills to effectively manage common problems and support optimal functioning in this population. The specific aims of this pilot project, which was partially supported by the Edmund J. Saffra Visiting Nurse Faculty Program, were to validate content and test the feasibility of an innovative method for delivering educational content to acute care nurses. Participants were provided with a hyperlink to a 30-minute screencast developed by the author. The content of the screencast was developed based on a review of the literature that identified acute care issues and challenges in caring for patients with Parkinson Disease. These included problems with drug administration and the management of motor and non-motor symptoms. The screencast which is a video with text and voice overlays, provided an overview of Parkinson Disease and suggested evidence-based approaches to symptom management through appropriate pharmacological and non-pharmacological interventions. In order to test feasibility, a staff nurse educator at a local hospital sent an email to all staff nurses with an embedded link to both the screencast and an electronic survey. The electronic survey was used to track utilization rates as well as gather participant feedback about the perceived utility and effectiveness of the design of the screencast. Discussions with key informants also provided invaluable feedback. These informants who viewed the screencast included: A regional coordinator of Parkinson Disease support groups, the head of the Saffra Visiting Nurse Faculty Program, staff educators, staff nurses and academics from local schools of nursing. In conclusion, this design proposes an innovative approach to educating acute care nursing staff about the unique needs of patients with Parkinson Disease. It provides suggested strategies to manage symptoms and improve outcomes. Acute care hospitals frequently do not have the resources to develop new educational content for staff. Synchronous learning within work settings can be cost prohibitive. The method utilized in this project can deliver content in an asynchronous manner at work or at home. Staff educators have indicated that this methodology might easily be adapted to learning management system platforms that are currently in use in order to track utilization and measure learning outcomes.

P23.02

Silver Snowflake Parkinson Fall Prevention Initiative: overview

Klaudia J. Cwiekala-Lewis¹, Klaudia J. Parkyn²

¹ University of Phoenix, Manchester, PA, USA

² Translate Nursing LLC, York, PA, USA

Parkinson's Disease (PD) prevalence is on the rise. According to the Parkinson's Disease Foundation there is an estimated 60,000 Americans that are newly diagnosed each year with PD. Many current evidence based studies have shown that falls are common in Parkinson's disease. The clinical impact of falls is significant, often leading to a debilitating fear of reoccurring falls. Costs

associated with post falls care are substantial. Falls are a serious problem among those with neurologic disorders like Parkinson's. This growing concern was supported by recently collected statistical data in the state of the science paper written by Allen, Schwarzel, & Canning in 2013 reported that 60.5% of Parkinson patients reported at least one fall and 39% reported recurrent falls within a one year period. Despite the fact the fall in Parkinsons patients are concerning and the cost of post falls care substantial, few if any clinical guidelines have specifically addressed prevention and interventional strategies for patients with Parkinson's disease. Silver Snowflake Parkinson's Fall Prevention Initiative (SSPFPI) was created during the Edmond J. Saffra Visiting Nurse Faculty Program (EJS-VNF) at the Parkinson's Disease Foundation (PDF). This initiative then was disseminated by Translate Nursing LLC. Silver Snowflake Parkinson's Fall Prevention Initiative (SSPFPI) is an ongoing initiative to close the gap and to educate healthcare providers, patients and their families about why the patients with Parkinson's prone to falls and provide some intervention currently available to prevent falls in patients with Parkinson's disease. All materials available for this initiative will be available in many languages and made available free of charge internationally.

P23.03

Longitudinal study of contrast sensitivity visual acuity defects in Parkinson's patients

Kenneth Dalton¹, Eric Thomas², Eric Barr², Michelle Ayazo², Charles Maitland²

¹ Tallahassee, FL, USA

² Florida State University College of Medicine, Tallahassee, FL, USA

Objective: A study of contrast sensitivity visual acuity (CSVA) in the earliest stage of Parkinsonism with a longitudinal follow-up.

Background: Deficiencies in CSVA are recognized in patients with Parkinson's disease (PD), putatively due to loss of retinal dopamine. These deficits can be identified simply by using contrast sensitivity wall chart testing at various efficiencies.

Design/Methods: Prospective study involving 26 early-stage PD subjects (Stage I-II H&Y) versus 26 controls. Subjects completed questionnaires about their vision, health, current medications, and four symptoms typically present in pre-motoric states of PD. Tests included UPDRS; directive and contrast sensitivity visual acuities (SLOAN) at 100%, 2.5%, and 1.25%; intraocular pressure; tear film formation; color vision (HRR); confrontational visual fields; fundoscopic exam; and Spectral Optical Coherence Tomography (Zeiss OCT) to assess inner retinal layers. Visual acuity <20/50 and recognized co-morbid ophthalmologic pathologies were exclusionary, as were other neurologic conditions and dementia. Statistical methods: Paired t-test, linear regression, and a one-way analysis of variance (ANOVA) with a Tukey post-hoc test. Significance levels were set at $\alpha=0.05$ for all analyses.

Results: A significant difference was noted in CSVA between PD patients and controls at baseline with subsequent deterioration over a 4 year period using a one-way ANOVA. Post-hoc analysis revealed that at both 2.5% and 1.25% contrast, controls had significantly better CSVA than PD patients. Over 4 years UPDRS scores increased by a mean of 4.625 ± 7.284 ($p < 0.05$). Although mean CSVA declined, neither changes in CSVA or Inner Plexiform Layer (IPL) + Ganglion Cell Layer (GCL) on OCT were statistically significant. There was no correlation between IPL+GCL and CSVA.

Conclusions: Early PD patients (11 of which were naïve to dopamine therapy) with normal directive visual acuity have significantly decreased CSVA, with subsequent decline over a four year period. The reduced efficiency of vision was not reflected in significant change in retinal layer thickness and has a weak correlation with changes in UPDRS scores.

P23.04

Online case-based education improves the recognition of risk factors for and treatment of NOH

Thomas Finnegan, John Maeglin
USA

Background: Neurogenic orthostatic hypotension (NOH) refers to the significant drop in blood pressure upon standing, which can result in dizziness, fatigue, and cognitive changes. Despite the fact that NOH is common and may contribute to disability and even death, many patients do not receive prompt and accurate diagnosis or treatment. Clinicians lack sufficient knowledge of risk factors to improve time to diagnosis of NOH and knowledge of appropriate treatments once diagnosed. The current study was undertaken to determine if an online, case-based intervention could effectively improve clinician knowledge of NOH risk factors and treatment strategies.

Methods: The educational intervention consisted of an online, case-based text CME activity using patient case scenarios that challenged clinicians to apply the most recent clinical data and evidence-based recommendations to the recognition and management of NOH. Educational effect was evaluated through the use of a pre- vs post-assessment design that linked responses of individual learners thus allowing each learner to act as his/her own control. Data were collected between March 16, 2015 and May 18, 2015. A paired 2-tailed t-test evaluated whether the mean pre- and post-assessment scores significantly differed from one another and Pearson's χ^2 test measured changes in paired responses to individual questions. Cohen's d was used to calculate the effect size of the intervention.

Results: Participation in the intervention resulted in a significant improvement in knowledge of risk factors and treatment strategies for NOH among neurologists (n=387; d=1.034; P<0.05). and cardiologists (n=65; d=1.031; P<0.05). Participation in the intervention resulted in a significant improvement (P<0.05 for all comparisons) in the proportion of pre- vs post-educational correct responses for both neurologists and cardiologists: risk factors for NOH (neurologists: +8%; cardiologists: +22%), nonpharmacologic treatment to improve symptoms of NOH (neurologists: +166%; cardiologists: +119%), initial treatment for a patient with supine hypertension: (neurologists: +25%; cardiologists: +14%), appropriate initial dosing of droxidopa for NOH (neurologists: +27%; cardiologists: +44%).

Conclusions: This study demonstrated the success of a targeted, online, case-based educational intervention on improving the knowledge of factors involved in the identification of, and treatment strategies for, NOH among neurologists and cardiologists.

P23.05

Impact of neurogenic orthostatic hypotension on healthcare costs in patients with Parkinson's disease

Clément François¹, Italo Biaggioni², Cyndya Shihao², Augustina Ogbonnaya³, Huai-Che Shih³, Eileen Farrelly³, Adam Ziemann¹, Amy M. Duhig³

¹ Lundbeck LLC, Deerfield, IL, USA

² Vanderbilt University Medical Center, Nashville, TN, USA

³ Xcenda, LLC, Palm Harbor, FL, USA

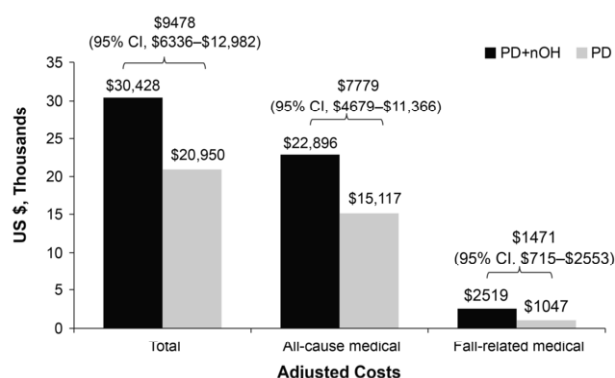
Purpose: Neurogenic orthostatic hypotension (nOH) is marked by a sustained blood pressure decrease upon standing that may cause symptoms of dizziness and syncope, and contribute to falls. nOH can occur in patients with Parkinson disease (PD) and related neurodegenerative disorders. Limited information exists regarding the healthcare cost of nOH in PD patients. The characteristics,

rates, and costs of medically attended falls were assessed in patients with PD vs PD+nOH.

Methods: PD patients (=1 PD diagnosis and PD prescription) and PD+nOH patients (=1 nOH diagnosis and nOH-related prescription plus =1 PD diagnosis and PD prescription) were identified using MarketScan® Commercial and Medicare Supplemental databases (1/1/2009-12/31/2013). The index date was defined as the first diagnosis-related medical or prescription claim. Characteristics (12-month pre-index period) and healthcare utilization and costs (12-month post-index period) were compared between groups. Multivariate analyses were used to adjust for baseline differences.

Results: Analyses included 281 PD+nOH and 17,421 PD patients. Significantly more PD+nOH than PD patients were aged =65 years (92% vs 76%) and male (68% vs 59%), and had Medicare coverage (93% vs 75%; P<0.005 for all). Pre-index, PD+nOH vs PD patients had significantly higher mean Charlson Comorbidity Index scores (1.5 vs 1.3; P=0.0084) and rates of syncope/collapse (26% vs 5%; P<0.0001) and dizziness/giddiness (17% vs 7%; P<0.0001). In the post-index period, significant differences were found in the PD+nOH vs PD groups in the proportion of patients who had a medically attended fall (30% vs 21%; P=0.0002) and the mean number of falls among patients who fell (2.5 vs 2.0; P=0.0176). After adjusting for baseline differences, PD+nOH patients had more medically attended falls than PD patients (difference, 0.26; 95% CI, 0.17–0.38). Adjusted costs for the PD+nOH group were higher by \$9478 for total costs, \$7779 for all-cause medical costs, and \$1471 for fall-related medical costs vs the PD group (Figure 1).

Figure 1. Adjusted Care Costs in the PD+nOH and PD Groups



PD=Parkinson disease; PD+nOH=Parkinson disease and neurogenic orthostatic hypotension.

Conclusions: Compared with PD patients, PD+nOH patients have a greater disease burden pre-index, as determined by comorbidity assessment and higher rates of syncope/collapse and dizziness/giddiness. Post-index, the PD+nOH group had increased falls and care costs vs the PD group. Whether nOH-directed therapies could impact these outcomes requires additional research.

Funding: Lundbeck

P23.06

Effects of STN-DBS on non-motor and axial symptoms in patients with Parkinson's disease

Maria Fraraccio¹, Christiane Lepage², Thi Thanh Mai Pham², Elise Lafleur-Prud'homme², Abbas Sadikot³, Nicolas Jodoin⁴, Michel Panisset²

¹ Centre de Recherche CHUM, Montreal, Quebec, Canada

² CHUM and Centre de Recherche CHUM, Montreal, Quebec, Canada

³ Montreal Neurological Institute and Hospital, Montreal, Quebec, Canada

⁴ CHUM and CRCHUM, Montreal, Quebec, Canada

Introduction: A clear consensus has yet to be established concerning the impact of STN DBS on non-motor symptoms (NMS) and axial signs for patients with Parkinson's disease (PWPDP). We aimed to investigate the effects of STN DBS on PWPDP using a battery of tests targeting NMS, axial function, and quality of life (QoL).

Methods: Consecutive PWPDP, enrolled in our inter-university (McGill University and Université de Montréal) functional neurosurgery program, were included in this study from October 2011 to March 2015. Patients were assessed prior to surgery and 7 to 18 months post-surgery in the ON-medication state. Scales measuring axial signs (gait and balance) and non-motor features (mental status, word fluency, sleep-related problems, mood, fatigue and quality of life) were administered as were measures of caregiver/family burden. The Wilcoxon signed-rank test was performed to compare pre- and post-surgical outcome. P-values were 2-sided and they were calculated at the 0.05 significance level.

Results: We analyzed the test scores of 40 patients with PD treated with STN-DBS for pharmaco-resistant complex fluctuations and dyskinesias. Mean age was 57.4 (± 8.31) years, median post-operative follow-up period between surgery and study evaluation was 53.4 weeks and mean disease duration was 10.3 (± 4.59) years. As expected, significant improvements on the UPDRS III motor scores were noted. Post-operatively, a significant decrease in performance was observed on tasks measuring category word fluencies (animal and vegetable) as well as on the Mini-Best Test which measures balance. Meanwhile, post-operative scores were significantly improved on the Parkinson's disease Questionnaire-39 (Table 1).

Discussion: Our results reveal a significant improvement for motor function, no effect on mental status, sleep problems, mood, fatigue, but word fluency and balance scores were decreased following STN-DBS. Overall however, patients report an improved quality of life and based on a self-assessment of treatment questionnaire, on average, patients indicate that they feel "... a definite improvement that has made a real and worthwhile difference".

TABLE 1 Test results	PRE-OP	POST-OP	p-value
Cognitive status			
MoCA	27.3 \pm 1.81	27.1 \pm 2.38	<i>ns</i>
Fluency P	16.2 \pm 5.48	15.5 \pm 4.83	<i>ns</i>
Fluency R	14.4 \pm 4.75	13.4 \pm 5.27	<i>ns</i>
Fluency Animal	18.4 \pm 4.65	16.5 \pm 4.17	<i>p</i> <0.05
Fluency Vegetables	12.6 \pm 3.04	11.6 \pm 3.68	<i>p</i> <0.05
Sleep related problems			
Epworth Sleepiness Scale	6.9 \pm 4.65	6.2 \pm 4.43	<i>ns</i>
Mood			
Geriatric Depression Scale	3.9 \pm 3.30	3.3 \pm 2.85	<i>ns</i>
HADS/A	7.0 \pm 4.32	5.9 \pm 3.11	<i>ns</i>
HADS/D	5.5 \pm 3.17	4.7 \pm 3.35	<i>ns</i>
Fatigue			
PDFS	51.3 \pm 15.94	45.8 \pm 14.06	<i>ns</i>
Quality of life			
PDQ-39 -global	51.2 \pm 22.27	41.4 \pm 24.81	<i>p</i> <0.05
Caregiver burden			
Zarit Caregiver Burden	16.9 \pm 13.26	18.5 \pm 17.12	<i>ns</i>
Mobility and gait			
TUG (sec)	9.2 \pm 2.50	11.2 \pm 9.20	<i>ns</i>
TUG motor (sec)	9.8 \pm 2.88	10.3 \pm 3.67	<i>ns</i>
TUG cognitive (sec)	11.5 \pm 5.05	11.7 \pm 7.39	<i>ns</i>
6MWT (m)	396.1 \pm 121.61	399.5 \pm 158.51	<i>ns</i>
Balance			
MiniBEST	23.8 \pm 2.94	21.6 \pm 5.54	<i>p</i> <0.05
Lower extremity strength			
Sit to Stand 5 times (sec)	15.8 \pm 6.34	15.3 \pm 5.89	<i>ns</i>
Sit to Stand (nb/30sec)	11.8 \pm 4.30	12.0 \pm 3.27	<i>ns</i>

Abbreviations: MoCA=Montreal Cognitive Assessment; HADS/A and D=Hospital Anxiety and Depression Scale; PDFS=Parkinson's disease Fatigue Scale; PDQ-39=Parkinson's disease Questionnaire-39; TUG=Time Up and Go; 6MWT=6 Minutes Walking Test; sec=seconds; m=meters; nb=number; plus-minus values are means \pm SD; *ns*=non-significant

P23.07

Vitamin D deficiency and severity of Parkinson's disease in veterans

Fariha Jamal¹, George Jackson², Suzanne Moore², Aliya Sarwar²

¹ Department of Neurology, Baylor college of medicine. Parkinson Disease Research, Education and Clinical Care Center, Michael E. DeBakey VA Medical Center, Houston, TX, USA

² USA

Background: Vitamin D deficiency is more prevalent in Parkinson's disease (PD) as compared to healthy controls and patients with Alzheimer's dementia. Data on the causal association of vitamin D deficiency with PD are inadequate. Despite previous reports of vitamin D deficiency in PD, estimation of vitamin D levels is not routinely done in PD patients.

Purpose: To study the relationship of vitamin D deficiency with different stages and clinical manifestations of PD in Veterans

Methods: This retrospective cohort study used data from Houston's Parkinson's Disease Research, Education and Clinical Center (PADRECC) database from 2001 to 2014. 1327 charts with ICD-9-CM code 332.0 (Parkinson disease) were queried for laboratory analysis of vitamin D levels. Vitamin D levels were available for 127 patients. Diagnosis of PD as per UK Brain Bank Criteria was confirmed in 68 patients. Clinical features of these 68 patients were further studied.

Results: 25 patients had vitamin D levels below 30ng/ml (25-OH vitamin D reference range: 30-100 ng/ml), while 43 patients had levels above 30ng/ml (36.8% vs 63.2%). Average age in both groups was 74 years. In vitamin D deficient group, 10 patients (40%) had Hoehn & Yahr (H&Y) stage less than or equal to 2, while 15 (60%) patients had H&Y stage above 2. Nineteen patients (44.2%) with normal vitamin D had H&Y stage less than or equal to 2 and 23 patients (53.5%) had H&Y above 2 (*p*=0.8). Five out of 17 patients in vitamin D deficient group reported falls within the first year of diagnosis while 13 out of 26 patients with normal vitamin D levels had falls within the same timeframe (*p*=0.56).

Conclusion: The distribution of vitamin D levels across H&Y stages of PD was the same. No association was found between serum Vitamin D level and motor disease severity including early falls in Veterans with Parkinson's disease. This finding highlights the need to determine whether low vitamin D is a risk factor for development of PD or PD related motor limitations lead to low vitamin D levels.

P23.08

Is there any correlation between symptoms of Parkinson's disease and cerebral white matter hyperintensity?: a Korean study

Oh Dae Kwon, So Young Choi, Ji Yeon Lee, Jang A Park

Daegu Catholic University Medical Center, Daegu, South Korea

Objective: This study was performed to identify any relationship between the severity of white matter hyperintensity and movement symptoms in Parkinson's disease

Background: Cerebral white matter hyperintensity seen with MRI is common in Parkinson's disease. There are reports of association of white matter hyperintensity with symptoms of Parkinson's disease.

Methods: Seventy-two patients with Parkinson's disease were recruited from a general hospitals in Daegu Metropolitan City. Diagnosis of Parkinson's disease was based on clinical symptoms, dopamine responsiveness, and CIT-PET. Rating movement symptoms including tremor, rigidity, bradykinesia, postural instability were done. The patients were divided to two groups according to the severity of white matter hyperintensity by modified Erkinjuntti criteria. We investigated any difference between the two groups in movement symptoms using statistical analysis.

Results: There were not differences of severity in Parkinsonian symptoms between the two groups according to the severity of white matter hyperintensity.

Conclusion: We could not find any differences in movement symptoms of patients with Parkinson's disease according to white matter hyperintensity in this study. Study with more numbers may find some differences according to the severity of white matter hyperintensity.

Key words: Parkinsonian signs, White matter lesions, Parkinson's disease, [123I]FP-CIT PET

P23.09

A comparison of the characteristics of those with Parkinson's disease who present with the postural instability/gait difficulty and the tremor dominant subtypes

Merrill Landers¹, Brach Poston²

¹ Department of Physical Therapy, University of Nevada, Las Vegas, Nevada, USA

² Department of Kinesiology and Nutrition Sciences, University of Nevada, Las Vegas, Nevada, USA

Objective: To compare the phenotypes of those with Parkinson's disease (PD) who present with the postural instability/gait difficulty (PIGD) and tremor dominant (TD) subtypes.

Background: Different clinical phenotypes of PD have been widely investigated but not with the new formulas developed for the Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS).

Methods: Fifty-nine individuals with PD (age=72.0 years, SD=9.4; males=45, females=14; Hoehn and Yahr Scale (HY) median=2.5, range=0–5) were classified into three subtypes using the MDS-UPDRS: PIGD (n=41), TD (n=13), and indeterminate (n=5). The phenotype of the two main subtypes were compared using five domains: demographics (age, gender, socioeconomic status (SES), education), PD symptoms (MDS-UPDRS, HY, Parkinson's Disease Questionnaire (PDQ-39)), balance and falls (fall history, Berg Balance Scale (BBS), Activities Specific Balance Scale (ABC), Fear of Falling Avoidance Behavior Questionnaire (FFABQ)), strength and conditioning (2-minute step test (2MST), 30 second Sit to Stand Test (30STS), Timed UP and Go Test (TUGT), activity monitor data), and psychological factors (Zung Anxiety Scale (ZAS), Beck Depression Inventory (BDI), Falls Efficacy Scale (FES), Catastrophizing About Falls Scale (CAFS), and Consequences of Falling Questionnaire (CoFQ)).

Results: There were no differences between PIGD and TD subtypes on age, gender, HY, SES, education, year of diagnosis, and fall history ($p>.202$). The PIGD subtype had poorer gait and balance performance scores (BBS, $p=.023$; TUGT, $p=.049$) and less balance confidence (ABC, $p=.040$). They also exhibited greater fall catastrophization (CAFS, $p=.003$; CoFQ, $p=.001$) and more avoidance behavior (FFABQ, $p=.014$; time stepping, $p=.049$; daily steps taken, $p=.029$). There were no other significant differences ($p>.054$).

Conclusions: Our results offer validity to the notion that the PIGD subtype is indeed related to gait and balance dysfunction and not related to disease severity or length of diagnosis. This balance dysfunction logically leads to decreased balance confidence and increased fall catastrophization. This, in turn, promotes increased fear of falling avoidance behavior which would explain why the PIGD subtype did not fall more than the TD subtype.

P23.10

Freezing of gait is associated with more fear of falling avoidance behavior and less participation in daily physical activity

Merrill Landers¹, Brach Poston², Jennifer Nash³, Jason Longhurst³

¹ Department of Physical Therapy, University of Nevada, Las Vegas, Las Vegas, Nevada, USA

² Department of Kinesiology and Nutrition Sciences, University of Nevada, Las Vegas, Las Vegas, Nevada, USA

³ Cleveland Clinic Lou Ruvo Center for Brain Health, Las Vegas, Nevada, USA

Objective: To compare those with and without freezing of gait (FOG) in Parkinson's disease (PD).

Background: The presence of FOG in PD has been shown to be related to postural instability and fall history. Some have asserted that this is a distinct phenotype with specific demographic, motor, non-motor, and genetic features. Further comparison is warranted.

Methods: Fifty-eight individuals with PD were dichotomized on FOG using a score >1 on Part II item 13 of the Unified Parkinson's Disease Rating Scale (UPDRS): FOG (n=9, age=68.6 \pm 7.0, males=6) and nonFOG (n=49, age=72.9 \pm 9.6, males=39). They were compared using five domains:

1. demographics (age, gender, year of diagnosis, socioeconomic status (SES), education);
2. PD symptoms (UPDRS, Parkinson's Disease Questionnaire (PDQ-39));
3. balance and falls (fall history, Berg Balance Scale (BBS), Timed UP and Go Test (TUGT), Activities Specific Balance Scale, Falls Efficacy Scale (FES), Catastrophizing About Falls Scale, Fear of Falling Avoidance Behavior Questionnaire (FFABQ));
4. strength and conditioning (2-minute step test, 30 second Sit to Stand Test (STS), activity monitor data); and,
5. mental and cognitive function (Mini Mental State Exam, Zung Anxiety Scale, Beck Depression Inventory).

Results: There were no differences on any demographic factor ($ps=.127$). PD motor-related dysfunction was more extensive in the FOG subtype: UPDRS Part II and III ($ps=.041$) and PDQ mobility ($p=.021$). The FOG subtype had a more extensive and recent fall history ($ps=.033$), poorer BBS scores ($p=.004$), slower TUGT times ($p=.048$), higher FES scores ($p=.032$), and higher FFABQ scores ($p=.031$). Also, the FOG subtype had fewer up/downs on the STS and spent less time daily in stepping ($p=.009$), more time sitting/laying ($p=.034$), fewer metabolic equivalents ($p=.023$), and fewer daily steps ($p=.014$) and up/down transitions ($p=.007$). There were no differences for the mental and cognitive factors ($ps>.135$).

Conclusions: Our results support previous data that the FOG subtype has a more extensive fall history and fall risk based on measures of gait and balance performance and balance self-efficacy. The FOG subtype exhibited more fear of falling avoidance behavior which was supported by activity monitor data indicating less participation in daily physical activity.

P23.11

Communicative efficiency and executive function in older adults with an acquired brain injury

Megan Loughnane, Laura Murray

Indiana University, Bloomington, IN, USA

The current study explored the relationship between idea density, macrolinguistic elements of spoken discourse, and the influence of executive functions on these linguistic skills within an older population with mild acquired brain injury. Participants included adults aged 65 and over who were either free from significant

cognitive impairment, or those with a mild, acquired brain injury. Inclusion criteria for the normally aging group included absence of dementia and normal or corrected hearing and vision. Inclusion criteria for the brain injury group included history of acquired brain injury including stroke, Parkinson's Disease, and mild dementia, among others, and normal to corrected hearing and vision. Of the planned sample size for this study (i.e., n=minimum of 20), 4 participants from the brain injury group have completed all testing (see Table 1), and 35 participants from the normal aging group have completed all testing (see Table 2). Data collection is scheduled for completion in August, 2016. Correlations between the rubric score, ID, age, and cognitive test performances will be run both within and between both groups. The macrolinguistic rubric score is expected to positively correlate with age, ID and verbal and nonverbal fluency scores. This study is using a narrative language sample analysis to examine the informativeness and macrolinguistic quality of narrative discourse produced by older adults with mild acquired brain injury, such as Parkinson's Disease. Associations between performances of executive function tests such as verbal fluency and the informativeness measures of language production will provide new insight into this aging population with an acquired brain injury. Additionally, by investigating the differences between normally aging adults and older individuals with mild impairments, such research might identify discourse measures sensitive to discriminating age-related changes from those due to mild brain injury/disease.

Table 1. Demographic and Measure Characteristics of Brain Injury Participants

(N=4)	M	SD	Range
Age	69.25	5.85	65-77
Education	19.00	3.46	16-22
Gender			
Male (N, %)	3	75	
Female (N, %)	1	25	
MMSE	28.66	1.52	27-30
Semantic Fluency	17.40	4.21	11.80-22
CIFA Acceptable Designs	12.50	4.65	6-17
RFFT Unique Designs	63.25	24.01	36-93
Rubric Total Score (Max. 30)	20.50	4.43	16-26
Rubric Main Concept (Max. 15)	10.75	3.20	8-14
Rubric Organization (Max. 5)	3.25	0.95	2-4
Rubric Language (Max. 10)	6.50	1.29	5-8

Table 2. Demographic and Measure Characteristics of Control Participants

(N=35)	M	SD	Range
Age	72.60	7.30	65-92
Education	17.00	1.86	13-20
Gender			
Male (N, %)	11	32	
Female (N, %)	24	68	
MMSE	28.40	1.54	26-30
Phonemic Fluency	16.20	5.17	8.00-34.25
Semantic Fluency	21.20	4.48	15.00-29.20
CIFA Acceptable Designs	16.94	5.65	7-28
RFFT Unique Designs	70.82	22.62	29-105
Rubric Total Score (Max. 30)	22.74	4.47	14-30
Rubric Main Concept (Max. 15)	12.00	2.09	5-15
Rubric Organization (Max. 5)	3.20	1.13	0-5
Rubric Language (Max. 10)	7.66	2.70	1-10
Idea Density	0.45	0.02	0.41-0.51

P23.12

Constipation and Parkinson's disease

Jean MacFadyen¹, Gwyn Vernon²

¹ MacFadyen Learning Enterprises, West Chester, PA, USA

² Nurse Practitioner, Univ. of PA Parkinson's Disease and Movement Disorders Center at the Pennsylvania Hospital, Clinical Instructor- Univ. of PA School of Nursing, National Director-Edmond J. Safra Visiting Nurse Faculty Program at the Parkinson's Disease Foundation, Philadelphia, Pennsylvania, USA

As if the involuntary movement of Parkinson's Disease (PD) is not embarrassing, add constipation to the uncomfortable mix of symptoms with which PD patients must deal! The topic is taboo, difficult to talk about with anyone, including one's closet friend or health care provider. But it is a symptom with which PD patients must manage to achieve a better quality of life. Can we give them relief?

Let's begin by giving them knowledge for which they can take responsibility to optimize their personal situation. Written for the PD patient, two nurses with more than 30 years of PD clinical experience developed a clinically tested monograph which is written in lay language with humor, sensitivity, and specifics...and is free online or by request from the Parkinson's Disease Foundation. It begins with an understanding of the physiological reasons for constipation. The PD patient is taught the spectrum of interventions with specific suggestions which promote optimal health, staged to the degree of difficulty the constipation poses. Comprehensively presented, the information is sequenced in a manner which is easily assimilated and applied. To promote a more in-depth exploration of all aspects of constipation, references online and in-print are provided. The monograph is a foundational starting point for anyone with PD and is useful for reiterating verbal directions given by any health care professional. A presentation about the monograph can be seen at the poster session where a hard copy of the monograph can also be obtained.

P23.13

Autonomic dysfunction in early Parkinson's disease: results from the United Kingdom Tracking Parkinson's study.

Naveed Malek¹, Michael Lawton², Katherine Grosset¹, Nin Bajaj³, Roger Barker⁴, David Burn⁵, Thomas Foltynie⁶, John Hardy⁶, Huw Morris⁶, Nigel Williams⁷, Nicholas Wood⁶, Yoav Ben-Shlomo², Donald Grosset¹, PPRoBaND Clinical Consortium⁸

¹ Institute of Neurological Sciences, Glasgow, United Kingdom

² University of Bristol, Bristol, United Kingdom

³ Queen's Medical Centre, Nottingham, United Kingdom

⁴ John van Geest Centre for Brain Repair, Cambridge, United Kingdom

⁵ University of Newcastle, Newcastle, United Kingdom

⁶ UCL Institute of Neurology, London, United Kingdom

⁷ University of Cardiff, Cardiff, United Kingdom

⁸ United Kingdom

Background: Autonomic dysfunction is common in later stage Parkinson's disease (PD), but less is known about its presence and severity in early stages.

Objective: To assess autonomic dysfunction in recent onset PD, and its relationship with motor and other non-motor domains.

Methods: Detailed patient-reported symptoms of autonomic dysfunction were assessed in the multicenter United Kingdom Tracking Parkinson's study, in cases diagnosed within the preceding 3.5 years. Statistical significance was tested after appropriate adjustment for sex, age, and disease duration differences across groups.

Results: There were 1,738 patients (65.1% male), mean age 67.6 years (SD 9.3), mean disease duration 1.3 years (SD 0.9), and mean Movement Disorder Society unified Parkinson's disease motor rating scale (MDS UPDRS 3) score was 22.5 (SD 12.1). Hoehn and Yahr (H&Y) was stage 1 or 1.5 in 855 cases (49.2%), stage 2 or 2.5 in 783 cases (45.1%), and stage 3 or higher in 100 cases (5.8%). Autonomic severity by SCOPA-AUT score increased significantly across the motor severity stages, from 10.7 (SD 6.2) for H&Y 1/1.5, to 12.7 (SD 7.6) for H&Y 2/2.5, and to 13.5 (SD 6.9) for H&Y 3+ (p<0.001). Urinary, bowel, and sexual dysfunctions were the most commonly reported. Results were intermediate between those previously reported in controls and PD at a mean duration of

10 years. Positive associations were present between autonomic severity and depression ($p < 0.001$), sleep disturbance ($p < 0.001$), postural instability gait difficulty motor subtype ($p < 0.001$), and dementia ($p = 0.016$).

Conclusions: Autonomic dysfunction is common from the earliest stages of PD, and correlates with other markers of disease severity.

P23.14

Clinical features Parkinsonism plus (+) in patients Uzbek population.

Rustambek Matmurodov
Tashkent, Uzbekistan

Parkinsonism may be a manifestation of other degenerative diseases of the central nervous system, combining these cases with oculomotor, pyramidal, cerebellar, cognitive impairment ("Parkinsonism plus").

The purpose of this paper is to explore the clinical features of Parkinson's tertiary developing on the background of other neurodegenerative diseases.

Material and methods. A total of 18 patients aged from 35 to 63 years, against the backdrop of various neurodegenerative diseases, including multiple sclerosis. The average age of patients was 58.5 ± 5.9 years. All patients underwent clinical and neurological, neuropsychological and biochemical studies. The control group consisted of 10 patients with Parkinson's disease (PD).

Results of the study. The results of our study show that resting tremors often occur in patients with PD (87.5%), when the spacecraft in patients with Parkinson's tremor plus met only 25% of patients. Almost all patients with Parkinson's disease distal muscle tone increased by plastic type with elements of "toothed wheel", while the tertiary parkinsonism increased axial muscle tone, and 2 patients met the phenomenon of "toothed wheel". Patients with PD symptoms were all asymmetric, and in patients with Parkinson's plus main symptoms were symmetrical. Patients with non-motor PD violations longer met before the onset of the main motor symptoms, including tremor and hypokinesia rest, whereas in patients with Parkinson's plus almost all patients after a motor symptoms observed non-motor symptoms. In patients with Parkinson's plus almost all patients met cerebellar and pyramidal symptoms, including tremors pronounced level arrangement, as well as in patients with multiple sclerosis in the background of these symptoms was observed with remission. Performance of autonomic disorders in patients with PD and 11.5 points in patients with Parkinson's plus was 8.5 points. The level of the neuron specific protein S100B in the blood plasma in patients with PD was 132.5 ± 6.5 ng/l, while the tertiary parkinsonism 206.3 ± 13.3 ng/l.

Conclusions. Thus, developing Parkinsonism compared to other neurodegenerative diseases has a clinical course that requires different diagnosis. Parkinsonism plus distinguishes by BP, not only motor disturbances and non-motor symptoms distinguish manifestations. S100B Blood plasma may live at a high level due to other neurodegenerative process, including multiple sclerosis.

P23.15

The level of neuron specific protein S100B and the degree of depression in Parkinson's disease.

Rustambek Matmurodov¹, Khanifa Khalimova²
¹ Tashkent, Uzbekistan
² Uzbekistan

One of the non-motor symptoms of affective occurring in Parkinson's disease (PD) is a depression. Parkinsonism is divided

into 3 groups: Parkinson's disease, Parkinsonism syndrome, and Parkinsonism plus (+).

Aim: To investigate the level of specific protein S100B in the blood plasma of patients with Parkinson's disease, depending on the degree of depression.

Material and methods: The material of this study was 51 patients with of Parkinsonism. Duration of the disease – is 0.5 to 8 years. The control group consisted of 9 patients without symptoms of PD. Determines the content of S100B in the blood serum by enzyme immunoassay performed with specific test systems developed on the basis of appropriate monoclonal antibodies on the analyzer Hospitex Diagnostics, Italy according to the instructions supplied with the kit. The level of depression was assessed using the Hamilton test.

Results: The results show that in patients the overall group of patients in the plasma protein level was with among – middle depression – average depression – severe depression – and very severe depression protein level was 114.2 ± 5.3 – 128.9 ± 5.4 – 163.1 ± 6.6 – 236.03 ng/l. In patients of PD with mild depression – average depression – severe depression – and very severe depression protein level was 99.2 ± 5.4 – 127.2 ± 6.4 – 161.6 ± 5.5 – 173.43 ± 4.3 ng/l. In patients of vascular parkinsonism 150.2 ± 5 – 151.5 ± 7.4 – 162.2 ± 4.5 – 259.9 ± 8.5 ng/l. At the tertiary parkinsonism these figures were 181.4 ± 3.6 – 188.6 ± 3.6 – 201.5 ± 4.6 – 253.7 ± 6.6 ng/l. A control group of patients with protein S100B level was 72.6 ± 5.4 .

Conclusions: The level of S100B protein in Parkinsonism not only depends on the form of the disease, and depends on the exact same depression. When Parkinsonism develops in the background of another neurodegenerative disease degree of depression increased.

P23.16

Is on-line motor control really impaired in Parkinson's disease?

Kate Merritt¹, Ken Seergobin², Melvyn Goodale³, Penny MacDonald⁴

¹ The Brain and Mind Institute; Department of Neuroscience, University of Western Ontario, London, Ontario, Canada

² The Brain and Mind Institute, University of Western Ontario, London, Ontario, Canada

³ The Brain and Mind Institute; Department of Psychology, University of Western Ontario, London, Ontario, Canada

⁴ The Brain and Mind Institute; Schulich School of Medicine and Dentistry, University of Western Ontario; Department of Clinical and Neurological Sciences, University of Western Ontario, London, Ontario, Canada

Rather than our actions being under the strict control of a predefined motor plan, fast and precise modifications can be processed and implemented on-line. In healthy controls, such an ability to rapidly correct movements on-line can occur both with and without conscious cognitive control. In contrast, patients with Parkinson's disease (PD) are thought to be selectively impaired in consciously-mediated on-line motor control, while their ability to perform subconscious on-line adjustments remains intact. Here, we argue that such a conscious-subconscious interpretation in PD is problematic. We propose that the alleged deficits in on-line motor control are not due to the consciousness of the correction, but rather are attributable to bradykinesia associated with PD. To address this idea, we modified the traditional double-step paradigm such that the timing of the target jump was adapted to account for confounding effects of PD-related bradykinesia. This was achieved by inducing target perturbations independent of hand movement onset. In addition, we investigated the effects of dopamine-replacement therapy on task performance by evaluating patients and controls on and off of dopamine medication in two identical consecutive sessions. Critically, in doing so, we demonstrated that PD patients

performed on-line corrections similar to that of healthy matched controls -regardless of the consciousness of the action and their medication status.

P23.17

Unmet needs in Parkinson's disease – a patients' and caregivers' perspective

Sarah Mufti, Laura Dixon, Craig Ziegler, Kathrin LaFaver
University of Louisville, Louisville, KY, USA

Background: Parkinson's disease (PD) is a chronic neurodegenerative disorder with motor and non-motor symptoms. Although multiple treatment options are available for PD, many symptoms remain challenging.

Objectives: The goals of this study were to determine most troublesome symptoms of PD, satisfaction with current treatments and need for development of new therapies from a patients' and caregivers' perspective. We furthermore aimed to correlate disease stage with treatment satisfaction and caregiver burden.

Methods: PD patients and caregivers were recruited from the University of Louisville Movement Disorder Clinic and the Parkinson's Support Center of Kentuckiana. Self-administered questionnaires inquired about PD symptom severity, most troublesome symptoms, benefit from treatment interventions and greatest need for development of new therapies. Patients completed a modified version of the patient centered outcomes questionnaire (PCOQ-PD) and the five-item geriatric depression scale. Caregivers completed the PCOQ-PD and the caregiver strain index.

Results: Ninety-seven patients and fifty-one caregivers completed the study. Patients had an average age of 68.4 (SD10.4) years and mean disease duration of 7 (1-24) years. 40% of patients were in early stages of PD (Hoehn and Yahr I/II), 33% in moderate stages (H&Y III) and 27% in advanced stages (H&Y IV/V). Most troublesome symptoms were tremor (25%), walking/ balance problems (21%), fatigue and slowness of movements (7% each). Patient satisfaction with treatment was rated highest for tremor, speech and swallowing problems and lowest for fatigue, constipation and sleep problems. Rating of most troublesome symptoms and treatment satisfaction differed by disease stage. Agreement between patients and caregivers on ratings of most troublesome symptoms and treatment benefit was good, but caregivers rated depression and sleep problems as more troublesome compared to patients ($p<0.05$). Greatest need for development of new therapies was seen for tremor (86%), walking/balance problems (79%) and fatigue (74%). Caregiver strain was present in 21.6%.

Conclusions: Currently available treatment options for PD are not providing optimal symptom relief. From a patient perspective, the symptoms with greatest need for new therapy development were found to be tremor, walking/balance problems and fatigue. Perspectives from PD patients and caregivers need to be taken into account in optimizing clinical care and guiding future research.

P23.18

What PD symptoms should be monitored and which most impact quality of life?

Leah Mursaleen¹, Soania Mathur², Tom Isaacs¹, Helen Matthews¹, Steve DeWitte³, Israel Robledo³, Jon Stamford⁴

¹ United Kingdom

² Canada

³ USA

⁴ Parkinson's Movement, London, United Kingdom

Background: Symptom measurement is integral to monitoring the severity of any condition and its response to treatment. For instance, in diabetes, one can measure blood sugar or in hypertension, blood pressure records are essential. In Parkinson's disease (PD), the criteria used to assess symptomatology are more subjective, principally measurements of the cardinal visible symptoms – tremor, rigidity, bradykinesia and balance. They do not reflect the motor symptoms that make up a large part of the symptom burden in PD.

Methods: Parkinson's Movement conducted a survey of PWPs for 8 weeks starting 13th July 2014 examining PWP attitudes to technology, symptom monitoring preferences and their implications for quality of life in PD.

Results: 492 PWPs took the survey and response rates per question vary between 81 and 100%. The sample was 47% male, 62.3±10.4 years old, with a seven year history of PD. 84% of survey respondents were receiving levodopa while 53% were taking dopamine agonists. The most common motor symptoms were slowness (82%), tremor (62%), rigidity (57%) and dyskinesia (39%). Most common nonmotor symptoms were lack of energy (61%), difficulties sleeping (55%), loss of sense of smell/taste (51%) and constipation (49%). 87% were interested in recording information about their Parkinson's to monitor their well-being (n=467). 97% felt it was 'very' or 'moderately' important to them to understand their own Parkinson's symptoms and recognise patterns in their condition (n=420). 49% of all respondents use a range of methods, from keeping a written diary (27%) to using technology such as apps (15%), to record information about their Parkinson's to monitor their wellbeing. Symptoms that PWPs most wanted to monitor were neuropsychiatric symptoms, postural and gait instability, sleep and fatigue.

Conclusions: PD symptoms that patients wish to monitor and feel most contribute to quality of life include more nonmotor symptoms than the classic diagnostic (motor) symptoms. PWPs are generally comfortable with technology and monitoring symptoms. Monitoring of the most appropriate symptoms for patients should feature in clinical trial design.

P23.19

Impact of levodopa-induced dyskinesias on health-related quality of Life: results from the French COPARK study

Santiago Perez-Lloret¹, Laurence Negre-Pages², Philippe Damier³, Arnaud Delval⁴, Pascal Derkinderen³, Alain Destee⁴, Wassilios Meissner⁵, Francois Tison⁶, Olivier Rascol⁷

¹ Cardiology Research Institute, National Council for Scientific Researc, Buenos Aires, Argentina

² LN Pharma, France

³ Department of Neurology, Hôpital Laënnec, CHU Nantes, Nantes, France

⁴ Department of Neurology, CHU Lille, Lille, France

⁵ Institut des Maladies Neurodégénératives, UMR 5293, CNRS, Bordeaux, France

⁶ Service de Neurologie, CHU de Bordeaux, Bordeaux, France

⁷ Department of Clinical Pharmacology and Neurosciences, University of Toulouse 3, Toulouse, France

Background: levodopa-induced dyskinesias (LIDs) often complicate the course of dopaminergic replacement therapy. The relative impact of LIDs and motor fluctuations has not been sufficiently explored so far.

Objective: To assess the impact of LIDs on HRQoL in this large sample of unselected Parkinson's Disease (PD) patients and to assess the factors related to its presence.

Methods: 683 PD patients of the COPARK survey were evaluated. All patients were assessed in a standardized manner: demographics, treatments, Unified PD Rating Scale (UPDRS), and

Hospital Anxiety and Depression Scale and HRQoL scales (primary outcome: PDQ-39, secondary outcome: SF-36). LIDs daily duration and disability were obtained from UPDRS IV items #32 and #33. Daily duration of wearing-off was obtained from UPDRS IV item #36 and disability was calculated as UPDRS II in OFF- minus ON-state. T-test was employed to compare HRQoL scores between PD patients with or without LIDs. Multivariate testing was performed by logistic regression. The relative contribution of LIDs or wearing-off duration and disability to HRQoL scores was modelled by ANOVA, with eta2 scores representing the effect size of each analyzed factor.

Results: 183 PD patients (26.8%) suffered from LIDs. Significant differences between patients with or without LIDs were detected in PDQ-39 total score (33.1 ± 1.1 vs 45.4 ± 2.1 , $p < 0.01$) as well as in SF-36 physical component score (70.4 ± 1.1 vs 59.1 ± 2.0 , $p < 0.01$) and mental component score (60.6 ± 0.7 vs 54.8 ± 1.3 , $p < 0.01$). Worse PDQ-39 mobility and bodily discomfort subscores. PDQ-39 was related to wearing-off duration ($\eta^2 = 3.0\%$, $p < 0.01$) and LIDs disability ($\eta^2 = 1.3\%$, $p < 0.04$). Factors independently and significantly related to LIDs were levodopa dose and therapy duration, daily equivalent dose of other dopaminergic drugs, age at PD onset, and anxiety. Exposure to oral hypoglucemians and tremor were protective factors.

Discussion: In this study, LIDs correlated with worse HRQoL, specially with feelings of altered mobility and bodily discomfort. PDQ-39 total scores was independently affected by LIDs disability and wearing-off duration. Anxiety affected LIDs negatively and exposure to oral hypoglycemics was a protective factor, which has not been reported before.

P23.20

Extensive training promotes performance improvement but not automaticity in patients with Parkinson's disease

Maria Elisa Pimentel Piemonte¹, Tatiana Oliveria², Camila Miranda², Erica Guelfi², Carolina Souza², Erika Okamoto², Gilberto Xavier²

¹ Sao Paulo, Brazil

² Brazil

Objective: This study evaluated the effects of extensive motor training in a finger-to-thumb opposition sequence task on performance and automaticity of patients at early and intermediate stages of Parkinson's Disease (PD).

Methods: Fifteen PD patients in stage 1 of Hoehn and Yahr classification, 15 patients in stages 2 and 3, and 20 healthy matched control individuals, were extensively exposed to a 5-element finger-to-thumb opposition sequence task, 2 sessions per week, along 5 weeks. On session 1 the participants performed a specified sequence of movements along 60 seconds in a single-task condition; the number of sequences completed correctly was recorded. On sessions 2 to 9 the subjects were exposed to 600 repetitions per session of the same sequence of movements. On session 10 the participants performed 4 different 60-second-duration trials including (1) the trained sequence and (2) a novel sequence, both in a single-task condition, and (3) the trained sequence and (4) a novel sequence, both concurrently with a verbal fluency task, therefore in a dual-task condition. The number of sequences completed correctly was recorded.

Results: All groups exhibited improvement of performance for the trained sequence. However, as expected, this improvement was relatively greater for the control subjects as compared to that seen for PD patients. Performance in the dual-task condition disrupted performance of all groups. However, while for control subjects this disruption was smaller for the trained as compared to the novel sequence, thus indicating automaticity for the trained sequence, for PD patients disruption was equivalent for trained and novel sequences.

Conclusion: Extensive motor training promotes improvement of performance in PD patients at different stages of the disease. However, this improvement is not associated with development of automaticity for the trained sequence. It seems important to take this information into account when planning therapeutic training approaches for PD patients.

P23.21

Association between deficiencies in implicit learning and balance control in patients with Parkinson's disease

Maria Elisa Pimentel Piemonte, Matheus S Alencar, Andre H.

Frazão, Bruno Monte, Antonio J. Galves

Neuromat project, Sao Paulo, Brazil

Aim: To investigate the relation between implicit learning capacity and balance efficiency in patients with Parkinson Disease (PD).

Background: Postural instability is an incapacitating disorder, which increases the risk of falls and the level of dependence in PD patients, marking a significant stage of disease progression. Evidence suggests that deficits in automatic control, hallmark symptom of PD, is associated with the lack of balance. Although all the neural processes of motor automaticity are not fully understood, the main role of implicit system for the process is a consensus.

Methods: Fifteen PD patients in stage 1 of Hoehn and Yahr classification, 15 patients in stages 2 and 3, and 15 healthy matched control individuals, were exposed to a probabilistic implicit learning experiment based on a computational game named "Goalkeeper" (GG) which simulated a soccer game and a balance evaluation by Balance Evaluation Systems Test (BESTest). On session 1 the participants performed the balance evaluation. On session 2, two days after session 1, participants were exposed to five trials of GG. Finally, on session 3, seven days after session 2, the performance in the GG was reassessed. All PD patients were tested in ON period of dopaminergic reposition medication.

Results: The ANOVA for repeated measure showed that PD patients were able to improve their performance in the GG. However, as expected, the improvement was relatively greater for the control subjects as compared to that seen for PD patients. Most important, the decline in balance control was correlated with the ability to improve the performance in the Goalkeeper game.

Conclusion: The decline in balance efficiency is associated to deficiency in probabilistic implicit learning in patients with PD. It seems important to consider this evidence in order to achieve the improved comprehension about the postural instability and to plan more efficient therapeutic approaches to improve the balance in patients with PD.

P23.22

Non motor symptoms dominant subtypes in PD: analysis of 264 cases

Thadshani Rajah¹, Pablo Martinez-Martin², Anna Sauerbier¹, Mubasher A Qamar¹, Alexandra M Rizos³, Lauren Perkins³, Carmen Rodriguez-Blazquez², K Ray Chaudhuri⁴

¹ King's College London and King's College Hospital, London, United Kingdom

² National Center of Epidemiology and CIBERNED, Carlos III Institute of Health, Madrid, Spain

³ King's College Hospital, London, United Kingdom

⁴ National Parkinson Foundation International Center of Excellence, King's College London and King's College Hospital, London, United Kingdom

Objective: To address the burden of non-motor symptoms staging (NMSB) in an ongoing multi-centre study currently with 264 cases.

Background: Non-motor subtypes have been described, however the relationship with NMSB is unclear. (Sauerbier et al 2016; Marras and Chaudhuri 2016). We have analysed cross sectional motor and non motor data from 264 cases.

Methods: An international PD database (part of the MDS non motor study group initiative) of 264 cases was analysed and 249 cases were evaluable. 3 specific groups could be identified; Group A: NMSB mild with mild HY stage (HY stages 1-2), Group B: NMSB severe with mild HY and Groups C: NMSB very severe with mild HY (groups B and C belonging to NMS subtypes). For analysis, Kruskal-Wallis (K-W) and the Mann-Whitney test were used.

Results: Groups B and C with NMS subtypes of sleep, cognitive, neuropsychiatric and autonomic dominant phenotypes had mild motor disease, were significantly younger and had significantly higher overall NMSB, sleep, anxiety, depression and worse quality of life.

Conclusions: This ongoing study provides evidence of the need to employ routine NMS measurements in clinic and identification of NMSB along with motor state to ascertain non motor subtypes which may influence prognosis and treatment.

P23.23

The integration between posture, manual control, and speech in people with Parkinson's disease

Hoda Salsabili, Jessica Huber, Sandy Huber, Kara Simon, Meghan McDonough, Shirley Rietdyk, Jeffrey Haddad
Purdue University, West Lafayette, IN, USA

The ability to modulate posture based on the demands of a concurrent manual task is critical when performing complex multi-task behaviors common to daily life (Haddad, Rietdyk, Claxton, & Huber, 2013). For example, individuals adopt a more rigid posture when performing a precision manual task. However, when less manual precision is required, adults adopt a more relaxed posture, which allows the body to remain more flexible and better attenuate any threat to balance (Haddad, et al. 2013). Multi-task behaviors such as speaking while walking or leaning forward to pick up an object are difficult for people with Parkinson's disease (PD) to perform due to reductions in cognition, mobility, and postural stability (LaPointe, Stierwalt, Maitland, 2010). It is therefore critical to understand how people with PD control reaching while performing complex real-world multi-task behaviors. In this study, we examined how manual movements are controlled in people with PD and healthy older adults while speaking.

Four people with PD and five healthy older adults fit a block into either a small or large opening and then held the block in the opening for 30 s while either speaking or not speaking. Wrist kinematics and center of mass were assessed. We analyzed the dependent variables using repeated measures ANOVA.

An interaction between speech and group was observed as the participants accelerated their arm toward the opening. Individuals with PD took longer to reach peak arm acceleration when speaking compared to older adults. However, when not speaking, arm acceleration towards the target opening was similar between older adults and people with PD. There were no significant differences in center of mass.

To perform a precision manual movement, the arm must first accelerate and then decelerate as it approaches a target (e.g. object to be grasped). Since acceleration time is measured relative to the total reach time, a longer acceleration time means a shorter deceleration time. The deceleration phase of this movement is a critical component to manual accuracy since this is when adjustments to the arm trajectory are made. Our results suggest that people with PD spend more time accelerating and less time decelerating. It appears people with PD have a difficult time performing a precision manual task while speaking. Speaking

appears to hinder relationship that naturally occurs between phases of a precision manual movement in people with PD and can result in less accurate reaching.

P23.24

Non-motor symptoms profiles in White Caucasian, Asian and Black African Caribbean patients with Parkinson's disease living in the United Kingdom

Anna Sauerbier¹, Alexandra Rizos², Lauren Perkins², Theresa Chiwera², Dhaval Trivedi², Pablo Martinez-Martin³, Mubasher Ahmad Qamar⁴, Philipp Loehrer⁵, Anne Martin⁶, Miriam Parry⁷, Thadshani Thavayogarah⁸, Nikolay Dimitrov⁷, Richard Brown⁸, K Ray Cahudhuri¹

¹ Neurology, King's College Hospital, London, UK; Institute of Psychiatry, Psychology and Neuroscience, King's College Hospital, London, UK, London, United Kingdom

² Neurosciences, King's College Hospital, London, UK, United Kingdom

³ National Center of Epidemiology and CIBERNED, Carlos III Institute of Health, Madrid, Spain, United Kingdom

⁴ Institute of Psychiatry, Psychology and Neuroscience, King's College Hospital, London UK, United Kingdom

⁵ Institute of Psychiatry, Psychology and Neuroscience, King's College Hospital, London UK; Department of Neurology, University Hospital Cologne, Cologne, Germany, United Kingdom

⁶ Neurology, King's College Hospital, London, UK, United Kingdom

⁷ Neurology, Lewisham and Greenwich NHS Trust, London, UK, United Kingdom

⁸ Institute of Psychiatry, Psychology and Neuroscience, King's College Hospital, London UK, United Kingdom

Background: Ethnic variations have been described in several conditions including diabetes, high blood pressure, and multiple sclerosis. Preliminary data indicate there may be differences in patients with Parkinson's disease (PwP).

Objective: To explore variations between motor and non-motor symptoms (NMS) in White Caucasian (WC), Asian, and Black African Caribbean (BAC) PwP living in the United Kingdom (UK).

Methods: In this prospective, longitudinal, observational study WC, Asian, and BAC PwP attending the outpatients' clinic at King's college hospital have been included. Demographics as well as motor, quality of life and non-motor data assessed with validated tools were recorded.

Results: Data from 67 UK-WC PwP (65.7% male; mean age 65.3±12.1 years; mean disease duration 7.2±5.2 years; mean age at PD onset 58.1±12.8 years; mean total SCOPA-Motor score 15.6±9.8; median Hoehn and Yahr 2 (range 1-4)), 20 UK-Asian PwP (70.0% male; mean age 61.1±11.3 years; mean disease duration 7.8±5.2 years; mean age at PD onset 53.3±10.9 years; mean total SCOPA-Motor score 20.8±13.9, median Hoehn and Yahr 2 (range 1-5)) and 21 UK-BAC PwP (81.0% male; mean age 63.3±11.5 years; mean disease duration 4.9±5.2 years; mean age at PD onset 58.4±12.5 years; mean total SCOPA-Motor score 20.7±8.1; median Hoehn and Yahr 2 (range 1-5)) are presented.

UK-Asian PwP and UK-BAC PwP had higher NMSScale total scores compared to UK-WC PwP. Applying the Kruskal Wallis equality-of-populations rank test we found a significant difference between the 3 ethnic groups in the mood and cognition domain as well as NMSScale total scores and Mini Mental State Examination total scores.

Conclusion: These preliminary results suggest that non-motor symptoms burden may be higher in the UK non-white Parkinson's disease population compared to the WC counterparts.

Acknowledgement: This study was supported by Kirby Laing foundation as well as Parkinson's UK Charity.

P23.25**Engaging people with Parkinson's in determining and defining research priorities: The PDF Community Choice Research Award**

Karlin Schroeder¹, Beth Vernaleo¹, Diane Cook¹, James Beck¹, Veronica Todaro²

¹ Parkinson's Disease Foundation, New York, New York, USA
² USA

Objective: To understand how engaging people with Parkinson's disease (PD) and their care partners in determining and defining research priorities can help address the unmet needs of patients and advance research.

Introduction: The Parkinson's Disease Foundation (PDF) is committed to ensuring that people living with Parkinson's disease are partners throughout the research process. This partnership begins with the creation of ways to identify patient needs and priorities as determined by patients themselves. PDF launched the Community Choice Research Award (CCRA) in 2013. The purpose of this award is to solicit priorities from patients, turn them into research questions and then fund a one and a half day workshop among scientific and clinical experts and people with Parkinson's and care partners on each of the selected priorities.

Methods: Research priorities were determined by questionnaires administered to people with PD and care partners via the PDF website and in person via electronic tablet. Research areas were reviewed and selected by PDF's scientific advisory board based on criteria as described above. The impact of patient involvement was determined via a survey administered to researchers and clinicians who attended the workshops.

Results: Responses for research priorities were far reaching but could be categorized into general areas. Unsurprisingly, Parkinson's therapies represented the topic area within which the greatest number of responses could be categorized. Based on these results PDF funded four CCRA workshops covering the following topics: gastrointestinal issues, fatigue, cognition and dystonia. The identified research areas were chosen because they are not well-managed with current therapies, lack a substantial body of research in current literature regarding etiology or treatment, are particularly disabling aspects of PD that lead to reduced quality of life and were suitable for the workshop format. Researchers felt patient input enriched the meeting dialog and were willing to including patients in future scientific conversations after the meeting.

Conclusion: Engaging people with PD and their care partners in determining research priorities can lead to identifying unmet needs that warrant attention by scientists. Research who collaborate with patients on defining research priorities find that it adds value, influences outcomes and increases the likelihood of patient involvement in future scientific conversations

P23.26**Evaluation of diagnostic criteria for idiopathic Parkinson's disease**

Nicholas Scott, Angus Macleod, Carl Counsell
University of Aberdeen, Aberdeen, United Kingdom

Background: New diagnostic criteria for idiopathic Parkinson's disease have recently been published, but these have not yet been evaluated. We sought to retrospectively apply the MDS diagnostic criteria in a population based incident cohort of PD and compare this with the UK PD Brain Bank criteria (UKPDBB).

Methods: The PINE study is a community-based incidence study of parkinsonism with lifelong follow-up in Aberdeen, UK, diagnosed between 2002-04 and 2006-09. The diagnostic criteria were retrospectively applied to clinical data from the PINE study

database, with reference to case notes where necessary, at baseline (diagnostic visit) and at five years of follow-up. We calculated the sensitivity and specificity of the MDS and UKPDBB criteria at these time-points against the most likely clinical diagnosis (both PD and dementia with Lewy bodies for the MDS criteria) as made by a movement disorder specialist at end of available follow-up. Only those surviving to five years were included in the analysis at five years.

Results: 333 incident parkinsonism patients at baseline were identified from the PINE database (60.9% male; median age at diagnosis of 76.9 years (IQR 11.0)). Patients were followed for between 5 and 12 years. 51 patients with parkinsonism had an autopsy. The sensitivity and specificity for expert clinical diagnosis of PD versus histology was 88% and 84% respectively. At baseline, the sensitivity and specificity for UKPDBB criteria versus clinical diagnosis was 83% and 72% respectively and versus histological diagnosis was 90% and 65%. At five years, the sensitivity and specificity for UKPDBB criteria versus clinical diagnosis was 71% and 73%. At baseline, the sensitivity and specificity for MDS criteria versus clinical diagnosis was 70% and 83% respectively and versus histological diagnosis was 62% and 93%. At five years, the sensitivity and specificity for MDS-defined PD versus clinical diagnosis was 68% and 99%. Insufficient autopsies have been performed so far in those surviving at least five years to allow meaningful comparisons with histology at this time point.

Conclusions: In this community-based sample of parkinsonism the MDS criteria tended to be less sensitive but more specific. We hypothesise that the relatively old age of this cohort may have led to a higher number of "red flags" than may be expected in younger cohorts, leading to lower sensitivities than were expected. Future analyses when more histology is available would be useful.

P23.27**Motor and non-motor symptoms of Parkinson's disease by gender and disease duration**

Ju Young Shin¹, Ryan Pohlig², Barbara Habermann¹

¹ University of Delaware, College of Health Sciences, School of Nursing, Newark, Delaware, USA

² University of Delaware, College of Health Sciences, Newark, Delaware, USA

Parkinson's disease (PD) is a neurodegenerative disease with a wide range of symptom presentations. However, only a few studies have examined gender differences in the simultaneous presentation of motor and non-motor symptoms in PD. Even less literature exists that examines the presentation of symptoms by disease duration.

The purpose of this research was to further explore these relationships comparing motor and non-motor symptoms of PD by gender and the duration of PD. This study was part of a cross-sectional descriptive survey, collected from March 2015 to February 2016 using community-dwelling people with PD in the U.S. Institutional Review Board approval was obtained.

A total of 141 participants (64.6% response rate) were included in this study. The mean age of participants was 69.7 (SD=8.21). Participants were mostly white (97.2%), married (87.2%) and not working (86.7%). The mean years of education were 15.8 (SD=3.15). There were no demographic differences between men (59.6%) and women (40.4%). Despite no gender differences in the number of motor symptoms (men 4.04 vs. women 3.49, $p=.11$) men reported more non-motor symptoms than women (9.71 vs. 8.09, $p=.049$). Men reported more rigidity, speech problems, sexual dysfunction, memory problems, and socializing problems in comparison to women. The number of motor symptoms in three groups divided by increments of five years was significantly increased ($p=.034$) while the number of non-motor symptoms did not. Postural instability, freezing, off periods, and dyskinesia in three

groups were significantly increased as the duration of PD increased. Speech problems and hallucinations/psychosis were significantly increased as the duration of PD increased.

Findings of this study showed differences in PD symptom reports by gender and duration of the disease. Given the multifaceted feature of symptoms, thorough assessment of motor and non-motor symptoms could decrease the risk of inadequate symptom management. Ongoing symptom assessment and treatment could improve function and quality of life in people with PD. Lastly, provision of information regarding PD symptoms at each stage may help people with PD and their caregivers in planning their future care and life.

P23.28

Egogram characteristics in Japanese patients with Parkinson's disease

Tomomi Shinoda¹, Tetsuya Maeda²

¹ Department of Neurology, Research Institute for brain and blood vessels-Akita, Japan

² Division of Neurology, Iwate Medical University and Department of Neurology, Research Institute for brain and blood vessels-AKITA, Japan

Objectives: This study aims to clarify personality characteristics in Japanese patients with Parkinson's disease (PD) by using the Tokyo University Egogram New Version II (TEG II).

Methods: Patients were consecutively enrolled from June to October 2015 in our institute and they completed TEG II. TEG II is a 53-item personality questionnaire and it is based on the theory of transactional analysis created by Erick Berne. Ego state is an important concept to understand personality in TEG II. Ego states include the patterns of thinking, feeling and behavior. The strength and the profile based on the scores of each ego state can indicate the personality characteristics. Ego states can be classified as 4 categories including Critical Parent (CP), Nurturing Parent (NP), Adult (A), Free Child (FC) and Adopted Child (AP). The score of each ego state and the profile in TEG II were statistically analyzed. All this study was approved by our institutional ethical committee.

Results: We enrolled 97 patients (41 males and 56 females) and their mean age was 69.7±8.9 (standard deviation). The median of Hoehn & Yahr stage was 2. Mean MDS-UPDRS and MMSE were 43.9±21.3 and 27.1±2.4. The scores of CP, NP, A, FC and AC were 12.2±4.6, 15.1±3.8, 11.1±4.8, 12.0±4.3 and 9.1±5.3, respectively. The score of CP and mean disease duration (90.9±62.3 months) ($r=0.3$, $p<0.05$), mean levodopa dose (381.4±155.8mg) ($r=0.2$, $p<0.05$) had significant correlation with low correlation coefficient. The score of NP was significantly higher than the score of CP, A, FC and AC ($p<0.001$). The score of AC was significantly lower than the score of CP, NP, A and FC ($p<0.001$). NP higher patterns (15.5%), CP higher patterns (12.4%) and AC lower patterns (11.3%) were observed frequently.

Conclusions: Egogram characteristics were changed in association with disease duration and levodopa dose. The score of NP was significantly higher than the scores of other ego states and most enrolled PD patients showed NP higher pattern, which indicates the personality taking care of others well but also sometimes interfering with them. The standardized analysis of healthy Japanese population has shown that AC higher pattern is the most common one. This study could suggest that NP higher pattern is a characteristic personality of the patients with PD in Japan.

P23.29

Assessment of several simple, low-tech "real-life" smell tests in PD patients and controls: an international, multicentre study designed, tested and analysed by PD patients

Jon Stamford¹, Jill Carson², Veerle Aertsen³

¹ Parkinson's Movement, London, United Kingdom

² Canada

³ Belgium

Background: Microsmia or even anosmia can precede both the development of motor symptoms and diagnosis in PD. The University of Pennsylvania Smell Identification Test (UPSIT), a 40 item scratch and sniff test is predominantly a research instrument rather than part of the battery of diagnostic tools. We wanted to look at more everyday olfactory assessments to determine loss of sense of smell in PD.

Methods: 66 experimental subjects (46 PD, 20 controls) participated in tests of olfactory function. In test 1, subjects smelt 29 male and female fragrances and had to ascribe the correct gender to each. In test 2, 63 subjects (44 PD, 19 controls) smelt 5 samples (all distilled water) and were asked to say whether they smelt roses, fruit, rubber, bleach or nothing. In test 3, 20 subjects (14 PD, 6 controls) were asked to identify 10 components of the bouquet of 4 wines from a list of 16 choices. Subjects also completed a questionnaire including questions about sense of smell.

Results: PD patients had significantly ($P<0.001$) poorer subjective sense of smell based on self-assessment ($4.1\pm2.4SD$) than controls ($8.5\pm1.8SD$) on a 0–10 scale. In test 1, there was no significant difference between PD and control groups identifying the gender of fragrances. Neither controls (16.9 ± 3.8) nor PD patients (15.6 ± 3.7) scored higher than random guesswork (14.5). In test 2, PD subjects and controls did not differ in the number of correct identifications (2.4 and 3.0 respectively out of 5). In test 3, there was no significant difference between PD subjects and controls in the number of bouquet components identified (3.7 and 4.0 out of 10 respectively).

Conclusions: An ideal olfactory test should allow sufficient dynamic range for differentiation of control and anosmia groups. Previous work by ourselves under equivalent test conditions demonstrated clear separation of PD and control groups on the UPSIT test [Stamford, 2016] and correlation with self-assessed anosmia. Despite comparable differences in self-assessed sense of smell with the previous trial [Stamford, 2016], the tests used here do not appear to differentiate between controls and PD patients. Largely, this appears to be due to low scores by the control cohort, thus allowing insufficient dynamic range for differentiation of normosmia and microsmia.

Stamford JA (2016) Smell perception and judgement in pd patients: results of a study designed, conducted, analysed and reported by PD patients (presented at MDS, Berlin, June 2016).

P23.30

The FDA is listening: integrating the voice of the patient in drug development for Parkinson's disease

Diane Stephenson¹, Theresa Mullin², Eric Bastings³, William Dunn³, Susanne Goldstein³, Gerald Podskalny³

¹ Critical Path Institute, Tuscon, Arizona, USA

² U.S. Food and Drug Administration, Silver Spring, MD, USA

³ FDA, Silver Spring, MD, USA

Background: Traditional drug development has not systematically incorporated patients' perspectives and preferences into the process. Two new initiatives are addressing this need: FDA's Patient-Focused Drug Development (PFDD) initiative, a commitment under the fifth authorization of the Prescription Drug User Fee Act (PDUFA V), which aims to more systematically gather

patients' perspectives on their condition and available therapies; and the Critical Path for Parkinson's (CPP) consortium, a public private partnership sponsored by C-Path and Parkinson's UK, to facilitate the path of PD drug development focused on patient needs. On September 22, 2015, the FDA hosted a public PFDD meeting focused on Huntington's disease and Parkinson's disease (PD) to gain patient feedback.

Objectives: To present the highlights from the first PFDD meeting held at the FDA for PD as a catalyst to raise awareness of the importance of listening to the needs of those living with PD.

Methods: 100 participants attended the FDA's PFDD meeting in person and >160 joined the four hour PD segment of the meeting remotely. Two-thirds of the participants who attended in person were diagnosed with PD. The FDA heard directly from participants with emphasis on symptoms and the inadequacy of the existing treatment options.

Results: FDA emphasized their commitment to safety as the utmost priority when reviewing new drugs and fully acknowledged the large unmet need for new, effective PD treatments. Participant testimonials focused on quality of life issues and the impact of PD on the daily life. Gathering of public input was extended for two months past the date of the meeting and all feedback was compiled to prepare a voice-of-the-patient report that has been made publically available. This information will be integrated into evaluation of improved outcome measures and assessment of risk/benefit in future trials.

Conclusions: By ensuring a thorough understanding of the impact of the diverse manifestations of PD from a patient perspective, the FDA's PFDD initiative promises to identify unmet needs and ensure that new PD therapies are given regulatory consideration. This goal aligns with those of the Critical Path for Parkinson's (CPP) consortium, to accelerate development of effective treatments for those with PD through a robust collaboration centered on data sharing.

FDA Patient Focused Drug Development Website and meeting materials: <http://www.fda.gov/Drugs/NewsEvents/ucm451807.htm>

P23.31

Depression in Parkinson's disease: prevalence, pharmacological treatment and association with brainstem raphe echogenicity

Toomas Toomsoo¹, Rene Randver¹, Inga Liepelt-Scarfone², Liis Kadastik-Eerme¹, Toomas Asser¹, Inna Rubanovits¹, Daniela Berg², Pille Taba¹

¹ Estonia

² Germany

Introduction: Depression is one of the most common non-motor manifestations of Parkinson's disease (PD). Depressive symptoms in PD patients often remain untreated, underlining the need to understand the factors that play a role in the prevalence of depression in PD. The objective of this study was threefold: to describe the prevalence (1) and pharmacological treatment (2) of depression, as well as analyze possible associations between brainstem raphe (BR) echogenicity and depressive symptoms (3) in an Estonian sample of patients with PD and age- and education-matched healthy (non-PD) controls.

Methods: The study included 266 PD patients and 168 age- and education-matched healthy controls. Disease and depression severity were assessed. In addition, data on independence in daily living and quality of life, cognitive functioning, and antidepressant use was documented. BR was visualized by transcranial sonography (TCS). Data was pooled and analyzed using group comparisons and correlation analysis.

Results: The mean age was 69.7 (±8.7). 55.4% of controls (n=168) were found to be depressed, whereas the percentage of depressed

individuals in the PD group (n=266) was 74.4, of which 35.7% had major depression. 6.8% and 13.7% of the patients with minor and major depression, respectively, were using antidepressants at study time. BR echogenicity in PD patients and controls was significantly correlated with the overall severity of depression as assessed by the BDI ($\bar{n}=0.593$, $p<0.001$ and $\bar{n}=0.663$, $p<0.001$, respectively).

Conclusion: Depression in PD patients is under-treated. BR echogenicity in both PD patients and controls was directly related to the overall severity of depression. The effect was stronger in the PD group, indicating a broader monoaminergic deficit. New efficacious treatment avenues to account for treatment-resistant depression should be pursued.

P23.32

mPower: an iPhone base study of Parkinson's disease provides personalized measure of disease

Andrew Trister, Elias Chaibub-Neto, Stephen Friend
Sage Bionetworks, Seattle, WA, USA

Objective: mPower is an observational study of Parkinson disease (PD) conducted completely through an iPhone app focused on the ability of sensors within the phone to measure symptoms of PD and detect variations within those symptoms.

Background: Despite the many advances in technologies to help measure the symptoms of PD, these measurements have had minimal impact on the clinical management of the disease. We hypothesize that these types of measurements can be more informative when performed repeatedly and outside the clinical context. mPower is a free iPhone app built on an open-source research framework (ResearchKit) that enables study participants to donate their data from sensor-based activities and survey instruments.

Methods: All iPhone users in the US over 18 years of age are eligible to participate in mPower. Informed consent was obtained using an electronic consent module within the app, as reviewed by the Western IRB. All activities and surveys within the study were optional. Participants answered a background survey, performed four separate activities to measure symptoms of PD as reflected by tapping, phonation, walking and balance that utilized the sensors within the iPhone: screen, microphone, accelerometer and gyroscopes. Each recording was analyzed with a series of statistical and signal processing methods to quantify over 300 different dimensions of performance. The multiple recordings for an individual before and after dopaminergic medication were used to build a mathematical model of disease changes with random forests approach.

Results: mPower was launched in the US app store in March 2015 with an enrollment of over 15,000 participants in the first nine months. Of those responding to the background survey, over 1,700 participants report a diagnosis of PD, with over 9,000 controls enrolling. Developing features of performance from each of the activities (tapping, gait, turning and balance, phonation), the heterogeneity and individual characteristics of the disease could be directly measured and quantified. These, in turn, were returned to participants as individual reports that can be shared with others.

Conclusions: Frequent assessment of symptoms of PD can be made with a personal smartphone using an app-based study. The features extracted from activities included in mPower provide a personalized quantified measure of changes to symptoms in PD that can be clinically validated.

P23.33**Attenuation of hyperalgesia responses via the modulation of 5-HT signaling in the rostral ventromedial medulla and spinal cord in a 6-OHDA-induced rat model of Parkinson's disease**

Fen Wang, Chentao Wang, Chengjie Mao, Yaping Yang, Xiaoj Zhang, Dongjun Lv, Chunfeng Liu
People's Republic of China

Background: Although pain is one of the most distressing non-motor symptoms among patients with Parkinson's disease (PD), the underlying mechanisms of pain in PD remain elusive. The aim of the present study was to investigate the role of 5-HT in the rostral ventromedial medulla (RVM) and spinal cord in pain sensory abnormalities in a 6-OHDA-treated rat model of PD.

Methods: The rotarod test was used to evaluate motor function. The radiant heat test and von Frey test were conducted to evaluate thermal and mechanical pain thresholds, respectively. Immunofluorescence was used to examine 5-HT neurons and fibers in the RVM and spinal cord. High-performance liquid chromatography (HPLC) was used to determine 5-HT and 5-HIAA levels.

Results: The duration of running time on the rotarod test was significantly reduced in 6-OHDA-treated rats. Nociceptive thresholds of both mechanical and heat pain were reduced compared to sham-treated rats. In addition to the degeneration of cell bodies and fibers in the substantia nigra pars compacta (SNpc), the number of 5-HT neurons was dramatically decreased in the RVM. Intra-RVM microinjection of 5,7-DHT partially reversed pain hypersensitivity. In addition, 5-HT concentrations in both the RVM and spinal cord were reduced. Interestingly, the enhancement of 5-HT levels via the administration of citalopram attenuated pain hypersensitivity.

Conclusions: These results suggest that the descending 5-HT facilitatory pathway in the RVM and the decreased 5-HT content in the RVM and spinal cord may play a role in hyperalgesia in the 6-OHDA-induced rat model of PD.

P23.34**The 3m Backward Walk Test and Its ability to assess fall risk among individuals with Parkinson's disease**

Emily White¹, Valerie Carter¹, Dirk Deheer¹, Kay Wing²

¹ Northern Arizona University Department of Physical Therapy and Athletic Training, Flagstaff, AZ, USA

² SWAN Rehab, Phoenix, AZ, USA

Background: Individuals with Parkinson's Disease (PD) often demonstrate disease specific functional deficits such as difficulty maintaining balance with backward stepping. Current tests and measures assessing fall risk among PD populations such as the Timed Up and Go (TUG) do not test the ability to maintain balance while walking backwards, and may not identify potential disease specific deficits that can lead to loss of balance and falling within this population.

Objective: Our goal was to determine whether among people with Parkinson's Disease (PD), the 3m Backward Walk Test (3MBWT) can more accurately classify people's fall history in the past year compared to the TUG.

Method: Twenty-nine individuals with PD were assessed for fall risk using the 3MBWT and the TUG. Fall history was documented within the last week, month, and six months to one year. Descriptive statistics were used to assess which cutoff most accurately captured falls in the previous year.

Results: Average time on the TUG was 10.9±4.26 seconds and 5.55±2.48 seconds for the 3MBWT. A total of 19 of the 29 people reported falling in the past 12 months. The TUG with 12 seconds as the cut off classified only 5 of the 19 people as risk for falls; 4 of the 5 reported a fall, and overall 44.8% of all people were correctly

classified. A 3MBWT cut off of greater than 4.8 seconds had the highest accuracy, with 14 individuals classified as high risk; 11 of the 14 reported falling, and over 62% of people were classified correctly. Of the 9 people classified as low risk with the TUG, but high risk with the 3MBWT, 8 of 9 reported falling.

Discussion: The TUG (using the cut off of 12 seconds) underestimated the number of people with PD who fell the previous year. The 3MBWT (using a cut off of greater than 4.8 seconds) was able to capture a substantially greater proportion of fallers, possibly due to capturing more disease specific limitations.

P23.35**Recognition, diagnosis, and management of neurogenic orthostatic hypotension in patients with Parkinson's disease**

Adam Ziemann¹, L. Arthur Hewitt¹, Timothy Harrison¹, Michelle Widolff¹, Steven Vernino²

¹ Lundbeck LLC, Deerfield, IL, USA

² UT Southwestern Medical Center, Dallas, TX, USA

Background: In response to a positional change from supine or sitting to standing, the baroreceptor reflex in the autonomic nervous system signals for vasoconstriction and heart rate (HR) increases to compensate for hemodynamic shifts in blood volume. Neurogenic orthostatic hypotension (nOH), defined as a sustained decrease in systolic blood pressure (BP) =20 mmHg or diastolic BP =10 mmHg within 3 minutes of standing or head-up tilt, is caused by an insufficient autonomic response to orthostatic stress. Estimates of prevalence suggest that symptomatic nOH occurs in 18% of patients with Parkinson disease (PD), and is common in other synucleinopathies characterized by either central autonomic failure (multiple system atrophy [MSA; 81%]) or peripheral autonomic degeneration (pure autonomic failure [100%] or dementia with Lewy bodies [31%]). In these disorders, nOH results from sympathetic failure due to inadequate production or release of norepinephrine (the effector neurotransmitter in the sympathetic nervous system).

Symptoms/Clinical Features: The cardinal symptoms of nOH are dizziness/lightheadedness and a sensation of presyncope; other signs and symptoms may include visual disturbances, head/neck pain ("coat hanger headache"), cognitive impairment, fatigue, syncope, and weakness. An increased risk for falls has been noted in patients with nOH. Patients often experience BP variability throughout the day and supine hypertension as a consequence of baroreflex failure. Studies in PD patient populations suggest that the clinical features of nOH have negative effects on quality of life.

Diagnosis: nOH diagnosis involves recognition of symptoms, consideration of other potential causes of orthostatic hypotension (ie, cardiac disorders or certain medications), orthostatic BP and HR measurements, a neurologic exam, and other assessments.

Treatments: If nOH symptoms do not improve with initial nonpharmacologic measures, pharmacotherapy with agents that cause vasoconstriction or expand blood volume may be considered. One recent option, the norepinephrine prodrug droxidopa, is approved by the US Food and Drug Administration for the treatment of orthostatic dizziness, lightheadedness, or the "feeling that you are about to black out" in adult patients with symptomatic nOH, caused by primary autonomic failure (PD, MSA, and pure autonomic failure), dopamine β-hydroxylase deficiency, or nondiabetic autonomic neuropathy.

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CLINICAL SCIENCES: PROGRESSION & PROGNOSIS

P24.01

Impact of Bdnf rs6265 variant on response to dopaminergic therapy and deep brain stimulation

D. Luke Fischer¹, John Goudreau², Barbara Pickut³, Brian Berryhill³, Peggy Auinger⁴, Mallory Hacker⁵, P. David Charles⁵, Jack Lipton¹, Allyson Cole-Strauss¹, Caryl Sortwell¹

¹ Michigan State University, Grand Rapids, MI, USA

² Michigan State University, East Lansing, MI, USA

³ Mercy Health Saint Mary's, Grand Rapids, MI, USA

⁴ University of Rochester, Rochester, NY, USA

⁵ Vanderbilt University, Nashville, TN, USA

The clinical response to levodopa and deep brain stimulation is heterogeneous; the ability to use genotyping to inform optimal treatment strategies would be a powerful tool. Pharmacogenetic considerations for Parkinson's disease (PD) have previously focused on genes that alter drug metabolism or dopamine transmission, and the influence of patient genotype on deep brain stimulation (DBS) outcomes has received little attention. Brain-derived neurotrophic factor (BDNF) is a critical modulator of neurotransmission and synaptic plasticity within the basal ganglia. Preclinical work in rodent models has implicated BDNF signaling in the antiparkinsonian efficacy of both levodopa and DBS. A common single nucleotide variant in Bdnf (rs6265) reduces activity-dependent BDNF release. Therefore, possession of the Bdnf rs6265 minor allele has significant potential to alter basal ganglia functioning. We have previously shown that early-stage PD subjects carrying the minor allele of the Bdnf variant rs6265 exhibit a less robust response to dopaminergic therapy following 12-18 months of treatment (and sustained at 24 months) compared to subjects who carry only the major allele, as measured by the UPDRS and the PDQ-39. In contrast, subjects who received STN DBS responded well to therapy over the identical treatment interval regardless of Bdnf rs6265 status. In the present study we will validate these findings in two larger subject cohorts: 1) 540 early-stage PD subjects from the NIH NINDS Exploratory Trials in Parkinson's Disease Long-term Study-1 (NET-PD LS-1) treated with dopaminergic medication and 2) 38 mid- to late-stage PD subjects treated with STN DBS. Subjects will be stratified by Bdnf rs6265 variant status, and response to therapy over time will be assessed by UPDRS and PDQ-39 metrics. Genotyping and clinical metric analysis is ongoing. Validation of our previous findings in these larger subject cohorts would suggest that Bdnf rs6265 genotyping is useful for predicting long-term response to drug therapy and counseling PD patients regarding the consideration of STN DBS.

P24.02

Economic burden in advanced Parkinson's disease patients uncontrolled on oral medications

Yash Jalundhwala¹, Prasanna Kandukuri¹, Thomas Marshall¹, Stephanie Dubow², Jorge Zamudio³, Cynthia Theigs⁴, Kavita Sail⁵

¹ Global Health Economics and Outcomes Research, AbbVie Inc., North Chicago, IL, USA

² US Medical Affairs, North Chicago, IL, USA

³ US Medical Affairs, AbbVie Inc., North Chicago, IL, USA

⁴ US Healthcare Solutions, AbbVie Inc., North Chicago, IL, USA

⁵ Global Health Economics and Outcomes Research, AbbVie Inc., North Chicago, Illinois, USA

Background: The progressive and disabling nature of Parkinson's disease (PD) imposes a significant economic burden on patients, caregivers and payers. The effectiveness of the oral medications in maintaining PD symptoms reduces with advances in the disease. Advanced PD (APD) patients may not be adequately controlled on oral medications.

Objective: To compare the direct costs of APD patients uncontrolled on oral medications with demographically matched non-PD and non-APD patients

Methods: PD patients (=2 PD ICD-9-CM codes; 332.0) from 1/1/2000-12/31/14 were selected from a large de-identified commercial insurance database. PD patients were classified as non-APD or uncontrolled APD. Uncontrolled APD was defined as PD patients taking 5 or more doses and = 1000 mg of oral levodopa per day. This definition was based on published clinical opinion on characteristics of PD patients eligible for device-aided treatments. The index date was the patient's first observed PD diagnosis for the non-APD cohort and the first sign of the advanced PD for the uncontrolled APD cohort. Uncontrolled APD patients were demographically (age, gender, region) matched (1:2) with non-APD patients and (1:5) with non-PD patients. Direct costs during the 12-month post-index period were compared between the cohorts using Wilcoxon rank sum test.

Results: Patients with uncontrolled APD incurred significantly higher direct costs [Mean (SD): \$26,075 (\$34,397); n=1066] compared with demographically matched non-PD patients [Mean (SD): \$7,694 (\$24,872), p<0.001] and non-APD patients [Mean (SD): \$15,766 (\$29,551), p<0.001]. The proportion of uncontrolled APD patients with hospitalizations or emergency room visits was 3.86 and 2.08 times higher than non-PD patients and 1.71 and 1.59 times higher than non-APD patients, respectively.

Conclusions: APD patients uncontrolled on oral medications exhibited higher direct costs and higher healthcare utilization compared with matched controls. These results provide preliminary evidence on the economic burden of APD uncontrolled on oral medications. Future analyses will address differences in comorbidities and the skewed nature of cost data.

P24.03

Identification of clinical and genetic predictors of Parkinson's disease progression via Bayesian machine learning

Jeanne Latourelle¹, Michael Beste¹, Tiffany Hadzi¹, Boris Hayete¹, Robert Miller¹, Jacob Oppenheim¹, Matthew Valko¹, Diane Wuest¹, Iya Khalil¹, Charles Venuto²

¹ GNS Healthcare, USA

² University of Rochester, USA

Background: The clinical progression of Parkinson's Disease (PD) is highly heterogeneous across patients. Identifying features predictive of the rate and nature of disease progression can inform disease management and provide insight into the disease process. The aim of this work was to apply a novel Bayesian machine learning platform, Reverse Engineering and Forward Simulation (REFS), to identify predictors of PD progression across three clinical domains: Motor, Function & Behavior, and Cognition.

Methods: Progression was measured as rates of change in the MDS-UPDRS parts II & III (Motor) and part I scores (Function & Behavior), and Montreal Cognitive Assessment (MoCA) scores (Cognition). Study data for 317 PD patients and 118 controls were obtained through the Parkinson's Progression Markers Initiative (PPMI), including in-depth longitudinal clinical assessments, DaTscan imaging data, CSF biomarkers, and comprehensive genotyping. REFS efficiently integrates a wide variety of data types for unbiased predictive modeling, resulting in an ensemble of models predicting rate of progression for each domain. Independent valida-

tion of the ensembles and replication of key associations were conducted in the Longitudinal and Biomarker Study in PD (LABS-PD).

Results: Multiple features were identified that are collectively predictive of the rate of PD disease progression. In 5-fold cross-validation, the percent variation explained was 0.41 (95% CI: 0.39–0.44), 0.21 (0.2–0.3), and 0.48 (0.4–0.6) for Motor, Function & Behavior, and Cognition progression, respectively. Ensemble accuracy varied across patient strata, with the greatest predictive accuracy in early-stage of disease (≈ 5 years). Genetic markers contributed significant explanatory power across all three domains, and CSF biomarkers were predictive of Cognitive and Functional/Behavioral progression. Replication of many clinical predictors was observed in LABS-PD. In addition, significant replication of a PD-specific interaction predictive of Motor progression was observed between an intronic LINGO2 SNP and intergenic 2q14.1 variant.

Conclusions: This analysis highlights the ability of Bayesian multivariate models to capture complex contributions of clinical, genetic, and molecular profiles to a highly heterogeneous PD progression phenotype. Identification of genetic, clinical, and molecular features with potential as biomarkers of PD progression may have important implications for patient interventions.

P24.04

Predictors of dependency in Parkinson's disease

Angus Macleod, Carl Counsell

University of Aberdeen, Aberdeen, United Kingdom

Background: Functional dependency, the need for help in basic activities of daily living, is an important patient-orientated outcome, which has been infrequently studied in Parkinson's disease (PD). We aimed to describe the development of dependency and identify independent prognostic factors for this outcome.

Methods: We analysed data from the PINE study, a prospective, community-based incident cohort of parkinsonism with ongoing long-term follow-up in Aberdeen, UK. Dependency was defined in two ways: Schwab & England score $< 80\%$ and Barthel index < 19 . We described the development of dependency in the cohort. We examined baseline factors for their association with dependency using multivariable Cox regression.

Results: In 198 patients with PD, the rate of development of dependency was 14 per 100 person years. Older age at diagnosis (hazard ratio [HR] for 10-year increase 2.23 [95% CI 1.66–2.98]), greater smoking history (HR for 10-pack-year increase, 1.15 [1.04–1.26]), more severe axial impairment (HR for 5-point increase in sum of axial items from UPDRS scale, 1.78 [1.30–2.44]), and lower MMSE score (HR 0.88 [0.79–0.98]) were independently associated with higher risk of dependency defined by the Schwab & England scale. Only older age (HR for 10-year increase 1.35 [1.04–1.76]) and severity of axial impairment (HR for 5-point increase 1.85 [1.31–2.62]) were associated with higher risk of dependency defined by the Barthel Index. Sex, deprivation, co-morbidity, overall UPDRS motor score and Hoehn & Yahr stage were not independently associated with dependency.

Conclusion: There is a high rate of development of dependency in PD. Older age, more smoking, more severe axial impairment, and poorer cognition are independent baseline risk factors.

P24.05

A disease specific exercise approach in independent community dwellers with Parkinson's disease: a pilot study

Alexis Okurily¹, Tarang Jain¹, Emily White¹, Valerie Carter²

¹ Northern Arizona University, Flagstaff, AZ, USA

² Northern Arizona University Department of Physical Therapy and Athletic Training, Flagstaff, AZ, USA

Background: Individuals with Parkinson's Disease (PD) often demonstrate functional deficits such as difficulty maintaining balance, turning while walking, and gait with hypokinesia and bradykinesia. Although individuals with PD are often advised to perform 'moderate or intense level' exercises to help improve their functional limitations, guidance as to the type of exercise required to accomplish this improvement is not clear. A disease specific approach to exercises in individuals with PD is necessary to improve and maintain physical functional performance and safety throughout their life and across disease severity.

Objective: To compare the effects of functional PD-specific exercise program which focuses on PWR!Moves® to a regular self-reported exercise program on physical functional performance in independent community dwellers with PD.

Methods: This cross-sectional study included 32 independent community dwellers with PD (> 3 years), all of which were in Hoehn and Yahr stages 1–3, were conveniently sampled into two groups: a disease specific emphasis group ($n=13$, age= 70.9 ± 8.5 y) and self-reported exercise group ($n=19$, age= 67 ± 9 y). The patients in the disease specific group participated in a program consisting of exercise activities that included high effort, large amplitude functional movements of rocking, twisting and stepping, in multiple postures for > 3 times per week. The individuals in the self-reported exercise group completed group sessions, independent exercises, or a combination of both for > 3 times per week. The primary functional outcome measures included: Timed Up and Go at self-selected speed, TUGSS; 3 meter backward walk test, 3MBWT; and self-selected walking speed, SSW. Mann-Whitney U test was used to compare the groups.

Results: Individuals with PD in the disease specific group demonstrated significantly better functional performance in all of the three outcome measures ($p < 0.05$). On an average, the individuals in the disease specific group were 37% faster during TUGSS (6.73 vs. 10.6 seconds), 34% faster during 3MBWT (3.31 vs. 5.02 seconds), and 92% faster during SSW (1.99 vs. 1.04 m/s).

Conclusions: Individuals with PD who exercise with a disease specific focus had significantly better physical function when compared to individuals in the self-reported exercise group. An exercise program that focuses on the disease specific movements (PWR!Moves®) is an effective training modality to improve physical function for PD.

P24.06

Mortality after deep brain stimulation surgery for patients with advanced Parkinson's disease

Ho-Sung Ryu, Sooyeoun You, Mi-Jung Kim, Young Jin Kim, Juyeon Kim, Kiju Kim, Sun Ju Chung

South Korea

Objectives: Despite the widespread use of deep brain stimulation (DBS) for patients with Parkinson's disease (PD), long-term outcome remains unclear. We aimed to analyze the mortality of advanced PD patients who received DBS surgery.

Methods: We assessed the survival rate of consecutive 158 advanced PD patients who underwent DBS surgery between April 2002 and May 2015. Kaplan-Meier survival curves were constructed using death as the endpoint. Cox proportional hazards regression models were used to assess the association of clinical risk factors with survival.

Results: Twenty-seven (17.1%) PD patients (13 men and 14 women) had died during the mean follow-up period of 4.9 ± 3.1 years. The survival rate was 97% at three years after DBS surgery and 85% at five years after DBS surgery. Pneumonia ($N=7$) was the most common specific cause of death. In a step-wise Cox

regression analysis, male gender (hazard ratio (HR)=2.58; 95% confidence interval (CI)=1.19–5.60; P=0.016), hallucination (HR=9.53; 95% CI=3.50–26.01; P<0.001), and the placement of nursing home (HR=6.76; 95% CI=2.40–18.99; P<0.001) predicted poor survival.

Conclusions: The poor survival of advanced PD patients who underwent DBS surgery was predicted by male gender, hallucination, and the placement of nursing home. Further studies with long-term follow-up will confirm these factors influencing mortality of these PD patients.

Keywords: Parkinson's disease, deep brain stimulation, mortality, outcome

CLINICAL SCIENCES: BEHAVIORAL DISORDERS

P25.01

Parkinson symptoms list

David Bunch

DABCO, Costa Mesa, California, Uzbekistan

Objective: To give people diagnosed with Parkinson's disease (PD) an easy tool for identifying, measuring and tracking their symptoms.

Background: I was diagnosed March 2013 with this typical scenario: "Mr. Bunch, we're afraid to have to tell you, but you have Parkinson's disease. Here is a prescription and we will see you in six months!" This happens all too often, leaving the person with numerous unanswered questions while fear is running rampant. My knowledge of PD was nonexistent except for Michael J. Fox and Muhammad Ali. I had heard that the symptoms identify a disease, so I started my search for those symptoms. I checked the internet for information at PD associations, major colleges and universities. All had symptoms lists, but none had a "complete list". I decided to create a comprehensive list. I elected to incorporate additional features to better serve the user.

Method: Features of the Symptoms List are: Multiple visit date columns to track progression

- Severity scale of 1–10
- Indication of the 10 Early Warning Signs
- Technical names for a symptom so a person can get further information
- Percentage of PwP with the same symptom

The Benefits of this form are: You and your doctor will be on the 'same page'

- Provides a method to communicate with caregivers, family and friends
- Track changes in the symptoms when starting new meds
- Track symptoms getting better or worse
- Keep accurate medical records electronically
- Less chance to forget something to ask or tell your doctor
- Make your doctor visit count (ie: Talk about the 6's and 7's first)
- Can be used at any type of doctors visit not just Neurologists
- Gives you back your power

Results: People using this form immediately are on 'the same page' with their doctor and have a better understanding of their disease. See Fig # 1 below:

Date:	Date:	Date:	Date:	Date:	Parkinson's Symptoms List®	Name:
-	-	-	-	-		-
					Acid Reflux - Heartburn - Indigestion - Sleeping on Left Side can help	
					Akathitic Discomfort - Inner restlessness - difficult to sit still - not Dyskinesia	
					Allergies - increased number	
					Anxiety - Fear - Guilt 40%	
					Apathy - Ennui - don't care about anything attitude 40%	
					Appetite - increased or reduced - many loose or gain 40-50# in 5 years	
					Arm Swinging - slowed - usually on one side when walking	
					Aspiration Pneumonia - swallowing incorrectly allows food to enter the lungs	
					Autonomic Nervous System - decline - can affect any of the Organ Functions	
					Back Pain - Lower - from mild to severe - aches - spasms	
					Balance - Dysequilibrium / loss of - Ataxia / falling backwards - Retropulsion	
					Bed - difficulty getting in / out - rolling over (Bed rail may help)	
					Blood Pressure Low - low when standing - Orthostatic Hypotension	
					Bowels - incomplete elimination	
					Breath - shortness - Dyspnea - panting - wheezing - Hyperventilation	
					Chewing - Choking - difficulties - keeping food moving toward the throat	
					Cognitive Function - diminished problem solving / decision making	
					Cogwheel rigidity - jerky movements - stiffness	
					Communication - slow at finding the right word - recall - Aphasia	
					Comprehension - difficulty understanding	
					Constipation - causes drugs to be less effective 80-90%	
					Coordination - Ataxia - less in general - especially with small things	
					Cramping / Burning / Pins & Needles - Toes - Legs etc. - Dysistonia	
					Daytime Sleepiness - Excessive - EDS - Somnolence 60%	
					Dementia - Dissociation - Psychosis - Schizophrenia 30%	
					Depression - Despondency - can not initiate activity - likes being house bound 60%	
					Diarrhea - may be caused by Autonomic Nervous System decline	
					Digestion - difficulty fully digesting food - Gastroparsis	
					Dizziness - Fainting - Lightheadedness - Vertigo	
					Drooling - excessive saliva - Sialorrhea - Botox shots can help - every 3mo.	
					Dry Mouth - excessively dry - cheeks may 'stick' to your teeth	
					Ears Ringing - Tinnitus	
					Early Satiety - feeling full after a few bites of food	
					Edema - Swelling of legs - retention of excess water	
					Emotional - higher sensitivity - more prone to cry	
					Erectile / Sexual Dysfunction - E.D. 80%	
					Executive Functions - trouble forming / executing concepts - goals - plans	
					Exhaustion - Lacks Strength - Tiredness - at times, rest doesn't help 60%	
					Eye Lids - can't open - Apraxia - Spasms - Blepharospasm - Botox helps	
					Eyes - Dry - Xerostomia + decreased blinking - slow - may cause Blurred Vision	
					Facial Expression - Hypomimia - "Masked Face"	
					Fatigue - Physical / Mental weakness - resting will help - not so with Exhaustion	
					Foot and Toe Cramping - can be very painful - Dysistonia	
					Freezing in Position - Akinesia - take one Big step to help get moving	
					Gait - Freezing Of Gait (FOG) stops walking / small steps / can't step forward	
					Hallucinations - Delirium - Delusions - Psychosis - 50% - may act out	
					Head Nodding - involuntary - can be slow or fast	
					Headaches - mild to severe - Migraines	
					Heart Palpitations - heart races	
					Impulse Control Issues - excessive eating - gambling - shopping	
					Light Sensitivity - Pupillomotor - more sensitive to light - Photophobia	
					Medications - unpredictable / changeable results	
					Melanoma - greater % chance of Cancer - Get checked up 2x per yr.	
					Memory Changes or Loss - slower at recalling words - ideas	
					Mood Swings - Irritability - Paranoia - Sadness	
					Movement - slowness of - Bradykinesia - 80% / limited range - Hypokinesia	
					Multi-Tasking - difficulty - causes anxiety / frustration - Be Careful Driving!	
					Muscle Jerks - Myoclonus	
					Muscle Spasms - Cramping - Dysistonia - Atrophy of muscles	
					Nausea - Vomiting - Acid Reflux	
					Numbness - Tingling - in the limbs	
					Olfactory Dysfunction - Small - can diminish to zero - Anosmia / Hypoemia	
					Pain - Central: burning - scalding - stabbing - insects crawling on the skin	
					Pain - Dystonia: due to posture of arms - feet - legs - neck	
					Pain - Nerves - Nerve Roots: compressed nerve roots - Radicular 50%	
					Panic Attacks / Paranoia / Suspicious Thinking / Worry	
					Pink-Rolling - rubbing the thumb with the forefinger - "Pill-rolling Tremor"	
					Pleasure - can't experience any longer - less smiling / laughter - Anhedonia	
					Posture Instability - Hunched - Stooped over - problems standing - walking	
					R.E.M. Disorder - improper sleep - Rapid Eye Movement - don't reach 4th level	
					Ratcheting - elbows - shoulders - temporary locking in position - see Shoulder	
					Restless Leg Syndromes (RLS) + Arms - constant moving - Mustard may help	
					Rigidity - Akinesia - Less Range of Motion - arms, legs, and torso	
					Rising from Seated Position - difficulty getting up - not balanced	
					Self Esteem - Low feeling of self	
					Sexual Desire - decreased or missing all together	
					Shoulder - Rotator Cuff - painful - Ratcheting - can't sleep on it	
					Skin - Dandruff - Flaky - Itchy - Oily - Rashes - Red - Seborrhea - Shingles	
					Sleep / Insomnia - awaken often - can't fall / stay asleep 60%	
					Sleep Apnea - snoring - stoppage of breathing - dangerous - can cause death	
					Speaking - soft or low volume - Hypophonia - monotone	
					Speech - hesitant - monotone - quick - slurred - Dysarthria - difficult Articulation 90%	
					Speech - Groping for the correct word - Aphasia or Dysnomia	
					Startle Easy - Hyperplexia - very easily surprised	
					Stiffness / Spasticity - in arms, legs, and torso areas	
					Stress and Tension - can increase Tremors and lack of concentration 75%	
					Stuttering - Dysfluency - slurring words	
					Sweats - greater desire for sweets	
					Swallowing and Eating - difficulty with - Dysphagia	
					Sweating - increased or excessive - Hyperhidrosis - "night sweats"	
					Taste - loss of = Ageusia - Partial loss = Hypogeusia	
					Tearing - excessive tearing for 20-40 seconds from only one eye	
					Teeth - excessive cavities - gum problems - may loose teeth - lack of saliva	
					Temperature Sensitivity - more so to Hot and/ or Cold than before	
					Thinking - Movements - slow and deliberate = Bradyphrenia - impaired 50%	
					Thirst - excessive - Polydipsia - constant and extreme 'dry mouth'	
					TMJ - Temporomandibular Joint Pain - jaw pain	
					Tremors (At Rest) - arms - face - hands - head - legs - voice 70%	
					Turning / Rolling over in bed - difficult - satin sheets/clothing may help	
					Twitches - just below the skin - Fasciculations	
					Urination - frequently - incontinence - may dribble - urgency - Nocturia	
					Vision - Blurred - Double = Diplopia - Dry Eyes - Eye Strain	
					Vitamin / Mineral Deficiency - B-12 & D-3 and Manganese (Mg)	
					Vivid Dreams - may act out - get physical	
					Walking - usually on one side; foot drag - no arm swing - shuffle - slow - stiff	
					Walking - quick short step - Festination - may over speed an fall	
					Weakness - Arms and Legs - Generalized Asthenia	
					Writing gets 5 on a 10 - Micrographia - difficult to read	
					Created by: David A. Bunch	

Fig. # 1

P25.02**Addicted to technology: Parkinson's disease and impulse control in the age of technology**

Michael J. Dodge, Erica A. Byrd, Caroline M. Tanner, Caroline A. Racine, Nicholas B. Galifianakis
Neurology, University of California, San Francisco, San Francisco, CA, USA

Objective: To ascertain the prevalence of problematic technology use (Technology-related ICDs, Tech-ICDs) in patients with PD.

Background: ICDs are a known complication of PD drugs causing serious harm, but problematic use of technology is not a recognized ICD. We have noticed multiple patients in our clinic with Tech-ICDs that were not detected using standard screens. To address this, we are systematically collecting detailed information on technology use in PD and matched controls. We hypothesize that Tech-ICDs are common in PD.

Methods: Consecutive PD cases and controls from our movement disorders center are being evaluated. Controls are cases' caregivers or family members. Subjects are evaluated once by clinical status, MoCA, QUIP and a structured screen for Tech-ICDs, the PUTS-PD (Problematic Use of Technology Scale-PD) elaborated by a semi-structured interview (SSI). Technology use was defined as problematic when it was excessive or disruptive enough to cause impairment or harm to an individual based on SSI.

Results: To date, 16 PD cases (mean PD duration 10 years, mean levodopa-equivalent daily dose 946mg, 44% ondopamine agonist) and 8 controls have completed the PUTS-PD. Mean MoCA was 27/30 in PD and 28/30 in controls.

QUIP was positive in 67% of PD and 33% of controls. Most subjects owned multiple devices (smartphone: 81% PD, 88% controls; tablet: 44% PD, 63% controls; laptop/desktop: 94% PD, 100% controls). 7 of 16 PD cases (44%) but only 1 control (13%) reported problematic use of technology now or in the past (among PD, 57% past, 29% now, 14% both; among control, both) on PUTS-PD. 9 PD completed the SSI; 44% were found to have Tech-ICD. All of PD with Tech-ICD also had classic ICD behaviors. Only 2 controls completed SSI and neither was found to have Tech-ICD or classic ICD behaviors. 55% of PD with Tech-ICD endorsed "escaping" or feeling in a "zone" with technology use. 100% with these feelings but only 25% without these feelings had a history of depression or anxiety.

Conclusions: Our preliminary result suggests that problematic technology use is common in PD and appears to occur more often in those with other ICDs. Additional screening methods are needed to identify these potentially harmful behaviors.

P25.03**Ages of onset of psychiatric symptoms in patients with Parkinson's disease**

Andreea Seritan, Marta San Luciano Palenzuela, Sarah Wang, Jill Ostrem
UCSF, San Francisco, California, USA

Objective: Psychiatric comorbidities, including anxiety, depression, impulse control disorders, psychosis, and neurocognitive disorders, are common in patients with movement disorders, including Parkinson's disease (PD). Psychiatric symptoms often precede the onset of motor symptoms. The purpose of this study is to explore the percentage of patients with PD who had psychiatric symptoms preceding the PD diagnosis and the frequency of lifetime psychiatric diagnoses in this group.

Methods: Patients with PD referred for psychiatric consultation during October 2015–April 2016 at the UCSF Movement Disorders and Neuromodulation Center were included (n=45). DSM-5

diagnoses were established through psychiatric evaluations. The age of onset of psychiatric symptoms was identified by chart review and compared with the patients' age at PD diagnosis.

Results: Of the 45 patients, 34 (75%) met DSM-5 criteria for lifetime depressive disorders, including MDD, dysthymia, and other depressive disorders; 32 (71%) met DSM-5 criteria for anxiety disorders, including generalized anxiety disorder, panic disorder, social anxiety disorder, and other anxiety disorders; 9 (20%) had impulse control disorders, current or historical; 5 (11%) had substance use disorders; 11 (22%) had either mild or major neurocognitive disorders, and 3 (6.6%) had psychosis (systematized paranoid delusions). The percentage of patients who had psychiatric symptoms prior to the PD diagnosis will be calculated (analysis is in progress).

Conclusion: Psychiatric comorbidities are common in patients with PD, and they often precede the PD diagnosis. Earlier onset of psychiatric conditions indicates a longer duration of illness, with multiple recurrent episodes. This informs the management of psychiatric conditions in PD.

CLINICAL SCIENCES: COGNITION/MOOD/MEMORY

P26.01**The effect of motor imagery on imitation of hand movements in Parkinson's disease**

Judith Bek¹, Emma Gowen¹, Stefan Vogt², Trevor Crawford², Emma Stack³, Jeremy Dick⁴, Ellen Poliakoff¹

¹ University of Manchester, Manchester, United Kingdom,

² Lancaster University, United Kingdom

³ University of Southampton, United Kingdom

⁴ Salford Royal NHS Foundation Trust, United Kingdom

Objective: Action observation and imitation activate motor representations, thereby improving movement and increasing learning, and may also offer an effective rehabilitation method for motor disorders. Few studies have directly investigated action observation and imitation in Parkinson's disease (PD), although some positive effects have been reported. We have used kinematic analysis to quantitatively investigate imitation of hand movements in PD. Previously, we found that people with PD imitate the timing of observed hand movement sequences. We also found a stronger effect of action observation than simple visual cues on the timing of movements. However, it was unclear whether people with PD also imitate spatial characteristics of observed actions. The current work addresses this question by examining imitation of a movement path. Moreover, behavioural and neural evidence has shown that combining action observation with motor imagery (imagination of a movement and its associated sensations) can increase effects on movement. We explored whether motor imagery can also increase imitation in PD, by comparing imitation of hand movement sequences before and after instructing participants to engage in imagery.

Methods: Participants with idiopathic PD (N=24; Hoehn & Yahr stage 1-3) observed videos of a human hand performing a two-movement sequence, and were asked to copy the observed action immediately afterwards. The hand moved between target positions following either a typical (direct, non-elevated) movement path or an atypical (indirect, elevated) trajectory. Modulation of movement in response to elevated vs. non-elevated stimuli provided a measure of imitation.

Following the first set of trials, participants were asked to imagine themselves performing the action while observing the subsequent videos (motor imagery), and then completed a second set of trials.

Results: Participants showed modulation of duration, peak velocity and vertical amplitude (all $p < .001$) in response to the observed movements. Following motor imagery instructions, the vertical amplitude of elevated movements was higher (time x elevation; $p = .005$), demonstrating increased imitation.

Conclusions: Imitation can be complemented by motor imagery in PD, as previously found in healthy young participants. This indicates the potential value of imitation and imagery in neurorehabilitation. These strategies may offer a form of internalised cueing that can be more easily applied in everyday life.

P26.02

Apathy in people with Parkinson's is alleviated while actively contributing towards improving lives of their Parkinson's communities

Leonore Gordon¹, Jillian Carson², Jackie Christensen³, Jean Burns⁴, Pamela Quinn⁵, Cynthia Gilbertson⁶

¹ Through Our Eyes: PD Speakers Panel; Brooklyn Parkinson's Group, Brooklyn, NY, USA

² WPC Ambassador; Parkinsons Canada, Brentwood Bay, British Columbia, Canada

³ Minneapolis, Minnesota, USA

⁴ PDPlan4life, Sun Lakes, Arizona, USA

⁵ Brooklyn Parkinson's Group; JCC/NYU Langone PD Wellness Program, New York, NY, USA

⁶ Brooklyn Parkinsons Group, Brooklyn, NY, USA

Apathy, a lesser variant of depression, is a non-motor symptom experienced by 40% of those with Parkinson's, frequently beginning early in evolution of disease, and lasting throughout. Unfortunately, it is rarely recognized or understood by either those with PD or by their support systems. Apathy can be characterized by a lack of interest in leaving the house for more than essential requirements, it can be quite disabling physically and emotionally, increasing isolation and preventing participation in activities necessary to reduce disease symptoms, such as group exercise, dance, boxing, support groups, etc. Without a clear diagnosis of depression, Apathy can be unfortunately mistaken by PWP's close family members for laziness or indolence, causing unwarranted resentment. Patients often report that anti-depressants, while lifting more crippling organic depression, doesn't seem to reduce their Apathy.

The good news is that many PWP's do report that their feelings of Apathy are lifted while engaging in activities to improve the lives of others globally, and especially of those with PD. Examples include participation in political advocacy, fund-raising activities for PD-research, signing up for PD-related clinical trials, participating in PD-focused conferences; educating peers, health care professionals, the larger PD community and the general public about living with PD; and leading or participating in self-help support groups or outreach to help others.

This study intends to use Survey Monkey, interviews, and anecdotal reporting by people with PD, their extended families and caregivers, and their health-care professionals to collect documentation that activities directed towards helping others reduces Apathy and isolation in people with Parkinson's. Study also intends to help leaders in PD world without Parkinson's (including physicians), and families and support systems of PWP's, to understand the necessity of inviting, encouraging and actively creating opportunities for those with PD to share their gifts and help with larger community. Doing so will improve the quality of life for both PWP's and for members of the world they live in.

P26.03

Effect of sleep quality on cognitive function in mild to moderate Parkinson's patients

Ping Gu, Huimiao Liu, Rui Han, Songxin Shi, Ci Dong, Binchuan Xie
People's Republic of China

Objective: To explore the sleep quality effects on cognitive function in mild-to-moderate Parkinson disease (PD) patients. Method 71 PD patients were divided into somniphathy group with normal group, according to the patients' situation whether the patients complained of decline in sleep quality, and the scores of Pittsburgh sleep quality index(PSQI). Compared to normal group and somniphathy group to find out the differences in cognitive function. Result 71 patients with mild to moderate PD. The number of patients with somniphathy was 37, and the incidence rate was 52.1%. UPDRS score of the patients with somniphathy (45.7 ± 15.9) was higher than that of the patients with normal sleep quality (35.8 ± 13.8), and the difference was statistically significant ($P < 0.01$). Among 71 PD patients cognitive dysfunction had appeared in 49 cases, and the total incidence rate was 69%. Furthermore, there were 28 patients with mild cognitive impairment, and the incidence rate was 39.4%. 21 cases with dementia had appeared, and the incidence rate was 29.6%. The average score of MMSE of the dementia group is 23.0 ± 1.7 , means mild dementia. There were significant differences in sleep quality between the two groups ($P = 0.05$).

Conclusion: The patients with mild-to-moderate Parkinson disease had the high incidence of somniphathy. The patients with severity degree of PD were more suffered from somniphathy. PD patients with poor sleep quality had the poor cognitive function. The sleep quality of patients with PD dementia was poorer than that of patients with normal cognitive function.

P26.04

Effect of emotion on cognitive function in patients with mild to moderate Parkinson's disease

Ping Gu, Huimiao Liu, Ci Dong, Fuchen Qiu, Bingchuan Xie, Changping Dun
People's Republic of China

Objective: To explore the effects of anxiety and depression on cognitive function in patients with mild to moderate Parkinson disease (PD). Methods A total of 71 patients with primary PD were enrolled in this study. Unified Parkinson Disease Rating Scale (UPDRS) and Hoehn-Yahr stage were used to evaluate the severity of the disease. Hamilton Anxiety Rating Scale (14-item version, HAMA-14) and Hamilton Depression Rating Scale (24-item version, HAMD-24) were used to evaluate the anxiety and depression. Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA, Beijing version) were used to evaluate the cognitive function. The impact of anxiety and depression on cognitive function was analyzed. Results All patients were diagnosed as mild to moderate PD, including 61 patients (85.92%) with anxiety, 55 patients (77.46%) with depression and 52 patients (73.24%) with concurrent anxiety and depression. The UPDRS score of patients with anxiety and depression were significantly higher than that of patients without anxiety ($P = 0.016$) or depression ($P = 0.000$). The MoCA score of PD patients with anxiety were significantly lower than that of patients without anxiety ($P = 0.042$). Among 71 patients, there were 49 cases (69.01%) with cognitive dysfunction, including 28 patients (39.44%) with mild cognitive impairment (MCI) and 21 cases (29.58%) with dementia. There was no statistical difference of HAMA-14 and HAMD-24 scores among PD patients with different cognitive levels ($P > 0.05$, for all). Logistic regression analysis showed only anxiety was the independent risk factor for cognitive dysfunction of PD patients (OR=10.816, 95% CI: 1.682–69.560; $P = 0.012$). Conclusions: The illness of PD patients

accompanied by anxiety or depression is more serious. PD patients with anxiety have higher prevalence of cognitive dysfunction.

P26.05

Trajectories of cognitive impairment in Parkinson's disease (PD-TCI)

Deepak Gupta¹, Jennifer Goldman², Judith Jaeger³, Curtis Tatsuoka⁴

¹ Cleveland, OH, USA

² Rush University Medical Center, Chicago, IL, USA

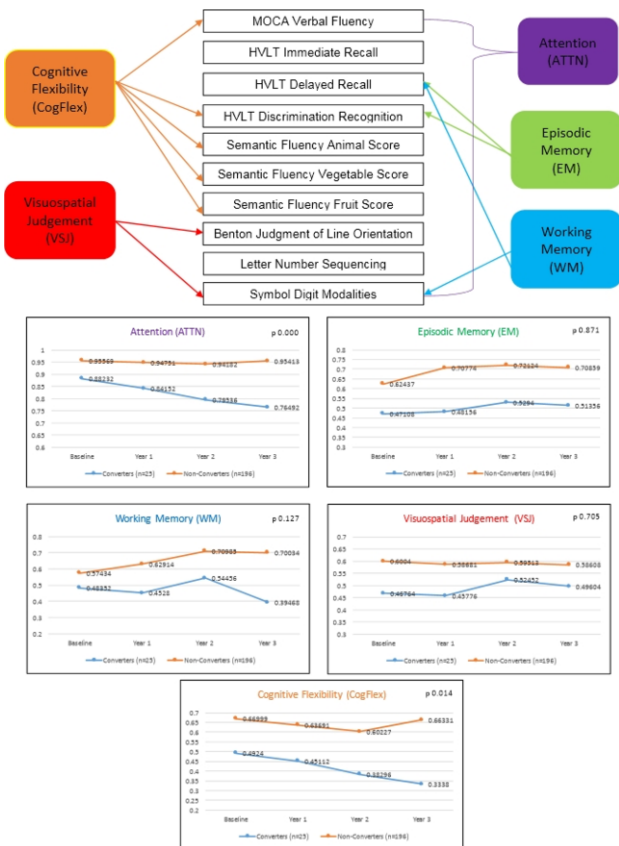
³ Psychiatry and Behavioral Sciences, Wilmington, DE, USA

⁴ Case Western Reserve University, Cleveland, OH, USA

Objective: To develop trajectories and delineate heterogeneity, of cognitive impairment (CI) in early Parkinson's Disease (PD).

Background: CI is common and heterogeneous in nature in PD. Current paradigms of classifying cognitive impairment lack specificity with regards to particular cognitive functions as many neuropsychological measures tap into several different or overlapping cognitive domains. Partially ordered set (POSET) models serve as a basis for novel methods to classify the performance of subjects with respect to specific functions.

Methods: Data of 418 PD and 196 healthy controls (HC) subjects were obtained from Parkinson Progression Marker Initiative (PPMI) database as of April 04, 2016. PD subjects with available follow-up data (baseline to year 3, n=264) for 6 cognitive test scores (Hopkins Verbal Learning Test-Revised[HVLT-R] Immediate Recall, HVLT-R Recognition Discrimination, Judgment of Line Orientation, Letter Number Sequencing, Symbol Digit Modalities Test, Semantic Fluency) were included and classified as having CI if they had at least 2 scores greater than 1.5 standard deviation below HC.



Based on expert opinion, we mapped five specific cognitive functions (Figure 1, flowchart) to above 6 scores (with splitting of Semantic Fluency into individual components for improving replication), HVLT-R Delayed Recall and Montreal Cognitive Assessment (MoCA) Verbal Fluency. We then calculated Cognitive function scores (CFS), representing respective posterior probabilities of a subject's highest level functioning, for PD subjects at baseline through POSET models and Bayesian analysis. We then derived CFS for year 1, 2 and 3 using baseline CFS as reference. After removing PD subjects with CI at baseline (n=43), we first plotted trajectories of CFS for subjects who developed CI by year 3 (Converters, n=25) versus who did not (Non-converters, n=196). We also compared differences in different CFS between year 3 and baseline using two-sided Mann-Whitney tests (p<0.05).

Results: Converters had a consistent and significant decline (Figure 1, graphs) in ATTN (p<0.000) and CogFlex CFS (p=0.014). Though VSJ, EM and WM CFS varied in their decline, these did not differ significantly between groups.

Conclusions: We report a novel approach for distinguishing different phenotypes of CI in early PD. This method and our findings may have important clinical and research implications (e.g., etiology and biomarker discovery for cognitive impairment) in PD.

P26.06

Prompting improves recall in Parkinson's disease with comorbid depression

Taylor Hendershott¹, Anisa Marshall², David Everling³, Gayle Deutsch³, Kathleen Poston⁴

¹ Stanford University School of Medicine, Stanford, CA, USA

² Department of Neurology and Neurological Sciences, Stanford University School of Medicine; Department of Neuroimaging, King's College London, Stanford, CA, USA

³ Department of Neurology and Neurological Sciences, Stanford University School of Medicine, Stanford, CA, USA

⁴ Department of Neurology and Neurological Sciences, Stanford University School of Medicine, Department of Neurosurgery, Stanford University School of Medicine, Stanford, CA

Objective: Categorical cues and recognition stimuli have been shown to improve recall in Parkinson's disease (PD) and depressed populations markedly more than in healthy controls. Understanding the relationship between PD, depression, and memory recall is crucial when interpreting neuropsychological test data because cognitive impairment is prevalent in both PD and depression, and because PD and depression are often observed comorbidly. Using both an internal and an external dataset, we examined how categorical cues and recognition stimuli influenced recall in depressed and non-depressed PD participants.

Method: We administered the California Verbal Learning Test-II (CVLT) and the Beck Depression Inventory-II (BDI) to 84 PD participants. Using the standard BDI cut-off scores we categorized the participants into three groups: non-depressed: BDI 0-13 (n=63), mildly depressed: BDI 14-19 (n=10), and moderately-severely depressed: BDI 20-63 (n=12). The external dataset was obtained from the Parkinson's Progression Markers Initiative (PPMI) database. Participants were 59 depressed and 59 non-depressed participants, who were matched on age, gender, education, and Montreal Cognitive Assessment (MoCA). Participants were administered the Hopkins Verbal Learning Test (HVLT) and Geriatric Depression Scale (GDS). Using the PPMI GDS cut-off scores we categorized the participants into three groups: non-depressed: GDS 0-4 (n=59), mildly depressed: GDS 5-7 (n=35), and moderately-severely depressed: GDS 8-15 (n=24). To determine level of memory improvement with categorical cues (CVLT) or recognition stimuli (HVLT), we calculated how many more items from the list were remembered with prompting as compared to free recall.

Results: Using multinomial regression on our internal dataset, we found a trend indicating that the amount of improvement with cueing predicted only the mildly depressed category ($p=0.052$). Because this first model used a small, unmatched dataset we analyzed the larger PPMI cohort, which was matched on several variables, including MoCA. In a logistic regression for improvement after recognition stimuli, predictors included depression category, age, and gender (OR=2.22, 95% CI=1.19–4.12, $p=0.012$; OR=1.10, 95% CI=1.04–1.17, $p=0.002$; OR=2.79, 95% CI=0.95–8.16, $p=0.06$, respectively). These results suggest that prompting increases recall in depressed PD populations, which could have clinical implications for treatment.

P26.08

The effect of dopaminergic therapy on stimulus-response learning and decision-making in Parkinson's disease using 3T fMRI

Nole Hiebert¹, Ken Seergobin², Adrian Owen², Penny MacDonald²

¹ University of Western Ontario, Canada

² Canada

Dorsal striatum (DS) function is impaired whereas ventral striatum (VS) processes are relatively spared in Parkinson's disease (PD). These brain regions are also differentially affected by dopaminergic (DA) medication in PD. DS function is improved by DA therapy, whereas VS processes are impaired, presumably due to DA overdose. Previously, we examined the neural correlates of stimulus-response (SR) learning in healthy individuals using functional magnetic resonance imaging (fMRI) and found that DS mediates SR decision-making and VS mediates learning. In addition, we examined a similar SR paradigm, behaviourally, in patients with PD both on and off their DA medication. Learning SR associations was impaired ON compared to OFF medication. Our aim here was to examine SR learning in patients with PD while brain activity was estimated using fMRI to directly examine the overdose effect of DA medication on VS-mediated cognitive function.

17 PD and 15 age- and education-matched healthy controls completed an SR learning task during which participants learned to associate abstract images with one of three button-press responses while in an fMRI machine. During learning, feedback was provided after each response, facilitating learning through trial and error. Patients with PD completed the task twice on consecutive days, once ON and the other OFF DA medication. Healthy controls also completed the task twice but did not take any DA medication. Data from the healthy control participants agreed considerably with data from the young healthy controls from the previous study. Activity in DS occurred during SR decision-making events, and VS was recruited when feedback was presented, indicating that this region is involved in learning. Behaviourally, the slope of learning, an indication of efficiency of learning SR associations, was higher in PD patients tested OFF compared to ON medication, suggesting again that VS-mediated functioning is impaired ON medication in patients with PD. Data analysis of the PD imaging data is still ongoing. We anticipate that DS will be recruited ON rather than OFF medication during decision-making events, whereas VS activity will be increased OFF compared to ON medication and will occur during learning events. The implications of this study inform cognitive complaints and medication strategies in PD. Understanding striatum-mediated cognition can guide medication titration in PD, considering individualized motor and cognitive symptoms.

P26.09

Pilot outcomes and patient satisfaction of a novel cognitive rehabilitation program: Parkinson's disease-cognitive rehabilitation for executive functioning (PD-CoRE)

Stella Kim¹, Brenna Renn², Angelle Sander³, Joohi Jimenez-Shahed¹, Michele York¹

¹ Baylor College of Medicine, Department of Neurology, Houston, Texas, USA

² Baylor College of Medicine, Department of Psychiatry and Behavioral Sciences, Houston, Texas, USA

³ TIRR Memorial Hermann/Baylor College of Medicine, Department of Physical Medicine and Rehabilitation, Houston, Texas, USA

Objective: Cognitive dysfunction is a prevalent feature of Parkinson's disease (PD) that contributes more to disability, caregiver strain, and diminished quality of life over the disease course than motor deficits. This study aims to investigate the pilot neuropsychological outcomes and patient satisfaction of the Parkinson's Disease-Cognitive Rehabilitation for Executive Functioning (PD-CoRE) program, a novel cognitive rehabilitation program that utilizes compensatory strategies to address executive dysfunction in PD.

Methods: The PD-CoRE program consists of 8 1.5-hour group sessions that provide education and hands-on experiences targeting inhibition, working memory, and set-shifting abilities. Nine patients with mild PD (67% men, mean age=66.9, mean Montreal Cognitive Assessment=25.7) who reported executive functioning difficulties completed standardized and ecologically valid measures pre- and post-treatment assessing memory, executive functioning, and mood in addition to a patient satisfaction questionnaire.

Results: At baseline, patients demonstrated low average to high average performances on all cognitive measures. Repeated measures t-tests found statistically significant improvement in set-shifting speed (Trail Making B; 95% CI=-1.44 to 38.33) but no changes on other cognitive measures. Mood evaluation showed subclinical symptoms at baseline and did not change after treatment. Participants expressed high satisfaction with the program; 100% enjoyed the social interaction with other PD patients, 89% agreed that the program provided them with ecologically valid skills for use in daily life, 78% reported improved problem-solving skills, and 89% would recommend it to other PD patients.

Conclusion: The pilot investigation of the PD-CoRE program demonstrated an improvement in set-shifting, a domain of executive functioning. Participants tended to be cognitively intact; therefore, ceiling effects may have limited detection of intervention effects. The high satisfaction ratings taken together with the preliminary outcomes suggest that the program should be further evaluated through a randomized clinical trial using a larger cohort of PD participants who are diagnosed with PD-Mild Cognitive Impairment secondary to executive dysfunction at baseline.

P26.10

Can we remediate mild cognitive impairment in Parkinson's disease? A randomized placebo-controlled trial of cognitive training and transcranial direct current stimulation

Blake Lawrence, Natalie Gasson, Andrea Loftus

Curtin Neuroscience Laboratory, School of Psychology and Speech Pathology, Curtin University, Perth, Western Australia, Australia

Aims: To compare the efficacy of cognitive training (CT), transcranial direct current stimulation (tDCS), and cognitive training combined with tDCS for improving cognition in people with Parkinson's Disease and Mild Cognitive Impairment (PD-MCI).

Methods: Participants were included if they met Movement Disorder Society Task Force Level II criteria for PD-MCI. Participants (N=42) were randomly allocated to one of six groups: (1) standard CT, (2) tailored CT, (3) tDCS, (4) standard CT+tDCS, (5) tailored CT+tDCS, or (6) a placebo-control group. Interventions lasted 4-weeks and participants' neuropsychological performance was measured at baseline, post-intervention (Week 5) and follow-up (Week 12). While controlling for moderator variables (e.g., education, disease duration), Generalized Linear Mixed Models (GLMMs) were used to analyze outcomes.

Results: Compared to the control group: (1) executive function significantly improved in the standard CT+tDCS ($p<.001$) and tailored CT+tDCS ($p=.024$) groups, (2) attention/working memory significantly improved in the tDCS ($p=.039$) and standard CT+tDCS ($p=.028$) groups, (3) memory significantly improved in the tDCS ($p<.001$) and tailored CT+tDCS ($p<.001$) groups, (4) language significantly improved in the standard CT+tDCS ($p=.008$) and tailored CT+tDCS ($p<.001$) groups and (5) activities of daily living improved in the standard CT ($p<.001$) and standard CT+tDCS ($p=.014$) groups.

Conclusion: Cognitive training, tDCS and cognitive training combined with tDCS showed improvements in cognition and activities of daily living in people with PD-MCI.

P26.11

Long term benefits from acetylcholinesterase-inhibitors for patients with Parkinson's disease dementia in real life clinic follow-up

Christiane Lepage, Nathalie L'Écuyer, Monica Béland
Centre Hospitalier de l'Université de Montréal, Montréal, Québec, Canada

Background: Acetylcholinesterase-inhibitors (AChEI) are routinely prescribed, and often for years, to patients with Parkinson's disease dementia (PDD). However studies proving their efficacy are based on a relatively short period of time and several factors may influence the benefits of AChEI: dosage, side effects, concurrent disease, anti-cholinergic medication...

Objectives: This presentation is to evaluate the long term benefits of AChEI (at 6 and 18 months) on MMSE scores and the subjective perception of change on cognitive functions for PDD patients, and on their caregivers.

Methods: We compiled MMSE scores completed at 6 and 18 months for 19 patients with PDD (MMSE scores between 17 and 26) to whom an AChEI was prescribed during their regular clinic follow-up. The patients, and or caregivers, were asked for their global subjective cognitive evaluation during the same period. Data were collected for patients who completed at least 18 months of treatment with one of the AChEI (Rivastigmine patch or pill, Donepezil or Galantamine). Dose adjustments and changes from one AChEI to another were done if side effects occurred.

Results: At 6 months, the mean (+/- SD) MMSE score was 25.10 (1.93) compared to 22.68 (2.49) at baseline. At that time, 42% of PDD patients, or their caregivers, reported a subjective improvement and 37% a stabilization of their cognitive functions. At 18 months, the mean MMSE score was 25 (2.36) and 58% of PDD patients, or their caregivers, noticed a decline in their cognitive functions. No patients stopped the medication.

Discussion: Even in this real life context (patients with different AChEI, at several dosages), this data collection corroborates the AChEI efficacy for PDD at 6 months and probably at 12 months according to the literature. At 18 months, mean MMSE score remained stable and more than half patients perceived a cognitive decline. However there is a sustained subjective benefit for 42% of patients, and it would be interesting to collect the same data at 24–36 months.

P26.12

Patterns of responses on the Montreal Cognitive Assessment in Parkinson's disease associated mild cognitive impairment

Melissa Mackenzie¹, Kristen Sundvick², Jiayue Cai³, Daryl Wile³, Adam Book³, Z. J. Wang³, Martin McKeown⁴, Silke Appel-Cresswell⁴

¹ Department of Neurology, University of British Columbia, Vancouver, British Columbia, Canada

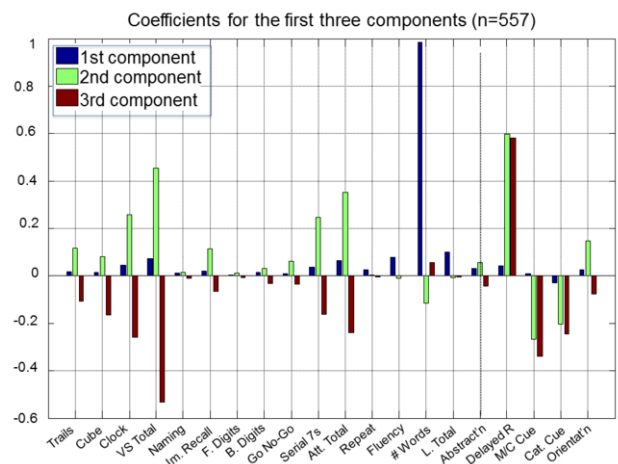
² Pacific Parkinson's Research Centre, University of British Columbia, Vancouver, British Columbia, Canada

³ University of British Columbia, Vancouver, British Columbia, Canada

⁴ Pacific Parkinson's Research Center, Department of Neurology, University of British Columbia, Vancouver, British Columbia, Canada

Rationale: Cognitive decline is a debilitating non-motor complication of Parkinson's disease (PD) that increases morbidity and care-giver burden, and is associated with poorer quality of life. The Montreal Cognitive Assessment (MoCA) has been validated for use in PD, and can be completed as part of a regular clinic assessment. It is not clear, however, if patients with PD-mild cognitive impairment (PD-MCI) exhibit a particular pattern of responses on the MoCA or what demographic factors may influence those patterns.

Methods: A total of 557 MoCA's completed by 213 patients with PD after meeting MoCA criteria for MCI (MoCA 21) were included. Principal Component Analysis (PCA) was performed to determine the patterns of responses that explained the majority of the variance. The subject-specific loadings on these patterns were assessed with ANOVA to identify the influences of demographic factors.



Results: Three patterns explain 83% of the variance in MoCA responses of patients with PD-MCI. Pattern 1 was largely based on the number of words on fluency testing in one-minute, and was heavily influenced by gender ($P=0.0008$) and Hoehn & Yahr (H&Y) stage ($P=0.001$). Pattern 2 was associated with a likelihood for scoring points on delayed recall without cue, as well as high scores on visuospatial components (trails-B, copy cube, clock), visuospatial total score, serial 7's and attention total score (digit span, go-no go, serial 7's). This pattern was heavily influenced by gender ($P=0.04$). Conversely, Pattern 3 was associated with a likelihood for higher scores on delayed recall, and lower scores on all visuospatial items (both independently and as a total score), as well as lower scores on serial 7's and attention total score. This pattern is influenced by rate of disease progression ($P=0.0002$), gender ($P=0.0001$) and H&Y disease stage ($P<0.003$).

Conclusions: The majority of PD-MCI patients fall into one of three patterns of responses on the MoCA. These patterns are influenced by different demographic factors, particularly gender, H&Y disease stage and rate of disease progression. These patterns of responses are not significantly influenced by years of education or Beck Depression Inventory scores. Further research is needed to determine if these patterns are predictive of a benign or pathological prognosis. There may need to be re-assessment of normative scores that take into account gender.

P26.13

Large-scale exploratory analysis of genetic risk factors for cognitive impairment in Parkinson's disease

Ignacio Mata, Catherine Johnson, James Leverenz, Daniel Weintraub, John Trojanowski, Vivianna Van Deerlin, Beate Ritz, Rebecca Rausch, Stewart Factor, Cathy Wood-Silverio, Joseph Quinn, Kathryn Chung, Amie Peterson-Hiller, Alberto Espay, Fredy Revilla, Johnna Devoto, Dora Yearout, Shu-Ching Hu, Brenna Cholerton, Thomas Montine, Karen Edwards, Cyrus Zabetian USA

Background: Cognitive impairment is a common and disabling problem in Parkinson disease (PD). Identification of genetic variants that influence the severity of cognitive deficits in PD might provide a clearer understanding of the pathophysiology underlying this important nonmotor feature.

Objectives/Methods: We genotyped 1,105 PD patients from the PD Cognitive Genetics Consortium for 249,336 variants using the NeuroX array. Participants underwent assessments of learning and memory (Hopkins Verbal Learning Test-Revised [HVLTR]), working memory/executive function (Letter-Number Sequencing and Trail Making A and B), language processing (semantic and phonemic verbal fluency), visuospatial abilities (Benton Judgment of Line Orientation [JoLO]), and global cognitive function (Montreal Cognitive Assessment). For common variants we used linear regression to test for association between genotype and cognitive performance with adjustment for important covariates. Rare variants were analyzed using the optimal unified sequence kernel association test. The significance threshold was defined as a false discovery rate corrected P-value (P_c) of 0.1.

Results: Thirty-three common variants in 32 genomic regions exceeded the significance threshold for one of the cognitive tests. These included GBA rs2230288 (E326K; P_c=2.7x10⁻⁴) and RAB25 rs34372695 (P_c=0.026), which were associated with lower performance on JoLO. Analysis of rare variants yielded only one significant gene region; PERP was associated with HVLTR delayed recall (P_c=0.053).

Conclusions: We have conducted the first large-scale PD cognitive genetics analysis and nominated several new putative susceptibility genes for cognitive impairment in PD. These results will require replication in independent PD cohorts.

P26.14

Gait at diagnosis, rather than cognition, predicts cognitive decline over three years in Parkinson's disease

Rosie Morris, Sue Lord, Rachael A Lawson, Alison J Yarnall, David J Burn, Lynn Rochester
Newcastle University, Newcastle upon Tyne, United Kingdom

Objective: Cognitive decline and dementia are significant in Parkinson's disease (PD). Identifying those at risk of cognitive decline is critical in order to optimise clinical management and improve therapeutics. Impaired cognitive function is associated with gait impairment in ageing and PD with discrete gait characteristics

showing promise as clinical biomarkers of cognitive decline in older adults. We sought to i) identify whether discrete gait characteristics at diagnosis could detect cognitive decline in PD and ii) compare gait and a global cognitive assessment as predictors of cognitive decline.

Methods: 119 idiopathic PD participants were recruited for ICICLE-Gait (an ICICLE sub-study) and assessed at; baseline (diagnosis), 18 and 36 months. Participants walked for two minutes around a circuit at preferred pace. Gait was quantified using a 7m GaitRite™ instrumented walkway deriving 16 gait characteristics representing five domains: pace, variability, rhythm, asymmetry, postural control. A cognitive battery assessed global cognition, attention, fluctuating attention, executive-function, working memory, visual memory and visuospatial. Linear mixed effect modelling was used to i) assess change in cognition over 36 months, ii) predict change in cognition from gait characteristics at diagnosis and iii) predict change in cognition from baseline MoCA. Models were determined using backward elimination to adjust for correct covariates including age, education, gender, depression and levodopa daily dose (LEDD). Log-likelihood tests were used to compare model fit. The significance threshold was set at p<.01.

Results: Significant cognitive deterioration was evident for attention, fluctuating attention, executive function and visual memory. A number of gait measures predicted cognitive decline. Pace, variability and postural control predicted decline in fluctuating attention (all p<.01). Pace predicted decline in visual memory (p<.01). In comparison, MoCA was unable to predict decline in fluctuating attention (p=.04) or visual memory (p=.15). Forced entry of the basic model plus gait characteristics and MoCA yielded the strongest model with most gait characteristics retaining significance (p.05).

Conclusions: This work demonstrates that discrete gait characteristics at diagnosis can predict cognitive decline in early PD. Gait may provide a simple, cost-effective clinical biomarker and contribute to a prognostic model of cognitive decline in PD.

P26.15

A case report of improvement of cognitive function after the endpoint of DASH-PD study (donepezil application for severe hyposmic Parkinson's disease)

Hidemoto Saiki
Japan

Background: The effect of acetylcholinesterase inhibitor, donepezil on cognitive function with dementia or mild cognitive decline in Parkinson's disease is not fully understood. Donepezil Application for Severe Hyposmic Parkinson Disease study (DASH-PD) is a double-blind placebo-controlled study which compares effects of donepezil and placebo on severely hyposmic Parkinson's disease (PD) patients. The end point of DASH-PD is emergence of cognitive decline.

Objective: To report a case who showed improvement of cognitive function after end point with administration of donepezil.

Patients and Methods: A 72 years old PD patient with ten years disease duration was screened as a candidate for DASH-PD. The examination revealed severe hyposmia and normal cognitive function. She was judged as competent for DASH-PD, and participated the study after informed consent.

Results: Six month after participation, she developed visual hallucination and delusion. The examination revealed emergence of cognitive decline. She was judged as reached to end point of DASH-PD. Her investigational drug was stopped, donepezil (3mg/day for initial two weeks, then 5mg/day) and low dose risperidone was prescribed. Six months after end point, neuropsychological examination showed recovery of cognitive

function to baseline. The examination at twelve months after end point revealed further improvement.

Conclusion: Although the content of her investigational drug is unknown, this case may suggest a strategy of early detection of cognitive decline by structured neuropsychological evaluation and active intervention is useful to prevent progression of dementia in advanced PD patients.

P26.16

Analysis of serum uric acid among Parkinson's disease subjects: is there a relationship between levels of serum uric acid and risk of PD dementia?

Richard Salazar

Jackson Hospital & Clinic, Montgomery, Alabama, USA

Objective: Compare levels of serum uric acid among subgroups of Parkinson's disease subjects based on the presence of PD dementia risk factors.

Background: Uric acid (UA), because of its antioxidant effect, might alter PD pathogenesis. Previous studies reported an inverse association between serum UA and the risk of PD. Risk factors for PD dementia include older age (>70 yo), REM sleep disorder, hyposmia and gait dysfunction.

Methods: 40 PD patients completed the Mayo Sleep Questionnaire and underwent the following tests: mental exam, timed sit-to-stand and walk 25 foot (TS-25FW), subjective identification of hyposmia, and HY staging. Gait dysfunction was determined based on the TS-25FW test (normal 30s). Mental exam comprised of executive function (F words fluency, similarities), memory (delayed recall) and visuospatial test (cube drawing). A single measurement of serum UA was undertaken (range 3.4–7.2 mg/dl).

Results: PD patients (N=40) mean age was 71±10.2 (66% male). Probable RBD or hyposmia was reported by 38% (15/40) and 48% (19/40) respectively. Mean TS-25FW time was 16.95±13.1. Prevalence of moderately severe gait dysfunction (TS-25FW >20 s) was 30% (12/40). PD subjects were further classified into cognitively intact (9/40, 23%), single domain MCI (16/40, 40%) and multiple domain MCI-Dementia group (15/40, 37%). Mean serum UA among the subgroups was as follows: cognitively intact (5.92 mg/dl±0.96); single domain MCI (5.16 mg/dl±1.0) and multiple domain MCI-dementia (4.61 mg/dl±1.39). Mean serum UA was lower in subjects carrying = 3 PD dementia risk factors (4.46 mg/dl±1.15) than in subjects with <3 PD dementia risk factors (5.28 mg/dl±1.24). Serum UA levels were similar between subjects experiencing moderately severe versus normal-to-mild gait dysfunction (5.10 mg/dl and 5.11 mg/dl, respectively). Mean serum UA didn't differ across the HY stages (I–II: 5.27 mg/dl; III–IV: 4.70 mg/dl; V: 5.35 mg/dl).

Conclusions: This study suggests a trend towards lower levels of serum UA among PD demented subjects and those at an increased risk of developing PD dementia. Serum UA was similar across disease stages or degree of gait dysfunction. Larger studies are necessary to confirm these findings.

P26.17

Outcomes of the PDF Community Choice Research Award: a workshop to address maintaining cognitive function in Parkinson's

Beth Vernaleo¹, Jennifer Goldman²

¹ Parkinson's Disease Foundation, New York, NY, USA

² Rush University Medical Center, Section of Parkinson Disease and Movement Disorders, Department of Neurological Sciences, Chicago, IL, USA

Background: In 2013, the Parkinson's Disease Foundation (PDF) launched the Community Choice Research Award (CCRA), designed to advance research in areas that were identified as unmet needs within the PD community. People with Parkinson's (PWP) and care partners (CP) were asked "what areas of research do you think scientists should be focusing on in order to make an impact in the PD community?" This year, over 300 people from eight countries responded with ideas. One unmet need identified by many PWP and CP was addressing cognitive problems in PD and how to maintain cognitive function for as long as possible. As a result, the PDF organized a working group of multidisciplinary experts to address this need. On June 3–4, 2016, a workshop will be held in Chicago, IL where the working group will meet to define the issues relating to PD cognitive problems and identify research and educational strategies to address these issues in Parkinson's and healthcare communities.

Objective: To define unmet needs regarding cognitive issues in PD, identify non-pharmaceutical interventions that may help maintain cognitive function, and formulate recommendations for what PWP can do at every stage of their disease to maintain cognitive health.

Workshop format: Nine topics will be covered at the meeting including: cognitive issues that affect PWP, cognitive aging, clinical measures, physical and cognitive exercise, nutrition, caregiver issues, and psychosocial aspects. The working group consists of 19 members from diverse clinical and research backgrounds. In addition, six members of the Parkinson's community (three PWP/CP couples) will attend the workshop to share their experiences with cognitive impairment.

Potential impact: This working group aims to provide recommendations to both PWP and healthcare professionals for what interventions regarding cognitive issues may be most helpful, not only at PD diagnosis, but also throughout the disease. The goal is to have a path forward so that PWP and their CP know what they can do at every stage of their disease in order to maintain cognitive health and function.

Conclusions: Cognitive impairment is recognized as a major issue in PD and frequently reported by PWP and CP as "one of their biggest fears." By addressing not only potential interventions but also when to start these interventions, the Parkinson's community can be armed with a personal toolkit to help mitigate both cognitive impairment and the fear of its development.

P26.18

SYN120, a dual 5-HT₆/5-HT_{2A} antagonist, for Parkinson's disease dementia (PDD) (SYNAPSE study): study design and partial blinded baseline data

Daniel Weintraub¹, Amy Cartaya², Eric Macklin², Keith Wesnes³, Jamie Eberling⁴, Christopher Kenney⁵, Karen Cravotto⁵, Michael Schwarzschild², Irene Litvan⁶, Lindsay Pothier², Hubert Fernandez⁷

¹ University of Pennsylvania School of Medicine, Philadelphia, PA, USA

² Massachusetts General Hospital, Boston, MA, USA

³ USA

⁴ Michael J. Fox Foundation, USA

⁵ Biotie Therapies, San Francisco, CA, USA

⁶ University of California San Diego, San Diego, CA, USA

⁷ Parkinson's Study Group (PSG), Cleveland, OH, USA

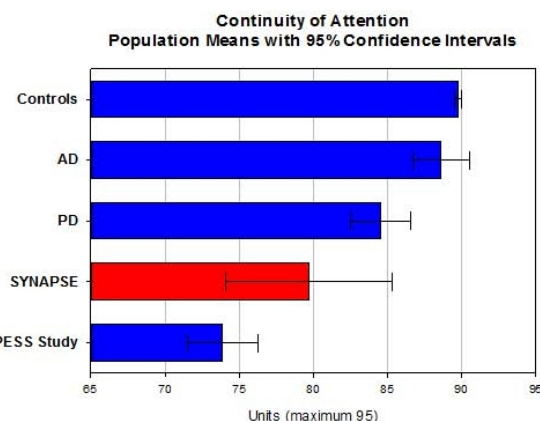
Background: Cognitive impairment, including dementia, is very common in Parkinson's disease (PD), ultimately affecting up to 80% of PD patients. PD dementia (PDD) is associated with worse quality of life, poorer clinical outcomes, and increased caregiver burden. Multiple neurotransmitter deficits are associated with cognitive impairment in PD. One medication has been approved for the treatment of PDD, rivastigmine, which targets the cholinergic system. The aim of the SYNAPSE trial is to assess the safety,

tolerability, and efficacy of SYN120, a dual 5-HT6/5-HT2A antagonist, in participants with mild to moderate PDD.

Methods: SYNAPSE is a 16-week, randomized, double-blind, placebo-controlled Phase 2a trial testing SYN120 at 100 mg daily in 80 subjects with PDD across 12 movement disorder centers in the USA. Additional key eligibility criteria include: diagnosis of PDD per MDS Task Force criteria, MoCA score of 10-23, age = 50 years, and on stable cholinesterase inhibitor therapy. The primary outcome measure is Continuity of Attention (CoA) which measures ability to sustain attention on the Cognitive Drug Research Computerized Cognition Battery (CDR). The key secondary outcome measure is the CDR Quality of Episodic Memory.

Results: Of 36 participants randomized to date (data through March 28th, 2016), participants were 86% male and 97% white. Mean (SD) age was 74.5 (8.3) years, with duration since PD and PDD diagnosis of 10.2 (5.6) and 3.5 (2.3) years. At baseline, the mean CDR CoA (maximum score=95, higher score indicating better attention) and MoCA scores were 79.7 (16.6) and 18.3 (3.6) respectively. Performance on the CDR Continuity of Attention suggests that dementia severity in SYNAPSE study population is milder on average compared to a comparable PDD study known as EXPRESS, but the attention deficits are greater than seen in controls, patients with Alzheimer's disease (AD), and PD patients without dementia (Figure 1). Longitudinally, there have been no serious adverse events, two early treatment discontinuations, and no significant changes in safety monitoring parameters. The most common individual adverse events in the population are nausea (11%) and urinary tract infections (8%).

Discussion: To date, subject enrollment for SYNAPSE is 45% complete. On average, SYNAPSE participants have mild dementia overall. Final results from the study will help determine if a larger Phase 3 study of SYN120 for the treatment of PDD is indicated.



CLINICAL SCIENCES: SLEEP DISORDERS/FATIGUE

P27.01

A survey of sleep fragmentation (SF) in patients with Parkinson's disease (PD)

Gaggandeep Singh Alg¹, Dhanushka Kulatunga¹, Helen Avery², Apurba Chatterjee³

¹ Specialist Registrar in General Medicine and Geriatric Medicine, Reading, United Kingdom

² Clinical Nurse Specialist in Parkinson's Disease, Reading, United Kingdom

³ Consultant Physician and Clinical Lead in Elderly Care Medicine, Specialist Interest in Movement Disorders, Royal Berkshire Hospital, Reading, United Kingdom

Objective: To assess the causes of sleep fragmentation in PD patients

Key Words: Sleep fragmentation, RBD, Parkinsonism, Nocturia

Background: SF is a common non-motor problem in PD patients, which affects their quality of life. The causes of SF are a combination of symptoms including: nocturia, nocturnal akinesia, restless legs and RBD. Intervention for nocturia include conene sheath catheter in males, pads in females and rotigotine patch can also be used in both males and females. REM sleep Behaviour Disorder (RBD) can be managed using drugs such as clonazepam.

Methods: Data was collected on a structured proforma from 25 consecutive patients attending the Elderly Movement Disorders Clinic at the Royal Berkshire NHS Foundation Trust, Reading, United Kingdom. Data was also collected by the PD nurse specialist during domiciliary visits.

Results: 17 male patients and 8 female patients were included in the survey, the average age of the patients was 79.6 years. 19 patients (76%) experienced SF. 68.4% (13/19) of the male patients suffered from SF and the remaining 31.6% (6/19) were female. 94.7% (18/19) of patients with SF had nocturia. 52.6% (10/19) patients with SF had RBD. 42.1% (8/19) of patients with SF had both nocturia and RBD. Of the male SF patients 46.1% (6/13) suffered RBD, while 92.3% (12/13) suffered from nocturia. 38.5% (5/13) of male patients suffered from both RBD and nocturia. 66.7% (4/6) of female patients with SF suffered nocturia and 100% (6/6) suffered RBD. 66.7% (4/6) of female patients suffered from RBD and nocturia. Interestingly, 100% of our patients suffering from Parkinson Disease Dementia (PDD) suffered SF and for 71.4% (5/7) of these patients the cause was RBD. 3 of our 10 RBD patients were prescribed Clonazepam.

Conclusions: The causes of sleep fragmentation should be explored in the clinic by the multi-disciplinary team, so appropriate intervention can be introduced and sleep hygiene can be improved. Nocturia should be investigated to exclude prostatism in males. The use of pads and conene sheath catheter should also be encouraged to improve sleep hygiene; Rotigotine patch may be used too. Management of RBD requires assessment of all dopaminergic drugs as this may be fuelling the para-somnia. However, the addition of clonazepam may be helpful to improve sleep hygiene.

P27.02

The association of fatigue and sleep problems with retention of daily life activities in people with Parkinson's disease

Cailin Donahue¹, Marie Saint-Hilaire², Cathi A. Thomas², Linda Tickle-Degnen¹

¹ Department of Occupational Therapy, Tufts University, Medford, MA, USA

² Department of Neurology, Boston University Medical Center, Boston, MA, USA

Background: Fatigue and sleep problems are under recognized and undertreated non-motor symptoms in Parkinson's disease (PD). Growing emphasis is placed on assessment and treatment of non-motor symptoms, but few studies explore the impact of fatigue and sleep problems on daily life activities in people with PD (PWP). This study evaluates the relationships between fatigue and sleep problems, and retention of activity participation in PWP.

Methods: 90 community dwelling PWP (Mean age=65, 34 women) self-reported on their experience living with PD as part of the 3 year

prospective cohort Social Self-Management of Parkinson's Disease Study (SocM-PD). Seven self-report items were related to fatigue and sleep problems. Tests of internal consistency and principal component analysis on these items led us to create a composite energy depletion score (7 items) and three separate but related factors: fatigue (3 items), daytime sleepiness (2 items), and nighttime sleep problems (2 items). Activity participation was measured using Baum and Edwards' Activity Card Sort, which yields a global score of how many activities a person retained over the past six months, as well as, four domain scores for retention of instrumental activities, low demand leisure, high demand leisure, and social activities. We calculated Pearson correlations to examine the relationships of energy depletion and its three factors to activity participation.

Results: Energy depletion showed significant negative correlations with global activity retention and with the four activity domains ($r = -.24$ – $-.36$, $p < .05$). The fatigue factor was also significantly and negatively correlated with all activity retention measures ($r = -.24$ – $-.37$, $p < .05$). The sleepiness factor was significantly and negatively correlated with global activity retention ($r = -.27$, $p < .05$) and with social activity retention ($r = -.30$, $p < .01$) but not with the other activity retention scores. The correlations between nighttime sleep problems and activity retention scores were in the expected negative direction but of small magnitude and non-significant ($r = -.04$ – $-.09$).

Conclusions: PWP who experience energy depletion, especially fatigue and daytime sleepiness, retained less of their daily activities over the last six months. More research is needed to understand the direction of causality in the relationship between energy depletion and activity retention, and if a third factor is contributing to this association.

P27.03

Neuroinflammation in pre-diagnostic Parkinson's disease: a multitracers pet study of idiopathic REM sleep behaviour disorder patients

Morten Gersel Stokholm¹, Alex Iranzo², Karen Østergaard³, Monica Seradell², Marit Otto², Kristina Bacher Svendsen³, Alicia Garrido², Dolores Vilas², Per Borghammer³, Arne Møller³, Carles Caig², Joan Santamaria², David J. Brooks³, Eduardo Tolosa², Nicola Pavese³

¹ Aarhus University Hospital, Aarhus C., Denmark

² Spain

³ Denmark

Objective: To investigate the in vivo occurrence of neuroinflammation in the brain of patients with idiopathic REM sleep behaviour disorder (IRBD) and its temporal relationship with striatal dopamine dysfunction using PET.

Background: Longitudinal follow-up studies in IRBD patients showed that a large number develop Parkinson disease or related Lewy body disorders over time. This implies that in IRBD the underlying pathology of developing neurodegenerative disorders can be investigated years prior to the development of manifest symptoms. Studies have indicated that chronic activation of microglia cells may have a detrimental effect on neurons, contributing to the development of neurodegenerative disorders. Using 11C-PK11195 PET, an in vivo marker of microglial activation, studies have shown increased uptake in multiple neurodegenerative disorders. Studying these mechanisms in patients with IRBD could provide significant insight into the earliest mechanisms of developing a synucleinopathy.

Methods: Patients with PSG-confirmed IRBD were recruited at Aarhus University Hospital and Hospital Clínic de Barcelona. Subjects underwent two PET scans with 18F-DOPA and 11C-PK11195 and a structural T1 MRI scan. Parametric images of specific tracer uptake (F-dopa Ki-values and PK11195 binding

potential) were constructed at voxel-level using Patlak graphical analysis and a supervised cluster-analysis with compartmental modelling respectively. A region of interest analysis was performed on a priori defined regions.

Results: 15 RBD patients and 16 matched control subjects were enrolled. Patients showed significantly reduced 18F-DOPA tracer uptake compared to control subjects in the putamen bilaterally ($p = 0.0072$ in left putamen, $p = 0.0045$ in right putamen) and similar uptake in the caudate and substantia nigra (SN). 11C-PK11195 tracer uptake was significantly increased in the left SN ($p = 0.0295$) and slightly increased in the right SN ($p = 0.0892$). Patients with more severe reductions in putamen 18F-DOPA uptake had significantly higher putamen 11C-PK11195 binding ($r = -0.444$, $p = 0.014$). There was a positive correlation between 11C-PK11195 tracer uptake in the SN and the ipsilateral posterior part of the putamen ($r = 0.38$, $p = 0.0368$).

Conclusion: In IRBD, microglial activation occurs in the SN and in the putamen. The latter correlates positively with dopaminergic dysfunction. Given this, anti-inflammatory agents could possibly delay progression to a manifest synucleinopathy in subjects with IRBD.

P27.04

A pilot study of obstructive sleep apnea (OSA) treatment in Parkinson's disease: effect on cognitive and motor function

Anne-Louise Lafontaine¹, Gabriel Leonard¹, Joelle Crane¹, Ann Robinson², Victoria Mery³, Andrea Benedetti⁴, Priti Gros⁵, John Kimoff⁴, Marta Kaminska⁴

¹ Montreal Neurological Hospital and Institute, Canada

² Research Institute of the McGill University Health Centre, Montreal, Canada

³ Clinica Alemana, Canada

⁴ McGill University, Montreal, QC, Canada

⁵ Canada

Introduction: Obstructive sleep apnea (OSA) can affect cognitive and psychomotor function in the general population. The impact of OSA in Parkinson's disease (PD) has not been well studied. Our global aim is to study cognitive and motor effects of OSA and its treatment in PD. In this pilot study, we evaluated the feasibility of a neurocognitive battery and preliminary effects of 6 months of OSA treatment.

Methods: Participants were recruited from a cohort study on OSA in PD, conducted at a tertiary care institution. Patients with idiopathic PD underwent overnight polysomnography and were offered continuous positive airway pressure (CPAP) therapy if they had OSA (apnea-hypopnea index [AHI] = 15/h). For this pilot project, subjects underwent a detailed neurocognitive assessment at baseline and at 6 months, including simple and complex manual motor testing (Leonard Tapping).

Results: Twelve participants were recruited from January to October 2014. Six (50%) were male with mean age 67.8 (SD 6.9) years, BMI 31.3 (43.7) kg/m² and MDS-UPDRS motor 24.2 (14.0). Six of the 12 (50%) were using CPAP at 6 months. The testing protocol at baseline was completed in 10/12 OSA+ subjects. At baseline, the mean Montreal Cognitive Assessment (MoCA) score of 24.8 (SD 5.0). They had reduced naming ability (Boston Naming Test [BNT] mean Z score -2.0), and prolonged completion time on the Tower of London (ToLT, mean standard score 84.7). Other tests were within normal range, though many were mildly reduced. Sequential tapping was significantly impaired for the right and left hands (mean Z scores -1.79 and -1.92, respectively). At 6-month follow-up, for CPAP+ subjects, there was a trend toward improvement on the BNT (Z score change 0.97, $p = 0.13$) and the ToLT (standard score change 7.3, $p = 0.15$). The bimanual tapping tasks also improved (mean Z score change for Balanced Tapping

0.45, $p=0.01$, and Unbalanced Tapping 0.35, $p=0.09$). No statistically significant differences were observed for other tests.

Conclusion: These pilot results attest to the feasibility of cognitive testing in PD patients with OSA at baseline and after 6 months CPAP treatment. Preliminary results suggest that treatment of OSA may improve elements of cognitive function in PD, such as naming (lexical search efficiency), as well as complex motor function requiring planning and inhibition. A larger study to clarify these effects is warranted.

P27.05

Differences between actual and perceived treatment groups in a double-blind placebo trial of acupuncture for fatigue in Parkinson's disease

Cynthia McRae¹, Sarah E. Rogers², Daniel Grine³, Benzi Kluger²

¹ University of Denver, Denver, CO, USA

² University of Colorado Anschutz Medical Campus, Aurora, CO, USA

³ University of Colorado, Denver Campus, Denver, CO, USA

Objective: To examine differences between actual (got real or sham acupuncture) and perceived (thought they got real or thought they got sham acupuncture) groups among persons with Parkinson's disease (PD) in a 6 week double-blind trial of acupuncture to treat fatigue. Variables included the UPDRS and standard measures of fatigue, apathy, optimism, anxiety, depression, sleepiness, personality, belief in acupuncture, and quality of life (QoL).

Methods: 94 participants were randomly assigned to two groups; one receiving acupuncture twice a week for 6 weeks and one receiving a sham procedure on the same schedule. All participants were examined by a neurologist and administered questionnaires at baseline and 6 weeks. Participants were asked if they thought they received acupuncture or the sham procedure at 6 weeks. In order to examine a possible placebo effect, differences between actual acupuncture and sham groups were investigated at baseline and 6 weeks, along with differences between perceived groups, or those who thought they received acupuncture and those who thought they received the sham procedure. Significance level was set at $p<.05$.

Results: There were few differences between actual or perceived groups at baseline. At 6 weeks the only difference between the actual groups was on the Acupuncture Belief Scale (ABS), with the sham group reporting stronger beliefs in acupuncture. Differences between perceived groups at 6 weeks included the ABS, level of fatigue, apathy, optimism, anxiety, depression, sleepiness, fatigue severity, and several subscales of the QoL measure. Those who thought they received acupuncture reported better scores on all measures than those who thought they received the sham procedure, regardless of actual treatment received.

Conclusions: Results indicated there were more differences between perceived groups than actual groups at 6 weeks. These results suggest the placebo effect was very strong in this study.

P27.06

Melatonin: risk or protection in PD progression?

Michael Rak¹, Paul Nicolai², Laurie Mischley¹

¹ Bastyr University Research Institute, Kenmore, WA, USA

² USA

Background: Melatonin deficiency is seen in PD, sleep disorders are common, and melatonin has been shown to improve insomnia and REM sleep behavior disorder in PD.

Objective: The goal of this study was to evaluate PD symptom severity among individuals who use melatonin.

Methods: An internet-based natural history study was designed to generate information useful to patients and providers. An assessment tool, the Patient-Reported Outcomes in PD (PRO-PD) scale, was designed to assess PD severity and was validated against the existing measures of disease severity. Individuals were queried on their use of supplements.

Results: 844 participants participated in the study with a mean age of 62.8 years and an average 5 years since diagnosis. Individuals who reported using melatonin consistently over prior 6 months had statistically significant worse PD symptoms than those not using melatonin. After adjusting for age, years since PD diagnosis, and income, patient-reported insomnia was associated with greater PD symptom severity ($P<0.000$, 95% CI: 8.17, 10.00). Of the 844 participants, 113 (13.39%) report using melatonin. Individuals who used melatonin had a worse overall PRO-PD score ($P=0.016$; 95% CI: 20.32, 194.16) compared to individuals who did not use, although this association diminished after adjusting for insomnia ($P=0.066$; 95% CI: -4.147138, 127.7816).

Conclusions: These data suggest that it is the underlying sleep disorder that is associated with worse PD prognosis, not the use of melatonin. Among individuals with insomnia, the use of melatonin did not appear to improve overall PD status. Melatonin, in the doses being used, does not seem to confer disease-modifying benefits, although it may improve sleep and REM sleep behavior disorder.

P27.07

REM sleep without atonia and dream-enactment behavior in Parkinson's disease

Yun Shen, Cheng-jie Xiong, Chun-feng Mao, Chun-feng Liu
People's Republic of China

Objective: REM sleep muscle atonia (RWA) and dream-enactment behavior (DEB) are subclinical REM sleep behavior disorder (RBD) symptoms. RBD is frequently associated with Parkinson's disease (PD). The aim of this study was to examine relationships between subclinical RBD symptoms and clinical characteristics in PD patients.

Methods: We conducted overnight polysomnography studies in 145 PD patients. Motor behaviors and/or vocalizations in REM sleep with a purposeful component other than comfort moves were identified as DEB. Tonic chin EMG density =15% and phasic =7% were identified as increased RWA (IRWA). PD patients were categorized into groups with clinical RBD (patients who had DEB and IRWA), subclinical RBD-DEB (patients who only had DEB), subclinical RBD-IRWA (patients who only increased RWA) and normal REM sleep.

Results: After adjusted for age, both groups who had DEB (clinical RBD and subclinical RBD-DEB) were higher H-Y stages, higher scores of UPDRS III than groups without DEB. Group who had IRWA (clinical RBD and subclinical RBD-IRWA) were higher H-Y stages, higher scores of UPDRS III than normal REM sleep group, separately. Clinical RBD group, subclinical RBD-DEB and subclinical RBD-IRWA had more levodopa-equivalent daily dose(LED) than normal group. Subclinical RBD-IRWA group had shorter PD duration and worse disease severity (higher H-Y stages and UPDRS III scores) than clinical RBD group, although the statistical significance is not very significant. After adjusted for age, partial correlation analysis was used to find the RWA were observed to be associated with PD duration, H-Y stages and LED.

Conclusion: These findings provided evidence that subclinical REM symptoms were associated with severity of illness in PD patients. When RWA increased to a certain degree, PD patients without DEB had worse condition. It was also possible DEB would disappear while RWA was increasing.

Keywords: Parkinson's disease, REM sleep muscle atonia (RWA), dream-enactment behavior (DEB).

Table 2. Clinical characteristic and PSG parameters of the cohort with a comparison of subjects grouping by DEB and increased RWA

Group	PD+RBD	PD+	PD+	PD+ cREM	P-value
	A	(sRBD-DEB) B	(sRBD-IRWA) C	D	
N	23	33	25	64	
Age (y)	69.2±8.2 ^a	66.6±8.5 ^b	68.2±7.5 ^c	60.7±10.3	0.000
Male : Female	19:4	21:12	14:11	40:24	0.239
Body mass index (kg/m ²)*	22.9±0.6	22.1±0.5	22.8±0.6	22.8±0.4	0.677
H&Y stage *	2.5±0.1 ^{a,d}	2.2±0.1 ^e	2.6±0.1 ^c	2.0±0.1	0.000
UPDRS I score*	3.8±0.6	4.0±0.6	4.2±0.6	3.0±0.4	0.298
UPDRS II score*	12.5±1.1	10.9±1.1	11.2±1.1	10.6±0.7	0.594
UPDRS III score*	23.6±2.2	18.9±2.2 ^e	26.6±2.1 ^c	20.5±1.3	0.041
PD duration (m) *	69.1±8.4 ^a	49.0±7.0	53.4±8.0	45.7±5.2	0.039
LED (mg/d) *	457.3±64.8 ^a	473.6±58.4 ^b	382.9±60.4 ^c	257.4±38.7	0.004

Abbreviations: PSG=polysonnography; y=years; H&Y=Hoehn & Yahr; n=number; UPDRS=Unified Parkinson's Disease Rating Scale; m=months; LED=levodopa equivalent daily dose;

Values are mean ± standard deviation, *: Adjusted for age.

a: significant between groups A and D

b: significant between groups B and D

c: significant between groups C and D

d: significant between groups A and B

e: significant between groups B and C

P27.08

Strength and central motor drive deficits in people with PD-related fatigability

A. Joseph Threlkeld¹, Dimitrios Katsavelis¹, Terry L. Grindstaff¹, Michele A. Faulkner², John M. Bertoni³

¹ Rehabilitation Science Research Lab, Dept. of Physical Therapy, Creighton University, Omaha, Nebraska, USA

² Dept. of Pharmacy Practice and Dept. of Neurology, Creighton University, Omaha, Nebraska, USA

³ Dept. of Neurological Sciences, University of Nebraska Medical Center, Omaha, Nebraska, USA

Objective: Muscle contractile force is determined by CNS motor drive (CMD) and muscle size, fiber-type and metabolism. Weakness and fatigue are key causes of disability and activity limitation in people with Parkinson's disease (PD). The withdrawal of dopaminergic medications (DMed) can further reduce muscle contractile force in people with PD. The purposes of this study were to assess muscle strength and CMD of people with PD-related leg fatigability (PD-LF) before and after exercise-induced fatigue and to evaluate the effects of DMed on strength and CMD.

Methods: Seventeen volunteers with PD-LF were assessed (14M, 3F; age=65.7±5.5; MDS-UPDRS Motor=35.6±9.6; PD Fatigue Scale=11.1±1.6). Two testing sessions were conducted >4 days apart: one ON prescribed DMed (ON) and another session OFF DMed (OFF). The order of ON vs OFF testing was alternated between subjects to minimize the effect of testing order. A control group of age and sex matched healthy older (HO) adults was also tested (14M, 3F; age=65.6±7). Quadriceps muscle strength was assessed by measuring peak knee extension torque during isometric contractions in a Biodex dynamometer. Peak torques were normalized to subject body weight (BW). CMD was assessed by calculating the percent activation (%Act) of the quadriceps using superimposed electrical stimulation and the twitch interpolation technique. Quadriceps strength and CMD were measured prior to (Tpre) and immediately after (Tpost) a fatiguing-inducing exercise protocol. The fatiguing exercise consisted of repeated 7-second maximum voluntary knee extension contractions followed by 3

seconds of rest. The 7-3 contract-relax cycle was repeated until reaching =65% of each subject's pre-fatigue peak torque.

Results: At Tpre and at Tpost, quadriceps strength was not different between PD-LF ON (Tpre 0.98±0.15BW; Tpost 0.65±0.11BW) and HO (Tpre 1.10±0.18; Tpost 0.69±0.12). In comparison to PD-LF ON, withdrawal of DMed induced a significant reduction (17% decrement; p<0.001) in quadriceps strength (PD-LF OFF Tpre 0.81±0.20; Tpost 0.55±0.12). At Tpre and at Tpost, CMD as measured by %Act was not different between PD-LF ON (Tpre 85.2±10.9; Tpost 79.5±13.3) and HO (Tpre 90.2±6.5; Tpost 87.3±8.5). In comparison to PD-LF ON, withdrawal of DMed induced a significant reduction (p<0.001) in %Act (PD-LF OFF Tpre 77.5±17; Tpost 67.4±18.2). These findings indicate that DMed fluctuations over time will increase disability by causing weakness and decreased CMD.

CLINICAL SCIENCES: DIAGNOSIS (DIFFERENTIAL, ACCURACY)

P28.01

Hyperechogenicity of substantia nigra for differentiation of idiopathic Parkinson's disease from other movement disorders: a systematic review and meta-analysis of transcranial ultrasonography (TCS) studies

Seyed-Mohammad Fereshtehnejad¹, Azin Shafieesabet², Azadeh Shafieesabet³, Ahmad Delbari⁴, Ronald Postuma⁵, Johan Lökk⁶

¹ Department of Neurology and Neurosurgery, McGill University, Montreal, Quebec, Canada

² Medical Students Research Committee (MSRC), Iran University of Medical Sciences, Tehran, Iran, Tehran, Iran

³ Student Scientific Research Committee (SSRC), Tehran University of Medical Sciences, Tehran, Iran, Tehran, Iran

⁴ Iranian Research Center on Aging, University of Social Welfare and Rehabilitation, Tehran, Iran, Tehran, Iran

⁵ Montreal General Hospital, Department of Neurology and Neurosurgery, McGill University, Montreal, Canada, Montreal, Quebec, Canada

⁶ Division of Clinical geriatrics, Department of Neurobiology, Care Sciences, and Society (NVS), Karolinska Institutet, Stockholm, Sweden, Stockholm, Sweden

Objective: Idiopathic Parkinson's disease (IPD) is the most common type of parkinsonian syndrome, however, about 30-40% of the patients suffer from other types generally called atypical parkinsonism (AP) with huge clinical overlaps in features and symptoms. Regarding various course of progression and response to levodopa, accurate differential diagnosis of IPD from AP and other movement disorders is important. We aimed to evaluate the diagnostic value of transcranial ultrasonography (TCS) to differentiate patients with IPD from those suffering from AP or essential tremor (ET).

Methods: In this systematic review and meta-analysis, any study using TCS to assess hyperechogenicity of substantia nigra (HSN) in patients with either IPD or any type of AP or ET published in biomedical databases namely PUBMED and/or EMBASE until November 2015 was screened for eligibility criteria, which were cross-sectional design, English language, and accessibility of the findings. After data extraction and quality assessment using the quality assessment of studies of diagnostic accuracy studies (QUADAS), we applied random effect models with restricted maximum likelihood method to calculate pooled estimates on prevalence rates and diagnostic accuracy.

Results: 115 studies with a total number of 6082 participants (IPD: 4528, AP: 981, ET: 573) were recruited. The pooled prevalence rate of HSN+ was estimated to be 76.8% (95% CI: 65.7–87.8%), 35.6% (95% CI: 25.2–45.9%) and 18.0% (95% CI: 9.9–26.1%) in IPD, AP and ET populations, respectively. Based on our meta-analysis, HSN has 77% (95% CI: 60–88%) sensitivity and 56% (95% CI: 34–76%) specificity to differentiate IPD from AP. Pooled sensitivity and specificity of HSN+ to diagnose IPD from ET were calculated as 75% (95% CI: 65–82%) and 85% (95% CI: 75–91%), respectively.

Conclusions: Findings from our meta-analysis showed that transcranial ultrasonography could provide useful information to accurately differentiate IPD. Diagnostic value of HSN+ is quite acceptable for differentiation between IPD and ET. HSN+ is two-folds more commonly found in IPD patients than the ones with AP. As a non-invasive and feasible method, TCS could be used in suspicious cases to increase the accuracy of IPD diagnosis.

P28.02

Smile!! You are on camera...

Christiane Lepage, Nathalie L'Écuyer

Centre hospitalier de l'universite de Montreal, Montréal, Québec, Canada

Objective: To present a new evaluation tool for motor complications in Parkinson's disease

Background: Most patients with Parkinson disease will develop motor complications with disease progression as a result of side effects from medication. Patients, caregivers and sometimes even first line health professionals are not always accurate in describing motor complications. Patients often confuse tremor and dyskinesia, and sometimes overestimate off periods which are not well tolerated from a psychological point of view. An objective observation is essential for medication adjustment and also surgical decision making.

Methods: We use a recording system with a fish-eye camera set on the wall of a large and comfortable examination room. The recording allows direct observation of the patient on any examination room computer. Patients can be observed during several hours, they are asked to move, walk or rest. UPDRS 3 is done on a regular basis during the observation period and the system allows zooming and searching for fine motor movement details.

The recording can be performed for clinical, teaching and/or research purposes.

Results: This direct observation helps the clinician pinpoint the nature of motor complications, how long they last and facilitates on the spot medication adjustments. It is also an educational tool for patients and caregivers. Finally this observational technique is very helpful when Levodopa challenges are done for surgical decision making and may be recorded for comparison purposes.

P28.03

Drug induced Parkinsonism

Nora Reznickova

Colorado Permanente Medical Group, Denver, CO, USA

Drug-induced parkinsonism (DIP) is a widely prevalent but often underrecognized disease process. It is perhaps the most important drug induced movement disorder from a functional point of view. Early diagnosis is difficult, particularly if the medication history is incomplete or unavailable. Furthermore, DIP is often indistinguishable from idiopathic parkinson's disease, particularly in the early stages of the disease.

"Rigid akinetic syndrome" secondary to introduction of dopamine-blocking medications is approaching an incidence of 1 million

individuals per year in the US, a figure that is fast approaching the incidence of traditional idiopathic Parkinson's disease (IPD). In addition, less common but significantly more serious disorders such as neuroleptic malignant syndrome, a rare, but life threatening reaction to introduction of neuroleptic medications are increasing as well. However, when caught early enough, many of these cases are reversible.

Education of individuals living with parkinsonism, as well as their care partners and physicians, among other providers is the goal of our efforts at Society of Postacute and Long Term Care Medicine. Over the years have launched a series of lectures on topics of parkinsonism as we found significant gaps in knowledge and management of the patients.

One of the reasons for this gap is a lack of training in movement disorders in the geriatric fellowship curriculum in US. In contrast, UK geriatricians receive at least three months of education in this area. Another issue is the extremely low percentage of geriatricians working in skilled nursing, long term care and assisted living facilities.

People with parkinsonism as well as their caregivers need to advocate for themselves to receive the correct diagnosis and consider alternatives to dopamine- blocking medications. If choosing skilled nursing or long term care facility, it is important to select one that has a physician and staff familiar with Parkinson's disease and related disorders.

Educating people with parkinsonism, their care givers and care partners as well as physicians and other health care providers is goal of the efforts at the Society of Postacute and Long Term Care Medicine, which has launched a series of lectures on topics related to identifying and treating different types of parkinsonisms in the populations they serve.

CLINICAL SCIENCES: CO-MORBIDITIES

P29.01

Injury rates for people with Parkinson's are predicted by Parkinson's severity independent of demographic data

Peter Schmidt¹, Connie Marras², Caroline Tanner³

¹ National Parkinson Foundation, USA

² University of Toronto, Toronto, Ontario, Canada

³ University of California – San Francisco, San Francisco, California, USA

Background: Injuries sustained due to postural instability and motor complications of Parkinson's disease represent a significant and substantial individual burden and an economic burden for society.

Methods: NPF's Quality Improvement Initiative (NPF-QII) is a long-term longitudinal clinical study of the natural history of PD in the context of expert care. The study includes 8,179 subjects evaluated 20,713 times at 21 expert clinics. It covers a broad range of demographic, social, clinical, and treatment variables. To assess the association between injury and PD severity, the frequency of reported injury was stratified by age and disease duration and then within strata, Cohen's D was calculated at various Hoehn and Yahr (H&Y) stage thresholds. The analysis was repeated twice, once in subjects with at least three years of data on injury (population P1) and again augmenting P1 with subjects who withdrew from the study for reasons that may have included deterioration in status due to injury (withdrawal other than for change of provider or diagnosis and death; population P2). Injury and withdrawal rates were adjusted for sex and comorbidities.

Results: Overall, 4,418 subjects met the inclusion criteria, with 2,981 in P1 and 1,437 added in P2. Population P1 averaged 65.0

years old (SD: 9.1), with 7.1 years since diagnosis (SD: 5.6), 64% male, and 35% reported symptomatic comorbidities. P2 was on average 71.8 years old (SD: 9.8), with 8.6 years since diagnosis (SD: 6.3), 39% male, and 51% reported symptomatic comorbidities. The population was divided into 25 tranches by the age at diagnosis and duration quintiles (age at diagnosis quintile boundaries: 48.1, 55.2, 61.0, and 67.2 years; duration, 2.5, 5.0, 7.8, and 11.8 years). The raw injury rates increased with age and duration across the tranches, with the duration effect dominating. For patients in the earliest duration quintile, their injury rate was 5.8%, while for patients in the latest quintile it was 14.7%. Comparing the injury rate between subjects at H&Y stage below 2.5 versus those 2.5 and above, Cohen's D was 0.219, indicating a significantly higher injury rate. In the expanded P2 population, the harm rate ranges from 17.7% to 51.8% across duration tranches with and Cohen's D for H&Y 2.5 and above increased to 0.460.

Conclusions: The rate of injury increases with Parkinson's severity independently of the patient's age or duration.

P29.02

High incidence of undiagnosed insulin resistance in non-diabetic people with Parkinson's disease

Elliot Hogg, Echo Tan, Kishore Athreya, Christina Basile, Michele Tagliati

Cedars-Sinai Medical Center, Los Angeles, CA, USA

Objective: To study the incidence of undiagnosed insulin resistance (IR) in people with Parkinson's Disease (PD)

Background: The role of IR in accelerating the deterioration of motor function in PD has been suspected for more than 20 years. It is also believed that broader neuropathology in PD may be accelerated by insulin resistance adversely impacting cognition. Additionally, IR and diabetes are both associated with the development of PD. IR is a potentially reversible state and may provide a target for drugs and lifestyle interventions fostering neuro-protection.

Methods: To identify the incidence of IR in Parkinson's disease, 85 consecutive idiopathic PD people attending the movement disorders clinic at Cedars-Sinai Medical Center in Los Angeles were offered testing for fasting insulin and glucose. Seven subjects were excluded from further analysis because of a pre-existing diagnosis of Diabetes Mellitus. HOMA index was calculated by the formula: $(\text{Insulin} \times \text{Glucose}) / 405 = \text{HOMA index}$. A cutoff HOMA of 2.7 was used to identify those with IR. Body Mass Index (BMI) and comorbid diagnosis of diabetes mellitus were noted. Additional testing of motor and non-motor features was performed for later analysis.

Results: 78 non-diabetic PD subjects (62 M, 16 F), with an average age of 63.2 ± 11.8 , were included in the analysis. 26 of 78 (33.3%) had an abnormal HOMA index (range: 2.71 to 9.92), consistent with IR. 59 of 78 (75.6%) subjects in our sample were overweight (BMI > 25) and 25 of these 59 (42.4%) had IR. Conversely, only 1 in 19 (5.2%) people with normal BMI had IR. All but 1 of the 26 (96%) non-diabetic PD patients with IR had normal fasting glucose levels, and 21 of 26 (80.8%) subjects with abnormal HOMA index had normal fasting insulin levels.

Conclusion: Preliminary data from this single center, ongoing study indicates that nearly half (42.4%) of non-diabetic, overweight people with PD may be insulin resistant. Importantly, the vast majority of individuals with IR had normal fasting glucose and insulin levels. Therefore, IR would go undetected by usual diabetic screening techniques, as also suggested by available hemoglobin A1C values in our cohort, which were all normal (data not shown). We conclude that IR in PD may be an undiagnosed problem in a large proportion of patients who are overweight. Given the putative role of IR in accelerating the progression of non-motor and motor features of PD, these data will deserve further attention and research.

P29.03

Modes of anesthesia exert no significant effects on the risk of venous thromboembolism in Parkinson's disease: a population-based study

Chun-Jen Huang¹, Pei-Shan Tsai²

¹ Taipei Tzu Chi Hospital, New Taipei City, People's Republic of China (Taiwan)

² Taipei Medical University, Taipei, People's Republic of China (Taiwan)

Background: We elucidated whether modes of anesthesia, i.e., general anesthesia and neuraxial (epidural or spinal) anesthesia, exerted significant effect on the risk of venous thromboembolism within 30 days after anesthesia in Parkinson's disease patients.

Methods: Data retrieved from the Longitudinal Health Insurance Database (LHID) 2010, released by the National Health Research Institutes, Taiwan, were analyzed. The LHID2010 includes medical claims data and registration files for 1 million enrollees randomly selected from the 2010 Registry for Beneficiaries (approximate 24 million) of the National Health Insurance program. The study subjects were Parkinson's disease patients who received general or neuraxial anesthesia. Subjects with history of venous thromboembolism or anesthesia were excluded. The study endpoint was the occurrence of venous thromboembolism events within 30 days after anesthesia. Logistic regression analysis was used to estimate the risk of venous thromboembolism event by calculating odd's ratios (ORs) and the 95% confidence intervals (CIs).

Results: A total of 2164 subjects (general anesthesia: 1442, neuraxial anesthesia: 722) were included for analysis. Subjects of the two groups were significantly different in age and history of cancer or blood transfusion (all $P < 0.005$). The incidences of venous thromboembolism within 30 days after anesthesia of these two groups were not significantly different (General vs. Neuraxial=0.4% vs. 0.6%, $P=0.739$). Logistic regression analysis revealed that the risk of aspiration pneumonia in subjects receiving general anesthesia and neuraxial anesthesia was not significantly different, either. The OR was 0.75 and 95% CI were 0.21–2.67 ($P=0.657$). The trend remained the same after adjusting for age and history of cancer or blood transfusion (OR=0.58, 95% CI=0.16–2.16, $P=0.416$) as well as for propensity score (OR=0.59, 95% CI=0.16–2.20, $P=0.430$).

Conclusions: Modes of anesthesia exert no significant effects on the risk of venous thromboembolism in Parkinson's patients.

P29.04

Two cases with acute dystonic reaction in Parkinson's disease

Woong-Woo Lee

Eulji General Hospital, Seoul, Seoul, South Korea

Objective: To report two Parkinson's disease (PD) patients who showed transiently acute dystonic reaction (ADR).

Background: ADR is generally caused by dopamine receptor blockers (DRBs). Antihistamines, selective serotonin reuptake inhibitors, opioids, methylphenidate, etc. sometimes could cause ADR. Although ADR occurs frequently in young patients receiving DRBs, it is rarely reported in patients with PD. Recently I have two PD cases presenting with ADR by levosulpiride and antihistamines.

Methods: Case report.

Results: A 71-year-old woman with a 3-year history of PD visited the clinic because of acute involuntary movement on her neck. It had developed at that morning. Her parkinsonian symptoms had been well-controlled by levodopa (600mg daily) before this event. On neurological examination, she showed intermittent, jerky retrocollis. It was revealed that she had taken levosulpiride at the

local clinic a day earlier. Her symptom was rapidly improved within 24 hours after discontinuing levosulpiride and using diazepam.

A 74-year-old man with PD also presented to the hospital due to involuntary movements on his face and neck. The resting tremor on right hand and bradykinesia were well responded to levodopa (600mg daily). He had fast dystonias on his face (facial grimacing) and neck (mild retrocollis) when he spoke or ate something. For 9 days before this unscheduled visit, he had taken doxycycline, olopatadine, azelastine, and chlorpheniramine because of itching skin. After ceasing these drugs, his dystonic symptoms disappeared gradually within 2 days.

Conclusion: ADR is generally reported in young males with DRBs. In half of patients with ADR, the first symptom occurs in 24 hours after initiation of offending drugs. The involved areas are mainly face and neck. However, it can progress into other body parts without proper managements. The reports of ADR in PD seem to be rare. Probably because PD patients are generally older, take dopaminergic drugs, and are seldom prescribed the DRBs.

These 2 cases presented with typical symptoms of ADR, but its clinical settings were unusual. They were typical PD patients with good responses to levodopa. Especially, in the first case, the offending drug was levosulpiride even though she took levodopa regularly. It is supposed that the postsynaptic mechanism such as super-sensitivities of dopaminergic, cholinergic, and other related receptors in basal ganglia system would take a more role in resulting in ADR.

P29.05

Impact of telephone intervention service provided at a community-based geriatrics clinic for Parkinson's: an observational study

Greta Mah, Joyce Lee, Michelle Lin, Harindra Rajasekeran, Harrison Mah

North York General Hospital, Toronto, Ontario, Canada

Introduction: Elderly patients with Parkinson disease (PD) are prone to experience multiple motor and non-motor complications, adverse drug events and medical co-morbidities resulting in frequent emergency department (ED) visits. Our Geriatrics Clinic for Parkinson's was established to provide comprehensive management and telephone intervention. Telephone intervention has been shown to be effective for the elderly in other settings, but limited data exists in the setting of a Geriatrics Parkinson's Clinic.

Objectives: This prospective observational study aimed to document:

1. whether pharmacist-administered telephone intervention in the Geriatrics Clinic for Parkinson's averts ED visits;
2. reasons for telephone calls from patients and caregivers.

Methods: All calls received from clinic patients and caregivers from August 2015 to March 2016 were analyzed. Demographic information, reasons for call, interventions and outcomes were documented. Calls were classified as crisis calls when caller indicated intention to visit ED, with follow-up within 2 weeks by telephone to document outcome.

Results: One hundred ninety-nine calls were received from 86 patients/caregivers with mean patient age of 79 years. Patients were on an average of 11 medications, with 9 medical co-morbidities. 80% had diagnosis of idiopathic PD with average duration of 11 years. Calls were initiated by caregivers (88%), patients (9%) and healthcare professionals (3%). Mean duration of calls was 18 min.

Top reasons for calls were: non-motor symptoms (36%); worsening motor symptoms (19%); request for referrals/equipment (16%); adverse drug effects (13%). 44 calls were classified as crisis calls (22%) with intention to visit ED. Reasons for crisis calls were hallucinations, presyncope/syncope, pain, anxiety, sleep disorders,

severe constipation/diarrhea, and acute bruxism. Only 4 crisis calls (10%) actually resulted in ED visits post-telephone intervention.

Conclusion: Forty-four (22%) out of 199 calls received at the Geriatrics Parkinson's Clinic during study period were crisis calls with intention to visit ED. 90% of crisis calls were resolved by telephone intervention, with only 4 calls (10%) resulting in ED visits. Reasons for crisis calls were non-motor symptoms and adverse drug effects. This study suggests that telephone intervention in the Geriatrics Parkinson's Clinic may be effective in averting potential ED visits for elderly patients with PD.

P29.06

Cardiovascular risk and statin use in recent onset Parkinson's disease: findings from the United Kingdom Tracking Parkinson's and Oxford Parkinson's Disease Centre (OPDC) discovery cohorts

Diane Swallow¹, Michael Lawton², Katherine Grosset¹, Naveed Malek¹, Johannes Klein³, Fahd Baig³, Claudio Ruffmann³, Nin Bajaj⁴, Yoav Ben-Shlomo², Roger Barker⁵, David Burn⁶, Thomas Foltynie⁷, Huw Morris⁷, Nigel Williams⁸, Nicholas Wood⁷, Michele Hu³, Donald Grosset¹, PProBaND Clinical Consortium⁹

¹ Institute of Neurological Sciences, Glasgow, United Kingdom

² University of Bristol, Bristol, United Kingdom

³ University of Oxford, Oxford, United Kingdom

⁴ Queen's Medical Centre, Nottingham, United Kingdom

⁵ John van Geest Centre for Brain Repair, Cambridge, United Kingdom

⁶ University of Newcastle, Newcastle, United Kingdom

⁷ UCL Institute of Neurology, London, United Kingdom

⁸ University of Cardiff, Cardiff, United Kingdom

⁹ Multicentre, sites, United Kingdom

Background: Cardiovascular risk quantification may be important in Parkinson's disease, as vascular problems may affect the PD phenotype, and increased vascular risk may merit statin therapy.

Objectives: To quantify vascular disease and risk along with statin use in recent onset PD, and to examine its relationship to PD severity and phenotype.

Methods: Recent onset PD cases were assessed for any history of cardiovascular disease, and for cardiovascular risk which was quantified using the QRISK2 calculator (high=20%, medium=10 and <20%, low risk <10%). Motor severity and phenotype were assessed using the Movement Disorder Society Unified PD Rating Scale (UPDRS), and cognition by the Montreal cognitive assessment.

Results: In 2,909 individuals with recent onset PD, the mean age was 67.5 years (SD 9.3), 63.5% were male, and mean disease duration was 1.3 years (SD 0.9). 441 cases (15.2%) had established cardiovascular disease. Of the remaining 2,468 cases 39.9% had high vascular risk, 33.9% medium risk, and 26.2% had low risk. Higher vascular risk was associated with older age (p<0.001), worse motor score (p<0.001), more cognitive impairment (p=0.01), and worse motor phenotype (p=0.004). Statins were prescribed in 37.2% with high vascular risk, 15.1% with medium vascular risk, and 6.5% with low vascular risk, which compared with statin usage in 75.3% of those with cardiovascular disease.

Conclusion: A high proportion of recent onset PD patients have high or medium cardiovascular risk (meriting statin usage), which is associated with a worse motor and cognitive phenotype. Statins are underused in these patients, compared to those with vascular disease, which is a missed opportunity for preventive treatment.

P29.07

Differential impacts of modes of anesthesia on the risk of aspiration pneumonia in Parkinson's disease: a population-based studyPei-Shan Tsai¹, Chun-Jen Huang²¹ Taipei Medical University, Taipei, People's Republic of China (Taiwan)² Taipei Tzu Chi Hospital, New Taipei City, People's Republic of China (Taiwan)

Background: This study compared the risk of aspiration pneumonia within 30 days after anesthesia between Parkinson's disease patients who received general anesthesia and those who received neuraxial anesthesia (i.e., epidural or spinal anesthesia).

Methods: We analyzed data retrieved from the Longitudinal Health Insurance Database (LHID) 2010 released by the National Health Research Institutes, Taiwan. The LHID2010 includes medical claims data and registration files for 1 million enrollees randomly selected from the 2010 Registry for Beneficiaries (approximately 24 million) of the National Health Insurance program. Parkinson's disease patients receiving general or neuraxial (epidural or spinal) anesthesia were enrolled in our study. Subjects with history of aspiration pneumonia or anesthesia were excluded. The study endpoint was the occurrence of aspiration pneumonia events within 30 days after anesthesia. The risk of aspiration pneumonia was estimated by calculating odd's ratios (ORs) and the 95% confidence intervals (CIs) using logistic regression analysis.

Results: A total of 2185 subjects (general anesthesia: 1454, neuraxial anesthesia: 731) were included for analysis. Subjects of the two groups were significantly different in age and cancer history (both $P < 0.001$). The incidences of aspiration pneumonia within 30 days after anesthesia of these two groups were also significantly different (General vs. Neuraxial=1.9% vs. 0.7%, $P=0.049$). Logistic regression analysis revealed that the risk of aspiration pneumonia in subjects receiving general anesthesia was significantly higher than subjects receiving neuraxial anesthesia (OR=2.75, 95% CI=1.05-7.16, $P=0.039$). The trend remained the same after adjusting for age and cancer history (OR=3.36, 95% CI=1.28-8.83, $P=0.014$) as well as for propensity score (OR=3.43, 95% CI=1.30-9.03, $P=0.013$).

Conclusions: Parkinson's patients receiving general anesthesia had at least twice the risk of a subsequent aspiration pneumonia event comparing to those receiving neuraxial anesthesia.

qualitative and quantitative signal loss in N1 in new onset PD (motor symptoms <1 year), and in a cohort of subjects with idiopathic REM sleep behavior disorder (RBD) without PD.

Methods: 16 subjects have thus far been recruited, 6 with idiopathic PD, 5 with idiopathic RBD, and 5 age-matched healthy controls (HCs). All subjects underwent clinical histories and exams, completed the SCOPA-AUT questionnaire of autonomic dysfunction, and the 40-item University of Pennsylvania Smell Identification Test (UPSIT). All subjects underwent 7T MRI with a specific protocol including T2* gradient echo sequences, with a voxel resolution of 0.28x0.28x0.8mm. Qualitative analysis of N1 signal was performed by two trained neuroradiologists blinded to subject status. Quantitative analysis of N1 signal was performed in 6 serial axial slices, the most rostral two slices containing the two most caudal slices of the red nucleus.

Results: Qualitative analysis of a predefined N1 region of interest by two blinded neuroradiologists was able to separate out PD subjects from HCs with 100% accuracy. Intraclass correlation between the blinded readers was perfect. Quantitative analyses of N1 image signal strength in PD and RBD subjects showed significant degradation in signal in the most rostral and two most caudal slices.

Conclusions: 7T MRI structural imaging of Nigrosome 1 is a reliable diagnostic biomarker of new onset and premotor PD. Nigrosome 1 signal loss is greatest at the rostral and caudal tails. Prospective changes in Nigrosome 1 signal are being tracked and may serve as a useful independent biomarker of disease progression.

P30.03

Prescribed gait tests versus continuous monitoring of gait in people with Parkinson's disease

Carolyn Curtze, James McNames, Mahmoud El-Gohary, John G Nutt, Martina Mancini, Patricia Carlson-Kuhta, Fay B Horak USA

Objective: To determine if prescribed self-administered gait tests are a valid measure of functional everyday mobility in people with idiopathic Parkinson's disease (PD).

Background: Motor fluctuations are a frequent complication of the long-term use of antiparkinsonian medication. Yet, the assessment of gait in the clinic at a singular moment may not adequately reflect functional everyday mobility. In this study we investigate quality of mobility in people with Parkinson's Disease over a week of continuous monitoring in the home and how it relates to self-administered gait tests in the home.

Methods: We recruited 20 people with PD (Hoehn and Yahr stage 2) and 10 age-matched healthy control subjects. Subjects wore three inertial sensors (Opals, APDM) attached to both feet and the lumbar region for a week of continuous monitoring. Each day subjects performed prescribed 2-min walking tests in the morning, before their levodopa medication intake ('Prescribed - OFF') and one hour after intake of the first dose of the day ('Prescribed - ON'). Gait was detected as walking bouts of at least 4 steps.

Results: Preliminary analyses of continuous monitoring of gait of a full-day and prescribed 2-min walking tests of a person with PD and a healthy control subject are given in Figure 1. In the person with PD, gait speed and stride length improved after levodopa intake (Prescribed - OFF vs ON). It appears that during continuous monitoring gait speed, stride length and double support was more variable than during prescribed gait test. The control subject showed high consistency between the two prescribed gait tests. Gait during continuous monitoring was again more variable and slower.

Conclusions: Prescribed gait tests accurately capture mobility at a singular moment. Continuous measures of gait might be more accurate to capture motor fluctuations due to medication intake in functional everyday mobility in people with PD.

CLINICAL SCIENCES: BIOMARKERS AND NEUROIMAGING

P30.01

Ultra high field MRI of nigrosome 1 is a biomarker of new onset and premotor Parkinson's disease

Matthew Brodsky, Jeff Pollock, David Lahna, David Pettersson, John Grinstead, William Rooney Oregon Health & Science University, Portland, Oregon, USA

Objective: An unmet need exists to develop a methodology to diagnose Parkinson's disease (PD) in the premotor stage, so that patients can be enrolled in neuroprotection trials at a stage when they're likely to be more effective.

Background: Nigrosome 1 (N1) is the 6x6x1 mm subregion of the substantia nigra pars compacta that degenerates earliest and to the greatest degree in PD. 7 Tesla magnetic resonance imaging (7T MRI) allows a high enough resolution to distinctly image N1 in healthy controls, and quantify N1 signal loss in PD. We report

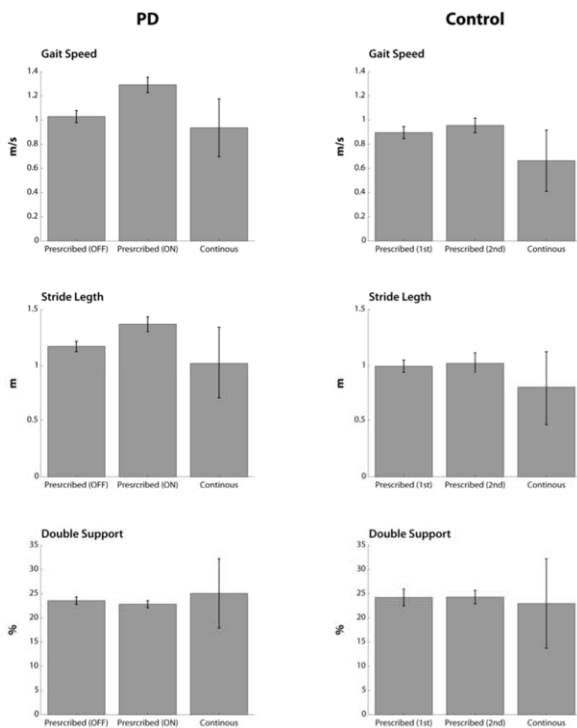


Figure 1: Exemplary data of a day of continuous recoding and prescribed 2-min walking tests of a person with PD and an able-bodied control subject.

P30.04

Biomarkers of catecholaminergic neurodegeneration predict Parkinson's disease: a first look at the NINDS PDRisk study

David Goldstein

DIR/NINDS/NIH, Bethesda, MD, USA

Objectives: The NINDS PDRisk study is testing whether individuals with multiple statistical risk factors for Parkinson's disease (PD)—family history of PD, olfactory dysfunction, dream enactment behavior, and orthostatic hypotension—and with neuroimaging or cerebrospinal fluid (CSF) neurochemical biomarker indicating catecholamine deficiency in the brain or heart develop symptomatic PD during follow-up. We report results of a first look at the outcome data after 3 years of follow-up.

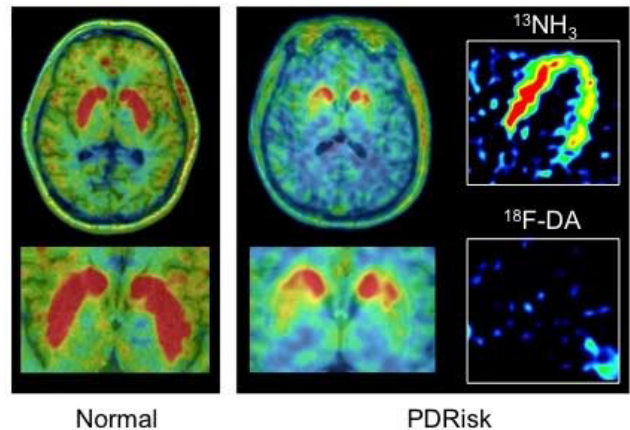
Methods: In this prospective cohort study, participants enter risk factor information at a protocol-specific website. After confirmation of = 3 risk factors during screening at the NIH Clinical Center, subjects undergo testing of central and cardiac catecholaminergic innervation, by putamen 18F-DOPA and myocardial 18F-dopamine positron emission tomographic scanning and by assays of CSF DOPA and 3,4-dihydroxyphenylacetic acid (DOPAC) levels. The subjects are then followed at about 18-month intervals. The primary endpoint is a diagnosis of PD by a neurologist blinded to the biomarkers data.

Results: Of 3,176 individuals providing risk factor data, 388 have had = 3 risk factors and 31 inpatient biomarkers testing, with 22 followed subsequently for = 3 years. Of the 22, 4 have developed PD, dementia with Lewy bodies (DLB), or both diseases. Low values for septal myocardial 18F-dopamine-derived radioactivity, the posterior/anterior ratio of putamen 18F-DOPA-derived radioactivity,

CSF DOPA, and CSF DOPAC have distinguished converters from non-converters ($p=0.0097, 0.0005, 0.0028, 0.0309$).

Conclusions: In people with increased risk of developing PD, biomarkers of central or cardiac catecholamine deficiency predict symptomatic PD, DLB, or both at 3 years of follow-up.

Figure Legend: Striatal and cardiac neuroimaging in a PDRisk participant who developed PD and DLB during follow-up. Note severely decreased posterior/anterior putamen ratio of 18F-DOPA-derived radioactivity and decreased 18F-dopamine-derived radioactivity diffusely in the left ventricular myocardium—2 biomarkers distinguishing at-risk people who convert.



P30.05

Denervation-dependent and -independent abnormalities of central dopamine metabolism in Parkinsonism

David Goldstein

DIR/NINDS/NIH, Bethesda, MD, USA

Objectives: Synucleinopathies such as Parkinson disease (PD) and multiple system atrophy involve decreased cerebrospinal fluid (CSF) levels of dihydroxyphenylacetic acid (DOPAC). One would expect this, because DOPAC is the main neuronal metabolite of dopamine, and parkinsonism in these conditions reflects nigrostriatal dopaminergic denervation. In this study we explored denervation-dependent and denervation-independent determinants of low CSF DOPAC levels in parkinsonian synucleinopathies.

Methods: Cysteinyldopamine (Cys-DA) is derived from and indicates spontaneous oxidation of intra-cellular dopamine. Central dopaminergic denervation alone should produce equivalent decreases in Cys-DA and DOPAC levels because of their shared source, whereas functional abnormalities such as decreased antioxidant capacity or low aldehyde dehydrogenase (ALDH) activity in central dopaminergic neurons should augment CSF Cys-DA compared to DOPAC. We assayed parent and cysteinyl catechols simultaneously in samples from patients with MSA-P ($n=32$), PD ($n=24$), pure autonomic failure (PAF, a non-parkinsonian synucleinopathy, $n=18$), and control subjects ($n=32$). Brain 18F-fluorodopa positron emission tomographic scanning was also done in most subjects.

Results: Cys-DA/DOPAC ratios in MSA-P (0.13 ± 0.03) and PD (0.12 ± 0.02) averaged more than twice those in PAF (0.05 ± 0.01 ; $p<0.0001$ each) or controls (0.05 ± 0.01 ; $p<0.0001$ each). Putamen/occipital cortex ratios of 18F-fluorodopa-derived radioactivity were lower and washout fractions of putamen radioactivity higher in the MSA-P and PD groups than in the PAF or control groups ($p<0.0001$).

Conclusions: In synucleinopathies, elevated cerebrospinal fluid Cys-DA/DOPAC ratios are associated specifically with parkinsonism, dopaminergic denervation, and increased dopamine turnover. Low CSF DOPAC levels in parkinsonian synucleinopathies reflect both denervation-dependent and denervation-independent determinants.

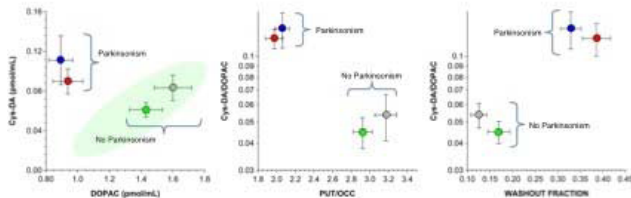


Figure Legend: Mean (\pm SEM) values for CSF Cys-DA, DOPAC, and Cys-DA/DOPAC and for putamen/occipital cortex (PUT/OCC) ratios and 18F washout fractions after 18F-fluorodopa injection in groups with MSA-P (blue), PD (red), or PAF (green) and controls (gray). Green oval indicates expected Cys-DA and DOPAC if there were denervation alone. In the parkinsonian synucleinopathies, CSF Cys-DA is higher than expected for DOPAC, CSF Cys-DA/DOPAC ratios and 18F washout fractions are increased, and PUT/OCC ratios are decreased compared to PAF and controls.

P30.06

A novel, non-invasive biomarker for Parkinson's disease: ceramide lipids from the skin

Jasmine Hammerstad¹, Joseph Quinn¹, Jill Kaspar¹, Susan Goelz¹, Philip Wertz²

¹ Dept. of Neurology, Oregon Health and Science University,
² Iowa City, Iowa, USA

Background: There is an urgent need for biomarkers in Parkinson's disease both for better understanding of disease pathogenesis as well as for use as an exploratory endpoint in early stage clinical trials. Altered lipid metabolism in Parkinson's disease has been reported both in the pattern of lipids in the brain and in CSF. In addition, mutations reducing the activity of glucocerebrosidase, an enzyme involved in ceramide synthesis, confer an increased risk of developing PD. In the context of clinical studies, non-invasive and inexpensive biomarker endpoints are desirable. In this study, the lipids from the skin of PD patients were analyzed using healthy subjects (HC) and AD patients as controls.

Results: In a blinded fashion, stratum corneum lipids were extracted from the surface of skin and the ceramides were analyzed by thin layer chromatography. Some differences were observed in the various ceramides, the most prominent being ceramide EOH where 9/10 HC vs 0/9 PD had detectable levels ($p=0.008$). Surprisingly, only 1/5 AD patients had detectable levels of ceramide EOH ($p=0.05$). In AD and PD the percentage of the ceramide lipid AS + NH appeared to be increased compared to HC (means PD=15.1, AD=16.9, HC=11.7; $p=0.16$ and 0.04 , respectively). Differences between AD and PD were also observed. For example, the percentage of ceramide AP + AH was lower in AD but not in PD compared with HC (mean: AD=29.1, PD=21.0, HC=17.7; $p=0.043$ and 0.39 , respectively).

Interpretation: In this small study of PD and AD patients, some intriguing differences in skin lipids were observed suggesting a possible link to neurodegenerative disease. To explore the use of skin lipids as a novel endpoint for PD and perhaps other neurodegenerative diseases, further studies may be warranted.

P30.07

Pontomesencephalic atrophy and postural instability in Wilson disease

Jayantee Kalita¹, Supriya Naik², Sanjeev Kumar Bhoi³, Usha Kant Misra⁴, Sunil Kumar⁴

¹ Professor, Neurology, Lucknow, Uttar Pradesh, India

² Senior Research Associate, Lucknow, Uttar Pradesh, India

³ Assistant professor, Lucknow, Uttar Pradesh, India

⁴ Professor, Lucknow, Uttar Pradesh, India

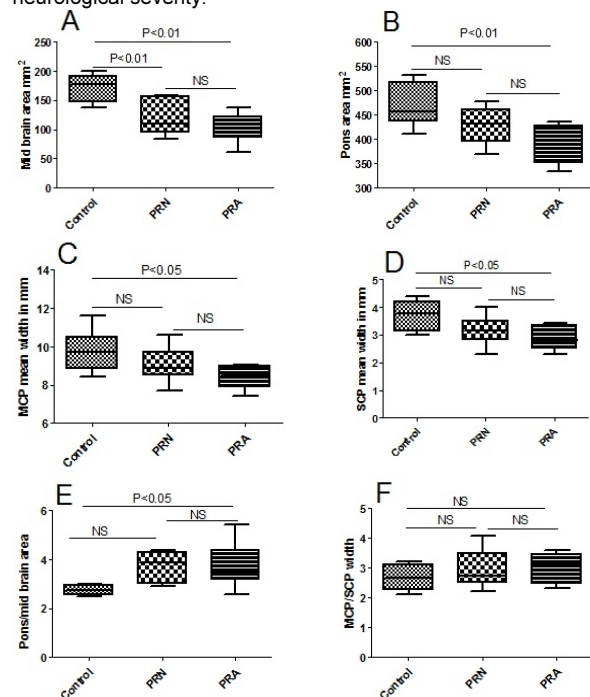
Background: Movement disorder and pontomesencephalic involvement are common in Wilson disease (WD) but there is no study correlating postural reflex with magnetic resonance Parkinson index (MRPI) and its indices in WD.

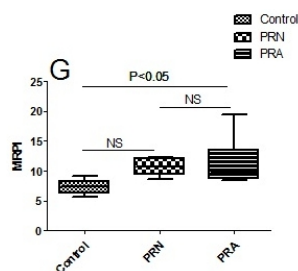
Objective: This study evaluates MRPI and its indices in WD and correlates these with postural reflex abnormality and clinical severity.

Methods: 13 WD patients with neurologic manifestations were included and their clinical details including neurological severity, postural abnormality and location of signal changes on magnetic resonance imaging (MRI) were noted. BRAVO 3D sequence was used for measurement of MRPI and its indices. MRPI and its indices were also obtained in 6 age and gender matched controls. The morphometric parameters on MRI were compared between the patients with and without postural reflex abnormality and healthy controls.

Results: The midbrain area was reduced in WD patients compared with the controls (112.08 ± 27.94 vs. 171.95 ± 23.66 mm²; $P=0.002$). The MRPI, and pons to midbrain ratio were increased in WD patients with abnormal postural reflex but not those with normal postural reflex compared with the controls. The patients with postural reflex abnormality had more severe illness evidence by higher Burke-Fahn-Marsden score (51.0 ± 32.27 vs. 13.75 ± 12.37 ; $P=0.04$) and neurological severity grade (2.57 ± 0.53 vs. 1.67 ± 0.82 ; $P=0.04$).

Conclusion: Increase in MRPI in WD is mainly due to midbrain atrophy and it correlates with postural reflex abnormality and neurological severity.





P30.08

Diurnal fluctuations of inflammatory factors in CSF and serum and identification of inflammatory markers that can be used to discriminate between Parkinson's disease and age-matched healthy controls

George Kannarkat¹, Lori Eidson¹, Jianjun Chang¹, CJ Barnum¹, Vicki Hertzberg², Malu Tansey¹

¹ Physiology Department, School of Medicine, Emory University, Atlanta, GA, USA

² Rollins School of Public Health, Emory University, Atlanta, GA, USA

Numerous attempts to identify fluid biomarkers for neurodegenerative diseases including Parkinson's disease (PD) have led to contradictory and confusing findings. As the role of inflammation in PD becomes increasingly recognized, many investigators aim to define the extent of alterations in cytokine and chemokine signatures that can help elucidate pathogenesis and detect PD earlier. However, the extent to which cytokines fluctuate or remain steady over a 24-hour period in serum and cerebrospinal fluid (CSF) in any given individual and the normal inter-individual variability of these molecules is unknown. In this study, we sought to address this and other related questions by measuring levels of 12 inflammatory markers (IL-1b, IL-2, IL-4, IL-6, IL-8, IL-10, IL-12, IL-13, TNF, IFNg, CRP, and NGAL) in serum and CSF from subjects with Parkinson's disease or age-matched healthy control (HC) subjects sampled over a 24-hour period and in relation to CSF levels of amyloid b(Ab)-40 and 42 and a-synuclein. Not surprisingly, 6 out of 12 inflammatory factors were found to be below the limit of detection in a majority of subjects. Surprisingly, CSF levels of inflammatory markers were more dynamic than serum levels and CRP was the only factor that displayed a strong linear relationship between CSF and serum. Regression analysis of each analyte across time for each individual identified a set of factors that show positive associations across time while others stability over time in serum or CSF and the percentage of PD vs HC that display these associations. Interestingly, serum CRP showed a positive association over time in 1/3 of PD subjects while it showed a negative association in 1/3 of HC subjects. The most stable analytes across time in a majority of PD patients and HCs were CSF IL-8, NGAL, TNF and serum IFNg, IL-8, NGAL, TNF. Analysis of covariance revealed significant differences between PD and HC with respect to the relationship between CSF levels of Ab-40, -42 and a-synuclein and specific inflammatory factors. Linear discriminant analysis revealed a minimal set of factors that can enable discrimination between PD and HC with sensitivity and specificity. In summary, our findings have identified a panel of inflammatory factors in serum and CSF that can be reliably measured and compared to distinguish between PD and HC as well as to monitor inflammation as disease progresses or in response to interventional therapies. [Funding by the MJFF].

P30.09

Characteristics and clinical implications of optic nerve integrity in Parkinson's disease

Jae Jung Lee¹, Yoonju Lee², Young Ho Sohn², Phil Hyu Lee²

¹ Department of Neurology, Inje University College of Medicine, Ilsan Paik Hospital, Goyang-si, Gyeonggi-do, South Korea

² Department of Neurology, Yonsei University College of Medicine, Seoul, South Korea

Objective: To explore the microstructural integrity of the optic nerve and its role as a cognitive predictor in patients with de novo Parkinson's disease (PD) using diffusion tensor image-based magnetic resonance scans.

Methods: We enrolled 82 patients with de novo PD, 36 patients with drug-induced parkinsonism (DIP), and 36 controls. Fractional anisotropy (FA) and apparent diffusion coefficient (ADC) were measured on the mid-portion of the intraorbital optic nerve. Using a multivariate analysis of variance with repeated measures, longitudinal changes in cognitive subscores of a comprehensive neuropsychological test were evaluated in PD patients according to optic nerve integrity.

Results: The mean FA value in PD was significantly lower (0.552 ± 0.103 , $p < 0.001$) than that in DIP (0.645 ± 0.099) or the controls (0.689 ± 0.089), whereas the mean ADC value was significantly higher in the PD group compared to the DIP or control group ($p < 0.001$). Optic nerve integrity was not associated with parkinsonian motor severity, striatal dopamine transporter activity, olfaction, or baseline cognitive performance in PD patients. In a longitudinal assessment of cognition in PD, the lower FA group demonstrated more significant cognitive decline in performance of Clock Drawing Test ($F = 3.39$, $p = 0.038$), yet not remarkable in otherwise cognitive subsets.

Conclusion: This study demonstrated that microstructural integrity in the optic nerve was distorted in PD patients, and that this nerve integrity might act as a cognitive predictor of visuospatial dysfunction.

P30.10

A quantitative mass spectrometry assay for measuring alpha synuclein in biological fluids

Amber Lothian, Malcolm Horne, Colin Masters, Blaine Roberts

The Florey Institute of Neuroscience and Mental Health, The University of Melbourne; Cooperative Research Centre for Mental Health, Melbourne, Victoria, Australia

The hallmark pathology of Parkinson's disease is the loss of dopamine neurons in the substantia nigra and the formation of Lewy bodies. The aetiology of Parkinson's disease can be either sporadic or be hereditary. Heredity risk factors are mainly associated with genetic mutations of SCNA, LRRK2, PARK16, PARK2 and DJ-1. The gene SCNA encodes the protein alpha synuclein. Alpha synuclein is 14 kDa abundant neurological protein. Mutations in this protein have been shown to affect the onset and progression of Parkinson's disease. Known familial amino acid point mutations include A53T, E46K, H50Q, G51D, A53E and A30P. Aggregated and misfolded alpha synuclein is a major component of Lewy bodies.

Like other neurological diseases there is an emphasis on identifying protein biomarkers that can be used for differential disease diagnosis, monitoring progression as well as early detection points. As one of the key proteins involved in Parkinson's disease alpha synuclein would be an ideal candidate to be investigated as a Parkinson's disease biomarker and the fact that it can be found in a large array of biological fluids and tissues, only strengthens its

potential. Its presence in both blood and saliva would give rise to a non-invasive, relatively pain free and cost effective biomarker.

Reported here is the development of a mass spectrometry based assay to measure the concentration of alpha synuclein in multiple biological fluids as well as tissues. The use of a mass spectrometry allows decreased interference from antibody cross reactivity, an inexpensive assay as no antibodies are required and the use of a true internal standard. As well as having the potential to measure modified, truncated and mutated forms of the protein, without the need for multiple antibodies or larger sample volumes. The use of a labelled alpha synuclein protein standard spiked into these samples at the beginning of their preparation allows for the correction of any variances between the samples during this process. These properties make mass spectrometry assays ideal for translation between labs and decreases interlab variability.

P30.11

Olfactory impairment predicts underlying dopaminergic deficit in presumed drug-induced Parkinsonism

James Morley

Philadelphia VA Medical Center/University of Pennsylvania School of Medicine, Philadelphia, PA, USA

Objective: To characterize underlying striatal dopaminergic denervation in presumed drug-induced Parkinsonism (DIP) and investigate its relationship to olfactory impairment (OI), a common prodromal finding in Parkinson disease (PD).

Background: DIP associated with dopamine receptor-blocking antipsychotic drugs is common and can be indistinguishable from idiopathic PD. When symptoms persist after drug withdrawal, DIP may represent "unmasking" of underlying prodromal PD. We have previously reported that OI was more common in patients with persistent DIP.

Methods: We reviewed 123I-loblupane (DAT-SPECT) scans that label striatal presynaptic dopaminergic neurons from 33 consecutive patients (29 male) evaluated for DIP. Scans were read as normal or abnormal by a radiologist without knowledge of clinical status. Semi-quantitative analysis of uptake in the caudate, anterior putamen and posterior putamen was performed on a subset of scans by a separate observer blinded to clinical and olfactory data. Olfactory scores (University of Pennsylvania Smell Identification Test or Brief Smell Identification Test) at or below the 10th percentile for age and gender were considered abnormal.

Results: DAT-SPECT was abnormal in 7/33 (21%) of DIP subjects. Olfactory testing was available for 30 subjects and was concordant with the DAT-SPECT result in 27/30 (Odds Ratio=63, 95% CI 4.8-820). In semi-quantitative DAT-SPECT, uptake was significantly lower in DIP subjects with OI (N=7) compared to those with normal olfaction (N=12) in the anterior putamen (1.8 ± 0.68 vs. 2.7 ± 0.46 , $p=0.02$), posterior putamen (1.4 ± 0.66 vs. 2.4 ± 0.53 , $p=0.009$) and lower posterior putamen (1.0 ± 0.51 vs. 2.1 ± 0.48 , $p=0.001$). Uptake in DIP/OI was similar to a PD group (N=3) whereas DIP subjects with normal olfaction were similar to tremor patients (N=4) in all striatal regions. Better olfactory score in DIP subjects was associated with higher uptake for the average anterior putamen ($r=0.64$, $p=0.003$), average posterior putamen ($r=0.74$, $p=0.04$) and lower posterior putamen ($r=0.79$, $p=0.<001$) adjusting for age and gender.

Conclusions: Olfactory testing may be a simple screen to help identify DIP subjects with underlying dopaminergic denervation, consistent with prodromal PD. Olfactory testing could also help guide therapy in patients where DAT-SPECT is not feasible. Identification of prodromal cohorts offers opportunities for study and intervention at the earliest stages of disease.

P30.12

Cerebellar volumes and cognitive differences between Parkinson's disease with and without freezing of gait

Peter Myers, Marie McNeely, Gammon Earhart, Meghan Campbell
Washington University School of Medicine, St Louis, Missouri, USA

Objectives: To examine potential differences in cognition and volumes of cerebellar structures between people with Parkinson disease (PD) with or without freezing of gait (FOG).

Methods: The study included 54 non-demented (MMSE=24) people with mild to moderate PD from a larger exercise intervention study. All testing was performed off anti-Parkinson medications.

The PD group was divided into PD with freezing of gait (PD+FOG, n=22) and PD without freezing of gait (PD-FOG, n=32), based on the new Freezing of Gait Questionnaire (nFOG-Q). To assess cognitive abilities, participants completed Verbal Fluency, Trail Making, and Stroop tests of executive function. Additionally, all participants completed structural T1 and T2 MRI scans. Imaging data were processed with FreeSurfer and the Spatially Unbiased Infratentorial (SUIT) template to segment the cerebellum into 10 distinct lobules per hemisphere. Lobular grey matter volume estimates were derived with white matter masking, and PD+FOG was compared to PD-FOG.

Results: All analyses controlled for participants' age and education. After controlling for estimated intracranial volume, there were no significant differences in cerebellar lobule volumes between PD+FOG and PD-FOG. There was a trend of decreased cognitive performance for PD+FOG compared to PD-FOG ($F=40.0$, $p=.086$), with univariate differences in phonemic Verbal Fluency ($F=7.624$, $p=.008$), semantic Verbal Fluency ($F=4.707$, $p=.035$), and category switch accuracy Verbal Fluency ($F=4.67$, $p=.036$).

Conclusions: Our results suggest potential cognitive deficits in PD with FOG, consistent with previous findings, and emphasize the difficulty with internally generated responses. In contrast, we did not find any cerebellar volumetric differences between PD +/- FOG groups. Although research on motor adaptation implicates the cerebellum in PD with FOG, our results indicate that altered cerebellar function in FOG is not reflected in altered cerebellar volume. It is possible that functional changes precede structural changes.

P30.13

Pre- and post-synaptic dopaminergic dysfunction and clinical features in multiple system atrophy

Kye Won Park, Ho-Sung Ryu, Min Young Oh, Mi-Jung Kim, Sooyeoun You, Young Jin Kim, Juyeon Kim, Kiju Kim, Jae Seung Kim, Sun Ju Chung
South Korea

Objective: To investigate the correlation between clinical features and pre- and post-synaptic dopaminergic dysfunction in patients with multiple system atrophy (MSA).

Background: Multiple system atrophy (MSA) is a sporadic adult-onset neurodegenerative disorder, which is clinically characterized by a combination of parkinsonism, cerebellar ataxia, pyramidal features, and autonomic dysfunction. MSA patients show considerable heterogeneity in clinical features, including parkinsonism and their levodopa responsiveness that is presumably related to heterogeneous nigrostriatal neuropathology.

Methods: We retrospectively analyzed clinical data of 63 MSA patients who underwent both [18F]-FP-CIT PET and [18F]-FDG PET. The tracer uptake of the striatum in [18F]-FP-CIT PET and glucose metabolism of the striatum in [18F]-FDG PET were quantitatively analyzed using eight striatal subregional volume-of-interest templates (bilateral ventral striatum, caudate, anterior

putamen, and posterior putamen). The differences of posterior putamen values between the glucose metabolism of the striatum in [18F]-FDG PET and the tracer uptake of the striatum in [18F]-FP-CIT PET were calculated and classified into two subgroups: MSA-STR group for those with lower quartile (below 25th percentile) value and MSA-SNpc group for those with upper quartile (above 75th percentile) value. The correlation between clinical features of MSA patients and the findings of [18F]-FP-CIT PET and [18F]-FDG PET were investigated.

Results: Levodopa responsiveness was significantly more prevalent in MSA-SNpc (N=16) than in MSA-STR (N=16) (P=0.043). Resting tremor and postural tremor were significantly more frequent in MSA-SNpc than in MSA-STR (P=0.02 and P=0.03, respectively). The proportion of clinical subtypes of MSA-parkinsonian type (MSA-P) and MSA-cerebellar type (MSA-C) was not different between MSA-SNpc and MSA-STR. There was no difference of age at onset of MSA, disease duration, and mini-mental status examination scores between MSA-SNpc and MSA-STR.

Conclusions: MSA patients who had predominant presynaptic dopaminergic dysfunction (MSA-SNpc) showed better levodopa responsiveness and more frequent resting and postural tremor compared with those who had predominant postsynaptic dopaminergic dysfunction (MSA-STR). Our findings may provide useful clinical information for the management of clinically heterogeneous MSA patients.

P30.14

Tau imaging in atypical parkinsonism: preliminary evidence with [11C]PBB3 PET in atypical Parkinsonisms

Alexandra Perez Soriano¹, Julieta Arena¹, Nasim Vafai¹, Elham Shahinfard¹, Qing Miao¹, Paul Schaffer¹, Hitoshi Shinotoh², Makoto Higuchi², Vesna Sossi¹, A. Jon Stoessl¹

¹ Canada

² Japan

Background: The differential diagnosis of parkinsonian disorders can be challenging due to their clinical overlap. Imaging tau pathology in vivo with PET is emerging as a clinical biomarker for more accurate diagnosis, and future assessment of disease modifying therapies.

Objective: To study selective regional binding for Tau pathology in vivo, with [11C]PBB3 ([11C]methylamino pyridin-3-yl buta-1,3-dienyl benzo[d]thiazol-6-ol) in atypical Parkinsonisms such as PSP (Progressive Supranuclear Palsy) patients, and CBS (Corticobasal Syndrome), and evaluate its correlation with clinical severity.

Methods: Dynamic PET scans were obtained for 70 min after the bolus injection of [11C]PBB3 (mean dose 518.97MBq) in five PSP subjects, 1 CBS subject, and 7 age-matched healthy controls. We selected [11C]PBB3 as a tracer due to its high specific activity, high binding specificity, good blood-brain barrier permeability, and good tracer kinetic properties. Subjects included five with a probable PSP diagnosis of 4, 8, 11, 12 and 16 years of disease duration since symptom onset, and one patient with a diagnosis of CBS of 5 year duration since symptom onset. Results were analyzed using a multilinear reference tissue model, using the lateral occipital cortex as reference region.

Results: In healthy controls, there was no regionally selective uptake. In PSP subjects, the highest retention of [11C]PBB3 was observed in putamen, thalamus, globus pallidus and substantia nigra. This was in keeping with areas known to be responsible for clinical symptoms, and with previous pathological evidence of tau accumulation. Longer disease duration and more advanced clinical severity were generally associated with higher tracer retention. The CBS case showed an asymmetric uptake in basal ganglia, as well as cortical uptake in right parietal lobe, correlating with left sided motor symptoms and apraxia.

Conclusions: All PSP patients, as well as the CBS patient showed increased retention of the tracer in the basal ganglia, as clinically expected, and giving in vivo evidence for tau pathology. Tau imaging is a promising tool for the assessment of diagnosis, prognosis, progression, and future monitoring of therapy in PSP and related conditions.

P30.15

Post-translationally modified alpha-1-microglobulin as a plasma biomarker for the early diagnosis of Parkinson's disease

Blaine Roberts¹, Anne Roberts¹, Scott Laffoon¹, Edward Dratz², Malcolm Horne¹

¹ CRC for Mental Health, Florey Institute of Neuroscience and Mental Health, Parkville, VIC, Australia

² Montana State University, Bozeman, MT, USA

Currently, there are no available molecular diagnostic tools to assist in the diagnosis of Parkinson's disease (PD). A diagnostic set of tools would be a highly significant advance and assist in the recruitment of subjects for clinical trials. This would aid in the effort finding a disease modifying therapy. Blood is a readily accessible bio-fluid and has many advantages over more invasive bio-fluids like CSF. We have used samples from the Victorian Parkinson's Disease registry and our patent pending blood biomarker assay to conduct a proteomic screen for plasma biomarkers of PD. We found that four proteins were significantly elevated in the PD samples with a diagnostic accuracy greater than 85%. We next analysed samples from newly diagnosed cases of PD that had yet to receive standard clinical treatment. We found that the protein biomarkers found in our discovery phase were significantly elevated. This indicates a potential for presymptomatic detection of PD. We also show that the protein markers are specifically elevated in PD and not in Alzheimer's disease cases.

Interestingly, one of the protein biomarkers, alpha-microglobulin, contained a specific post-translational modification that may provide a direct insight to the redox chemistry that occurs in PD brain. Our results indicate that a blood based test for the early detection of PD maybe possible and that the four markers we have discovered could form the basis of diagnostic screen to detect PD at the earliest stage possible.

P30.16

Investigation of exercise vs. repetitive transcranial magnetic stimulation induced dopamine release: [11C]Raclopride PET study

Matthew A. Sacheli¹, Bimal Lakhani², Jason L. Neva², Danielle K. Murray³, Nasim Vafai⁴, Nicole Neilson⁵, Jessamyn McKenzie⁵, Katie Dinelle⁴, Lara A. Boyd⁶, Vesna Sossi⁴, A. Jon Stoessl⁵

¹ Pacific Parkinson's Research Centre, Djavad Mowafaghian Centre for Brain Health, University of British Columbia, Vancouver, BC, Canada

² Department of Physical Therapy, Faculty of Medicine, Djavad Mowafaghian Centre for Brain Health, Faculty of Medicine, University of British Columbia, Vancouver, BC, Canada

³ Parkinson's Research Centre, Djavad Mowafaghian Centre for Brain Health, University of British Columbia & Vancouver Coastal Health; Faculty of Medicine, University of British Columbia, Vancouver, BC, Canada

⁴ Department of Physics and Astronomy, University of British Columbia, Vancouver, BC, Canada

⁵ Parkinson's Research Centre, Djavad Mowafaghian Centre for Brain Health, University of British Columbia & Vancouver Coastal Health, Vancouver, BC, Canada

⁶ Department of Physical Therapy, Faculty of Medicine, Djavad Mowafaghian Centre for Brain Health, Vancouver, BC, Canada

Objective: To investigate differences in exercise induced dopamine (DA) release and repetitive transcranial magnetic stimulation (rTMS) induced DA release in subjects with Parkinson's disease (PD).

Methods: DA release was examined in 28 subjects with mild to moderate PD. Subjects were allocated into habitual (n=8) or sedentary (n=20) based on their regular weekly exercise regime. All subjects participated in two [¹¹C]Raclopride (RAC) PET scans separated by either (a) 30 min of cycling at 60% of VO₂ reserve with aerobic exercise (cycling on a stationary bicycle) (habitual n=8, sedentary n=9, total n=17) or (b) rTMS over the primary motor cortex of the less affected hemisphere (sedentary n=11). The post stimulation (exercise or rTMS) scan was compared to the baseline scan to determine the change in binding potential (Δ BPND), a measure of dopamine release, in 8 regions of interest (ROIs); caudate and anterior, middle and posterior putamen on each brain hemisphere. ANCOVA with the baseline scan BPND used as a covariate was conducted to determine differences between exercise and rTMS DA release in habitual exercisers, and sedentary PD subjects.

Results: There was no difference in BPND at baseline between the groups. A group-by-hemisphere interaction ($F(2, 23)=8.31, p<.01$) for Δ BPND was found in caudate. Fisher's LSD post-hoc test revealed a significant difference between exercise induced DA release in PD habitual exercisers and sedentary PD subjects (in both the more and less affected hemispheres, $p<.01$) and exercise induced DA release in habitual exercisers and rTMS induced DA release in sedentary PD subjects ($p<.01$ in both hemispheres) (Figure 1). There were no differences between rTMS and sedentary PD and no differences observed in the putamen of either hemisphere between the groups.

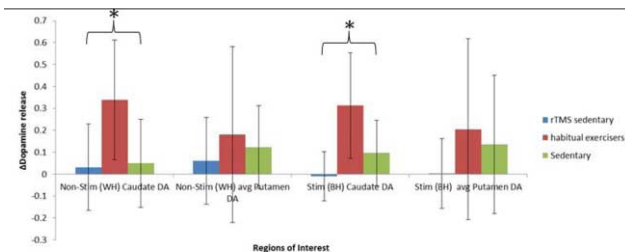


Figure 1. Change in binding potential with [¹¹C]Raclopride in Parkinson's disease subjects who are sedentary or habitual exercisers. Regions of interest (ROIs) include the caudate and average putamen (mean of anterior, middle and posterior ROIs). Δ Dopamine release, baseline binding potential - Post stimulus. Exercise stimulus: 30 minutes of aerobic exercise (cycling on a bicycle at 60 rpm) at 60% of maximal oxygen consumption (VO₂) reserve in PD habitual exercisers and sedentary PD subjects. Repetitive transcranial magnetic stimulation, rTMS: 4x150 stimulations at 90% motor threshold at 10Hz, 10 min rest between blocks in sedentary PD subjects. WH, worse hemisphere contralateral to the more affected side of the body (non-stimulated hemisphere), BH, better hemisphere (stimulated hemisphere). * $p<.01$

Conclusion: These findings suggest that aerobic exercise is a suitable stimulus to elicit DA in caudate regardless of affected hemisphere in habitual exercisers. Additionally, rTMS did not elicit consistent DA release in sedentary PD subjects. However, additional analysis (e.g. cluster analysis) needs to be conducted as spatial differences in DA diffusion to more distal regions in the striatum may explain the lack of detectable rTMS induced DA release in sedentary PD subjects. Based on the differences in DA release between habitual exercisers and sedentary PD subjects, fitness/amount of exercise should be considered when designing future studies investigating DA release.

P30.17

NAMPT mRNA is a potential blood biomarker for de novo Parkinson's disease patients

Jose A Santiago, Alyssa M Littlefield, Judith A Potashkin
Rosalind Franklin University of Medicine and Science, North Chicago, IL, USA

Background: Emerging research indicates that major depressive disorder (MDD) could be one of the earliest prodromal symptoms or risk factors associated with the pathogenesis of Parkinson's disease (PD), the second most common neurodegenerative disorder worldwide, but the mechanisms underlying the association between both diseases remains unknown. Understanding the molecular networks linking these diseases could facilitate the discovery of novel diagnostic and therapeutics.

Methods: We performed a transcriptomic meta-analysis and network analysis of blood microarrays from untreated patients with PD and MDD. The most significant gene identified in these analyses was evaluated in RNA prepared from whole blood from 99 untreated PD patients and 101 healthy controls (HC) nested in the cross-sectional Parkinson's Progression Markers Initiative (PPMI) by quantitative real-time PCR assays.

Results: Integrative transcriptomic meta-analysis and network analysis identified genes enriched in pathways related to the immune system, metabolism of lipids, glucose, fatty acids, nicotinamide, lysosome, insulin signaling and type 1 diabetes. Nicotinamide phosphoribosyltransferase (NAMPT), an adipokine that plays a role in lipid and glucose metabolism, was identified as the most significant dysregulated gene. Relative abundance of NAMPT was significantly upregulated in blood of PD patients compared to HC in PPMI.

Conclusions: Here we demonstrate that shared molecular networks between PD and MDD provide an additional source of biologically relevant biomarkers. Evaluation of NAMPT in a larger prospective longitudinal study and in patients at risk of PD is warranted.

P30.18

Does walking exercise and music change the structures of brains afflicted with Parkinson's disease?

Sun Nee Tan¹, Robert Baumeister², Martin McKeown³, Bin Hu⁴

¹ Pacific Parkinson's Research Centre, University of British Columbia, Vancouver, Canada, Vancouver, British Columbia, Canada

² Department of Biomedical Engineering, University of British Columbia, Vancouver, British Columbia, Canada

³ Faculty of Medicine, Pacific Parkinson's Research Centre, University of British Columbia, Vancouver, British Columbia, Canada

⁴ Department of Clinical Neurosciences, University of Calgary, Calgary, Alberta, Canada

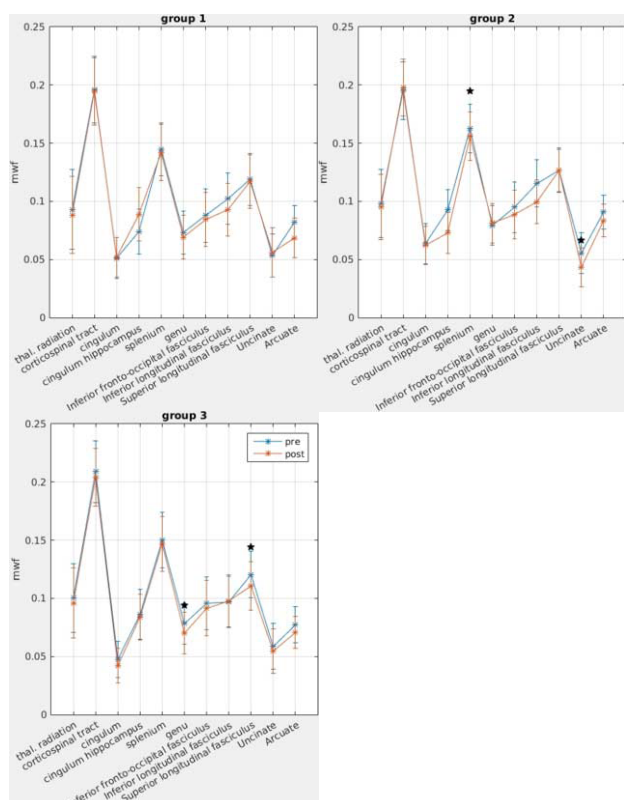
Objective: This study aims to investigate whether walking exercise with and without music (Ambuloso™) is related with structural changes to myelinated nerve tracts in Parkinson's patients.

Methods: PD participants were randomly assigned into 3 groups of walking exercise routine: Gp1: walking only (n=5), Gp2: walking while listening to music (n=7) and Gp3: large step walking with music (n=6). An ipod installed with the GaitReminder™ app is strapped on to the patient's knee to play music and measure various gait parameters while patients walk. In the third group, patients were cued by music playing when they walked with larger than usual step sizes. All participants completed at least 100km walking distance off-site in this program. 3T MRI brain scans include multicomponent T2 relaxation imaging to indirectly measure the structural changes

of white matter tracts in the brain. One trained operator assessed all participants using the United Parkinson's Disease Ratings Scale (UPDRS)-III which indicates quantitatively measures severity of motor symptoms in PD.

Results: Myelin water fraction (MWF) values are significantly different ($p < 0.05$) walking exercise in Gp2 and Gp3 only. In Gp2, alterations were seen in the splenium and uncinate tracts. In Gp3, the genu and superior longitudinal fasciculus are nerve tracts that demonstrated a change in MWF post-exercise. Severity of motor symptoms are significantly reduced (lower UPDRS scores) in Gp2 and Gp3 only.

Conclusion: Preliminary data suggest that walking exercise with exposure to music appears to be more effective in ameliorating motor symptoms in PD. Further research is critical to further understand the relation between changes in white matter tracts and influence of music during walking exercise in PD patients.



P30.19

Relationship between plasma uric levels and Parkinson's disease in a Nigerian population

Yusuf Zubair¹, Shyngle Oyakhire², Saheed Alimi², Lukman Owolabi³, Sunday Bwala⁴

¹ Abuja, FCT, Nigeria

² Neurology Unit, Department of Internal Medicine, National Hospital Abuja, Abuja, FCT, Nigeria

³ Department of Medicine, Aminu Kano Teaching Hospital, Kano, Kano, Nigeria

⁴ Neurology unit, Department of Medicine, National Hospital Abuja, Abuja, FCT, Nigeria

Introduction: Parkinson's disease is the second most common neurodegenerative disease worldwide and overwhelming evidence shows oxidative stress plays an important role in its pathogenesis. Uric acid (UA), a product of purine metabolism and a natural antioxidant in humans seems to reduce the risk and progression of PD. There is paucity of data on the relationship of UA levels and PD in Africa.

Objectives: The study aimed to examine the plasma UA levels among Nigerian PD patients attending National Hospital Abuja (NHA) compared with age and sex-matched healthy controls. The other objectives were to relate disease duration and disease severity with plasma UA levels.

Methods: The study was a cross-sectional study of 60 consecutive Nigerian PD patients attending Neurology clinic, NHA from July 2014 to March 2015 and 60 age and sex-matched healthy controls. The participants underwent clinical evaluation. Disease duration, Hoehn and Yahr (H&Y) and Unified Parkinson Disease Rating Scale (UPDRS) part III were documented. Plasma creatinine was also measured to roughly reflect renal function.

Results: The mean age of PD patients studied was 61.18 ± 8.53 years; while that of the controls was 61.11 ± 8.80 years. Male to female ratio was 3.3: 1. Plasma UA levels were found to be significantly lower in PD patients compared to controls (4.43 ± 1.23 mg/dl vs 5.26 ± 0.89 mg/dl) $p = 0.001$. This association was observed in both gender, but weaker in females. Only plasma UA level was found to significantly decrease the odds of PD (OR 0.495; $p < 0.001$; 95% CI [0.344–0.714]). Smoking, well water ingestion, coffee intake, weight did not significantly increase the risk of PD. The mean duration of disease was 40.23 ± 23.58 months. Median score of H&Y and UPDRSIII were 2 (1–5) and 43 (11–76) respectively. Disease duration showed a very weak, inverse, linear correlation with plasma UA levels but this was not statistically significant (Spearman's correlation ($r = -0.121$, $p = 0.545$)). Furthermore, there was no significant statistical difference between short term (<36 months) and long term (≥ 36 months) PD patients (4.61 ± 1.15 mg/dl vs 4.31 ± 1.29 mg/dl) $p = 0.364$. However, correlation analysis showed a statistically significant, moderate, inverse, linear relationship between plasma UA and both H&Y ($r = -0.541$, $p < 0.001$) and UPDRS III ($r = -0.544$, $p < 0.001$).

Conclusion: Our study showed consistent findings that UA might be protective against PD and a potential marker for disease progression.

CLINICAL SCIENCES: PHARMACOLOGICAL THERAPY

P31.01

Levodopa carbidopa infusion gel to treat very advanced idiopathic Parkinson's disease: a case series of atypical LCIG patients

Jason Aldred¹, Anne Marie Bergeleen²

¹ Northwest Neurological, PLLC, Spokane, WA, USA

² USA

Objective: To demonstrate LCIG is well-tolerated and effective in advanced Parkinson's disease in a group of patients who are not typical candidates.

Methods: 4 patients with advanced idiopathic Parkinson's received t-GJ tube for delivery of LCIG. In addition all had risk factors considered relative contraindications for LCIG including significant cognitive impairment or placement of DBS for with concomitant use of LCIG has not been well studied. Of these patients Patient #1 had advanced dementia with hallucinations associated with levodopa

peak dose dyskinesia. Patient #2 patient had received DBS bilateral STN for five years with prior responsiveness before developing disabling ON freezing of gait despite adjustment of DBS and oral anti-parkinson medication. Patient #3 was determined to have moderate cognitive impairment and deemed high risk for worsening cognitive impairment from DBS. Patient #4 had young onset Parkinson's disease with severe motor fluctuation and dyskinesia and severe dementia.

Results: All 4 underwent outpatient IR guided t-GJ tube placement without complications. All 4 patients initiated LCIG the day following the procedure in outpatient neurology clinic completing satisfactory maintenance LCIG dose by day 3. Patient #1 had experienced dramatic improvement in motor fluctuations with improved UPDRS to X with reduction in derlerium from severe to mild and this was sustained over entire treatment duration to date. Patient #2 experienced dramatic improvement in ON FOG on day 1 of titration that was sustained for 6 weeks. Over time subjective increase of FOG increased but was not witnessed in two clinic follow up visits. Patient #3 showed improvement in all motor symptoms associated with PD but experienced mild irritation near stoma site that improved within 2 weeks. Patient number #4 experienced significant improvement in motor symptoms without significant worsening of cognitive impairment.

No patients discontinued LCIG therapy. Minor GI pain was noted by patient #2 but this resolved by day 3 post-tube placement and no other patients reported significant abdominal pain or significant adverse events.

Conclusion: Those with Parkinson's disease with cognitive impairment or who have received DBS and have ON FOG may benefit from LCIG therapy.

P31.02

Positive allosteric modulators of metabotropic glutamate receptor 4 (mGlu4) for the symptomatic and disease-modifying treatment of Parkinson's disease

Anna Blobaum, Corey Hopkins, Colleen Niswender, P. Jeffrey Conn, Craig Lindsley

Vanderbilt Center for Neuroscience Drug Discovery, Franklin, TN, USA

Disorders of the CNS remain some of the most elusive targets for the pharmaceutical industry and academic researchers to tackle in drug discovery and development. Although, Parkinson's disease (PD) is the second most common neurodegenerative disease, no effective long term treatment or cure has been developed. The gold standard therapy for PD is to replace lost dopamine using either levodopa (L-DOPA), which is converted into dopamine, or to treat patients with dopamine receptor agonists. Due to adverse effects, it has been hypothesized that the core symptoms of patients might be more effectively treated if lower doses of these drugs could be co-dosed with mechanistically distinct pharmacological agents or, alternately, if dopaminergic-based treatments could be avoided altogether. Metabotropic glutamate receptor 4 (mGlu4) is highly expressed presynaptically in projections from the striatum to the external globus pallidus (GPe) in the brain. Activation or potentiation of mGlu4 activity at the striato-GPe synapse leads to reductions in GABA release in the GPe, ultimately normalizing output from the basal ganglia. To generate drug candidates that are highly selective for mGlu4, we and others have developed positive allosteric modulators (PAMs) of mGlu4 that exhibit antiparkinsonian effects in numerous PD animal models after acute dosing. These results suggest that mGlu4 PAMs should induce an acute reversal of PD motor symptoms. Utilizing a functional HTS and medicinal chemistry approach, we have discovered a novel series of mGlu4 PAMs with ideal pharmacokinetic and other properties important for advancing into clinical development. These preclinical candidates display

robust brain penetration, are suitable for chronic oral dosing, and demonstrate robust in vivo efficacy in models of PD. We are now poised to select the optimal development candidate and advance to IND-enabling studies required for future clinical testing.

P31.03

Prokinetic pharmacologic intervention as a novel method for optimization of levodopa pharmacokinetics and pharmacodynamics in Parkinson's disease: results from a pilot study using erythromycin

Leslie Cloud¹, Serendipity Zapanta Rinonos¹, Jeffrey Hoder¹, Virginia Norris¹, John Kuemmerle², Jurgen Venitz³, Matthew Halquist³, Wen Wan⁴

¹ Parkinson's Disease & Movement Disorders Center, Virginia Commonwealth University School of Medicine, Richmond, VA, USA

² Division of Gastroenterology, Hepatology, and Nutrition, Virginia Commonwealth University School of Medicine, Richmond, VA, USA

³ Department of Pharmaceutics, Virginia Commonwealth University School of Pharmacy, Richmond, VA, USA

⁴ Department of Biostatistics, Virginia Commonwealth University School of Medicine, Richmond, VA, USA

Objectives: To assess the effect of erythromycin (EM) on gastric emptying in Parkinson's disease (PD) and to determine its effects on levodopa (LD) pharmacokinetics and pharmacodynamics (PK/PD).

Background: Studies suggest that the prevalence of delayed gastric emptying (DGE) in PD may approach 100%, occurring in early-stage, untreated patients as well as treated, advanced-stage patients. DGE has the potential to profoundly affect LD delivery, efficacy, and response fluctuations in PD. LD exacerbates DGE. This has key PK implications, as LD must reach the small intestine for absorption. Unfortunately, there are no FDA-approved drugs for DGE that are safe in PD. Metoclopramide is contraindicated in PD due to central dopamine receptor antagonism. We predicted that EM, a motilin agonist in widespread off-label use for gastroparesis, would mitigate LD-induced DGE, thereby enhancing both LD absorption and its pharmacodynamic response.

Methods: This study followed a randomized, double blind, placebo-controlled, crossover design. Eight eligible PD patients were randomized to either sequence: Intravenous placebo-EM (100 mg) or EM-placebo, with intervening 2-week washout. Following each EM infusion, patients received their usual oral levodopa dose. Gastric emptying time (GET) was measured by SmartPillTM, AUC 0-4hour and Cmax were estimated from serial LD plasma concentrations (determined by validated LC-MS/MS assay), while the pharmacodynamic response was measured by motor United Parkinson Disease Rating Scale (UPDRS), Abnormal Involuntary Movement Scale, 9-hole peg test, five times sit-to-stand, comfortable 20 feet gait speed, and timed-up-and-go.

Results: A statistically significant improvement in GET by 36 minutes ($p=0.036$) was observed after EM. A corresponding 15% increase in LD AUC 0-4hour was not statistically significant, however, likely due to the small sample size. Of the pharmacodynamic assessments, only UPDRS score was significantly improved by 35% ($p=0.0314$) after EM.

Conclusions: EM accelerates gastric emptying in PD patients, which may have the potential to improve LD PK/PD.

P31.04

Five-year's of levodopa-carbidopa intestinal gel treatment: safety and efficacy from an open-label phase 3 study in advanced Parkinson's disease patients

Hubert H. Fernandez¹, James T. Boyd², Victor S.C. Fung³, Mark F. Lew⁴, Ramon L. Rodriguez⁵, John T. Slevin⁶, David G. Standaert⁷, Cindy Zadikoff⁸, Krai Chatamra⁹, Susan Eaton⁹, Maurizio F. Facheris⁹, Coleen Hall⁹, Weining Z. Robieson⁹, Janet Benesh⁹

¹ Center for Neurological Restoration, Cleveland Clinic, Cleveland, Ohio, USA

² University of Vermont College of Medicine, Burlington, Vermont, USA

³ Westmead Hospital and Sydney Medical School, Sydney, Australia

⁴ Keck/University of Southern California School of Medicine, Los Angeles, CA, USA

⁵ Orlando Veteran's Affairs Medical Center, Orlando, FL, USA

⁶ University of Kentucky Medical Center, Lexington, Kentucky, USA

⁷ University of Alabama at Birmingham, Birmingham, Alabama, USA

⁸ Feinberg School of Medicine, Northwestern University, Chicago, IL, USA

⁹ AbbVie Inc., North Chicago, IL, USA

Objective: To assess the 5-year safety, tolerability, and efficacy of levodopa-carbidopa intestinal gel (LCIG, carbidopa-levodopa enteral suspension in the US) in advanced Parkinson's disease (PD) patients in the final phase 3, open-label, continued-access-to-treatment study from the US registration program.

Background: LCIG is continuously delivered via percutaneous gastrojejunostomy (PEG-J) in advanced PD patients with motor fluctuations inadequately controlled by oral anti-Parkinsonian medications.

Methods: The study enrolled advanced PD patients (N=262) who had completed either a 12-week double-blind study and its 52-week open-label extension or a separate 54-week open-label study. Patients could remain in this continued-access-to-treatment study until LCIG was commercially available. Adverse events from start of this extension through October 2015 and efficacy data (collected from US patients only per protocol amendment, n=86 with =1 post-baseline measure) were summarized.

Results: In the entire safety and efficacy cohort, mean age was 64.1 years, PD duration was 11.4 years, and total exposure to LCIG was 4.1 years (range 1.2-6.9 years). At the data cutoff, 110 (42%) patients had successfully completed the study and begun treatment with commercial LCIG, 63 (24%) continued LCIG treatment within the study, and 89 (34%) had prematurely discontinued. While most patients (246, 94%) had an AE and 140 (53%) had a serious AE (Table 1), fewer (62, 24%) discontinued treatment due to an AE. There were 38 deaths (15%), of which 2 were considered possibly related to treatment and the rest unrelated. Efficacy-cohort patients who began LCIG infusion in the double-blind study had a significant change in mean daily hours of "off" time from first infusion to final visit (-4.9 [SD=2.3], n=19, P<0.001), with no significant change from baseline of this extension study to the final visit (-0.33 [SD=2.5], P=0.569). Efficacy-cohort patients who began LCIG infusion in open-label studies (total n=56) had similar efficacy results.

Conclusions: Most advanced PD patients who enrolled in the continued-access study experienced sustained and clinically meaningful long-term benefits from LCIG, and successfully transitioned to commercial LCIG or continued to participate in the open-label study. While a high incidence of AEs was noted, the discontinuation rate due to AEs was relatively low in this population.

Table 1: Adverse events (AEs) and serious AEs during the continued-access-to-treatment extension study

AEs occurring in ≥ 10% of patients	n (% of N=262)
Postoperative wound infection	59 (23)
Vitamin B6 decreased	58 (22)
Fall	55 (21)
Urinary tract infection	50 (19)
Blood homocysteine increased	48 (18)
Excessive granulation tissue	41 (16)
Incision site erythema	38 (15)
Weight decreased	36 (14)
Complication of device insertion ^a	33 (13)
Parkinson's disease ^b	33 (13)
Procedural site reaction	33 (13)
Nausea	32 (12)
Depression	30 (11)
Constipation	29 (11)
Insomnia	29 (11)
Abdominal pain	27 (10)
Dyskinesia	27 (10)
Procedural pain	27 (10)
Serious AEs occurring in ≥ 3% of patients	
Pneumonia	17 (6.5)
Complication of device insertion ^a	14 (5.3)
Fall	12 (4.6)
Pneumonia aspiration	8 (3.1)
Postoperative wound infection	8 (3.1)
Weight decreased	8 (3.1)

Adverse events are summarized from start of the continued-access study (i.e. from 52-74 weeks into LCIG treatment) through the October 2015 data cutoff. A single event could be coded to ≥ 1 MedDRA preferred term descriptive of the event. Events associated with the procedure or device are italicized.

^aEvents with this term were most often additionally coded to abdominal pain, abdominal discomfort, abdominal distention, flatulence, pneumoperitoneum.

^bRefers to the re-emergence of Parkinson's symptoms, often due to a problem with drug delivery.

P31.05

Impact of droxidopa on symptoms, functionality, and health-related quality of life at 1 month following treatment initiation in a prospective study of patients with neurogenic orthostatic hypotension

Clément François¹, Kim McLeod², Amy Duhig², Augustina Ogbonnaya², Apryl Quillen², Joan Cannon¹, Byron Padilla¹, Steven Kymes¹, Cyndya A. Shibus³, Italo Biaggioni³

¹ Lundbeck, LLC, Deerfield, IL, USA

² Xcenda, LLC, Palm Harbor, FL, USA

³ Vanderbilt University Medical Center, Nashville, TN, USA

Background: Patients with neurodegenerative disorders such as Parkinson's disease (PD) may have associated autonomic nervous system impairment with neurogenic orthostatic hypotension (nOH). In 2014, droxidopa was approved in the USA for treatment of dizziness/lightheadedness symptoms in adults with symptomatic nOH due to autonomic failure. Persistence of benefit beyond 2 weeks has not been established.

Methods: A 6-month, prospective cohort study of patients initiating droxidopa for treatment of nOH is being conducted. The first patient was recruited June 30, 2015, and follow-up will be completed in June 2016. Patients reported on their dizziness/lightheadedness symptoms, rated from 0 (none) to 10 (worst possible), measured using the Orthostatic Hypotension Symptom Assessment Item 1 (OHSA Item 1), functionality assessed by the Sheehan Disability Scale (SDS), and health-related quality of life (HR-QoL) using the 8-item Short-Form Health Survey (SF-8). Interim study results for 1-month outcomes following droxidopa initiation are reported.

Results: Initial study enrollment was 179 patients; 139 patients completed 1 month follow-up. The initial cohort consisted of 51.4% women and 85.5% non-Hispanic whites; mean age at baseline was 62.8 years. The most frequent diagnoses were autonomic failure (no cause identified; 65.4%) and PD (33.0%). At 1 month following droxidopa initiation (mean ± SD daily dose, 1015±448 mg), statistically significant improvements in the OHSA Item 1 score

(dizziness/lightheadedness symptoms) were demonstrated (mean change from baseline, 1.5 units; $P < 0.001$). Statistically significant improvements in functionality were also demonstrated by changes in the SDS global functional impairment score ($P = 0.0011$) and in ratings for impact on work/school, social life/leisure activities, and family life/home responsibilities ($P = 0.0417$ for all). On the SF-8, droxidopa was associated with significant improvements from baseline in the physical component score ($P = 0.0011$), and in 4 of the 8 individual domains (general health, physical function, role-physical, and vitality; $P = 0.0414$ for all).

Conclusions: After 1 month of droxidopa treatment, improvements in nOH symptoms, functionality, and HR-QoL from baseline were reported in this first real-world study of nOH patients. Future reports will examine persistence of the benefit of droxidopa at 3 and 6 months. This observational study complements an ongoing long-term randomized trial.

Funding: Lundbeck

P31.06

Initiating intra jejunal infusion of levodopa/carbidopa intestinal gel with the naso-jejunal (NJ) tube test phase.

Benoit Gagnon

Centre Hospitalier Universitaire de Montreal, Montreal, Quebec, Canada

Objective: To present our experience with naso-jejunal (NJ) test phase with levodopa/carbidopa intestinal gel (LCIG) for patients with Parkinson disease during one week prior to percutaneous endoscopic gastrostomy with jejunal tube (PEG-J)

Background: During the LCIG study which took place at CHUM Movement Disorders Unit in 2011, all patients were started with a nasal tube for 2–3 days to validate the treatment efficiency and confirm the patient and caregiver's commitment. Our team decided to go on with this naso-jejunal test phase before the PEG-J surgery for all the patients when LCIG was approved from Health Canada.

Methods: All patients underwent endoscopic nasal tube placement as outpatient by a gastroenterologist. The next morning, we started the titration of the LCIG at our walk-in clinic. Patients have to come at the clinic for 2 or 3 days in a row for dosage adjustments. Then they stay at home with the NJ tube between 5 to 7 days before the surgery to learn the pump manipulation and certify their satisfaction with the LCIG response. A few patients, who live far from our hospital and a few with special needs, will be hospitalized for the titration only.

If patient has at least 50% improvement of their condition, PEG-J will be installed as outpatient and LCIG treatment is restart right after the PEG-J placement, the same day.

Results: 27 patients were recruited since July 2013 and 19 are still on LCIG treatment. Three stopped treatment during NJ phase test and did not undergo the PEG-J surgery. For the 3 of them, the response with LCIG did not differ from the PO medication. Three others stopped after PEG-J installation for different medical reasons. One developed peritonitis and gastrostomy was removed. One patient died and cause of death was not related to LCIG.

Discussion: Useless PEG-J placement was avoided for 10% of PD patients. The NG test phase allowed us to make dosage adjustment and patient's education prior to PEG-J installation and to restart LCIG treatment just after.

P31.07

Adjustments of antiparkinsonian medication due to long-term subthalamic deep brain stimulation in patients with Parkinson's disease

Anna Gamaleya¹, Ekaterina Bri², Alexey Tomskiy¹, Anna Poddubskaya¹, Nataliya Gubareva², Vladimir Shabalov¹, Nataliya Fedorova²

¹ Burdenko Neurosurgical Institute, Moscow, Russia

² Russian Medical Academy of Postgraduate Education, Moscow, Russia

Introduction: Following DBS STN, antiparkinsonian medication could be optimized. However, the strategy of postoperative PD management differs between movement disorder centers.

Objective: To assess long-term changes in medication under DBS STN in PD patients with in our clinic.

Methods: We evaluated 76 PD patients treated with DBS STN. Minimal follow-up was 2 years. Mean age at surgery was 54.3 ± 9.1 years; disease duration – 12.2 ± 4.4 years; Hoehn&Yahr stage – 3.5 ± 0.5 . We analyzed antiparkinsonian medication scheme preoperatively and appropriate adjustments under continuous DBS STN yearly, maximum follow-up was 5 years.

Results: All patients received levodopa before surgery; 14 patients (18%) – more than 2000 mg daily. 59 patients (78%) were on combined therapy; 37 patients (49%) took three and more types of antiparkinsonian drugs. Under DBS STN, we aimed primarily to minimize levodopa dosage preserving dopamine antagonists' dose at the therapeutic level. In the first year of DBS STN, levodopa-dose was reduced by $63 \pm 27\%$ and total levodopa equivalent daily dose (LEDD) was reduced by $50 \pm 27\%$; in the second year, by $62 \pm 27\%$ and $50 \pm 24\%$; in the fifth year, by $56 \pm 31\%$ and $41 \pm 31\%$ (37 patients analyzed), respectively. No patients stopped medication completely. After the second year of DBS STN, 20 patients (26%) stayed on monotherapy (levodopa or dopamine agonist); in 13 patients (17%) levodopa could be withdrawn; proportion of patients receiving dopamine agonists increased from 61% before surgery to 78%. After the fifth year of DBS STN, 8 patients (22%) were still on monotherapy, 5 patients (14%) did not receive levodopa, 33 patients (89%) had dopamine agonists in medication scheme. Number of patients taking levodopa/COMT-inhibitor combinations and prolonged-release levodopa preparations significantly decreased to the fifth year of DBS STN. Anticholinergics could be discontinued in most of the patients. At the same time, 11 patients (30%) still needed multi-drug treatment; in 16% of patients, antidepressants were required.

Conclusions: DBS STN allowed a considerable persistent reduction in dopaminergic medication (levodopa-dose and levodopa equivalent daily dose). Medication could be partially simplified. Therapeutic regimens based on predominant decrease in pure levodopa-dose with increasing role of dopamine agonists showed safety in long-term follow-up. Optimization of therapeutical scheme due to DBS STN might contribute to improving in quality of life of PD patients.

P31.08

Pharmacological inhibition of the NLRP3 inflammasome in the CNS with an orally active inhibitor protects against synuclein pathology and dopaminergic degeneration in Parkinson's disease models

Richard Gordon¹, Eduardo Albornoz², Daniel Christie¹, Monica Langley³, Vinod Kumar¹, Susanna Mantovani⁴, Mark Butler², Avril Robertson², Dominic Rowe⁵, Anumantha Kanthasamy³, Kate Schroder², Matthew Cooper², Trent Woodruff¹

¹ School of Biomedical Sciences, The University of Queensland, Brisbane, QLD 4072, Australia, Brisbane, Queensland, Australia

² Institute for Molecular Bioscience, University of Queensland, Brisbane, Australia., Brisbane, Queensland, Australia

³ Parkinson Disorders Research Program, Department of Biomedical Sciences, Iowa State University, USA, Ames, Iowa, USA

⁴ Wesley Medical Research, Brisbane, Queensland, Australia., Brisbane, Queensland, Australia

⁵ Department of Neurology, Faculty of Medicine and Health Sciences, Macquarie University, Sydney, New South Wales, Australia

Parkinson's disease (PD) pathology is characterized by a profound loss of nigral dopaminergic neurons that is accompanied by chronic neuroinflammation and extensive α -synuclein inclusions in the form of Lewy-bodies. Fibrillar synuclein has recently been shown to be the major neurotoxic species in PD, mediating cell-to-cell transmission and neuropathology. However, the mechanisms by which synuclein pathology and spread contributes to dopaminergic degeneration is unclear. Chronic activation of the NLRP3 inflammasome in the CNS by insoluble protein aggregates, is emerging as a major pathological mechanism that can drive progressive neurodegeneration. Herein, we demonstrate that activation of the microglial NLRP3 inflammasome is a common pathway triggered by both fibrillar synuclein and by dopaminergic degeneration in the absence of synuclein aggregates. Key hallmarks of inflammasome activation including cleaved caspase-1 p20, and ASC upregulation are evident in the substantia nigra of PD patients. Similarly, we also found extensive NLRP3 inflammasome in multiple pre-clinical mouse models of PD. Our mechanistic studies with primary microglia demonstrate that fibrillar Syn activates the NLRP3 inflammasome with delayed kinetics compared to canonical NLRP3 agonists. Crucially, we demonstrate that the potent NLRP3 inhibitor, MCC950, is active in the central nervous system following oral dosing, and can effectively block inflammasome activation and neuropathology in PD models. Significantly, chronic daily oral dosing of MCC950 effectively protected against motor deficits and nigrostriatal dopaminergic degeneration induced by synuclein fibrils in the pre-formed fibril (PFF) model of synuclein pathology. Collectively, these findings suggest that the microglial NLRP3 inflammasome pathway could be a sustained source of neuroinflammation that drives PD pathology, and highlights microglial NLRP3 as a novel therapeutic target for PD.

P31.09

PD MED – update on a pragmatic randomised clinical trial of Parkinson's disease medication using patient-rated outcomes and involving 2120 people with Parkinson's disease, 1306 of their carers and up to 15 years of follow-up

Richard Gray¹, Natalie Ives², Smitaa Patel², Caroline Rick², Alastair Gray¹, Crispin Jenkinson¹, Emma McIntosh³, Francis Dowling², Keith Wheatley², Adrian Williams⁴, Carl Clarke²

¹ University of Oxford, Oxford, United Kingdom

² University of Birmingham, Birmingham, United Kingdom

³ University of Glasgow, Glasgow, United Kingdom

⁴ University Hospital Birmingham, Birmingham, United Kingdom

Aim: PD MED aimed to determine which class of drug as initial treatment for newly-diagnosed PD provides the most effective control and best quality of life (QoL). A second aim was to determine which drug to add when symptoms became poorly controlled with the initial treatment.

Methods: 1620 people with newly diagnosed PD were randomised 1:1:1 between levodopa-sparing therapy (dopamine agonist (DA) or MAOBI) and levodopa alone. 500 experiencing uncontrolled motor complications were randomised 1:1:1 between dopamine degradation inhibitors (DDI; COMTI or MAOBI) and DA. Primary

outcome: mobility dimension on the patient-rated PDQ-39 QoL scale. Secondary outcomes: other dimensions of PDQ-39, EQ-5D, motor complications, dementia and mortality analysed using repeated measures regression and logrank methods.

Results: With a median follow-up of 3 years, patients randomised to levodopa had slightly better mobility, activity of daily living and overall PDQ-39 quality of life scores than those allocated levodopa-sparing. Fewer patients in the levodopa group developed dementia, entered institutional care or died but these differences were not significant perhaps because longer follow-up was needed to assess any neuroprotective effect of levodopa. Quality of life was rated better with MAOBI than DA as levodopa-sparing therapy. MAOBI also outperformed COMTI when added to levodopa in later disease with mobility and overall quality of life rated better and a suggestion that the risk of dementia, institutionalisation and death may also be reduced though longer follow-up is, again, needed for confirmation. Follow-up of PD MED is currently being updated and results will be presented with a median of 6 years of follow-up.

Conclusion: First results of the PD MED trial (Gray et al, Lancet 2014) suggested that both levodopa and MAOBI inhibitors might have neuroprotective effects. However, such effects may take many years to emerge so large trials of long duration are needed to detect them. Longer follow-up of PD MED provides a unique opportunity to confirm, or refute, these possible neuroprotective effects.

P31.10

Istradefylline and Preladenant as an adjuvant therapies for patients with Parkinson's disease

Zeinab Hassan¹, Hussien Ahmed¹, Abdallah El-sherbiny¹, Shady Azzam², Omnya Osama³, Yasmeim Hany Ibraheim¹, Ahmed Negida¹

¹ Faculty of Medicine, Zagazig University, Zagazig, El-Sharkia, Egypt

² Faculty of Medicine, Al Azhar University, Cairo, Egypt

³ Kasr Al ainy School of Medicine, Cairo University, Cairo, Egypt

Introduction: The aim of this meta-analysis is to synthesize evidence about the efficacy of the Istradefylline and Preladenant for patients with Parkinson's disease.

Methods: We searched PubMed through, November, 2015, using relevant keywords. Records were screened for randomized controlled trials assessing the efficacy of istradefylline and Preladenant in comparison to placebo. Data were extracted and were analysed by RevMan version 5.3 for windows and Open[META-analyst].

Results: Ten RCTs (istradefylline: 7 RCTs, n=2231; and preladenant: 3 RCTs, n=1507 patients) were pooled in the final analysis. The overall effect estimate favored istradefylline than placebo in terms of: (1) daily time off (20 mg/day: WMD -0.621, 95% CI -1.064 to -0.178; 40 mg/day: WMD -0.801, 95% CI -1.221 to -0.381); (2) on time without troublesome dyskinesia (20 mg/day: WMD 0.747, 95% CI 0.313 to 1.180; 40 mg/day: WMD 0.856, 95% CI 0.401 to 1.312); and (3) UPDRS III "on state" (20 mg/day: WMD -0.917, 95% CI -1.717 to -0.117; 40 mg/day: WMD -1.612; 95% CI -2.491 to -0.734). However, the overall effect estimate did not favor istradefylline over placebo in terms of: (1) on time with dyskinesia (20 mg/day: WMD 0.891, 95% CI -0.662 to 2.444; 40 mg/day: WMD 0.982, 95% CI -0.083 to 2.048); (2) UPDRS II during off state (20 mg/day: WMD -0.488, 95% CI -1.130 to 0.155; 40 mg/day: WMD -0.519, 95% CI -1.301 to 0.263); and (3) UPDRS II during on state (20 mg/day: WMD 0.094, 95% CI -0.545 to 0.734); 40 mg/day: WMD -0.189, 95% CI -0.491 to 0.114). For the Preladenant, the overall effect size favored Preladenant than Placebo in terms of "daily time off" (WMD -0.303, 95% CI -0.543 to -0.064). However, in the subgroup analysis, this effect size was not significant for the 2 mg, 5 mg, and 10 mg doses compared to placebo. In terms of "ON time without troublesome dyskinesia", the overall effect size did not

favor either of the two groups (WMD 0.239; 95% CI -0.032 to 0.509) and the effect size was not significant for the subgroups of 2 mg, 5 mg, and 10 mg doses in comparison to placebo.

Conclusion: Istradefylline could improve the motor functions during the "on state" and it was effective in reducing the "off time" without increasing the "on time with troublesome dyskinesia". Current evidence suggests that Preladenant can reduce the "off time". However, further randomized controlled trials on Preladenant are needed.

P31.11

Patient global impression of improvement in advanced Parkinson's disease patients treated with IPX066, extended-release carbidopa-levodopa capsules (RYTARY®, NUMIENT™)

Robert Hauser¹, Nishit B. Modi², Sarita Khanna², Suneel Gupta²

¹ University of South Florida, Tampa, FL, USA

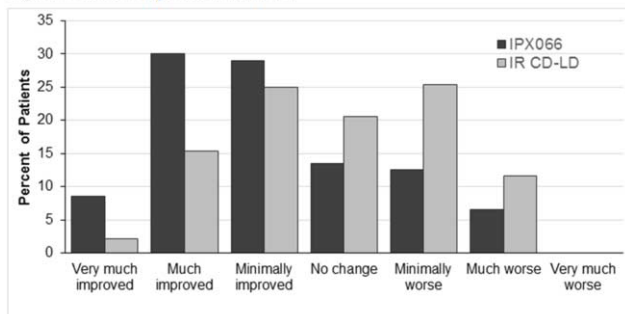
² Impax Laboratories, Inc., Hayward, CA, USA

Background: IPX066 [RYTARY®, NUMIENT(TM)] is an extended-release capsule formulation of carbidopa-levodopa (CD-LD). Following an initial peak at about one hour after ingestion, plasma levodopa concentrations are maintained for approximately 4–5 hours. In clinical trials, IPX066 significantly improved motor function and activities of daily living in early and advanced Parkinson's disease (PD) patients.

Objective: Describe the magnitude of change in clinical measures in patients who rated themselves as minimally or much improved after treatment with IPX066.

Methods: ADVANCE-PD examined the efficacy and safety of IPX066 vs. immediate-release (IR) CD-LD in patients with advanced PD. Patients underwent open-label conversion to IPX066 followed by 13 weeks of double-blind treatment with either IR or IPX066. Study endpoints included Patient Global Impression of Change (PGI), PD patient diaries, and Unified Parkinson Disease Rating Scale (UPDRS) activities of daily living (ADL) and motor scores.

Figure 1. Patient responses on the PGI



Results: Of the 471 patients enrolled, 393 (87.3%) patients were randomized to double-blind treatment. On the PGI, a greater proportion of patients rated themselves as improved (minimally, much, or very much) compared to baseline after IPX066 treatment than with IR (67.5% vs. 43.2%) (Figure 1). Patients treated with IPX066 who rated themselves as "minimally improved" compared to baseline had mean (SD) improvements in "off" time of 2.1 (2.3) hours/day, in UPDRS ADL score of 2.0 (4.3) points, and in UPDRS motor score of 3.6 (8.6) points. A similar rating by those in the IR treatment group reflected improvements of 1.1 hours/day in "off" time, 0.6 (3.9) points in UPDRS ADL, and 3.9 (7.3) points in UPDRS motor score. IPX066 patients who were "much improved" compared to baseline had mean improvements in "off" time of 3.2 (2.5) hours/day, in UPDRS ADL of 1.7 (4.0) points, and in UPDRS motor

score of 6.7 (7.9) points, vs. improvements of 2.5 (2.1) hours/day in "off" time, 2.0 (3.2) points on UPDRS ADL, and 4.6 (8.7) points on UPDRS motor score for IR-treated patients.

Conclusions: Patients treated with IPX066 more frequently reported global improvement compared to those treated with IR CD-LD. Generally, improvements with IPX066 for a given PGI rating were associated with greater improvements in "off" time, ADL, and motor scores compared to IR CD-LD. Supported by Impax Laboratories, Inc.

P31.12

MYSTICOL: a controlled study of Myobloc in the treatment of sialorrhea in Parkinson's disease (PD) and other neurological conditions

Stuart Isaacson¹, William Lawrence Severt², Jean Hubble³, Thomas Clinch³

¹ Parkinson's Disease and Movement Disorders Center of Boca Raton, Boca Raton, Florida, USA

² Mount Sinai Beth Israel, New York, NY, USA

³ US WorldMeds, LLC, Louisville, KY, USA

Background: Uncontrolled sialorrhea (drooling) can be troublesome and even disabling due to embarrassment, social isolation, perioral skin breakdown, and deterioration of dentition. RimabotulinumtoxinB, also known as brand name Myobloc (MYO), has been reported to improve sialorrhea stemming from various causes including PD. We report on the largest controlled study of MYO in the treatment of sialorrhea due to PD and other etiologies.

Methods: Eligible patients were individuals with troublesome sialorrhea due to PD, Stroke, Amyotrophic Lateral Sclerosis (ALS) or other neurological conditions. Subjects were blindly and randomly assigned to receive either MYO 2500U total or MYO 3500U total or placebo; dosing and injection sites were: 250U into each submandibular gland in both treatment groups; 1000U and 1500U into each parotid gland in the lower dose group and higher dose group, respectively. Subjects were followed for 13 weeks post-injection. Co-primary outcomes were: Unstimulated Salivary Flow Rate (USFR) and Clinical Global Impression of Change (CGI-C) at Week 4 post-injection compared to baseline. Also collected were multiple secondary outcomes as well as safety data.

Results: A total of 187 subjects were enrolled (safety population) and 184 subjects comprised the Intention-to-Treat (ITT) analysis group having received either 2500U MYO n=63; 3500U MYO n=64; or placebo n=57. Sialorrhea etiologies by percentage were: PD 65%, Stroke 7%, ALS 7%, Other 21%. MYO injection sites were localized by anatomical landmarks in 75% and ultrasound (US) guidance was used in 25%. Both co-primary outcomes were significantly improved at week 4 compared to baseline pre-injection vs placebo: both USFR and CGI-C p<.0001 in both active treatment arms. Secondary analyses revealed significant improvement in both USFR and CGI-C at week 1 extending through week 8 post-injection in both active treatment groups with maintained improvement in the USFR only in the high dose group at the last observation point at week 13. Initial analyses as planned revealed no significant differences in outcomes based on injection technique using Anatomical Landmark vs US guidance. No unexpected side effects were reported.

Conclusions: MYO is effective for troublesome sialorrhea in PD and in other neurological conditions. Doses of both 2500U and 3500U are effective when injected into the parotid and submandibular glands; the higher dose may provide longer duration of benefit.

P31.13

Use of Ryтары (carbidopa-levodopa ER) in Parkinson's disease patients also treated with deep brain stimulation

Karen Merchant¹, Sarah Wang², Michael Dodge², Lorna Beccaria², Jill Ostrem²

¹ UC San Francisco Movement Disorder and Neuromodulation Center, San Francisco, CA, USA

² UCSF, San Francisco, CA, USA

Objective: Ryтары (carbidopa-levodopa ER) is a relatively new FDA-approved anti-parkinsonian medication with an improved pharmacokinetic profile over traditional carbidopa-levodopa formulations. Patients treated with deep brain stimulation (DBS) may have a lower anti-parkinsonian medication requirement but many still experience motor fluctuations or side effects from traditional PD medications. We sought to understand the use of Ryтары in a high-volume DBS practice during the first year post market approval.

Methods: A retrospective medical chart review was conducted on patients in our clinic treated with DBS and prescribed Ryтары since it came to market in early 2015. Thirty-seven patients (26M/11F) were identified for inclusion in the study, 20 patients with subthalamic nucleus (STN) implanted leads and 17 patients with globus pallidus interna (GPI) implanted leads. The mean age at diagnosis was 55 (± 8.2) years and mean time from diagnosis to DBS surgery was 11.5 (± 4.5) years. Parameters such as disease duration, time since DBS surgery, and post-surgical medication adjustments will be evaluated. Documented reasons for Ryтары prescribing and determination of continued use of the medication will be reported.

Initial Results: Several categories of DBS patients have been prescribed Ryтары in our practice: (1) For patients with DBS implantation for less than one year, Ryтары has been prescribed to minimize wearing off or to reduce dyskinesias while stimulation therapy was being optimized, as well as for those with unilateral DBS who are awaiting a second sided surgery. (2) Patients with unilateral DBS therapy and no planned second surgery have been prescribed Ryтары to reduce motor fluctuations. (3) Patients taking a number of medications even with DBS, including older formulations of carbidopa-levodopa, dopamine agonists, Amantadine and COMT inhibitors, with medication simplification as a goal. (4) Patients with motor fluctuations that improved with DBS therapy, but motor symptoms reappeared with PD progression. (5) Patients with a low threshold for tolerating DBS induced side effects.

Use of Ryтары for each of the categories above will be further investigated.

Conclusion: Ryтары was prescribed in a population of PD patients treated with DBS. Many patients found this medication beneficial, in addition to other standard PD medications, at various time points over the course of DBS treatment.

P31.14

A successful quality improvement process for improving timely levodopa administration in the hospital

Martha Nance, Lesa Boettcher, Joan Gardner, Ron Kitzmann, Catherine Wielinski

USA

Introduction: Previous reports have shown suboptimal levodopa administration in hospitalized patients with Parkinson's disease (PD), and that late or missed levodopa doses are associated with greater morbidity and longer lengths of stay. We report a successful quality improvement process to improve timely levodopa administration in a hospital linked to a National Parkinson Foundation Center of Excellence.

Methods: To date, the quality improvement process has included the following:

1. Identification of the problem: acknowledging patient concerns and complaints; collection of data available in the computerized medical record system regarding a) the number of patients with a diagnosis of PD present in the hospital each day, and b) the time of scheduled and actual levodopa administration as recorded in the Medication Administration Record (MAR)
2. Increasing awareness: presentations to the hospitalist monthly conference and Nursing Grand Rounds; in-service presentations on key nursing units and for rehabilitation staff; article in Pharmacy monthly newsletter
3. Interventions: development and later modification of an Epic alert to remind nurses when levodopa doses are scheduled; stocking immediate release and oral dissolving levodopa on key nursing units; creation of a monthly PD Medication Compliance Scorecard for nursing units; development of a flag "SBAR") within the MAR to remind nurses about timely admission of levodopa; pharmacy staff rounding on hospitalized PD patients to ensure reconciliation with outpatient levodopa schedules

Results: Levodopa administration within 30 minutes improved from 65.8% of 4446 doses in 2014 to 71.3% of 4029 doses in 2015, and 82.2% for 428 doses in the first six weeks of 2016; administration within 15 minutes improved from 42.9% in 2014 to 63.3% by early 2016.

Discussion: We have significantly improved timely administration of levodopa to hospitalized PD patients through this quality improvement process, which has included the collaborative efforts of Center of Excellence neurology, nursing, rehabilitation, and research staff; hospital nursing administration, hospitalist physicians, pharmacy, information technology, rehabilitation staff, and most importantly, nurse managers and floor nurses in the hospital.

P31.15

Levodopa-carbidopa intestinal gel in routine care of advanced Parkinson's disease patients: final long-term efficacy results on motor complications from the GLORIA registry

Werner Poewe¹, Thomas Kimber², Bruno Bergmans³, Per Odin⁴, Angelo Antonini⁵, Ovidiu Bajenaru⁶, Koray Onuk⁷, Ashley Yegin⁷, Lars Bergmann⁸, K Ray Chaudhuri⁹

¹ Medical University of Innsbruck, Innsbruck, Austria

² Royal Adelaide Hospital and University of Adelaide, Adelaide, Australia

³ AZ Sint-Jan Brugge-Oostende AV, Campus Brugge, Department of Neurology, Bruges, Belgium

⁴ Lund University, Lund, Sweden

⁵ Institute of Neurology, IRCCS San Camillo, Venice, Italy

⁶ Bucharest University Emergency Hospital, Bucharest, Romania

⁷ AbbVie Inc., North Chicago, IL, USA

⁸ USA

⁹ King's College Hospital, London, United Kingdom

Objective: To evaluate the effect of levodopa-carbidopa intestinal gel (LCIG, carbidopa-levodopa enteral suspension in the US) on motor fluctuations and dyskinesia in advanced Parkinson's disease (PD) patients during routine care.

Background: LCIG is continuously delivered via percutaneous gastrojejunostomy (PEG-J) in advanced PD patients with motor fluctuations and dyskinesia not adequately reduced by anti-Parkinsonian medications. LCIG treatment significantly improved motor complications and dyskinesia in this registry at interim (12 months [M]). [ref1]

Methods: GLORIA was a multinational (18 countries, 75 centers) registry designed to collect efficacy and safety data from routine

clinical care use of LCIG over 24M via PEG-J. Daily hours of "off" time and "on" time with dyskinesia were measured by modified Unified Parkinson's Disease Rating Scale Part IV items 39 and 32, respectively. Adverse drug reactions (ADRs) were monitored.

Results: Of the 375 patients enrolled, 225 (60%) were LCIG-naïve and 150 (40%) were treated with LCIG for =12M prior; 258 (69%) completed the 24M follow-up. At baseline, mean (SD) age was 66.4 (8.8) years, PD duration was 12.7 (6.3) years and "off" time and "on" time with dyskinesia were 6.0 (3.2) and 4.3 (3.8) hours, respectively. The mean (SD) levodopa dose was 1412 (606) mg on D1 (first day of LCIG infusion via PEG-J) [n=348] and 1512 (646) mg at M24 [n=257]. The percentage of patients on LCIG monotherapy ranged 36-40% over the study (98/273, 126/316); the most frequently used concomitant medication was oral levodopa including rescue or nighttime use (45-52%). LCIG-treated patients had significant decreases from baseline in mean (SD) daily hours of "off" time and "on" time with dyskinesia, which were maintained over 24M (-4.1[3.5], $P<0.0001$ and -1.1[4.8], $P=0.0064$ at 24M respectively, Figure 1). ADRs were reported by 194 (54%) patients; serious ADRs by 109 (31%). Forty-six patients (12%) discontinued because of an ADR. Of the 29 deaths reported, 23 were judged not related to treatment, 5 possibly related (to drug/device) and 1 probably related (to tubing).

Conclusions: LCIG led to significant improvements in motor fluctuations and dyskinesia in advanced PD patients in this long-term registry. The observed tolerability was consistent with the established safety profile of LCIG. [ref 2]

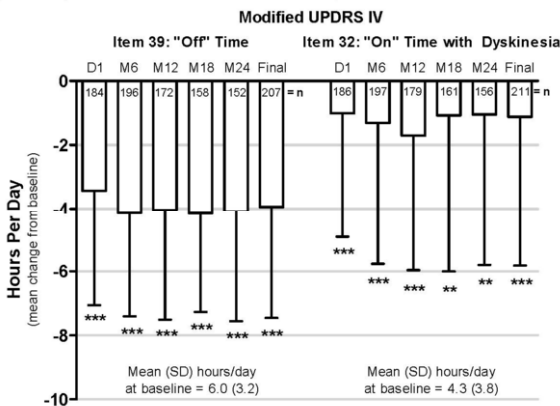
References:

[1] Antonini et al. Parkinsonism Relat Disord. 2015

[2] Lang et al. Mov Disord. 2015

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Figure 1: Mean change from baseline of daily hours in "Off" time and "On" time with dyskinesia (modified UPDRS Part IV Items 39 and 32)



Asterisks indicate statistical significance compared to baseline in a paired t-test at the $P<0.01$ (***) and $P<0.001$ (***) levels. UPDRS = Unified Parkinson's Disease Rating Scale; D1 = first day of LCIG infusion via PEG-J after titration via nasogastric tube; M = month; Final = last visit

P31.16

ND0612 – a newly developed liquid levodopa/carbidopa formulation administered continuously subcutaneously by a mini-pump – patient use perspective

Tamar Rachmilewitz, Sophie Nash, Moran Gera, Eran Shor, Sheila Oren

NeuroDerm Ltd., Rehovot, Israel

Levodopa is the gold standard treatment for Parkinson's disease (PD). However, due to short half-life its blood levels fluctuate sharply leading to motor complications such as OFF time and

dyskinesia. ND0612 is an investigational drug-device combination utilizing the first and only liquid formulation of levodopa/carbidopa (LD/CD) administered continuously subcutaneously by a mini-pump. In clinical studies to date, ND0612 was shown to achieve constant levels of LD in the blood and improvement in disease symptoms such as off time.

Human factor/usability studies focus on the interactions between the patient and the device. In this work, we examined the usability of the ND0612 associated mini-pump among patients with moderate-severe PD in order to confirm safe and effective use of the device by the target population. For this purpose 15 PD patients, along with their partner (spouse or caregiver) were invited to partake in 4 sessions of 90 minutes during which they were trained on how to set up and operate the pump system. Participants also simulated the infusion to a dummy skin pad. The study was conducted in two sites in the US. For the training process, training aids such as step-by-step live demonstration and use of a highly pictorial patient guide were used as well as a quick link for a 24/7 helpline. The training was followed by an assessment. The outcomes measures were the ability to assemble and operate the pump independently or with the help of a caregiver and to comprehend and appropriately respond to potential use errors.

All of the 15 pairs that participated in the study were able to assemble and operate the pump following training, demonstrating user-learning ability and overall user satisfaction from the device use. Training materials were shown to be effective in aiding PD patients to achieve safe and effective operation of the pump. Despite inherent motor difficulties, patients were able to perform the tasks requiring fine motor skills such as drug loading and connection of infusion line.

We conclude that from the user perspective the ND0612-associated device is well perceived by PD patients and their caregivers, following appropriate and effective training and the use of training aids. ND0612 product candidate offers a novel, patient-controlled, easy to use solution to achieve constant levels of LD in the blood and improve motor fluctuations that cannot be adequately controlled with oral therapy and might otherwise require surgical intervention.

P31.17

Simpler prescribing patterns are associated with a lower rate of falls

Peter Schmidt¹, Bastiaan Bloem²

¹ National Parkinson Foundation, USA

² Radboud University, Nijmegen, Netherlands

Objective: Evaluate center medication strategies for associations with outcomes.

Background: Expert Parkinson's neurologists today deliver care as art, however it would benefit all patients and also improve power in clinical trials to establish a standardized approach to care. Such a standard could be continuously and systematically evaluated through tracking outcomes by experts versus deviation from the standard; positive deviations providing insight and negative, opportunities for remediation. The development of such a standard is predicated upon the identification of differences in clinical outcomes with different medication approaches.

Methods: NPF's Quality Improvement Initiative is a longitudinal clinical study of the natural history of PD that has been previously described. Using machine learning approaches, patient outcomes across 8,179 subjects evaluated 20,713 times at 21 expert clinics were evaluated against observed medication strategies. A vector was computed representing the tendency of centers to use each of the ten most common medication strategies and, across centers, medication strategies and outcomes were compared based on a simulated clinical model informed by measured outcomes.

Results: The top ten medication patterns were levodopa (l-dopa) alone (14.3% of participants in the study), l-dopa and a dopamine agonist (DA; 8.4%), l-dopa and an anti-depressant (AD; 7.9%), l-dopa and a MAO-B inhibitor (4.4%), l-dopa, DA, and AD (4.1%), l-dopa, DA, and a MAO-B inhibitor (3.5%), l-dopa and amantadine (2.8%), l-dopa, DA, and amantadine (2.7%), and l-dopa, DA, and COMT inhibitor (2.1%). No medication was used by 1.3%. The remaining 48.3% of participants utilized one of 336 other combinations of medications to treat their Parkinson's symptoms. While 50.4% of participants were on one of these 10 common patterns, from center to center the standardized use of the common patterns varied from 24% to 82% (mean, 50%; SD, 12%). The frequency of the use of the simplest medication strategy, l-dopa alone, varied from 2% to 54% (mean, 16%; SD, 11%), and the linear relationship between propensity to use of l-dopa alone at the center and the patient-reported frequency of falls explained 39.7% of the variation in the falls outcome ($p=0.002$).

Conclusions: Different clinics appear to have different strategies in their use of medication, from highly standardized to highly customized. These differences are associated with differences in outcomes.

P31.18

ND0701: a novel safe concentrated apomorphine formulation for continuous subcutaneous administration via a patch pump

Ronit Shaltiel-Karyo¹, Oron Yacoby-Zeevi¹, Yonit Tsarfati¹, Eduardo Zawoznik¹, Irena Weinstock¹, Mara Nemas¹, Anna Rubinski¹, Yael S. Schiffenbauer², Abraham Nyska³

¹ NeuroDerm Ltd., Rehovot, Israel

² Aspect Imaging, Shoham, Israel

³ Timrat and Tel Aviv University, Tel Aviv, Israel

Objective: To characterize the local safety and PK of a novel apomorphine formulation, ND0701, in comparison to a commercially available apomorphine-HCl solution.

Background: Apomorphine is the most potent dopamine agonist that provides anti-Parkinson's effect comparable to levodopa, and potentially improves dyskinesia. Nevertheless, its long-term use is limited by poor compliance and local site skin reactions, resulting in the formation of nodules that can cause discomfort and may impact the effectiveness of the drug.

Methods: The experiments were conducted in domestic pigs. For the evaluation of local site reactions, four drug formulations, 1% ND0701, 2.5% ND0701, 0.5% apomorphine-HCl or 1% apomorphine-HCl, were administered by subcutaneous continuous infusion of 50 mg apomorphine during 24h, at a volume of 5, 2, 10 and 5 ml, respectively. For the determination of steady state plasma concentration of apomorphine, the drug formulations were administered by subcutaneous continuous infusion of 14 mg apomorphine during 7h, at a rate of 0.2, 0.08, 0.4 and 0.2 ml/h, respectively. Local safety was evaluated using ex-vivo & in-vivo MRI and histopathology.

Results: MRI analysis showed that local site reactions following continuous subcutaneous administration of ND0701, at concentrations as high as 2.5–5^x than those of Apomorphine-HCl, were significantly smaller and exhibited better recovery. Histopathological evaluation supported these findings showing only a minimal, chronic inflammatory reaction following continuous subcutaneous administration of 1% and 2.5% ND0701, while mild, chronic, granulomatous inflammation and necrosis of the subcutis were observed following Apomorphine-HCl administration. Steady state plasma concentrations of apomorphine were attained after

P31.19

Effects of levodopa-carbidopa intestinal gel on non-motor symptoms and safety of outpatient titration: a phase 3 study in advanced Parkinson's disease patients

David Standaert¹, Ramon L. Rodriguez², John T. Slevin³, Michael Lobatz⁴, Susan Eaton⁵, Coleen Hall⁵, Krai Chatamra⁵, Maurizio F. Facheris⁵, Janet Benesh⁵

¹ University of Alabama at Birmingham, Birmingham, Alabama, USA

² University of Central Florida, Orlando, FL, USA

³ University of Kentucky Medical Center, Lexington, KY, USA

⁴ Neurology Center of Southern California, CA, USA

⁵ AbbVie Inc, North Chicago, IL, USA

Objective: To assess the efficacy of levodopa-carbidopa intestinal gel (LCIG, designated in the USA as carbidopa-levodopa enteral suspension [CLES]) on non-motor symptoms (NMS) and the safety of outpatient titration in a phase 3 study of LCIG in advanced Parkinson's disease (PD) patients.

Background: LCIG, delivered via percutaneous gastrojejunostomy (PEG-J) and titrated in the inpatient setting, is reported to reduce motor fluctuations in advanced PD patients. The effect of LCIG on NMS and the long-term safety of outpatient titration at 60-week follow-up have not been reported.

Methods: In this 60-week, open-label Phase 3 study, LCIG titration was initiated as a monotherapy in an outpatient setting following PEG-J placement. The change in NMS from baseline (BL) to Week 12 (primary outcome) and Week 60 was measured by the Non-Motor Symptom Scale (NMSS) total score; additional measures included NMSS domain scores, and normalized "off" time and "on" time without troublesome dyskinesia (TSD) as measured by a patient diary. Treatment extension was permitted for patients who completed their Week 60 visit before LCIG was commercially available. Adverse events (AE) were monitored.

Results: Of the 39 advanced PD patients enrolled, 28 completed the treatment. The mean total duration of LCIG infusion was 427 (189) days ($n=38$). The mean NMSS total score and 6 of the NMSS domain scores were significantly reduced at Week 12 compared to BL, and these reductions were maintained at Week 60 with the exception of the urinary domain. [table1] There were accompanying improvements in normalized "off" time and "on" time without TSD at Week 12 that were also maintained at week 60. [table1] There were 37 (94.9%) patients with AEs and 8 (20.5%) with serious AEs; the most frequently reported AE was procedural pain (33.3%). Five (12.8%) patients discontinued due to AE. There was one death, which was deemed unrelated to the therapeutic system.

Table 1: Mean change from baseline on the Non-Motor Symptom Scale (NMSS) and in PD diary measures

	BL (n= 38)	Week 12 (n= 35)		Week 60 (n= 28)	
	Mean (SD)	LS Mean (SE) Change from BL	P Value	LS Mean (SE) Change from BL	P Value
NMSS total score	48.3 (35.6)	-17.6 (3.6)	<0.001	-11.8 (4.0)	0.004
NMSS domains:					
Cardiovascular ^a	1.4 (2.1)	-0.2 (0.4)	ns	0.5 (0.4)	ns
Sleep/Fatigue	11.6 (9.2)	-6.0 (1.2)	<0.001	-5.4 (1.3)	<0.001
Mood/Cognition	4.1 (6.2)	0.0 (1.1)	ns	0.5 (1.2)	ns
Perceptual problems/					
Hallucinations	1.9 (3.8)	-0.5 (0.4)	ns	0.4 (0.4)	ns
Attention/Memory	4.6 (6.4)	-2.1 (0.8)	0.010	-2.2 (0.9)	0.013
Gastrointestinal tract	5.3 (6.1)	-2.0 (0.6)	0.001	-1.9 (0.7)	0.006
Urinary	8.3 (8.4)	-2.2 (1.1)	0.044	0.1 (1.2)	ns
Sexual function	2.7 (3.6)	-1.8 (0.4)	<0.001	-1.1 (0.5)	0.021
Miscellaneous ^b	8.3 (9.4)	-3.4 (1.0)	0.001	-3.4 (1.1)	0.003
"Off" Time, hours ^c	6.6 (1.6)	-4.1 (0.4)	<0.001	-4.9 (0.5)	<0.001
"On" Time without TSD, hours ^d	8.4 (2.2)	3.7 (0.5)	<0.001	4.3 (0.6)	<0.001

Diary data were normalized to 16 waking hours. Diary and NMSS endpoints were analyzed by a mixed-effect model for repeated measures using factors of study site, visit, and baseline and the baseline-by-visit interaction.

^a Including falls

^b The Miscellaneous domain includes questions on pain, change in the ability to taste and/or smell, weight change and excessive sweating.

^c For Week12 N=32, Week 60 N=21

BL = baseline; NMSS = Non-Motor Symptom Scale; SD = standard deviation; LS = least squares; SE = standard error; ns = not significant, TSD = troublesome dyskinesia

Conclusions: LCIG treatment following outpatient titration led to reductions in NMS burden and motor fluctuations in advanced PD patients. The safety profile was consistent with previous studies that used inpatient titration and outpatient titration does not appear to pose additional risks.

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P31.20

Baseline characteristics associated with therapeutic response to levodopa-carbidopa intestinal gel treatment for advanced Parkinson's disease

David Standaert¹, James T. Boyd², Per Odin³, Weining Z.

Robieson⁴, Jorge Zamudio⁴, Krai Chatamra⁴

¹ University of Alabama at Birmingham, Birmingham, Alabama, USA

² University of Vermont College of Medicine, Burlington, Vermont, USA

³ Lund University, Lund, Sweden

⁴ AbbVie Inc., North Chicago, IL, USA

Objective: To identify baseline (BL) clinical characteristics associated with a therapeutic response to levodopa-carbidopa intestinal gel (LCIG, designated in the USA as carbidopa-levodopa enteral suspension [CLES]) in patients with advanced Parkinson's disease (PD) during a 54-week, open-label phase 3 study.

Background: A previous report demonstrated that LCIG, administered via percutaneous gastrojejunostomy, reduced motor fluctuations in advanced PD patients, however the correlation between baseline clinical characteristics and response to treatment was not examined.

Methods: Of the 354 patients enrolled, 307 patients had both BL and post-BL PD symptom diary data and were included in this post-hoc analysis. Patients with a change from BL to final visit of at least 1 hr improvement in "Off" time were categorized as "Responders"; those with <1 hr improvement or worsening were "Non-Responders". BL demographics and disease characteristics were analyzed in the 2 subgroups. The correlations between BL characteristics and the change from BL in normalized "Off" time as well as "On" time with troublesome dyskinesia (TSD) were determined. Correlations with baseline PD symptom scales were also examined.

Table 1: Baseline Patient Demographics and Clinical Characteristics

BL Characteristics	Responder (N=272)	Non-Responder (N=35)	Correlation with Change in PD Diary Assessments	
			Change in "Off" Time r (P Value)	Change in "On" Time with TSD r (P Value)
Age (years), mean (SD)	64.1 (9.0)	64.0 (9.5)	0.015 (0.794)	0.003 (0.958)
< 65, n(%)	133 (88)	18 (12)		
≥ 65, n(%)	139 (89)	17 (11)		
Gender				
Female, n(%)	115 (88)	15 (12)		
Male, n(%)	157 (89)	20 (11)		
BMI, mean (SD)	25.0 (4.6)	23.4 (4.2)	-0.105 (0.068)	0.010 (0.867)
< 25, n(%)	146 (85)	25 (15)		
≥ 25, n(%)	126 (93)	10 (7)		
PD duration (years), mean (SD)	12.3 (5.6)	12.6 (5.3)	0.088 (0.123)	-0.021 (0.715)
< 10, n(%)	107 (91)	11 (9)		
≥ 10, n(%)	165 (87)	24 (13)		
UPDRS Total Score, mean (SD)	48.9 (18.6)	45.0 (22.4)	-0.156 (0.009)**	0.103 (0.086)

Asterisks indicate statistical significance compared to baseline in a paired t test at the $P < 0.01$ (**) level. BL = baseline; BMI = body mass index; TSD = troublesome dyskinesia; PD = Parkinson's disease; UPDRS = Unified Parkinson's Disease Rating Scale

Results: Out of the 307 patients, 272 (89%) were categorized as Responders and 35 (11%) were Non-Responders. Baseline characteristics were remarkably similar between Responders and Non-responders [table1]. No significant relationships were observed between change in "Off" time, or "On" time with TSD, and BL patient age, PD duration, or BMI [table1]. Baseline UPDRS Score did not differ between the 2 subgroups, but a higher baseline Total UPDRS

score was associated with a greater reduction in "Off" time ($r = -0.156$; $P = 0.009$). Adverse events were common and mostly mild to moderate in severity in this patient population as previously described.

Conclusions: LCIG treatment led to an improvement in "Off" by at least 1 hour in 89% of advanced PD patients. Notably, Responders to LCIG were observed independent of the range of BL demographics and clinical characteristics and a higher UPDRS was associated with a greater response to treatment.

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P31.21

Individual levodopa dosing suggestions based on a single dose test

Ilias Thomas¹, Moudud Alam¹, Filip Bergquist², Dag Nyholm³, Marina Senek³, Jerker Westin⁴

¹ Statistics, Dalarna University, Borlänge, Dalarna, Sweden

² Dept. of Pharmacology, University of Gothenburg, Gothenburg, Sweden

³ Neuroscience, Neurology, Uppsala University, Uppsala, Sweden

⁴ Computer Engineering, Dalarna University, Borlänge, Dalarna, Sweden

Objectives: To construct patient-specific models from dose-effect experiment and use the models to make optimized dosing suggestions for oral administration of levodopa.

Dataset: 19 patients with Parkinson's disease that participated in a clinical study (Uppsala University Hospital, Sweden, 2015). They were given a single dose of levodopa-carbidopa, 150% of their normal morning dose. Three movement disorder specialists rated the patients' condition on a seven-level treatment response scale from very off (-3) to very dyskinetic (+3) in regular time points after the dose. The mean values of the raters' assessments at each point were used as target values for model parameter estimation.

Methods: An established pharmacokinetic-pharmacodynamic model, together with different optimization methods were used to identify patient-specific dose effect profiles. Simulations were then conducted to identify patient specific optimal dosing routines for oral administration of levodopa. Optimized dosing for the algorithm was defined as the dosing routine that minimizes motor fluctuations and maximizes the "on" time throughout the day, and was restricted to a maximum number of doses.

Results: Preliminary results show the ability of the optimization routines to identify individual dose-response curves and fit individual models. Examples of individual models can be seen in Figure 1. The simulation algorithm makes optimized individualized dosing suggestions according to the models. The suggestions are similar to the real-life dosing regimens of the patients (Pearson's correlation 0.84, p-value 0.07), but still changes are proposed.

Discussion: As Parkinson's disease progresses the levodopa response duration gradually changes. Our findings suggest that the response to a single dose of levodopa provides enough information to propose individualized dosing regimens that may reduce motor fluctuations. Evaluation of single-dose response profiles could be automated using objective motor performance measurements with accelerometry, and may in combination with individualized dose-response simulations be used to aid patient and physician in dose regimen optimization when patients start to develop motor fluctuations.

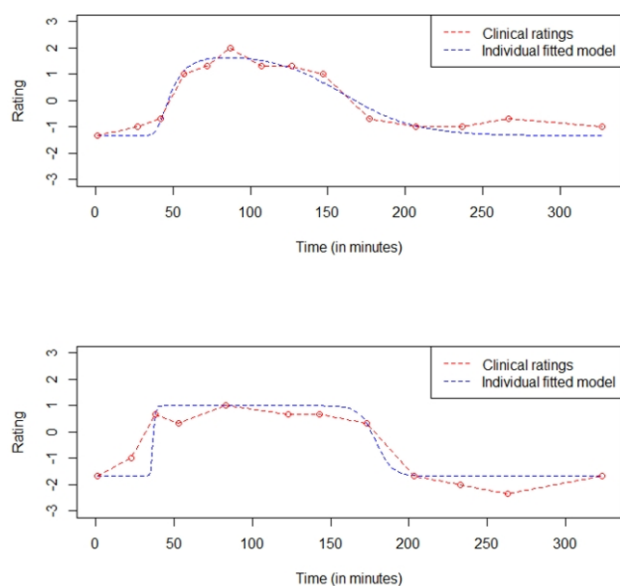


Figure 1: Individually fitted patient profiles in accordance with clinical ratings. The red line represents the ratings at each time point and in the blue line the fitted individual curves.

P31.22

Efficacy of IPX066, extended-release carbidopa-levodopa, in advanced Parkinson's disease patients with limited levodopa treatment duration

Leo Verhagen-Metman¹, Elizabeth Lindemulder², Robert Rubens², Suneel Gupta²

¹ Rush University Medical Center, Chicago, IL, USA

² Impax Laboratories, Inc., Hayward, CA, USA

Background: IPX066 [RYTARY®, NUMIENT(TM)] is an extended-release capsule formulation of carbidopa-levodopa (CD-LD). Following an initial peak at about one hour, plasma levodopa concentrations are maintained for about 4–5 hours.

Objective: To evaluate whether IPX066 can significantly reduce Parkinson's disease (PD) symptoms compared to immediate-release (IR) CD-LD when given relatively early on in the LD treatment course, we examined a subset of patients who had recently begun treatment with LD.

Methods: ADVANCE-PD was a randomized, active-controlled, double-blind study examining the efficacy and safety of IPX066 vs. IR in patients with advanced PD. Patients (n=393) received 13 weeks of treatment with either IR or IPX066. To investigate the efficacy of IPX066 vs. IR in PD patients with limited LD treatment history, those in the lowest quartile of LD treatment duration at study baseline (n=118) were examined in this post-hoc analysis. The changes from baseline in PD diary measures and the Unified Parkinson Disease Rating Scale (UPDRS) Part II (activities of daily living) plus Part III (motor score) were examined in IPX066 and IR treatment groups.

Results: In the overall study population, IPX066 reduced "off" time by 1.2 hours more than IR (P<.0001) and improved UPDRS Parts II+III scores (P<.0001) more than IR. Patients with the shortest exposure to LD had a median (range) duration of PD of 3.0 (1–16) years, duration of LD therapy of 2.0 (0.2–3.0) years, daily LD dose of 600 (400–1600) mg, and dosing frequency of 4 (4–7) times/day. In this subgroup, IPX066 decreased "off" time by [mean (SD)] -2.4 (3.0) hours compared to baseline vs. -1.1(2.5) hours for IR (P=.05). This was accompanied by increased "on" time without troublesome dyskinesia [IPX066: +2.1 (3.2); IR: +1.1 (2.6) hours], without an

increase in "on" time with troublesome dyskinesia [IPX066: +0.2 (1.1); IR: +0.2 (1.3) hours]. The change from baseline in UPDRS Parts II+III was improved more by IPX066 [-8.4 (12.8)] than by IR [-3.9 (9.6)] (P<.01).

Conclusions: IPX066 improved PD diary measures and UPDRS scores in patients with limited exposure to LD to a similar degree as in the entire study population, suggesting that IPX066 is effective early in the LD treatment course.

P31.23

Comparison of once-daily versus twice-daily combination of Pramipexole extended release in Parkinson's disease

Ji Young Yun¹, Beom S. Jeon²

¹ Ewha Womans University School of Medicine, Ewha Womans University Mokdong Hospital, Seoul, South Korea

² Department of Neurology, Seoul National University College of Medicine, Seoul, South Korea

Pramipexole extended release (PER) is a once-daily formulation. However, there may be individual pharmacokinetic differences so that multiple dosing may be preferred in some individuals. This study compares once-daily and twice-daily PER in patients with Parkinson's disease (PD).

Methods: This study was an open-label crossover study. We enrolled PD patients on dopamine agonist therapy with unsatisfactory control such as motor fluctuation, dyskinesia and sleep-related problems. Agonists were switched into equivalent dose of PER. PER comes in dosages of 0.375, 0.75, 1.5 mg; therefore, the actual conversion was the nearest higher possible dose in undivided tablets. Subjects were consecutively enrolled into either once-daily first or twice-daily first groups, and received the same amount of PER in a single and two divided dosing for 8 weeks respectively in a crossover manner without a washout period. The primary outcome was a questionnaire of the preference completed by patients in the last visit. The secondary outcome measures included the Unified Parkinson's Disease Rating Scale part 3 (mUPDRS), Hoehn and Yahr stage (HY) at medication-on state; Parkinson's disease sleep scale (PDSS); Epworth Sleep Scale (ESS); visual analogue scale (VAS) for duration and severity of dyskinesia; VAS for duration and severity of off-symptoms; compliances and patient global impression (PGI).

Results: A total of 48 patients were enrolled; 45 completed the questionnaire, and 44 completed the study. Of the 44 subjects who completed the questionnaire for preference, 18 patients preferred twice-daily regimen, 12 preferred the once-daily regimen, and 14 had no preference. And, at final visit, 13 subjects chose once-daily regimen and 22 patients chose twice-daily regimen, and 5 wanted to maintain the previous regimen. The main reasons to choose twice-daily regimen were: decreased off-duration (n=15), more tolerable off-symptoms(n=13) and psychological stability(n=10). Their mean mUPDRS, HY, PDSS, PGI, VAS score of dyskinesia and off-symptoms, compliance and adverse events were not statistically different in both regimens. The daytime sleepiness was statistically severe in once-daily (P=0.04). The proportion of patients' impression on wearing-off and dyskinesia was not statistically different.

Conclusions: PER is a once-daily formulation, but multiple dosing was preferred in many patients. Multiple dosing of PER needs to be tried if once-daily dosing is unsatisfactory. [NCT No: 01515774]

P31.24

Integrated analysis of droxidopa for the treatment of neurogenic orthostatic hypotension in patients with Parkinson's disease

Adam Ziemann¹, Italo Biaggioni², L. Arthur Hewitt¹, Yekaterina Dribinsky¹, Steven Vernino³

¹ Lundbeck LLC, Deerfield, IL, USA

² Vanderbilt University Medical Center, Nashville, TN, USA

³ UT Southwestern Medical Center, Dallas, TX, USA

Background: Droxidopa is approved in the USA for the treatment of symptomatic neurogenic orthostatic hypotension (nOH), based on 3 randomized placebo-controlled trials in patients with nOH resulting from primary autonomic failure, including Parkinson's disease (PD). Using integrated trial data, the efficacy of droxidopa (100–600 mg, 3 times daily) was examined for the subgroup of patients with PD.

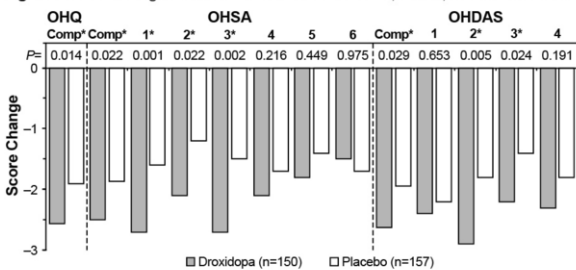
Methods: In 2 studies, responders during an open-label optimization period were randomized to receive an individualized double-blind dose of droxidopa or placebo for 1 or 2 weeks. In the third study, patients were randomized to receive double-blind droxidopa or placebo in an optimization period, followed by 8 weeks of stable-dose treatment. Key efficacy outcomes included standing blood pressure (BP) measurements and patient-reported evaluations using the Orthostatic Hypotension Questionnaire (OHQ), which includes domains for nOH symptoms, the Orthostatic Hypotension Symptom Assessment (OHSA), and their impact on daily activities, Orthostatic Hypotension Daily Activity Scale (OHDAS). Mean changes from baseline to end of study/week 1 of randomized treatment were compared for droxidopa vs placebo.

Results: A total of 307 patients with PD were randomized to droxidopa (n=150) or placebo (n=157). Significant increases in standing mean±SD systolic/diastolic BP were found for droxidopa vs placebo (9.4±20.2/6.7±16.1 mmHg vs 2.4±21.5/0.7±19.0 mmHg; P=0.003/0.002). Compared with placebo, droxidopa treatment was associated with significant improvements in OHQ, OHSA, and OHDAS composite scores (P=0.014, P=0.022, and P=0.029, respectively; Figure 1). Compared with placebo, droxidopa was associated with statistically significant improvements in 3 of 6 OHSA individual items and 2 of 4 OHDAS individual items, including dizziness/lightheadedness (OSHA Item 1; P=0.001). Droxidopa was generally well-tolerated. Common adverse events associated with droxidopa included headache, dizziness, nausea, and fatigue.

Conclusions: This pooled analysis supports the clinical benefit and tolerability of droxidopa for the treatment of nOH in patients with PD. Significant improvements in standing systolic BP, nOH symptoms, and their impact on activities of daily living were demonstrated, including the cardinal symptoms of nOH, dizziness/lightheadedness.

Funding: Lundbeck

Figure 1. Mean Change From Baseline to Week 1 in OHQ, OHSA, and OHDAS Scores



OHQ=Orthostatic Hypotension Questionnaire; OHDAS=Orthostatic Hypotension Daily Activity Scale; OHSA=Orthostatic Hypotension Symptom Assessment.
 OHSA Items: 1=Dizziness/lightheadedness; 2=Visual disturbances; 3=Weakness; 4=Fatigue; 5=Trouble concentrating; 6=Head/neck discomfort.
 OHDAS Items: 1=Standing a short time; 2=Standing a long time; 3=Walking a short time; 4=Walking a long time. OSHA/OHDAS ratings on a scale of 0 (none/no interference) to 10 (worst possible/complete interference).

*Statistically significant difference for droxidopa vs placebo (P<0.05).

CLINICAL SCIENCES: SURGICAL THERAPY, INCLUDING CELL AND GENE THERAPY

P32.01

Gait improvement with modification of frequency parameters after bilateral STN DBS in patients with Parkinson's disease

Rupam Borgohain¹, Rukmini Mridula Kandada², Aneel Kumar Puligopu³, Vani VP Kagita², Shaik Afshan Jabeen², Meena A Kanikannan²

¹ Department of Neurology, Hyderabad, Telangana, India

² Department of Neurology, Nizam's Institute of Medical Sciences, Punjagutta, Hyderabad, Telangana, India

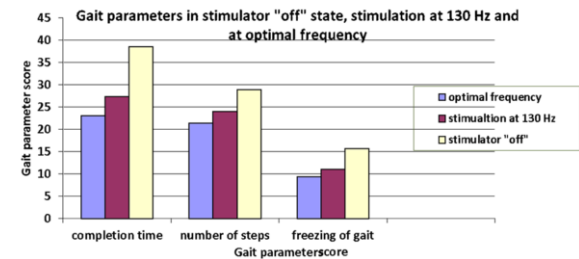
³ Department of Neurosurgery, Nizams Institute of Medical Sciences, Punjagutta, Hyderabad, Telangana, India

Background: Bilateral subthalamic nuclei DBS improves most motor symptoms with a commonly used frequency of 130 Hz. Severe gait disturbances including festination and freezing episodes often appear in advanced Parkinson disease (PD) and may worsen or may be unresponsive to standard frequency of stimulation. Lower frequency in DBS have been found to be more beneficial for gait.

Aim: To study various frequency settings and to identify the optimal frequency of bilateral subthalamic nuclei deep brain stimulation (DBS) for improvement in gait parameters in Parkinson's disease(PD) patients.

Methods: We conducted an open label interventional study. Ethical committee approval was taken and informed written consent were taken from all patients. 20 patients who underwent STN-DBS atleast 1 year prior to the study with meaningful response after DBS (improvement in UPDRS III "off" score by atleast 5 points) with complaints of gait problems were included in the study. Patients with surgical complications and unable to walk post operatively were excluded. Patients were assessed during medication 'ON' state. Every patient was assessed using 4 frequency settings i.e., 60Hz, 90 Hz, 130 Hz, 180Hz and device "off" state. Gait was assessed using The Stand-Walk-Sit (SWS) and Freezing of gait scoring. Best response was calculated based on improvement on SWS score and FOG score was used to confirm the improvement.

Results: 20 post DBS patients were studied, out of which 6 were female. Mean age was 55.1±10.2 years, mean disease duration disease was 13.97±6.87 years. Mean pre DBS UPDRS III motor score in 'ON'/OFF' was 12±4.5/51±15. There was marked variation in the response to the stimulation frequencies. We determined the frequency, which lead to the best response in each patient. FOG test also demonstrated significant improvement with the same settings. Gait was best with 180 Hz in 8 (40%), 90 Hz in 7 (35%), 60 Hz in 3 (15%), and 130 Hz in 2 (10%) (fig 1). There was no statistical significant difference in demographic details, pre-operative UPDRS III scores, duration of disease and amplitude settings of patients with best response at each frequency.



Conclusions: Optimization of frequency setting for each patient can improve gait and each patient may have a different optimal frequency. Both higher and lower frequencies may be beneficial and every PD patient with gait abnormality should be evaluated for best frequency.

P32.02

Patient-specific cell therapy for Parkinson's disease

Andres Bratt-Leal¹, Ha Tran², Sherrie Gould³, Wenbo Zhou⁴, Curt Freed⁴, Melissa Houser³, Jeanne Loring²

¹ USA

² The Scripps Research Institute, La Jolla, California, USA

³ The Scripps Clinic, La Jolla, California, USA

⁴ The University of Colorado, Aurora, Colorado, USA

Objectives: Our objective is to develop a patient-specific cell therapy for Parkinson's disease using induced pluripotent stem cells. Recent advances in reprogramming adult somatic cells and directed differentiation of dopaminergic neurons from pluripotent stem cells has made it feasible to treat patients by direct cell replacement of dopaminergic neurons using an autologous source. Several other groups around the world are using other cell sources including allogeneic iPSCs, embryonic stem cells and fetal tissue. Our challenge is to create a robust protocol and develop quality control measures to enable production of autologous dopaminergic neurons of consistently high quality for cell therapy.

Methods: Dermal fibroblasts from patients diagnosed with Parkinson's disease were taken with patient consent under IRB approval. Fibroblasts were reprogrammed using the Cytotune® Sendai virus kit and pluripotency was verified using whole-genome gene expression analysis (PluriTest) and embryoid body differentiation. Patient iPSCs were differentiated using a modification of the dual-SMAD inhibition protocol (Kriks et al 2011). Patient dopaminergic neurons were characterized in vitro by electrophysiology, neurotransmitter secretion, whole-genome gene expression. Additionally, dopaminergic neurons from three patients were transplanted in a 6-OHDA hemiparkinsonian rat model. Amphetamine-induced rotations were characterized over 20 weeks after which, histological analysis was performed on the rat tissue.

Results: Patient iPSCs differentiated efficiently into dopaminergic neurons after 25 days of differentiation. Patient neurons displayed mature electrophysiological signatures of dopaminergic neurons including hyperpolarization-activated cation current and released dopamine after stimulation. Gene expression analysis demonstrated that cells produced from different patients are of consistently high quality and that gene expression can be used to identify sub-optimal cell preparations. In vivo results demonstrated that patient neurons can survive and produce neuronal outgrowth over a 6 month period. Transplantation of the patient neurons resulted in a consistent reduction in amphetamine rotations indicating the potential use for these cells in a patient-specific cell replacement therapy.

P32.03

Clinical outcomes in Parkinson's disease for asleep deep brain stimulation with electrodes placed using intraoperative imaging versus awake deep brain stimulation with microelectrode recording

Matthew Brodsky, Shannon Anderson, Aaron Vederman, Jennifer Wilhelm, Kitty Leelaamornvichet, Joanna O'Leary, Mara Seier, Kim Burchiel

Oregon Health & Science University, Portland, Oregon, USA

Objective: To compare the difference in clinical outcomes for deep brain stimulation (DBS) surgery for Parkinson's disease (PD) when

target localization is performed via intraoperative computed tomography imaging (iCT) versus microelectrode recording (MER).

Background: MER has been the gold standard for lead targeting in DBS, however patients must be awake during this surgery, it requires more instrumented passes into the brain, and operative time is longer. Targeting can be performed using iCT to place electrodes with equal accuracy, which is appealing to patients since it is performed under general anesthesia and may result in lower morbidity and cost.

Methods: Patients with PD and motor complications referred for DBS were prospectively enrolled and underwent STN or GPi implantation using iCT. A historical control PD cohort underwent DBS by the same surgeon at the same medical center using MER. Baseline Unified PD Rating Scale (UPDRS), motor diaries, the PD Questionnaire (PDQ39) and neuropsychological testing was performed at baseline and 6 months following optimization.

Results: 30 subjects underwent DBS using iCT (9 STN and 21 GPi, mean age=61.1) and 34 subjects underwent DBS using MER guidance (15 STN and 19 GPi, mean age=62.7). Mean improvement in the off medication/on DBS motor UPDRS at 6 months in the iCT group of 14.3 (10.88) was not significantly different than the improvement in the MER group of 17.6 (12.26), (p=0.25). Significant improvement in quality of life (QoL) in the iCT group (9.6 points on PDQ-39, p=0.005) was not significantly different from a 7.6 point improvement in the MER group (p=0.3). Improvement in ADLs in the iCT group (5.6 points on UPDRS II, p=.01) was not significantly different from a 4.6 point improvement in the MER group (p=0.7). iCT patients had a significant increase in ON time without dyskinesia by 4 hours per day (p=.04), not significantly different from changes in the MER group (+4.5 h/d, p=0.6). Changes in mean scores of phonemic and semantic fluency in the iCT group were significantly superior to changes in the MER group (p<.001). There were no serious adverse events in the subjects who underwent DBS using iCT.

Conclusions: Motor, ADL and QoL outcomes for asleep DBS using iCT were equivalent to awake DBS using MER. Speech fluency outcomes with iCT were superior MER DBS. Asleep DBS was well tolerated with no complications, and should be an option that is offered to PD patients who are candidates for this therapy.

P32.04

Objective measures of balance and gait to improve mobility outcomes for deep brain stimulation

Patricia Carlson-Kuhta, Katherine J. Ladwig, Martina Mancini, Shannon Anderson, Matthew A. Brodsky, Fay B. Horak

Oregon Health & Science University, Portland, OR, USA

Background: Deep Brain Stimulation (DBS) is a common treatment in advanced stage of Parkinson's Disease (PD), but it is unclear whether it improves balance and gait. A number of studies have shown that DBS helps reduce the cardinal symptoms of PD (tremor, rigidity, and bradykinesia). Use of objective measurements of balance and gait with inertial sensors could improve pre-surgery assessments and DBS programming after DBS surgery.

Objective: To examine the feasibility of measuring balance and gait in people with Parkinson's disease during clinic visits before and after DBS surgery.

Methods: Sixteen subjects were recruited and tested when arriving for scheduled pre-surgery assessment in Rehabilitation clinic and post-surgery appointments in the Neurology clinic (between 30 days and 6 months post-surgery). Before DBS surgery, the subjects were tested OFF and ON levodopa medication. After surgery subjects were tested ON DBS and sometimes both OFF and ON medication. The DBS target was the subthalamic nucleus (N=10) or globus pallidus internus (N=6). Subjects wore inertial sensors (APDM, Portland, OR) on the wrists, ankles, chest and waist while

completing the ISAW (instrumented stand and walk) test, that consisted of standing quietly for 30 seconds, walk 7 meters, turn 180°, and walk back to start. This allowed assessment of postural sway, step initiation, walking, and turning.

Results: The post-surgery best-treated state (ON DBS+levodopa) was not better (or worse) than pre-surgery ON medication for all balance and gait measures, except for step initiation and arm swing during gait. Postural sway centroidal frequency and jerk improved with DBS ($p=0.009$, $p=0.03$) and with the combination of DBS+levodopa ($p=0.0005$, $p=0.0002$) (compared to pre-surgery OFF medication). Stride length and stride velocity also improved with, DBS ($p=0.03$, $p=0.03$) and with the combination of DBS+levodopa ($p=0.004$, $p=0.0002$). Peak turn velocity also improved but only with DBS+levodopa ($p=0.02$). However, arm swing range of motion during gait and amplitude of anticipatory postural adjustments prior to gait initiation were worse post-surgery.

Conclusion: The quick assessment of gait and balance using inertial sensors in the clinic setting was able to discern changes in walking and standing performance before and after surgery. This supports a proof of concept that inertial sensor tests could be useful for clinicians in assessing patients with DBS.

Funding: NIH AG006457, Parkinson Alliance.

P32.05

How to deal with the poor treatment acceptance for deep brain stimulation in Parkinson's disease

Lars Dinkelbach¹, Bettina Möller², Karsten Witt², Alfons Schnitzler¹, Lars Wojtecki¹, Martin Südmeyer¹

¹ Department of Neurology and Institute of Clinical Neuroscience and Medical Psychology, Heinrich Heine University, Düsseldorf, Germany

² Department of Neurology, University of Kiel, Kiel, Germany

Introduction: Deep Brain stimulation (DBS) is an effective and well-tolerated treatment for Parkinson's disease (PD). The patients' way to receive this treatment usually consists of two steps: general neurologists refer them to a specialized DBS center where the final decision for or against this treatment is made upon further diagnostic assessment. Noteworthy, only 28% of the patients who were preselected as promising DBS candidates by general neurologists actually consented in the referral to a specialized center (Wächter et al., J Neurol 2011;258:641–646).

Methods & Results: To increase the treatment acceptance of DBS for PD, two projects were initiated:

(A) 51 general neurologists located all over Germany identified DBS candidates by using the electronic preselection tool STIMULUS. The patients' acceptance or refusal to undergo further diagnostic assessment at a DBS center as well as several clinical characteristics and details of the patient briefing were documented. In total, 264 patients were identified as appropriate candidates for DBS. Within 16 months, 114 (43.2%) had accepted to be referred to a DBS center. The patients' decisions were significantly influenced by their age, their classification as an akinetic-rigid type and when, during the clarification talk, the following topics were mentioned: a potential reduction of dopaminergic side effects with DBS and the optimal time frame for DBS.

(B) A collaboration of 20 general neurologists and two movement disorder specialists at the University Hospital Düsseldorf was established.

Between 2006 and 2015, 912 PD patients were examined in those joint consultation visits. In 92 cases (10.1%), a referral to undergo further diagnostic assessment was recommended. Within 16 months, 69 (70.4%) of those patients showed up in the University Hospital Düsseldorf.

Conclusion: Our findings underline the importance of a comprehensive and ethical clarification talk for the treatment acceptance of PD patients for DBS. Joint consultation visits

between general neurologists and movement disorders specialists for patient education and pre-selection are a promising perspective for a better patient-centered DBS care. [Some results were presented previously at the II. International Conference on Deep Brain Stimulation in Düsseldorf, Germany from 15–16 March, 2016]

P32.06

Can living micro-tissue engineered axonal tracts reconstruct the nigrostriatal pathway in PD?

John E. Duda, Laura A. Struzyna, Kevin D. Browne, Justin Burrell, H. Isaac Chen, D. Kacy Cullen

Corporal Michael J. Cresenz Veterans Affairs Medical Center and the Perelman School of Medicine at the University of Pennsylvania, Philadelphia, Pennsylvania, USA

Introduction: The classic motor symptoms of PD result from selective degeneration of the nigrostriatal pathway, including dopaminergic neurons in the substantia nigra and their long-projection axonal inputs to the striatum. We are developing a micro-tissue engineering strategy to directly reconstruct the lost nigrostriatal pathway and, as a result, restore motor function following PD neurodegeneration.

Methods: We create micro-tissue engineered neural networks (micro-TENNs), which are living 3-D neural constructs comprised of a tubular hydrogel (340–550µm OD) containing an extracellular matrix (ECM) core that supports robust axonal extension. Isolated neurons are precisely delivered to one end of the micro-TENN, and cultured for 4–20 days based on desired length of axon growth. The cytoarchitecture of the micro-TENNs consists of a population of dopaminergic neurons at one end with long axonal tracts extending through the ECM to the other end. For transplantation, adult rats are anesthetized, and preformed micro-TENNs are stereotactically microinjected.

Results: These miniaturized living neural constructs – less than half the diameter of a deep brain stimulation lead – have been constructed with dopaminergic neurons and unidirectional axonal tracts. To date, these dopaminergic axonal tracts have spanned at least 6mm – a suitable length to reconstruct the nigrostriatal pathway in rats. Following in vitro characterization, dopaminergic micro-TENNs have been delivered to physically reconstruct the nigrostriatal pathway in rats. Following transplantation into the brains of rats, we have demonstrated that these dopaminergic micro-TENNs survive and maintain their axonal architecture for at least 1 month. Ongoing implants are being assessed with behavioral, electrophysiological, and histological outcomes to assess functional and structural integration.

Conclusions: These studies demonstrate that micro-TENNs can be generated in vitro with dopaminergic neurons and long unidirectional axonal tracts, and survive transplantation into rat brain. By virtue of their long axonal tracts, micro-TENNs may be capable of directly replacing the entirety of the nigrostriatal pathway, integrate into the cellular milieu of the substantia nigra and striatum, and respond to the normal intracellular inputs regulating the uninjured nigrostriatal pathway, for the alleviation of the motor symptoms of PD.

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P32.07

Patient expectations and outcome after DBS: 24-Month results

Nasrin Esnaashari, Steffi Chen, Joanna Liang, Christopher Liao, Mark Liker, Jennifer Hui, Daniel Togasaki

Keck School of Medicine at University of Southern California, Los Angeles, CA, USA

Background: Many publications have examined the outcome of deep brain stimulation (DBS) for Parkinson's disease, but none have assessed patient satisfaction and fulfillment of patients' expectations. This study determined patients' expectations preoperatively, evaluated their fulfillment postoperatively (24 months) and correlated this with their self-rated motor improvement and with clinical evaluations.

Methods: Patients undergoing surgery completed a questionnaire recording three goals for DBS. These goals were sorted into one of thirteen categories (which had been formulated from initial observations). At 6, 12, 18, and 24 months after surgery, patients completed follow-up surveys. Clinicians assessed each patient before and at 6, 12, 18, and 24 months after DBS placement using the Clinical Global Impression-Improvement (CGI-I) scale.

Results: 35 patients have 24-month data. Patient satisfaction scores (self-rated) were stable after 12 months up to 24 months. All patients reported improvement in their neurologic symptoms, but the extent of improvement did not correlate with physician CGI-I scores. Self-rated improvement in neurologic symptoms correlated more strongly, however, with how well preoperative expectations were fulfilled. Of the thirteen goal categories, the three that correlated best with patient satisfaction were: (i) reducing medications; (ii) reducing dyskinesias; and (iii) improving gait/balance.

Conclusions: At 24 months after DBS implantation, patients' self-rated improvement in neurologic status after DBS for Parkinson's disease was more strongly correlated with the degree of fulfillment of their initial expectations than with the physician-related improvement (CGI-I). Patient satisfaction scores were more variable at 6 months and stabilized after 12 months.

P32.08

What do people with Parkinson's disease who are potential candidates for surgery think about deep brain stimulation?

Gun-Marie Hariz¹, Maria Sperens¹, Katarina Hamberg²

¹ Department of Community Medicine and Rehabilitation, Occupational Therapy, Umeå University, Umeå, Sweden

² Department of Public Health and Clinical Medicine, Family Medicine, Umeå University, Umeå, Sweden

Background: According to estimates, about 140 000 patients worldwide, the majority of them men, have undergone Deep Brain Stimulation (DBS) for Parkinson's disease (PD). DBS is an alternative when medication no longer can control the symptoms. Regardless of its beneficial effects, DBS has been mitigated by side-effects, such as dysarthria, impaired balance and changes in behaviour. Notwithstanding careful selection criteria and thorough information before recommending DBS, the final decision has to be taken by the patient.

Objective: To explore male and female patients' perceptions of, and reasoning about, DBS as a possible future treatment option.

Material & method: 23 patients with PD (10 women; mean±SD age: 52±7.4 years, range 40–63) were interviewed at a mean±SD of 8.3±5.3 years after diagnosis. Their mean±SD Levodopa equivalent daily doses (LEDD) were 1167±526mg. Thematic interviews were conducted to obtain information on the patients perception of DBS as a possible future treatment alternative. The 1–2 hours-long interviews were transcribed verbatim and analysed in line with the technique of similarities and differences in grounded theory.

Results: Patients considered DBS as something dramatic, not easy to decide about, and a treatment modality that required careful consideration. Both men and women expressed worries about the procedure and whether they themselves would be suitable candidates for DBS. Although the participants were knowledgeable about the indications for DBS, their thoughts were mainly related to negative effects rather than a positive outcome. The risk of impaired balance was frequently mentioned as a concern. They stressed the

need for individual timing of different treatment options. Most of the participants considered DBS as being a very last treatment alternative when the disease had progressed to a level where they would have great difficulties managing their daily lives.

Conclusion: Our patients who have had PD for several years, and who were on relatively high doses of dopaminergic drugs, seemed to be quite knowledgeable about DBS as a potential future treatment option. However, they emphasized eventual side-effect more than the advantages with DBS, and their expectations were not overly high. DBS was seen as the last treatment option to be considered 'when needed' in the future. The perception of DBS among our patients does not seem to support the "Earlystim" strategy recently advocated in the literature.

P32.09

Once DBS, always DBS? — clinical, ethical, and financial considerations related to deep brain stimulation for Parkinson's disease.

Marwan Hariz

Institute of Neurology, London, United Kingdom

Background: Deep Brain Stimulation (DBS) has become a popular method for treatment of patients with advanced Parkinson's disease (PD). DBS is advertised as reversible and adaptable, as opposed to stereotactic lesions, which are described as permanent and irreversible. However, little has been said about the issue of patients becoming "addicted" to DBS, especially DBS of the subthalamic nucleus (STN), which has become the main DBS procedure for PD thanks to its efficacy. DBS hardware can become infected, necessitating its removal and the patient cannot be re-implanted until infection is cleared which can take several months. Also, DBS requires regular replacements of the implanted pulse generator (IPG), which is very costly and involves a new surgical procedure every 3-5 years, with increased risk for infection. In case of withdrawal of DBS, either due to infection or due to inability for patients to pay for a new IPG, a "DBS withdrawal syndrome" can develop resembling a malignant parkinsonian crisis that may be refractory to intensive medical treatment and includes akinetic crisis with severe impairment of motor function as well as hyperthermia and rhabdomyolysis that may lead to renal failure and eventually multi-organ failure and death. This issue is seldom discussed in the narratives about DBS.

Objective: To explore the literature about the occurrence of a "DBS withdrawal syndrome", and ponder the ethical and financial issues when advising patients about a surgical procedure that will entail life-long maintenance at recurring high financial costs.

Material & method: A search of PubMed using the words "deep brain stimulation" and "withdrawal syndrome" was conducted.

Results: Only three peer-reviewed publications were found describing a total of 6 patients in whom cessation of STN DBS led to a severe medication-refractory malignant parkinsonian syndrome, leading to death in three of them. Other cases have been reported anecdotally in meetings but never published.

Conclusion: Patients considered for STN DBS should be informed that they may become "addicted" to a device that will need regular replacements, and which they may not afford in the long run, unless it is reimbursed by insurance or by the Healthcare system. Upon abrupt cessation of STN stimulation, a severe potentially fatal withdrawal syndrome may occur despite intensive medical treatment. In these instances, a stereotactic lesioning procedure (pallidotomy or subthalamotomy) may be lifesaving.

P32.10**Intervention with shutdown of the entopeduncular nucleus output to motor thalamus is protective in a progressive MPTP mouse model of Parkinson's disease**

Will Liguore, Cindy Moore, Charles Meshul
USA

Objective: Basal ganglia circuit imbalances lead to gait disturbances and problematic symptoms in Parkinson's Disease (PD). Electrode based manipulation of brain regions can be effective in correcting these imbalances and treating the symptoms of PD; however deep brain stimulation (DBS) can cause damage and effect axons of passage. Viral based gene knockdown can be more targeted and less damaging. It is our objective to determine if intervening with viral knockdown of the internal segment of the globus pallidus (GPi) output can protect against dopamine cell loss, terminal loss, or gait changes induced by progressive administration of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) or by overexpression of a mutant form of α -synuclein.

Methods: Mice were infused intracerebrally with an AAV vector into the GPi that excised the vesicular GABA transporter (VGAT). Infusions into the substantia nigra (SN) of a virus containing a mutant form of α -synuclein or four weeks of intraperitoneal injections with increasing doses of MPTP were administered. Following toxin administration gait measures, paw grip strength, and protein levels were measured.

Results: Viral excision of VGAT and knockdown of GPi output prior to MPTP administration was protective against the toxin-induced loss of striatal tyrosine hydroxylase (TH), a marker for dopamine, loss of nigral dopaminergic neurons, as well as increases in paw grip strength and changes in gait measures. GPi knockdown midway (i.e., intervention) through MPTP administration also prevented gait measure changes and decreases in striatal TH but did not protect against increases in forepaw grip strength. Viral knockdown prior to α -synuclein infusion protected against increases in forepaw grip strength and gait measure changes but did not yield a significant protection against striatal TH decreases.

Conclusion: DBS of the GPi can correct some circuit imbalances, but has inherent problems. Viral knockdown of the GPi can protect against changes in behavioral measures and decreases in dopaminergic markers in our model. Viral dampening of brain nuclei outputs, specifically the GPi, promises less complications and more specificity than DBS. Many technologies such as crispr and long acting siRNA's are broadening the applications of this therapy in humans. As these technologies improve we may be approaching an era where viral infusion replaces DBS as the preferred therapy for correcting circuit imbalances in PD.

P32.11**Meta-analysis of mortality after subthalamic versus pallidal deep brain stimulation in patients with Parkinson's disease**

Ahmed Negida
Faculty of Medicine, Zagazig University, Zagazig, El-Sharkia, Egypt

Aim: Deep brain stimulation (DBS) is an effective surgical treatment for patients with advanced Parkinson disease (PD). Our study aims at comparing mortality after subthalamic (STN) and pallidal (GPi) deep brain stimulation (DBS).

Methods: We searched PubMed for clinical trials comparing STN DBS and GPi DBS. Death events were pooled as risk ratio in fixed effect model using RevMan 5.3. Subgroups analysis was performed according follow up duration.

Results: Four clinical trials (479 patients) met our inclusion criteria. The overall relative risk favoured GPi DBS than STN DBS (RR=0.27, 95% CI [0.13, 0.59] (with statistical significance (P=0.001).

Conclusion: Death was more common after STN DBS than GPi DBS in PD patients. Since most of death cases were due to postoperative complications not related directly to stimulation, our results highlight the importance of considering postoperative complication while choosing surgical target for PD patients.

P32.12**Meta-analysis comparing subthalamic and pallidal deep brain stimulation for patients with Parkinson's disease**

Ahmed Negida¹, Hussien Ahmed¹, Attia Attia²

¹ Faculty of Medicine, Zagazig University, Zagazig, El-Sharkia, Egypt

² Faculty of Medicine, Al Azhar University, Cairo, Egypt

Aim: This meta-analysis aims at comparing motor improvement after subthalamic (STN) and pallidal (GPi) deep brain stimulation (DBS) for patients with Parkinson's disease (PD).

Methods: We searched PubMed through November,2014 for prospective controlled studies comparing STN DBS and Gpi DBS for PD patients. Changes in UPDRS motor score, activities of daily life, verbal fluency score and levodopa equivalent dose were pooled as standardized mean difference between two groups in a meta-analysis model using RevMan 5.3.

Results: Nine controlled trials with a total of 497 patients were eligible for this study. The overall effect did not favor either of the two groups in terms of improvement in UPDRS motor score (off medication SMD=-0.11, 95% CI=[-0.30, 0.09] and on medication SMD=0.04, 95% CI=[-0.15, 0.23]), activities of daily life (SMD=-0.10, 95% CI=[-0.31, 0.11]), semantic verbal fluency (SMD=-0.04, 95% CI=[-0.25, 0.16]) and phonemic verbal fluency (SMD=-0.15, 95% CI=[-0.35, 0.06]). The levodopa equivalent dose was less in patients undergoing STN DBS than GPi DBS (SMD=-0.29, 95% CI=[-0.48, -0.10]).

Conclusion: STN DBS allows more reduction in medication than GPi DBS. Subthalamic and Pallidal DBS achieved the same motor improvement in PD patients, so we recommend that choosing surgical target in PD patients should be based on other non-motor outcomes.

P32.13**Subthalamic deep brain stimulation in Parkinson's disease: impulse control disorder and affective behavioral complications**

Sabina Omarova
Moscow, Russia

Objective: In this 1-year prospective study, we evaluated the effect of bilateral deep brain stimulation (DBS) of the subthalamic nucleus (STN) on neuropsychiatric complications of Parkinson's disease (PD), including impulse control disorders (ICD), depression, apathy, anxiety, anhedonia.

Background: There are various data on the effect of STN-DBS on behavioral complications of PD. Either improvement or worsening after surgery of ICD, depression, apathy, anxiety, anhedonia has been reported.

Methods: A consecutive series of 23 PD patients (disease duration: 10.7±4.1 years; age: 47.5±6.7 years) were evaluated longitudinally before surgery and 3, 6, 12 months after bilateral STN-DBS. Behavioural evaluation included the following scales: Hamilton Rating Scale for Depression, (HDRS), The Hamilton Anxiety Rating Scale, (HARS), Snaith-Hamilton-Pleasure-Scale, (SHAPS), apathy scale Starkstein S. et al., (ASS), Questionnaire for Impulsive-Compulsive Disorders in Parkinson's disease (QUIP), Parkinson's Disease Quality of Life-39 Scoring System, (PDQ-39).

Results: 12/23 patients presented at least one ICD at baseline, most frequently punding. At last follow-up, dopamine dysregulation syndrome disappeared in 5/5, gambling in 3/5, compulsive shopping in 7/8 and hypersexuality 4/6. New onset hypersexuality occurred just in one patient at 3 months follow-up, with resolution up to 9-months years switching from ventral to dorsal stimulation. Severity of the following ICD significantly decreased over time: dopamine dysregulation syndrome, gambling, compulsive shopping and hypersexuality. Reduction of levodopa and dopamine agonists equivalent daily dose was associated to significantly improvement of ICD after surgery.

Conclusions: Based on our observations, we can conclude that successful STN-DBS is efficacious in treating behavioral symptoms associated to PD, through a decrease of dopaminergic medications

P32.14

Impact of deep brain stimulation on walking and balance on people with Parkinson's disease; preliminary results

Michel Panisset¹, Elise Lafleur Prud'homme², Mélissa Foucault³, Cindy Gagnon³, Soanie Labelle³, Andréanne Laurin-Fournier³, Dorothy Bathélemy⁴, Abbas Sadikot⁵

¹ CHUM Hopital Notre-Dame, Montreal, Qc, Canada

² CHUM Hopital Notre-Dame, unité des troubles du mouvement André-Barbeau, Montreal, Qc, Canada

³ Programme de physiothérapie, école de réadaptation, Université de Montreal, Montreal, Qc, Canada

⁴ CRIR, Montreal, Qc, Canada

⁵ CHUM Hopital Notre-Dame; Montreal Neurological Hospital, Montreal, Qc, Canada

Introduction: Subthalamic nucleus (STN) deep brain stimulation (DBS) in Parkinson disease (PD) is effective for the treatment of fluctuations related to dopa-therapy, and has a significant impact on tremor, rigidity and bradykinesia. The effect of DBS on gait and balance disorders is not as clear with contradictory results in the literature.

Objective: To contribute to a better understanding of STN DBS on walking and balance in an OFF medication state with people with PD (PWP).

Method: Gait and balance assessments were performed in stimulation ON and OFF state. Patients were evaluated in a technical OFF state (no anti-PD medication for 12 hours). Walking evaluation was done with a GAITRite mat, comparing spatio-temporal information for comfortable, fast, cognitive dual-task walking. Balance was assessed using the Mini BESTest balance scale. Global mobility was assessed using the MDS-UPDRS section III.

Results: 8 subjects with STN-DBS were included. Statistically significant differences have been observed in favour of STN DBS for cadence and speed in fast walking, balance and MDS-UPDRS III. A trend in favour of STN DBS as also been observed regarding speed in cognitive dual-task walking. No trend was observed for comfortable walking.

Conclusion: Our preliminary results show a positive effect of STN DBS on balance, global mobility and certain aspects of walking in PWP. These preliminary results will have to be validated when final results are available after assessing a larger number of subjects.

P32.15

The effect of deep brain stimulation on gait and freezing of gait in Parkinson's disease – a systematic review and meta-analysis

Christian Schlenstedt¹, Ali Shalash², Muthuraman Muthuraman¹, Karsten Witt¹, Günther Deuschl¹

¹ Germany

² Egypt

Aim: To analyze the short and long-term effects of deep brain stimulation (DBS) on gait and freezing of gait (FOG) in Parkinson's disease (PD).

Methods: A comprehensive review of the literature was conducted until October 2015 using Medline-Ovid databases for studies analyzing the effect of bilateral STN DBS on gait and FOG. Sixteen studies with available data of the gait item 29 of the UPDRS and six studies with available FOG item 14 were included in this meta-analysis. Data were summarized for the following follow-up periods: 6-15, 24-48 and >48 months (5-6 years).

Results: For the condition Med OFF, DBS significantly improved gait by 59.4%, 47.3% and 44.8% from baseline to 6-15, 24-48 and >48 months follow-up, respectively (p48 months follow-up, respectively (p<0.05). There was no significant effect of DBS on gait and FOG under medication (condition Med ON).

Conclusions: This meta-analysis shows that without antiparkinsonian medication gait and FOG can be improved by DBS for more than 4 years. Preoperative gait and UPDRS-III severity (Med OFF) and levodopa-responsiveness are the predictors of the effect of DBS on gait. However, no effect was found of DBS on gait and FOG when patients took their antiparkinsonian medication. These findings support the underlying dopaminergic-like effect of DBS.

P32.16

Combining biological therapy with deep brain stimulation for the treatment of Parkinson's disease

John Slevin¹, Jorge Quintero², Julie Gurwell², Greg Gerhardt², Craig Van Home²

¹ University of Kentucky, Lexington, KY, USA

² USA

Objective: Provide update on clinical trials using DBS surgery as a platform for neurotrophic delivery.

Introduction: Deep brain stimulation (DBS) therapy is FDA approved for the treatment of several conditions including Parkinson's disease (PD). However, many PD-related symptoms are not relieved through the use of DBS. We have coupled biological therapy delivery with DBS surgery to provide neurotrophic factors to areas of the brain affected in PD. We recently completed a 1-year Phase I study (NCT01833364). Here we describe a follow-up, ongoing clinical trial examining the safety and feasibility of implanting autologous peripheral nerve grafts into an area of the brain affected by PD in patients undergoing DBS surgery.

Methods: Multi-stage, DBS surgery targeting the subthalamic nucleus or internal globus pallidus was performed using standard procedures. After the DBS electrodes were implanted, a section of sural nerve was unilaterally delivered into the substantia nigra. Adverse events were continuously monitored. Assessments included neurocognitive performance, quality of life, gait, (123I-ioflupane) SPECT imaging, and MR imaging at baseline and at the end of the study, 24 months after surgery. Participants also undergo a UPDRS evaluation before surgery and at 6, 12, 18 and 24 months after surgery.

Results: We have begun a follow-up open-label two-year study of safety and feasibility (NCT02369003) that expands the location where the DBS electrodes are placed from an earlier study. Mean age for participants is 67.3±5.9, Hoehn & Yahr score: 3.2±0.5, UPDRSIII OFF medication: 37.5±9.7, and UPDRSIII ON medication: 17.8±9.6. Participants showed a unilateral or bilateral decrease in 123I-ioflupane binding with SPECT imaging. In total, we have completed peripheral nerve graft delivery to the substantia nigra in 20 participants. Immediate post-operative magnetic resonance scans did not indicate evidence of abnormal tissue disruption. Adverse event profiles were comparable to standard DBS surgery.

Conclusions: Initial results from two clinical trials indicate a potentially safe and feasible means of delivering biological therapy

at the time of DBS surgery. On-going evaluations will further help assess the safety and feasibility of implanting peripheral nerve tissue in conjunction with DBS implant surgery for patients with PD and the potential benefits it may provide.

Disclosures: CVH: Medtronic

P32.17

Rechargeable deep brain stimulator (DBS) batteries: exploring possible predictors of patient satisfaction and experience

Monica Volz

San Francisco, CA, USA

Objective: Deep brain stimulation (DBS) is an effective therapy for suppressing motor symptoms in patients with movement disorders. Relatively new to patients are rechargeable systems with implantable pulse generator (IPG) (battery life >9 years) compared to traditional non-rechargeable IPGs (battery life typically 2-5 years). Little information exists about patient satisfaction and experience using rechargeable devices. Here we seek to measure patient satisfaction in a cohort of patients treated with rechargeable DBS systems.

Methods: This single-center questionnaire-based study will invite all patients implanted with rechargeable IPGs (n=80) at UCSF since 2009. Patient's demographic information will be collected. An in-person or a phone questionnaire (5-point Likert scale, based on a modified version of a questionnaire used in a previous study of Timmerman, et. al., 2013) will be used, consisting of statements assessing satisfaction of battery size, training received on how to recharge the device, training materials received, patient programmer use, recharging process, recharging equipment, recharging burden, level of anxiety associated with recharging. For those patients who switched from a non-rechargeable battery to a rechargeable battery, they will also be asked to rate their relative satisfaction with the rechargeable device and decision to switch IPG type. Patients will also be asked open-ended questions about their experience with recharging, such as the frequency of recharging and the length of time spent recharging.

Results: We will present overall satisfaction results from the questionnaire and examine patient demographic differences in satisfaction results.

Conclusion: We anticipate ease of recharging and length of time spent recharging will be key predictors of patient satisfaction with the rechargeable device, and patients implanted with the rechargeable battery as their first and only battery will be more satisfied than patients treated with a rechargeable battery after a non-rechargeable IPG.

CLINICAL SCIENCES: REHABILITATION SCIENCES (PT, OT, SLP)

P33.01

Post-traumatic Parkinsonism in diffuse axonal injury: a case report

Poonam Bajaj, Aashish Contractor, Ankita Pramanick

Sir H N Reliance Foundation Hospital & Research Center, Mumbai, Maharashtra, India

Introduction: This study describes the onset of Parkinsonian features in a previously normal 23 year old female, 6 weeks after a road traffic accident. Magnetic Resonance Imaging (MRI) showed presence of a diffuse axonal injury with no evidence of a basal

ganglia lesion. However clinical features and temporo-spatial features in a gait analysis show concurrence with Parkinsonian features.

Description: 23 year old, previously normal, female presented with abnormalities in gait and balance after a road-traffic accident. Post head injury she was comatose for 18 days, following which she became conscious with significant paucity of speech and left sided weakness. Over a six week period her neurological status improved, and she achieved independent gait. However her gait was significantly slow and balance was poor. She had facial hypomimia and monotonous speech. Muscle tone was mildly rigid on the left side, more than the right. Alteration in handwriting was noted. MRI showed petechiae in bilateral dentate nuclei of the cerebellum and the right cerebral peduncle, suggestive of diffuse axonal injury. Gait analysis (12 camera motion analysis system) showed temporo-spatial parameters consistent with Parkinsonian features – significant reduction in step length (left more than right), stride length significantly reduced bilaterally, step width and double-support time were significantly increased. Cadence, single limb support time and percentage swing phase were significantly reduced. Kinematic analysis showed a marked reduction of plantar flexion at toe-off, right more than left.

Balance tested by the Mini-Balance Evaluation Systems Test showed fall risk with a score of 16 out of 28.

Discussion: The persistence of Parkinsonian features (bradykinesia, initiation difficulties, rigidity, tremor) over the last one year, and significant responsiveness of temporo-spatial parameters in gait (to auditory cues) during therapy are suggestive of post-traumatic Parkinsonism after a single closed head injury. In addition, findings met the historical criteria established by Crouzon and Justin-Besancon (1929). However, lack of response to dopaminergic agents and a lesion in the basal ganglia or the mid brain (criteria suggested by Factor et al more recently) are suggestive that this may not be qualitatively consistent with Parkinsonism. Therapeutic intervention based on lines similar to those for Parkinson's disease were effective in improvement of the temporo-spatial parameters in gait.

P33.02

The effects of progressive aerobics and functional, amplitude-focused whole body training (PWR!Moves®) in an individual with advanced PD through an integrated physical therapy and PD-specific community exercise program – a case study?

Jennifer Bazan-Wigle, Kevin Moynahan, Emily Borchers, Becky Farley

Parkinson Wellness Recovery, Tucson, AZ, USA

Purpose: Progressive (vigorous) aerobic training and skill acquisition have emerged as forms of exercise that are capable of not only improving function, but of mediating brain health and repair mechanisms in people with mild to moderate Parkinson disease (PD). This case study will evaluate their effect in an individual with advanced PD (HY Stage 4/5).

Methods: The subject (CC) is a 68-year-old male with disease duration of ~23 years, DBS for 8 years. CC lives in an assisted living facility where he needs assistance with walking, activities of daily living, and is confined to a bed or wheelchair unless aided.

The subject was seen for physical therapy ~3x/week for 1 year, at which point he met the criteria for group programming. For the last 6 months, he has reduced physical therapy to 1x/week, and participates in a group exercise class 3x/week.

Initial assessments included: 1X Sit to Stand (STS), Timed Sit to Supine, 10-Meter Walk Test, and the 2-Minute Walk Test. Due to progress, additional assessments were added at 5-month assessment: 5X STS, Berg Balance Scale (BBS), and 6-Minute Walk Test.

The interventions for both individual and group class consisted of: progressive aerobic treadmill training with a safety harness (unweighted) and a functional, amplitude-focused whole body skill training program called PWR!Moves®. These functional exercises target PD-specific skills (posture, weight shift, axial rotation, transitions) and were performed repetitively and in various positions, with emphasis on maximum range of motion and high effort.

Results: All pre- to post-assessments improved: 1X STS was 34.6X faster (64.1 sec to 1.85 sec); Sit to Supine was 31.1X faster (152.47 sec to 4.91 sec); 10 Meter Walk Test was 4.47X faster (.15 m/s to .67 m/s); 2 Minute Walk Test was 7.7X farther (9.8 meters to 75 meters); 5x Sit Stand was 1.7X faster (14.13 sec to 8.15 sec); BBS indicated significant change (35/56 to 42/56; 6 Minute Walk Test is 1.4X farther (68 m to 98 m).

Conclusion: This case study demonstrates that progressive aerobics and a PD-specific skill training program can result in significant changes in functional mobility for an individual with advanced PD. The ability to make these gains, despite advanced PD, illustrates the need for continuous access to therapy and exercise programming for life to put off the motor deterioration that occurs secondary to inactivity/deconditioning. The subject continues this program to determine his full potential.

P33.03

Perceptual deficits of gait asymmetry during split-belt walking in patients with Parkinson's disease with and without freezing of gait

Esther Bekkers¹, Wouter Hoogkamer², Aniek Benghevoord³, Elke Heremans¹, Sabine Verschueren⁴, Alice Nieuwboer¹

¹ KU Leuven, Department of Rehabilitation Sciences, Neuromotor Research Group, Leuven, Belgium

² University of Colorado, Boulder, Colorado, USA

³ KU Leuven, Leuven, Belgium

⁴ KU Leuven, Department of Rehabilitation Sciences, Musculoskeletal Rehabilitation Group, Leuven, Belgium

Background: Freezing of gait (FoG) in Parkinson's disease (PD) has been associated with impairments in gait rhythmicity, bilateral coordination and gait symmetry. In addition, freezers (FR) are known to have increased difficulties in gait adaptation during prolonged split-belt walking and re-adaptation to tied-belt walking. This problem has been hypothesized to be caused by an underlying perceptual deficit.

Objectives: In the present pilot study, it was investigated whether FoG is related to perceptual deficits of asymmetrical gait speed changes.

Methods: 5 FR, 5 non-freezers (NFR) and 7 healthy controls (HC) were tested while walking on a split-belt treadmill. Both belts started at an equal speed of 3.0 km/h and after a random time interval, the speed of one of the belts was increased with 0.01 km/h per second. Participants had to indicate the moment at which they perceived belt speeds to be different by pressing a handheld button and verbally indicating which belt ran faster. Trials ended after the button press, or in case no difference was detected, after two minutes. As main variables, perception accuracy, i.e. the number of correct answers and the perception threshold, i.e. the difference between belt speeds at the moment of detection, were calculated. Each participant performed 7 trials in random order, including three in which the left and three in which the right belt accelerated and 1 sham trial in which none of the belts accelerated. In between all trials a one-minute walk with belts at equal speed (3.0 km/h) was provided to wash out any adaptation effects.

Results: Perception accuracy significantly differed between groups ($p=0.030$). Post-hoc comparisons showed that FR had a lower perception accuracy than NFR during the trials in which the belts moved at different speed ($p=0.042$). As well, significant differences

between groups were found for the sham trials ($\chi^2=0.013$). Although speed remained equal between both belts during these trials, 80% of the FR and 40% of the NFR erroneously perceived a difference in belt speed, compared to 0% of HC. The perception threshold of locomotor asymmetry did not differ between groups.

Conclusion: The current results provide evidence for the hypothesis that the difficulties in gait adaptation during split-belt walking in FR are at least partially caused by an underlying perceptual deficit. These results may contribute to the development of novel methods for gait rehabilitation in PD, and more specifically in patients with FoG.

P33.04

Short-term benefits of a progressive aerobic exercise and skill acquisition program for people with mild to moderate Parkinson's disease in a community group setting

Emily Borchers¹, Erin Borchers¹, Kaitlin Krauss², Becky Farley¹, Jennifer Bazan-Wigle¹

¹ Parkinson Wellness Recovery, Tucson, Arizona, USA

² University of Arizona, Tucson, Arizona, USA

Objective: To examine the short-term effects of a progressive aerobic exercise and skill acquisition program conducted at The Parkinson Wellness Recovery Gym (PWR!Gym®), a model community neurofitness center specializing in early intervention and ongoing access to research-based therapy and fitness programming for individuals with Parkinson Disease (PD). **Methods:** Sixteen members of the PWR!Gym with mild to moderate PD participated over the course of 7 weeks. Each session was led by a physical therapist, and trained volunteers provided individualized feedback regarding perceived effort based on the Modified Borg scale. Group 1 (8 participants with moderate stage PD) exercised 3 times per week with total cardio times increasing from 30 to 40 minutes. Group 2 (8 participants with mild to moderate stage PD) exercised 3 times per week with total cardio times increasing from 40 to 50 minutes. Both groups utilized treadmills and stationary bikes for the cardio portion of the session followed by functional, amplitude-focused training called PWR! Moves® for the remaining time to total a one hour session. **Results:** Preliminary findings suggest improvements in motor and cognitive assessments as well as reported non-motor symptoms. The majority of participants improved in the 6 minute walk test, 2 minute walk test, timed up and go, and 5 times sit to stand suggesting gains in endurance and functional mobility. Improvements were also found in verbal fluency and a trailmaking task. In addition, subjects reported less fatigue, improved sleep quality, better mood, less pain, and higher quality of life. **Conclusions:** These findings suggest that a 7 week progressive aerobic group exercise and skill acquisition program based upon the Modified Borg scale at high-intensity intervals paired with functional, amplitude-focused training can improve motor, cognitive, and non-motor symptoms of PD. A second bout of a similar 8 week program was performed approximately 3 months later with similar results. This pilot study has encouraged the incorporation of progressive aerobic exercise into all mobility levels of group programming at the PWR! Gym where there will be ongoing investigation into its effects.

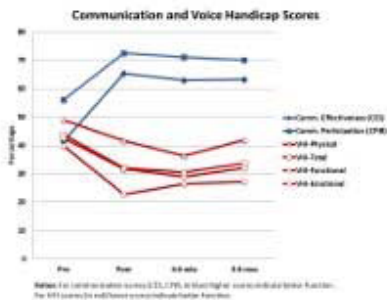
P33.05

The impact of Lee Silverman Voice Treatment (LSVT) on functional communication and voice handicap: findings from a prospective study

Linda Bryans, Andrew Palmer, Shannon Anderson, Joshua Schindler, Donna Graville

Oregon Health and Science University, Portland, Oregon, USA

Individuals with Parkinson's Disease (PD) often present with hypokinetic dysarthria which may include hypophonia, imprecise articulation, reduced prosody, palilalia, and hypernasality. Lee Silverman Voice Treatment (LSVT), an intensive 4-week program of voice therapy, is regarded as the most well-researched, efficacious treatment for these symptoms. Although numerous studies have been published reporting acoustic and perceptual findings, there are comparatively few data regarding functional outcomes. According to one systematic review, more evidence of treatment efficacy is needed particularly with regard to the impact of treatment on the adequacy of communication in natural settings. The current data are preliminary findings from a prospective, longitudinal study undertaken to investigate the functional impact of LSVT on communication and whether LSVT affects all aspects of communication equally. The study also utilized the first validated instrument dedicated entirely to the measurement of the domain of "communicative participation" which is defined as taking part in life situations in which knowledge, information, ideas, or feelings are exchanged. Measures were taken at baseline, immediately following treatment, 4–8 weeks following treatment and 3–6 months following treatment. LSVT resulted in significant improvements in acoustic measures of vocal function and loudness from pre- to post-treatment. There were also significant improvements in functional measures of communication as recognized by individuals with PD and their partners, including voice handicap, communication effectiveness, and communicative participation. Functional outcomes improved significantly post-treatment and the majority remained significantly above baseline at an average of 4.3 months after treatment. Significant correlations between measures suggested that the new measure of communicative participation was associated with other validated measures and was sensitive to change for individuals with PD. Specific findings suggested that LSVT promotes an increased sense of personal control over the communication difficulties resulting from PD as well as increasing engagement in more complex communicative activities such as asking questions, giving detailed information, and speaking in groups. These findings are important because patients with PD often withdraw from conversations, placing them at risk for social isolation. Participation in LSVT may reduce those risks by increasing communication effectiveness and social participation.



P33.06

Characteristics of falls in individuals with Parkinson's disease

Monthaporn Bryant
USA

Purpose: To study fall characteristics in individuals with Parkinson's disease (PD). We reviewed fall records completed by individuals with PD to understand circumstances and consequences surrounding their falls.

Method: Fall records from 53 individuals with idiopathic PD were reviewed. All individuals were able to ambulate independently and were cognitively intact. During a five-month recording period, they

were asked to record falls in a falls diary and were called once a week to verbally report any falls as well as to provide details about each fall (e.g. location, activity, time of day, cause, landing, saving reaction, injury). We coded responses and counted frequencies of these fall characteristics.

Results: Mean age of the study subjects was 70.1 years. The average time since diagnosis was 8.5. There were a total of 249 fall incidences recorded from the sample.

- Activity: 56.6% during walking, 16.9% during turning, 12.4% during transferring from sit to stand, 6.4% during talking and 7.6% not specified.
- Location: 18.9% in bedrooms, 12.9% in kitchens, 10.4% in bathroom, 18.9% outside the house (e.g. walkway, garden, and driveway) and 6% in the living room.
- Time of day: 25.3% in the morning, 37.3% in the afternoon, 21.7% in the evening and 15.3% at night.
- Cause of fall: 42.6% loss of balance, 23.3% due to freezing, 11.2% misjudgement, 3.6% distraction, 3.6% foot dragging and 15.3% others not specified.
- Landing: 37.3% on hands and knees, 11.2% landing on head, 12% sideways, 20.5% backward and 11.6% not specified.
- Saving reaction: 22.9% used arms and legs, 20.5% used external assistance, 13.3% used arms to get up and 4.8% used legs.
- Injury: 32.5% no injury, 26.1% bruises and cut, 4.4% some bleeding, 0.8% joint sprain and 0.4% bone fracture.

Conclusion: Of 249 falls circumstances reviewed, a majority of these falls were 1) indoors (i.e. inside the house), 2) during walking, 3) in the afternoon time, 4) commonly caused by loss of balance, 5) resulted in landing on hands and knees, 6) used arms and legs to get up, and 7) most of them did not cause injury. Clinicians should consider these common fall circumstances when designing an intervention to prevent falls in the PD population.

P33.07

Multidirectional treadmill training in de novo patients with Parkinson's disease: gait, balance and kinematics changes

Monthaporn Bryant, Craig Workman, Hao Meng, Beom-Chan Lee, Fariha Jamal, George Jackson, Michele York
USA

Purpose: To study the effect of multidirectional treadmill training (MDTT), a novel treadmill training strategy, in patients with Parkinson's disease (PD) who were not receiving L-dopa therapy. We aimed to study the changes in gait and balance performances, as well as gait kinematics after the intervention.

Participants: Three patients with PD who were diagnosed with idiopathic PD participated in the study. Average age, year of PD, Hoehn and Yahr stage and Unified Parkinson Disease Rating Scale motor score were 65.7 years, 4.2 years, 1.3 and 23.3, respectively. Intervention: MDTT consisted of walking on a treadmill in 4 directions (forward, backward, left and right sideways) and while being supported in a harness for safety. The patients walked at the fastest, tolerated speed that allowed a full step while walking forward, backward, and left and right sideways on the treadmill. They walked continuously in each direction in the support system for about 7 minutes each session.

Measures: Gait parameters, time to perform 5-step test, timed up and go test (TUG), postural instability and gait disorders (PIGD) score, turning 360 degrees, computerized posturography and gait kinematics were measured before and after 6 weeks of MDTT.

Results: Percent improvements of gait speed of the forward, backward and sideways walks ranged from 9.9% to 40.84%, and of stride length ranged from 5.3% to 25.1%. Time to perform 5-step test decreased 6.03%, TUG decreased 20.59%, time to turn 360 degrees decreased 13.84%, number of step to complete the turn

reduced 24.39%, Equilibrium score increased 0.91%, Limit of Stability (LOS) composite reaction time decreased 12.5%. Hip right and left mean angles increased by 10.94% and 22%, respectively.

Conclusion: Six weeks of MDTT showed a tendency to improve spatiotemporal gait measures of all walking directions, balance performances (i.e. 5-step test, turning, TUG, posturography) and gait kinematics in de novo patients with PD.

P33.08

Speech-related sensory impairment in Parkinson's disease

Yu-Wen Chen¹, Peter Watson²

¹ Department of Speech, Language and Hearing Sciences, University of Minnesota, Portland, OR, USA

² Department of Speech, Language and Hearing Sciences, University of Minnesota, Minneapolis, MN, USA

Speech impairments in persons with Parkinson's disease (PD) are not solely accounted for by motor impairment. Somatosensory deficits were suggested associated with movement abnormalities of the trunk and limbs, but less is known about speech-related sensory systems in PD and their link to parkinsonian speech characteristics. This study investigates the relationship between the speech of persons with PD and their sensory acuity, using the sibilants /s/ and /ʃ/ as the speech target. The study seeks to answer three questions: 1) Do persons with PD show decreased auditory acuity in discriminating spectral shapes? 2) Do persons with PD show decreased acuity to tactile stimuli on the tongue tip? And 3) Are there relationships of auditory and lingual-tactile acuity to /s/-/ʃ/ contrast in persons with PD?

Ten participants with PD and ten age- and gender-matched healthy participants were studied. Participants performed three tasks: an auditory acuity task, a tactile acuity task, and a speech production task. In the auditory task, participants discriminated three aperiodic sounds acoustically modified from /s/ and /ʃ/ and differing in spectral shapes. In the tactile task, they judged the orientation of a dome-shaped grating probe gently touching their tongue tip. Auditory and tactile acuity measures were determined from the psychophysical functions based on participants' responses. For the production task, participants read a passage and eight sentences with /s/- and /ʃ/-initial words; acoustic contrast between the two sibilants was measured using difference between the average first spectral moments of /s/ and /ʃ/. Group comparisons were made for every measure, and correlation analyses were done between the sensory acuity measures and the measures of sibilant contrast.

Results showed that the PD participants had significantly reduced auditory acuity in discriminating spectral shapes relative to healthy controls, and significantly reduced tactile acuity of the tongue tip. For speech production, the PD group showed smaller sibilant contrast in their sentence readings, but the difference was not statistically significant. Correlation analyses showed significant correlation between tactile acuity and sibilant contrast for the PD group.

P33.09

Deep brain stimulation in Parkinson's: common speech characteristics & strategies for intervention

Jennifer Cody

Richardson, TX, USA

Deep Brain Stimulation (DBS) is a surgical intervention currently being used to treat Parkinson's disease. In DBS, electrodes implanted in the brain deliver electrical stimulation to specific areas that can alter Parkinson's symptoms. DBS has largely replaced earlier surgical treatments because it is reversible, adjustable, and less invasive. Ideal candidates for DBS have had good

responsiveness to levodopa, but are now experiencing greater fluctuations in medication effectiveness, dyskinesias, or suffer from increased "off" times. For patients who are good candidates for DBS, the improvement of motor function can be dramatic and can significantly impact quality of life. Furthermore, research has suggested that people who have undergone DBS may even have longer survival rates and be less likely to be in residential care. However, there are many common Parkinson's symptoms that do not improve with DBS therapy, including speech. In fact, DBS may even negatively impact speech in some patients. While there has been little formal research addressing the differences in therapeutic approaches for Parkinson's patients with DBS compared to those without DBS, patients with DBS have been seen at Parkinson Voice Project's clinic for more than 10 years. This presentation will focus on the ways we have observed that DBS may affect speech and communication as well as the ways these changes may impact the patient's ability to participate in speech therapy. It will also discuss how therapeutic approaches can be modified to accommodate the needs of patients with DBS to maximize patient success.

P33.10

Group speech therapy programs for people with Parkinson's

Jennifer Cody

Richardson, TX, USA

Though group therapy is not currently a common a part of speech-language pathology services for people with Parkinson's, group maintenance therapy potentially provides a number of benefits to both patients and therapists. These benefits include providing a more natural communicative environment, helping patients to gain more insight into their speech deficits, peer support and motivation, and increased likelihood of long-term use of communication strategies. Group therapy also allows the therapist to better understand each patient's individual needs. Because group therapy allows the patient regular opportunities to practice speech strategies with the support and encouragement of peers while also gaining a better understanding of how Parkinson's affects speech and communication, group therapy can be an integral part of improving the communication of the whole person. Parkinson Voice Project, a nonprofit organization based in North Texas, has developed a unique group maintenance program that utilizes the advantages that group therapy provides. Participants in Parkinson Voice Project's group program, The LOUD Crowd, have been observed to maintain, and even improve, functional speech for more than 10 years after initial contact and decades after their Parkinson's diagnosis. While funding and running a group maintenance therapy program can be challenging, Parkinson Voice Project's model program has been replicated in facilities across the country. This presentation will cover both the challenges and the benefits of group therapy for Parkinson's and will discuss models for implementing group therapy programs in multiple settings. Suggestions for "best practices" when planning a group program will be offered to maximize the viability and success of such programs. If selected for an oral presentation, we will lead a "demo" group of what group therapy looks like at our clinic. 15-20 of our patients will be attending WPC and will be available to participate.

P33.11

Perceptions related to participation in a community-based exercise program in people with Parkinson's disease: a case series

Stephanie Combs-Miller, Connie Fiems, Rachel Milne, Sarah Shaw, Janelle Snyder, Brittany Swygart

University of Indianapolis, Indianapolis, IN, USA

Background/Purpose: Exercise regularity is important for people with Parkinson disease (PD). The purpose of this case series was to explore perceptions and change over time related to participation in a community-based exercise program for people with PD.

Methods: Seven individuals with PD [mean age 66.7(9.5) yrs; mean time post diagnosis 31.1(31.4) mos; 5 male], newly enrolled in a community-based exercise program participated. Participants were encouraged to attend 1-2 sessions per week for 12 months, but attendance was not mandatory. The PD-specific exercise program offered two or more classes per week at two locations and was staffed by physical therapists and personal trainers. Multiple dimensions of exercise were addressed including strength, flexibility, balance, and/or cardiovascular fitness. Number of sessions attended was recorded. After 12 months, semi-structured interviews were conducted including questions about initial attraction to the program, motivators/barriers to participation, and program fit. Change in motor symptoms (Unified Parkinson Disease Rating Scale, subsection III), walking speed (Fast 10-meter walk) and stepping activity (steps per day) were calculated from baseline to 12 months.

Results: Six participants completed all testing sessions over the 12 month period. Two participants regularly attended classes over 12 months (1–2 times/week). The other four participants inconsistently attended classes over 12 months (1–3 times/month). Regular attendees indicated an initial self-motivated attraction to the program, whereas three of four non-regular attendees started the program due to family/friend encouragement. Non-regular attendees commented that accessibility, convenience and transportation were barriers to participation. Regular attendees felt the program was a good fit for them based on the variety of exercises offered; however, three of four non-regular attendees specified that they would prefer a more intensive exercise program. Only one participant, a regular attendee, demonstrated consistent improvements across all measures, exceeding minimal detectable change scores.

Conclusions: Self-motivation and perceptions of minimal barriers and potential benefit contributed to more regular participation and may have led to improvements in function over time for regular attendees. Convenience of class schedules and stratifying exercise intensity are important considerations for community-based exercise programs for people with PD.

P33.12

Building collaborative, community-based partnerships between physical therapists and community-based fitness trainers

Stephanie Combs-Miller¹, Jeff Mestrich², Christine Timberlake³, Cara Riesner⁴

¹ University of Indianapolis, Indianapolis, IN, USA

² Ortho Indy, Indianapolis, IN, USA

³ Rock Steady Boxing, Inc, Indianapolis, IN, USA

⁴ Community Health Network, Indianapolis, IN, USA

Purpose: Development of community partnerships for ongoing health promotion of patients with chronic neuromuscular diseases is needed. The purpose of this report is to describe a novel, collaborative, community-based model that encourages an ongoing interactive approach between physical therapists (PTs) and fitness specialists for long-term support and access to services for patients with Parkinson disease (PD) in the community.

Description: Rock Steady Boxing (RSB) is a community-based, group exercise program serving over 200 people with PD in Indianapolis, Indiana. Local PT volunteers were recruited to build an ongoing partnership with RSB to provide regular health screening sessions for RSB members in need of further health-related services. Members are triaged to 30-minute screening sessions with either a Neurologic or Orthopedic PT screener based on their primary complaint. Neurologic screens consist of basic clinical

assessments and use of selected outcome measures. Orthopedic screens consist of region specific assessments that include basic clinical assessments as well as application of special tests as needed to rule in or out pathology. Findings on outcomes and special tests are interpreted using established norms and cut-off scores to determine next steps in care.

Summary of Use: Seventeen PTs have volunteered to participate in the screening sessions, with three PTs volunteering per month. On average 18 members of RSB are screened monthly for health-related complaints, with six being seen for neurologic issues and 12 for orthopedic issues. Balance, low back pain and knee pain are the most common health conditions screened by the PTs. Approximately one-half of patients screened are provided with a home exercise program appropriate for their condition and are contacted by the screener for follow up on progress within 2–4 weeks. The other half of patients screened typically receives referral recommendations for continued services. Within a three month period of providing the screens, 98% of members screened were retained within the RSB program.

Relevance: This novel, collaborative community-based partnership has advantages for all parties involved. Physical therapists, in particular, benefit through enhanced outreach and direct access to patients that will, in turn, reduce health care costs via immediate and appropriate referrals and use of services.

P33.13

Effect of double the task training motor-traction in PD

Mávia Maria Almeida Tavares da Cruz¹, Renata Amanajás de Melo¹, Lucieny da Silva Pontes², Erica Feio Carneiro Nunes², Edileia Monteiro de Oliveira², Dayse Danielle de Oliveira Silva³

¹ Universidade da Amazônia, Belém, Pará, Brazil

² Universidade do Estado do Pará, Belém, Pará, Brazil

³ Belém, Pará, Brazil

Objective: Analyze the effect of the double motor-motor task training in walking parkinsonian patients. **Method:** This is a pilot study of type randomized clinical trial conducted in the Amazon University Clinic physiotherapy School in the period of August to October 2014, composed of 10 parkinsonian subjects, divided by lot into two groups. Both groups were evaluated before and after the treatment protocol, through the test Timed Get Up Go (TGUG), the Protocol was in turn divided into three phases, totaling 20 minutes each session, the Group A held heating/acceleration, maintenance (constant speed) and deceleration. The Group B held heating/acceleration, maintenance (constant speed) associated with double motor-motor task and deceleration. The sessions were held twice a week on alternating days, for four consecutive weeks.

Results: 90% of participants were male, with an average age in the Group A of 58.00±9.57 years and the Group B of 7.78±60.00 years. Both groups achieved a significant reduction in the time and number of steps in the implementation of the TGUG test, and team B showed a significant increase in speed. When comparing the effects in both groups, there were no significant differences between them.

Final Considerations: It was noted that the treatment protocol promoted in both groups a significant decrease in execution time and number of steps, however, compared the effects of both groups in the variables studied did not statistically significant differences.

P33.14

Eliminating handicaps: a binocular view of therapy

Jennifer Davis

Kadlec Regional Medical Center, Richland, WA, USA

Client motivation is pivotal to successful outcomes in Parkinson's disease (PD). (Sapir, Raming, & Fox, 2011) Therapy must empower clients to be active participants, not just in therapy sessions, but practicing on their own. This is a particular challenge for PD clients because PD involves deficits in motivation and learning as well as motor deficits. (Foerde, Braun, Higgins, Shohamy, 2014) Drawing clients into the process of determining their most important needs, and building toward those goals, is essential for supporting the intrinsic motivational framework. Therapy must be client-centered, not just client-focused. (Levitt, 2014)

PD is in part a disorder of perception. Clients coming to their first visit are aware there is a problem (Haberman, 1999), but they often believe the problem belongs to others who are having trouble understanding them. What clients need from a therapist is reassurance that there is hope – a way to make it better. It is critical in the initial evaluation to include data on a client's present level of functioning and exploration of the client's unique strengths and needs. Through careful probing, a therapist develops targets that are relevant, motivating and empowering for the client. Therapy activities relevant to daily life motivate ongoing practice – and improve outcomes.

At age 41, the presenter, an SLP for 16 years, was diagnosed with PD. She experienced a rapid decline in vocal intensity. The changes impacted her work – and her daily activities like reading to her children, talking on the phone, participating in conversation, etc. After completing an intense therapy program herself, she began helping clients regain their speech and voice. Her experience on both sides of the table – as a client and as a therapist – gives her a unique perspective on what great therapy can look like.

Foerde, K., Braun, E.K., Higgins, E.T., Shohamy, Deb. (2014) Motivational modes of learning in Parkinson's disease. *Social Cognitive and Affective Neuroscience Advance Access*.

Habermann, B. (1999). Continuity challenges of Parkinson's disease in middle life. *Journal of neuroscience Nursing*, 31(4), 200–207.

Levitt, J. (2014). A Case Study: The Effects of the "SPEAK OUT!" Voice Program for Parkinson's Disease. *International Journal of Applied Science and Technology*, 4(2), 20–28.

Sapir, S., Ramig, L., & Fox, C. (2011). Intensive voice treatment in Parkinson's disease: Lee Silverman Voice Treatment (LSVT). *Expert Reviews in Neurotherapeutics*, 11(6), 815–830.

P33.15

Repeating postural perturbations in Parkinson's disease: effects on postural instability

Bauke Dijkstra
Leuven, Belgium

Reactive postural control is often studied via perturbations during dynamic posturography. It has already been shown that people with Parkinson's disease (PD) have greater first trial reactions in response to balance platform rotations. First trial reactions may yield important information, reflecting the true automatic balance deficit. We aimed to determine the feasibility of studying first versus subsequent trials of platform translations in the anterior direction. Therefore, we tested a group of 23 people with PD and 11 healthy controls on a Computed Assisted Rehabilitation Environment (CAREN) platform with dual force plates. Twelve people with PD (12/23, 52%) and 3 healthy controls (3/11, 27%) responded with a compensatory stepping response to the first perturbation. During the consecutive trial more people with PD (17/19, 89%) and all controls were able to respond without compensatory stepping. Interestingly, no between group differences in center of mass (CoM) displacements were found in the first ($t(15)=-.34$, $p=.74$, $N=17$) and the consecutive trial ($t(24)=-.53$, $p=.60$, $N=26$). However, people with PD decreased their CoM displacement significantly ($t(8)=3.23$, $p<.05$) from the first to the consecutive trial unlike healthy controls

($t(6)=1.27$, $p=.25$). Altogether, our findings confirm that people with PD show greater postural instability in the first trial. Differences in the first trial between people with PD and healthy controls were not confirmed by the CoM analysis as the presence of compensatory strategies precluded analysis of the full sample. We also found that people with PD learned to suppress a stepping response and became more stable during the consecutive perturbation. We conclude that while first trial responses may have high ecological validity, the variety seen in postural response strategies is a limiting factor for posturography analysis. Future interpretation of balance platform data need to take into account that in PD remarkable adaptation of postural responses occurs even after one perturbation, indicating a first trial effect.

P33.16

Comparison between virtual reality through the Wii therapy and physiotherapy on conventional balance and gait speed in individuals with PD

Carla Ramos Do Carmo¹, Kamila Paoloni Nunes¹, Nélia Haruka Ramos Sasaki¹, Luciane Lobato Sobral Santos², Dayse Danielle de Oliveira Silva¹

¹ Universidade da Amazônia, Belém, Pará, Brazil

² Universidade do Estado do Pará, Belém, Pará, Brazil

Parkinson's Disease (PD) is the second most common neurodegenerative disease after Alzheimer's, affecting more than 1% of the elderly population, and despite the treatment is progressive and disabling. The motor phenotype is characterized by bradykinesia, postural instability, rigidity, muscle-type plastic, which can take the signal cog and resting tremor. Other clinical data of importance are: gait disturbances, mask facies, voice alteration, dysarthria, drooling, olfactory dysfunction, orthostatic hypotension, cramps, pain, paresthesia, sleep disorders, depression and dementia. Objective: This study aimed to compare the virtual reality through the Wii Therapy and Physiotherapy on conventional balance and gait speed in individuals with PD. Method: a sample of 6 subjects with a mean age of 56.6 years who had a diagnosis clinical staging of Parkinson and between 2.5 and 4 seconds to Hoehn and Yahr. They were divided into two groups, one undergoing conventional physiotherapy and other Wii therapy for 10 sessions over the period of June 18 to July 9, 2012, attended the School of Physiotherapy Clinic at the University of the Amazon – Fisioclinica. Data were collected through the Berg balance scale, dynamic gait index and Timed Get Up And Go The significance level was set at 5% (p -value <0.05). Results: It was found that the groups did not show significant improvement in balance and gait speed at end of treatment compared to Wii Therapy with conventional physiotherapy. However, the group that underwent conventional therapy showed significant improvement in walking speed.

P33.17

The applicability of a multitask boxing program using the BoxMaster® for individuals Parkinson's disease.

Josefa Domingos
Campus Neurológico Sénior, Portugal, Portugal

Background: Parkinson's Disease (PD) typically results in significant functional disabilities including gait, postural deficits, cognition, and vocal problems. There is growing evidence for the positive benefits of non-pharmacological interventions, such as physiotherapy, cognitive training and speech therapy for PD for such problems. This evidence is now being translated into PD-specific community programs, such as boxing. Yet, translating this nontraditional modality of exercise into a Parkinson-specific

community approach is still a challenge for health professionals since it requires high-level multitasking.

Objective: To test the applicability of a multitasking boxing program using the BoxMaster® in individuals with PD.

Methods: The Multitask BoxMaster® program consisted of PD-specific physical, cognitive and voice exercise sessions using boxing activities. The program was conducted by physiotherapist specialized in PD and was done using the BoxMaster® boxing equipment (from StarTrac® and GIMNICA, Lda) that has punching pads identified with numbers, placed in an adjustable tower with specific angles that allow any combination of punching sequences and functional activities relevant to PD (sitting, standing, walking, turning). Applicability was assessed based on patient satisfaction and any types of problems that arose during the sessions.

Results: Eight participants were included, with a diagnose of PD, medically stable, Hoehn & Yahr I-III, with mean age of 68 years. Twelve individual sessions were done during 3 months, once per week. During the sessions, modifications to the exercises included adjustments to the type of cognitive, voice and physical activities applied into the boxing sequences, length, use of verbal feedback, time for learning, among others. Patients referred that using the BoxMaster® made learning the boxing sequences easier because of the numbers placed on the boxing pads. Risk of falling and changes in posture had to be corrected continuously. Yet, all participants completed the study with no adverse events during the sessions. A satisfaction questionnaire at the end of each session showed participants were satisfied with the intensity and type of exercises.

Conclusions: Our results suggest that using the BoxMaster® with the selected combination of physical, cognitive and voice exercises was acceptable to people with PD and facilitated patients leaning capacities. Safety precautions are needed when doing dual task training.

P33.18

A study of the effect of a one year community-based group exercise program for people with Parkinson's disease in Mumbai, India: A quasi-experimental design.

Nicole Dsouza, Anjali S, Komal Parikh Sanghavi, Maria Barretto
Parkinson's Disease and Movement Disorder Society, Mumbai, Maharashtra, India

Objective: The Parkinson's Disease and Movement Disorder Society conducts group therapy sessions where patients at different stages of the disease (Hoehn and Yahr stages 1 to 4) exercise together at a community centre under the supervision of a physiotherapist. This study aimed to investigate the effects of participation in such an exercise program in people with Parkinson's disease (PD) after a duration of 1 year.

Methods: Unified Parkinson's Disease Rating Scale (UPDRS) was administered to 50 people with PD at baseline. Group therapy sessions were conducted once weekly (60 minute sessions) for PD patients who voluntarily participated in the program and consisted of exercises aimed at improving posture, range of motion, strength, balance and gait. Those participants who attended at least 45 of the 48 sessions were allocated to Group A (cases). Those who didn't attend more than 2 of the 48 sessions due to logistical reasons like far distance to travel to the session, lack of an accompanying person, unsuitable session timings etc were allocated to Group B (controls). UPDRS was administered at the end of 1 year to all patients in Group A and B.

Results: At baseline, there was no statistically significant difference between the UPDRS mean scores of Group A and Group B (U=163.5, NA=20, NB=19, P=0.456) however at the end of 1 year the mean score of Group B was significantly higher than Group A indicating greater progression of the disease in patients in Group B

(U=79.0, NA=20, NB=19, P<0.05). There was a statistically significant difference between the pre and post UPDRS scores for Group B (NB=19, Z=-3.724, P<0.001) while there was no statistically significant difference between the scores for Group A (NA=20, Z=-1.169, P=0.243) indicating the effectiveness of the exercise program in retarding the progression of the disease.

Conclusion: The results show that a community based group exercise program for people with PD is effective in slowing the progression of the disease.

P33.19

Effect of a group based short intense lyengar yoga program on gait characteristics in people with Parkinson's disease- a pilot study.

Nicole Dsouza¹, Rajvi Mehta², Maria Barretto¹

¹ Parkinson's Disease and Movement Disorder Society, Mumbai, Maharashtra, India

² lyengar Yogashraya [div of Light on Yoga Research Trust], Mumbai, Maharashtra, India

Objective: Parkinson's disease is a progressive condition which affects movement primarily. Gait, in particular, when affected can lead to falls and significantly affect the quality of life. Studies have shown the positive effects of traditional exercise in improving gait characteristics in Parkinson's disease. Yoga, an ancient Indian science, is now being recognised and accepted as a form of complementary medicine. Of the different styles of yoga, lyengar Yoga is internationally recognised as a therapeutic form of yoga. This study aimed to study the effects of a short intense group lyengar yoga program, in improving gait in people with Parkinson's Disease.

Methods: Twenty seven people with Parkinson's disease (Hoehn and Yahr stage 2 to 4) participated in the study. lyengar yoga sessions were conducted for 90 minutes daily for 10 continuous days. A set of asanas (yoga postures) utilizing special props (chair, rope, belt) was taught to the participants by a trained yoga therapist and supervised by 4 assistants. Participants were tested pre and post the intervention in their "Best ON" time on the Timed Up and Go Test (TUG), 10 Meter Walk Test (10MWT) and through footprint analysis.

Results: Data from twenty four people with Parkinson's Disease was analysed. Statistical analysis showed a significant improvement in the TUG (P=0.019) and walking speed (P=0.011) and a trend towards significance for step length and stride length (P=0.075 and P=0.066 respectively.) In addition to this one of the participants who was unable to perform the initial testing independently was able to do so post the intervention.

Conclusion: Results show that lyengar yoga improves certain gait characteristics in Parkinson's disease even through a short intense program. Future larger studies are required to confirm and expand our findings on this form of yoga for people with Parkinson's Disease.

P33.20

Characterizing maximum step length test performance in people with Parkinson's disease

Ryan Duncan, Marie McNeely, Gammon Earhart

Washington University in Saint Louis School of Medicine – Program in Physical Therapy, Saint Louis, MO, USA

Purpose: To characterize Maximum Step Length (MSL) Test performance in PD, determine the effects of anti-PD medication on MSL performance, and determine the relationships between MSL performance and balance and motor symptom severity.

Methods: Thirty-eight subjects (mean age: 65.7±8.0; 45% female) with idiopathic PD performed the MSL, using the dominant (DOM) and non-dominant legs (NDOM), in four directions: forward, backward, and lateral (to DOM and NDOM sides). Subjects performed three practice trials and five test trials, measured to the nearest centimeter and normalized to leg length. Subjects were tested both OFF and ON anti-PD medication. Subjects also completed the Mini-BESTest (a measure of balance) and the MDS-UPDRS III (a measure of motor sign severity in PD). Analyses of variance with direction, lower extremity dominance, and medication status as factors were used to characterize MSLT performance. Spearman correlations were used to describe relationships between the MSL, Mini-BESTest, and MDS-UPDRS III.

Results: Subjects' MSL was greater ON meds compared to OFF ($p=0.003$) regardless of direction. The MSL was greater in the forward and lateral directions compared to backward ($p<0.001$). DOM MSL was greater than NDOM in the forward ($p=0.001$) and backward ($p=0.018$) directions. NDOM MSL was greater than DOM in the lateral direction ($p<0.001$). DOM MSL differed between all directions with the largest MSL in forward, followed by lateral, then backward ($p<0.001$). For the NDOM, MSL for forward and lateral were similar, but both were different from backward ($p<0.001$). OFF MDS-UPDRS III was significantly correlated with OFF and ON backward DOM and NDOM MSL only ($P<0.05$). ON MDS-UPDRS III and Mini-BESTest, both OFF and ON, were significantly correlated with MSL regardless of medication status, direction, or leg dominance ($P<0.05$).

Conclusions: Subjects with PD have improved MSL performance when ON anti-PD medication compared to OFF. The lowest MSL was in the backward direction consistent with reports suggesting people with PD have poor balance in the backward direction. Finally, the MSL is related to the Mini-BESTest and MDS-UPDRS III. Physical therapists may choose to use the MSL to measure balance in individuals with PD.

P33.21

Whole body vibration therapy with exercise enhances motor function and improves quality of life in Parkinson's disease

Drucilla Edmonston, Olivia Gruder

Florida State University College of Medicine, Tallahassee, FL, USA

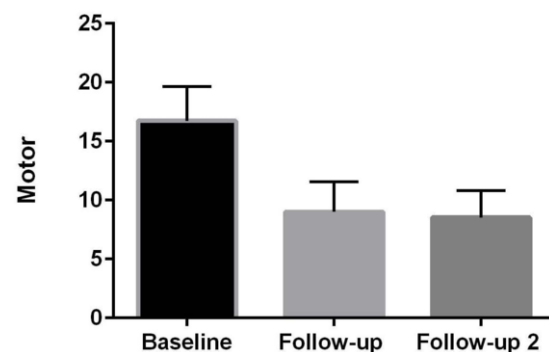
Background: Pharmacologic intervention is the current standard of care for Parkinson's Disease (PD), yet medications frequently fail to control some symptoms, including tremor and postural instability, which degrade functional performance and quality of life. Non-pharmacological treatments, including Whole Body Vibration (WBV) and exercise therapy may reduce these symptoms.

Objective: To investigate the influence of combined WBV and exercise therapy on functional performance and quality of life in PD.

Methods: A total of fifteen individuals diagnosed with PD (stages I-IV) were identified via the National Parkinson's Foundation Center and recruited on a voluntary basis. Exclusionary criteria included a history of dementia, heart disease, exercise intolerance, stroke, peripheral neuropathy, open wounds and recent surgical implantation. Participants underwent twelve sessions of combined WBV and exercise therapy over the course of six weeks. The treatment regimen consisted of static and dynamic lower body exercises performed on a vibratory platform. Motor performance, functional outcome, and quality of life were assessed using the GAITrite@System, Unified Parkinson's Disease Rating Scale (UPDRS parts 2-3), Beck Depression Inventory (BDI), Fatigue Symptom Inventory (FSI), and Healthy Days Measure (HRQOL-14). Data was collected in three sessions; at baseline before therapy initiation, one day after the conclusion of the six-week program, and again at four days after concluding the program.

Results: One-way repeated measures ANOVA showed statistically significant improvements in combined UPDRS scores $F(1.474, 20.64)=26.37$, $p<0.001$, decreasing from 29.53 ± 7.60 (baseline) to 18.00 ± 7.09 (1 day post-intervention) and 17.53 ± 5.78 (4 days post-intervention). Post-hoc analysis revealed a UPDRS score decrease from baseline to 1 day post-intervention (10.13 (95% CI, 4.86,15.41) $p<0.001$), and from baseline to 4 days post-intervention (10.73 (95% CI, 6.22, 15.25) $p<0.001$). Significant improvements were also observed in post-interventional examinations for gait velocity, cadence, and double support time. No significant change was observed in FSI, BDI, and HRQOL-14 scores. In conclusion, combination WBV-exercise therapy has significant positive short-term influence on motor performance, activities of daily living, and postural stability. Further investigation is needed to determine long-term effects.

UPRS MOTOR



P33.22

Regain and maintain speaking abilities with a two-part therapy approach

Samantha Elandary

Parkinson Voice Project, Richardson, TX, USA

Up to eighty-nine percent of people with Parkinson's struggle with their communication. While intensive speech therapy can be beneficial, people with Parkinson's require continuous vocal exercise in order to maintain the strength of their voices. Parkinson Voice Project, a nonprofit speech therapy clinic in Texas, has developed an effective two-part therapy approach that helps those with Parkinson's both regain and maintain their speaking abilities. Patients also report an improvement in their swallowing abilities.

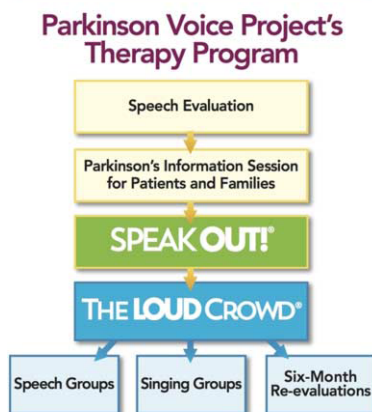
Patients enter the program and undergo a speech evaluation first. Then, they, along with their family members, attend a "Parkinson's Information Session" where they learn basic information about Parkinson's and the specifics of the two-part therapy approach. Understanding why the speech and voice are affected in Parkinson's is an important part of the remediation process.

Next, patients are scheduled for SPEAK OUT!®. This unique program is based on the teachings of Daniel R. Boone, PhD, a speech-language pathologist who in the 1950s discovered that people with Parkinson's spoke better when they used "intention." Since automatic movements are disrupted due to the depletion of dopamine, speaking with purpose and intention can improve volume, clarity of speech, breath support, vocal quality, intonation, and even facial expression. In addition, patients also report a decrease in drooling and state that it is "easier to swallow" and "food doesn't get stuck" when using intention. SPEAK OUT! consists of twenty-five lessons laid out in an easy-to-follow workbook that is provided by Parkinson Voice Project as a gift to every person with

Parkinson's in the U.S. who is receiving SPEAK OUT! Patients typically receive twelve therapy sessions conducted by a speech-language pathologist who instructs them on six different exercises aimed at strengthening the muscles used for speaking and swallowing.

Upon completion of SPEAK OUT!, patients transition to the second part of the therapy approach called "The LOUD Crowd®" which focuses on maintaining the improvements made in SPEAK OUT! Patients are assigned to a weekly speech therapy group and have the opportunity to participate in a singing group. Patients then receive a re-evaluation by a speech-language pathologist every six months.

By following this two-part therapy approach, people with Parkinson's have the ability to maintain their speaking abilities despite the progressive nature of Parkinson's.



P33.23

Proprioception and motor performance can be enhanced in early Parkinson's disease by visuomotor training

Naveen Elangovan¹, Paul Tuite², Juergen Konczak¹

¹ School of Kinesiology, University of Minnesota, Minnesota, USA

² University of Minnesota, USA

Background and Purpose: People with Parkinson's disease (PD) are known to exhibit proprioceptive impairments along with motor deficits. Recent research on healthy adults shows that sensorimotor training that challenges the proprioceptive system improves proprioceptive acuity and translates to improved motor function. It is unknown whether proprioceptive function can be enhanced in PD and whether improved proprioceptive function translates to improved motor performance. Here, we evaluate the possibility of improving proprioceptive function in PD by specialized visuomotor training that emphasizes precise movements and determine if such training directed towards improving proprioception leads to improved motor performance. We administered a sensorimotor training to PD patients using a wrist robotic device coupled with a real-time virtual visual environment.

Method: 12 participants (Mean age=61.8 yrs; mean disease duration=2.5 yrs) diagnosed with PD were tested in their ON medication state. Training involved tilting a virtual table to position a virtual ball on a target by making precise small amplitude wrist flexion/extension movements. With increasing proficiency, task difficulty increased by adjusting the responsiveness of a virtual ball. Wrist position sense acuity and the spatial precision of an untrained goal-directed wrist reaching movements were assessed without

vision before and after training. Wrist position sense discrimination thresholds were obtained using controlled robotic motion to passively rotate the wrist joint. Mean movement precision error was determined using the absolute difference between passively presented target of 15° wrist flexion and subsequent active movement to the target by the participant.

Results: All 12 participants showed improvements in wrist proprioceptive thresholds (mean: pre/post=1.6°/1.1°). Wrist movement precision in the untrained reaching improved in 9/12 participants (mean: pre/post=2.6°/1.9°).

Conclusion: Wrist proprioceptive function improves after brief specialized visuomotor training in PD patients. Movement precision in an untrained motor task also improved on average by 27% in most participants, indicating that such sensory-based training directly benefits motor function. These initial findings are promising and suggest that somatosensory-based training may enhance sensorimotor function in PD.

P33.24

A model community neurofitness and wellness center for people with Parkinson disease: 1-year group pilot data

Becky Farley¹, Alexi Okurily², Jennifer Bazan-Wigle³, Kevin Moynahan³, Emily Borchers³

¹ USA

² Northern Arizona University, Flagstaff, Arizona, USA

³ Parkinson Wellness Recovery Gym (PWR!Gym), Tucson, Arizona, USA

Background: Progressive aerobic training and skill acquisition have emerged as forms of practice for people with PD that are capable of not only improving function, but of mediating brain health and repair mechanisms. Translating neuroplasticity-principled research protocols into real world models effectively is a challenge and will require new healthcare paradigms. The Parkinson Wellness Recovery Gym (PWR!Gym®) offers integrated therapies with ongoing specialty group classes for people with Parkinson disease of varying severity in a community center.

Objective: Report preliminary one-year benefits of ongoing research-based community group exercise programs integrated with 6-month therapy coaching for people of varying disease severity.

Methods: All participants were provided an initial consult with a PD-specialized physical therapist to determine the class that would best meet their fitness, cognitive, and mobility goals. Measurements were collected at initial intake and at ~6 month intervals thereafter. All classes met for 1-hour 2-3x/week and targeted 30' of progressive aerobic training plus 30' of functional amplitude-focused training program called PWR!Moves®. Intensity of practice (physical/attentional effort) was high across groups (7+/10 on modified Borg Scale). Complexity of training (cognitive effort) varied across groups from high (HIIT, N=32); High-moderate (Circuit, N=46); Moderate (Moves 3, N=26); to least (Moves 1-2, N=22).

Results: HIIT, Circuit and Moves3 maintained or improved function and endurance from baseline to 1 year for all assessments (timed stand to floor and back, 5x sit to stand, 10MWT, TUG self-selected and fast/safe, 6 MWT, 3-meter backward walking). Moves 1 and 2 show decreased performance from baseline to one year and this was consistent with greater cognitive or mobility challenges.

Conclusions: We propose that the unique environment, coaching, psychosocial support, education, and access to PD specialized therapists, exercise and wellness programming is a win-win for individuals with Parkinson disease, healthcare, and research. This model offers an infrastructure for multisite research to demonstrate disease modification and healthcare utilization. We will continue to re-assess needs at 6 months and add intermittent bouts of intensive physical therapy through insurance/medicare reimbursement to

optimize an individuals ability to fully participate in everyday life and benefit from exercise programming.

P33.25

Dual-task interference on postural sway, postural transitions and gait in people with Parkinson's disease and freezing of gait

Ana Claudia Fortaleza¹, Fay Horak², Martina Mancini², Patty Carlson-Kuhta², John Nutt², Laurie King², Ismael Freitas Junior³

¹ State University of Sao Paulo, São Paulo, Brazil

² Oregon Health and Science University, Portland, Oregon, USA

³ State University of Sao Paulo, Presidente Prudente, São Paulo, Brazil

Objective: It is unclear if postural sway and postural transitions (i.e gait initiation and turning) are more or less automatic compared to ongoing gait, and thereby more or less affected by a secondary, dual task. Subjects with Parkinson's disease (PD) and freezing of gait (FoG+) usually present more cognitive impairments that can interfere with mobility compared to subjects with PD without FoG (FoG-). Therefore, our aim was to compare the effects of a cognitive dual task on postural sway, postural transitions and gait in FoG+ and FoG-.

Methods: Thirty FoG- and 26 FoG+ performed an Instrumented Stand and Walk test (standing quietly for 30 seconds, initiating gait, walking 7 meters, turning 180 degrees and walking back) in the practical OFF medication state, with and without a secondary cognitive task. The cognitive dual task consisted in counting backwards by 3s. Measures of postural sway (Root mean square-RMS and Sway Jerkiness-JERK in antero-posterior-AP and medio-lateral-ML directions), Step Initiation (Anticipatory postural adjustments-APA peaks in AP and ML directions, APA duration, First step Range of Motion-ROM), Turning (Turning Peak Velocity and Turning Duration) and Walking (Stride Length and Stride Velocity) were extracted using Mobility Lab (by APDM, Inc.).

Results: FoG+ showed altered RMS-ML compared to FoG- (group effect, $p=0.021$), while higher values of JERK AP and JERK ML were revealed for the dual task condition compared to the single task in both FoG+ and FoG- (condition effect, JERK AP- $p=0.015$; ML- $p=0.048$). FoG+, but not FoG-, showed a longer First Step in the dual-task compared to single-task condition ($p=0.028$). Both groups showed a slower turning speed in the dual-task compared to single task condition, and FoG+ turned significantly slower than FoG-. Lastly, FoG+ exhibited significant shorter stride length and slower stride velocity compared to FoG- both in single, and dual-task conditions.

These findings did not support our hypothesis that dual task costs on postural transitions (initiation and turning) would be larger than on straight ahead in FoG+ compared to FoG, this could suggest that automaticity in postural transitions is impaired in PD, despite showing or not freezing of gait.

P33.26

Increased access to training in a Parkinson-specific rehabilitation approach through online learning

Cynthia Fox¹, Laura Guse², Lorraine Ramig³

¹ LSVT Global, Tuscon, Arizona, USA

² LSVT Global, Inc., Lexington, KY, USA

³ LSVT Global, Inc., New York, NY, USA

Objective: Compare online versus live training of physical and occupational therapists in an evidence-based, Parkinson-specific rehabilitation approach.

Background: LSVT BIG® is an effective physical/occupational therapy for people with PD (Ebersbach et al, 2010). A challenge is

that many people with PD who could benefit from this treatment do not have access to therapists trained to administer it. Online learning is an effective way to increase access to educational content (Anderson & Elloumi, 2004). Our previous NIH-funded work documented that online and live training of a PD-specific speech treatment (LSVT LOUD®) was comparable across learners. If we can demonstrate that online and live LSVT BIG training for physical and occupational therapists are comparable, it may expand access to this effective treatment for people with PD.

Methods: The online LSVT BIG training was developed to rigorously parallel the live course. It consists of 40 modules of content (including 99 videos), 142 review questions, a 40 question exam (85% required to pass), and a 90 day period for completion. After a pilot launch in 2014, the first year of implementation of online training was 2015. Data from the total number of online and live LSVT BIG learners in 2015 were analysed. Measures included number of clinicians trained, exam scores, course evaluations, and a post-completion practice survey.

Results: A total of 1133 therapists from 18 countries and 2227 therapists from 12 countries completed the online and live training, respectively. Preliminary data analysis revealed comparable outcomes in exam results for both groups (99% pass; 1% fail). Course evaluations were also comparable with 100% of online and live learners reporting they "received effective training" and 98% online and 100% live learners reporting they "were well-prepared to deliver LSVT BIG." Online users identified technical issues as the greatest challenge and convenience as the greatest benefit of online learning. Additional data from the post-completion practice survey will be presented.

Conclusions: Online training for physical and occupational therapists in LSVT BIG appears to be comparable to live training, and may be a more effective format for some learners. Utilizing online learning can increase access to PD-specialty training for rehabilitation professionals globally, thus improving patient care.

P33.27

Functional movement disorders and the role of physical therapy.

Joellyn Fox, Heather Cianci

Dan Aaron Parkinson's Rehabilitation Center/Penn Therapy and Fitness, Philadelphia, Pennsylvania, USA

Objective: To present an overview of functional movement disorders (FMD) and the role of physical therapy (PT) in their treatment via 3 case studies.

Method: A literature review of FMD, and of FMD and rehabilitation was completed. A sample of 3 patients with FMD who received PT at the Dan Aaron Parkinson's Rehabilitation Center in Philadelphia, Pennsylvania was chosen. All patients were referred from physicians at the University of Pennsylvania's Parkinson's disease and Movement Disorder Center in Philadelphia, Pennsylvania. A best-practice treatment plan was established based on the literature review and on-going communication with the referring physician. This included the therapists' acknowledgement of the patients' symptoms as not being "fake," and how symptoms can commonly be handled and improve with therapy. Therapists received specialized training in effective communication and education strategies in working with patients with FMD. All treatments were individualized to each patient's needs.

Results: All patients showed a decrease in their symptoms and an improvement in symptom management. While receiving PT, 2 patients recognized a need for psychotherapy in conjunction with their therapy. A multi-disciplinary approach that emphasizes effective communication and begins with PT before psychotherapy can have a positive effect on the lives of those living with FMD.

P33.28**Yearly periods of challenging balance training to prevent decline in gait and balance.**

Erika Franzén, Martin Benka Wallén, David Conradsson, Maria Hagströmer
Karolinska Institutet, Huddinge/Stockholm, Sweden

Introduction: Balance training has an important role in the treatment of Parkinson's disease (PD). We recently demonstrated, in a randomized controlled trial, that a highly challenging balance training (HiBalance) induced significant short-term improvements for older adults with PD. Specifically, the training group had positive effects on balance performance, gait (single-task and dual-task), as well as activities of daily living (ADL) and physical activity. Although these results add to the growing body of research demonstrating short-term benefits of balance training on mobility, our understanding about how long the effects are retained after training periods is limited. Such information is especially important for knowing how often to provide periods of training. Thus, the aim of this study was to predict the course of reversion back to baseline levels in older adults with PD after participating in the HiBalance program.

Methods: One-hundred older adults with mild to moderate PD were randomly assigned into a training- or control group. The training consisted of 10 weeks, 1 hour, 3 times/week balance and gait exercises incorporating dual-task exercises. Long-term follow-ups were carried out 6 and 12 months after the intervention. Outcomes included balance performance (Mini-BESTest), gait performance (gait velocity and step length), dual-tasking ability (cognitive task during gait), objectively assessed physical activity (daily steps) and ADL measured with the UPDRS. Assuming an intention-to-treat protocol, piecewise regression models were estimated to predict the course of reversion for each outcome after the end of treatment.

Results: The effects of the training diminished after conclusion of the intervention. The fastest reversion back to baseline showed physical activity (4 months) while the benefits on cognitive dual-task ability were predicted to persist over a very long period of time. Balance performance was predicted to reach baseline levels after 13 months, gait velocity after 11 months, step length after 9 months and ADL after 13 months.

Conclusions: These results suggest that the positive effects on gait and balance ability seen at the end of the training period are back at baseline levels after 9 to 13 months. Hence, yearly periods of challenging balance training might be necessary to prevent decline in ability. The retained effect seen in cognitive dual-task ability might be associated with a shift in strategy thus further studies are needed.

P33.29**A combined cognitive- and balance-based training intervention for people with Parkinson's disease: COBALT**

Jeffrey Haddad¹, Sandy Snyder¹, Meghan McDonough¹, Shirley Rietdyk¹, Kara Simon¹, Peter Altenburger², Hoda Salsabili¹, Sarah Zaubner³, Jessica Huber¹

¹ Purdue University, West Lafayette, IN, USA

² Indiana University, School of Health and Rehabilitation Sciences, Indianapolis, IN, USA

³ Indiana University, School of Medicine, Indianapolis, IN, USA

Falls and fall related injuries are common in people with Parkinson's disease (PD). Following diagnosis, 50–70 percent of the people will fall at least once, leading to long-term pain and impairment (Ashburn, Stack, Pickering, & Ward, 2001; Wood, Bilclough, Bowron, & Walker, 2002). Falls are likely to be precipitated by the inability to simultaneously manage the motor and cognitive

demands inherent in daily balance activities (Bloem, Grimbergen, van Dijk, & Munneke, 2006; Brown & Marsden). Current therapies often target motor or balance outcomes but not the cognitive limitations associated with PD. We have developed a COgnitive-based BALance Training (COBALT) that simultaneously trains cognitive and balance skills, as we expect that combined training will significantly reduce falls in people with PD. COBALT utilizes repurposed gaming technology so that patients can train in the comfort of their own home with minimal supervision by therapists. This drastically increases convenience and availability and reduces health care costs. As of 2010, the economic burden of PD was over \$14 billion (Kowal, Dall, Chakrabarti, Storm, & Jain, 2013). The training program prompts the user to make therapeutic type movements that are used to control and play cognitively challenging games, customized to the specific impairments of individuals with PD. To date 4 individuals with PD have completed eight weeks of training, 3x per week, (2 in COBALT, 1 in cognitive control training, and 1 in balance control training). We are assessing improvements in cognition, functional reaching, speech, mobility and quality of life. This poster will focus on the protocol and training we are using, presenting the cognitive, reaching, and gait data in a set of pilot subjects to demonstrate the potential of the training. Preliminary results suggest that reaching kinematics, such as the arm velocity, and gait speed improve after COBALT training. We are currently assessing how these improvements compare to training in our control groups. Improvements in standardized cognitive assessments were greatest in the participants who trained with COBALT and smaller for those who used the balance control training. Our goal is to provide effective treatment that is inexpensive and readily available by implementing an "app"-style dissemination. A home-based training plan such as COBALT will mitigate insurance issues currently faced by most patients with PD enrolled in rehabilitation.

P33.30**Parkinson patient reported outcomes of voice and communication pre, post and 6 months following LSVT LOUD® and LSVT ARTIC.**

Angela Halpern¹, Lorraine Ramig², Katherine Freeman³, Jennifer Spielman¹

¹ National Center for Voice and Speech, Denver, Colorado, USA

² University of Colorado, Boulder, Colorado, USA

³ Extrapolate Statistics LLC, Delray Beach, Florida, USA

Objective: To evaluate the functional impact of LSVT LOUD and LSVT ARTIC on voice and communication in individuals with Parkinson disease (PD) immediately post and at 6 months following treatment via two standardized self-rating scales: the Voice Handicap Index (VHI; Jacobson et al., 1997) and the modified Communication Effectiveness Index (CETI-M).

Background: LSVT LOUD is an intensive voice treatment developed for PD. Over 20 years of research data have demonstrated the efficacy of this treatment (e.g., Ramig et al, 2001). LSVT LOUD targets the hallmark PD voice symptoms of decreased loudness, hoarseness, and monotonicity. LSVT ARTIC is an intensive articulation treatment that was designed to be a contrastive, parallel treatment to LSVT@LOUD with potential to improve speech articulation. In combination with objective measures, patient reported functional outcomes following behavioral treatment are key. Thus, the VHI was utilized to investigate voice specific changes, and the CETI-M to evaluate overall communication effectiveness.

Methods: 64 individuals with PD (disease duration: 4.7 (5.2)) were randomly assigned to one of three groups: LSVT LOUD, LSVT ARTIC, or no treatment (Notx). Both treatments included 4-one hour individual sessions a week for 4 weeks (16 sessions). 20 individuals

without PD served as healthy age matched controls (HC). CETI-M and VHI were collected Pre, immediately Post and at 6 months (FU) following the treatment phase.

Results: There were no significant differences among the 3 PD groups at Pre, but there was a significant difference between HC and the 3 PD groups Pre, with the HC scoring better. Significant improvement was noted for LSVT Pre-Post and Pre-FU for both CETI-M and VHI; for LSVTA Pre-Post for CETI-M, Pre-Post and Pre-FU for VHI. Notx and HC had no significant changes Pre-Post or Pre-FU.

Conclusions: Results of this study demonstrate that prior to treatment, subjects with PD rated themselves worse than HC on perceptual measures of voice and communication, and these ratings significantly improved from Pre-Post for both treated groups, maintaining improvement at FU for LSVT and for LSVTA on the VHI. These results indicate a positive impact of voice and articulation treatment on patient reported outcomes of voice and communication in individuals with PD.

P33.31

Singing as a cue to improve gait in Parkinson's disease: a feasibility study

Elinor Harrison, Marie McNeely, Gammon Earhart

Washington University School of Medicine, St. Louis, MO, USA

Objectives: While external rhythmic auditory stimulation is well-established as an effective tool to stabilize gait in PD, little is known about whether self-generated cues such as singing have the same beneficial effect. The purpose of our study was to determine if people with PD could generate their own cues through singing and if this novel cueing technique could improve gait in the same way that traditional cueing techniques do.

Methods: We compared gait patterns of 23 people with mild to moderate PD under five cued conditions: uncued, music only, singing only, singing with music, and a verbal dual-task condition. Participants completed three walking trials in each condition. Velocity, cadence, stride length, and variability measures were recorded on a GAITRite computerized walkway.

Results: Cueing in the form of listening to music, singing, or singing to music did not alter velocity, cadence, or stride length relative to UNCUED walking. The DT condition, however, elicited significant decreases in normalized velocity ($F(4,19)=16.418, p<.001$), cadence ($F(4,19)=7.04, p=.001$), and stride length ($F(4,19)=10.115, p<.001$) compared to all other conditions.

Variability was significantly lower for SING compared to MUS+SING and DT for step time ($F(4,19)=7.172, p=.008, F(4,19)=7.172, p=.003$, respectively) and single support time ($F(4,19)=6.806, p=.031, F(4,19)=6.806, p=.004$, respectively). For step time, DT was more variable than UNCUED walking ($F(4,19)=7.172, p=.003$), MUS ($F(4,19)=7.172, p=.021$), and SING ($F(4,19)=7.172, p=.003$). For single support time, DT walking was more variable than UNCUED walking ($F(4,19)=6.806, p=.003$) and SING ($F(4,19)=6.806, p=.004$).

Conclusions: In our single-session study, singing while walking did not significantly alter velocity, cadence, or stride length, indicating that it was not excessively demanding for people with PD. In addition, singing positively impacted gait variability as compared to other cued conditions. This was further supported by a comparison to a verbal dual-task condition that negatively affected gait performance. These findings suggest that singing holds promise as a useful cueing alternative that may be as effective or better than traditional cueing techniques. The potential benefits of this technique are that it could be used at any time and in any place, without the need for a device to play music, and that it can be customized to match one's cadence.

P33.32

PERFORM: rationale and design for a controlled study in fluctuating PD patients examining the effects of motor state on the outcomes from a structured physical therapy (PT) program

Jean Hubble, Beth Fisher, Kelly Lyons, Claire McLean, Giselle Petzinger, Rajesh Pahwa
USA

It is well established that exercise and physical therapy (PT) have an immediate and potentially long-term impact on motor function in PD patients. However, to date, most PT studies have not addressed the role that dopamine replacement therapy and/or motor state may contribute to enhancing the practice of the PT intervention and thus its functional outcomes. Published studies in animal models of dopamine depletion support the role of dopamine replacement in facilitating motor learning. PERFORM is an ongoing multicenter, outpatient study to evaluate if outcomes following a PT program are improved if PT sessions are conducted while PD patients are in an on motor state vs. an end-of-dose off motor state. The study was initiated in November 2015, with a planned enrollment of 100 patients. Patients currently using apomorphine (APO) injections to manage motor fluctuations are randomized (1:1) to 2 treatment groups (Group 1: PT sessions conducted with patients in an on state with APO & Group 2: PT sessions conducted with patients in an end-of-dose off state. All patients will arrive for the PT visit in an end-of-dose off state and will participate in a standardized PT intervention (3 visits/week to a total of 18 visits). To ensure that PD patients in Group 1 are in the on state during each PT training period, a subcutaneous injection of their usual dose of APO will be administered a few minutes prior to each session; the use of rescue therapy is prohibited during the PT visits. The primary endpoint is the mean change from baseline to study end in the Activities-specific Balance Confidence Scale (ABC) total score. Secondary outcome measures include MDS-UPDRS (Parts 1, 2, 3 and 4) scores, Modified Physical Performance Test, Timed Up & Go, 6-minute walk, Montreal Cognitive Assessment, and Clinical Global Impressions of Severity and Change. PERFORM is one of the first studies to prospectively address the role of the motor state in PT training and outcomes. The first results are expected Q3 2016.

P33.33

Use of the SpeechVive device improves communication in people with Parkinson's disease

Jessica Huber¹, Sandy Snyder¹, Carrier Rountrey², Christy Ludlow²

¹ Purdue University, West Lafayette, IN, USA

² James Madison University, Harrisonburg, VA, USA

Objective: To examine the effectiveness of the SpeechVive device for improving communication in persons with Parkinson's disease (PD).

Background: Speech impairments are common in PD and lead to social isolation and reduced quality of life. Generalization of behavioral speech therapy to everyday communication remains difficult for many patients, possibly due to the sensory and cognitive problems associated with PD. A potential solution is the SpeechVive device, a wearable device that produces cocktail noise in one ear triggered by the patient's voice onset. This noise elicits the Lombard Effect, a reflexive increase in the person's vocal intensity that does not interfere with their ability to hear others' speech.

Methods: Sixteen persons with PD wore the SpeechVive regularly for 3 months. During pre- and post-testing, participants produced a variety of speech tasks first without and then with the SpeechVive. Tasks included connected speech (monologue), reading, and tasks meant to examine prosody. Objective acoustic measurements

determined if speech changed over time with and without the device ($p < 0.01$).

Results: While wearing the SpeechVive, significant changes were apparent in that participants produced speech at higher vocal intensity, used longer utterances, and paused more often at major syntactic boundaries. Variability in fundamental frequency significantly increased during sentence production, particularly in question production. Based on means inspection, participants produced fewer revisions and disfluencies when wearing the SpeechVive.

Conclusions: Overall, wearing the SpeechVive resulted in improved communication. Participants learned to use a higher vocal intensity and better intonation patterns after treatment, even when not wearing the SpeechVive. Some effects occurred with continued use of the SpeechVive suggesting long-term use of the device may be helpful to speech. Larger controlled trials are needed to determine the level of benefit of such a device in PD and to determine what patients are the best candidates for treatment.

P33.34

The efficacy of continuous dopaminergic stimulation in patients with movement disorders in their activities of daily living

Jelka Janša¹, Nina Zupancic Kriznar¹, Milica Kramberger Gregoric¹, Rok Koritnik¹, Robert Rajnar¹, Sabina Posar Budimic¹, Lidija Kambic¹, Klara Trpkov¹, Zvezdan Pirtosek¹, Lidija Ocepek², Ales Praznikar³, Maja Troš³

¹ Slovenia

² MS, Ljubljana, Slovenia

³ MD, Ljubljana, Slovenia

Background: Advanced movement disorders patients (Parkinson's disease (PD), essential tremor (ET) and dystonia (DY)) can be effectively treated with deep brain stimulation (DBS), additionally PD patients could receive intrajejunal infusion of levodopa-carbidopa intestinal gel (IJLC). We were evaluating the effect of this treatments on patients' perception of their performance of self-chosen activities of daily living (ADL), in PD in their best "ON" phase.

Methods: Patients: 17 patients with various movement disorders; twelve with PD, three with DY and two with ET were included in study. Their average age was 60 ± 18 years, there were 7 male, 10 female. Assessment tool: Canadian Occupational Performance Measure (COPM)[1]. The use of COPM assists a person with PD to identify those daily tasks that he/she wants to do, needs to do, is expected to – but cannot do, or are not performed to a satisfactory level for the individual. It measures patients' perception and satisfaction of meaningful and self-chosen ADLs. It is therefore patient-centred assessment. Patients scored their current level of performance and satisfaction with their performance from 1 (with great difficulty or not satisfied) to 10 (with no difficulties or completely satisfied). Procedure: Seven movement disorders patients were treated with IJLC (all with PD, 10 patients with DBS treatment (5 with PD, 2 with ET, 3 with DY). They were assessed in terms of ADL by using the COPM prior to treatment (PD in their best ON phase) and at three, six and twelve months post treatment follow ups.

Results: The average initial COPM-performance was 6.5 ± 2.5 . At month three it was 6.4 ± 2.5 , at month six 6.4 ± 2.5 and at 1 year 6.1 ± 2.6 . The differences between initial scoring and follow ups for COPM-performance were not significant ($p=0.49$; $p=0.48$; $p=0.89$). Initial average COPM-satisfaction score was 6.1 ± 2.3 at month three 6.3 ± 2.5 , at month six 6.5 ± 2.5 , at 1 year 6.0 ± 2.6 respectively. The differences between initial scoring and follow ups for COPM-satisfaction were not significant ($p=0.78$; $p=0.55$; $p=0.85$).

Conclusion: Continuous dopaminergic stimulation, measured by patients' perception of their performance, has enabled patients

functioning to the similar level of ADL performance as they have experienced before therapy and PD in their best "on" phase.

Literature 1. Law M, Baptiste S, Carswell A, McColl M, Polatajko H, Pollock N. Canadian Occupational Performance Measure (3r.ed.). Ottawa, Canada: CAOT Publications, 1998.

P33.35

Perceived walking difficulties in relation to motor aspects in Parkinson's disease

Manzur Kader¹, Susanne Iwarsson¹, Per Odin², Maria H Nilsson³

¹ Department of Health Sciences, Lund University, Lund, Sweden

² Department of Clinical Sciences, Lund University, Lund, Sweden, and Department of Neurology, Central Hospital, Bremerhaven, Germany, Lund, Sweden

³ Department of Health Sciences, Lund University, Lund, Sweden, and Memory Clinic, Skåne University Hospital, Malmö, Sweden, Lund, Sweden

Objective: Walking difficulties are one of the earliest signs of disability in people with Parkinson's disease (PD). However, few studies have investigated contributing factors to perceived walking difficulties in daily life. This study aimed to investigate which motor aspects that contribute to perceived walking difficulties in people with PD.

Methods: The study involved 243 (62% men) participants; their median (min-max) age and PD duration were 70 (45–93) and 8 (1–43) years, respectively. A postal survey including self-administered questionnaires preceded a home visit, which included observations, clinical tests, questions and questionnaires that were administered as a structured interview. Perceived walking difficulties were assessed by using the generic Walk-12 (Walk-12G, scored 0–42, higher=worse), which constituted the dependent variable. Independent variables included bradykinesia and postural instability assessed with the motor examination (part III) of the Unified PD Rating Scale (UPDRS) as well as lower extremity function assessed with the timed Chair-Stand Test. An additional variable tapped freezing of gait (FOG) assessed with the self-administered version of the FOG (dichotomous) Questionnaire, item 3. Linear multiple regression analysis was used to identify factors that independently contributed to perceived walking difficulties.

Results: The results showed that FOG was the most important motor factor contributing to perceived walking difficulties (explaining 26% of the variance, $p < 0.001$) followed by lower extremity function (7% of the variance, $p = 0.001$), postural instability (3% of the variance, $p = 0.003$) and bradykinesia (1% of the variance, $p = 0.033$).

Conclusions: The findings highlight the impact of motor aspects on perceived walking difficulties in people with PD. These findings might have important implications for rehabilitation targeting walking ability in people with PD. In order to increase the knowledge further, future studies should include a broader variety factors (e.g., personal factors, environmental aspects, non-motor symptoms) that may contribute to perceived walking difficulties in people with PD.

P33.36

The LSVT BIG intervention in clients with Parkinson's disease: a systematic review

Dennis Klima¹, Mary DiBartolo², Michael Rabel¹

¹ University of Maryland Eastern Shore, Princess Anne, Maryland, USA

² Salisbury University, Salisbury, Maryland, USA

Introduction: Exercise is a fundamental constituent of rehabilitation management for individuals with Parkinson's disease. Evidence-based interventions should be employed to maximize benefits of

rehabilitation sessions and target performance parameters likely to improve. The LSVT Big® program is a 16 session exercise intervention which incorporates high amplitude/high intensity exercise to recalibrate hypokinetic movement and enhance functional mobility. LSVT Big rehabilitation practitioners are trained and certified worldwide. Aim: The objective of the study was to examine the effects of LSVT Big on motor symptoms and physical performance (gait, balance, and reaction time) in persons with Parkinson's disease through a systematic review of the literature.

Methods: Inclusion criteria required that studies contain the LSVT Big treatment as the primary independent variable in intervention studies within the 2002 to present time corridor. Major data bases searched were the Ovid portal (including PubMed, CINAHL, and EMBASE), PsycINFO, and the Cochrane Library. Two independent raters classified studies according to Sackett's Level of Evidence and analyzed intervention effects and outcomes exceeding minimal detectable change. Randomized control trials (RCT) were graded with the Physiotherapy Evidence Data Base (PEDro) scale. Results: Six studies met the inclusion criteria, including: 3 RCT's (LEVEL 1b), one cohort study (Level 2b), one small RCT (Level 2b), and one case series (Level 4). Pooled findings support that LSVT Big resulted in significant improvement in motor performance on the UPDRS (Levels 1b), gait speed (Level 1b, 2b), and cued reaction time (Level 1b). Conclusions: The LSVT Big intervention demonstrates benefits in motor performance, gait speed, and reaction time supported by salient Level 1 RCT evidence. LSVT BIG, through its focus on high amplitude and high effort exercise, impacts the physical performance profile of clients with Parkinson's disease. Large scale studies are needed to explore the effect on other physical and psychosocial variables.

P33.37

'Pushing the limits' – rethinking motor and cognitive resources after a highly challenging balance training program for Parkinson's disease

Breiffni Leavy¹, Kirsti Skavberg Roaldsen², Kamilla Nylund², Maria Hagströmmer², Erika Franzén²

¹ Department of Physiotherapy, Dept of Neurobiology, Care sciences and Society, The Karolinska Institute., Stockholm, Sweden

² Department of Neurobiology, Care Sciences and Society, Division of Physiotherapy, Karolinska Institute., Stockholm, Sweden

Background: There is growing evidence for the positive effects of exercise training programs on balance control in Parkinson's disease (PD). To be effective, balance training needs to be specific, progressive and highly challenging. Little evidence exists however for how people with PD-related balance impairments perceive highly challenging and progressive balance training programs with dual-task components.

Objective: To explore and describe perceptions of a highly challenging balance training program among people with mild to moderate PD.

Design: This study was qualitative in nature. In-depth interviews were conducted with 13 individuals with mild-moderate PD who had participated in a highly-challenging balance training program. Interview transcripts were analysed using qualitative content analysis, with an inductive approach.

Results: The analysis revealed three sub-themes concerning participants' perceptions of highly challenging and progressive balance training: Movement to counter the disease, reflects how physical activity was used as a long and short-term strategy for counteracting PD symptoms and their progression; Dual-task training in contrast to everyday strategies, incorporates the described experiences of being maximally challenged in a secure and supportive group environment, circumstances which stood in contrast to participants' everyday lives; The struggle to maintain

positive effects, describes participants' long-term struggle to maintain program effects on cognitive and physical function in the face of disease progression. Interpretation of the underlying patterns of these sub-themes resulted in one overarching theme Training at the limits of balance capacity causes a rethinking motor and cognitive resources.

Conclusions: Findings from this study suggest that involvement in highly challenging balance training programs may strengthen feelings of empowerment and self-confidence among people with mild-moderate PD. Training at the limits of balance capacity provoked participants to rethink their individual motor and cognitive resources, a process which was further enabled by the PD-specific group setting. Clinicians and people with PD alike may consider these findings in support of the feasibility of performing challenging and progressive balance training as a treatment method for PD.

P33.38

The influence of cerebellar transcranial direct current stimulation on skill acquisition in Parkinson's disease

Lidio Lima de Albuquerque¹, Merrill Landers¹, Katherine Fischer¹, Sharon Jalene², Brach Poston²

¹ University of Nevada, Las Vegas, Las Vegas, Nevada, USA

² Department of Kinesiology and Nutrition Sciences, University of Nevada, Las Vegas, Las Vegas, Nevada, USA

Objective: The purpose was to determine the influence of cerebellar transcranial direct current stimulation (c-tDCS) on motor skill acquisition in Parkinson's disease (PD).

Background: c-tDCS is a non-invasive brain stimulation technique that has been shown to acutely increase motor performance in young and old adults. Since the cerebellum contributes to PD pathology through increased compensatory activation, excitatory c-tDCS could enhance this process and improve motor function.

Methods: This study was a double-blind, sham-controlled, cross-over experimental design. Twelve individuals with PD participated in two experiments that were separated by a 7 day washout period. Each session involved performance of both a rapid, goal-directed arm movement task (AMT) and a precision grip task (PGT) (practice tasks) performed during either c-tDCS or SHAM stimulation. For the AMT, 4 blocks of 20 trials were performed, whereas the PGT involved matching a target sine wave (target force range: 5-25% of maximum) for 10 trials of 30 seconds each. These two practice tasks were completed over a time course of 25 minutes, which corresponded to the c-tDCS or SHAM stimulation period. c-tDCS was applied over the cerebellum ipsilateral to the primarily affected hand using accepted guidelines (anode 3 cm to the right of theinion, cathode on the ipsilateral buccinator muscle, current strength 2mA). SHAM stimulation was applied in the same fashion using accepted blinding procedures. The dependent variables were endpoint error (AMT) and force error (PGT). Endpoint error was quantified as the final positional error relative to the target, whereas force error was quantified as the average error in force relative to the target force.

Results: There were no significant differences between the two stimulation conditions for either the AMT or PGT.

Conclusion: These findings indicate that a single session of c-tDCS does not elicit improvements in motor skill acquisition in hand and arm tasks in PD. Based on previous research involving tDCS applied to the motor cortex in various populations, c-tDCS may need to be applied over several consecutive days or weeks to elicit improvements in motor performance in PD.

P33.39

Provision of a posture drop-in clinic to improve posture in people with Parkinson's

Fiona Lindop
Derby, Derbyshire, United Kingdom

Background: In Parkinson's, posture can become increasingly flexed, particularly in the hips, knees and trunk. This can begin early with subtle changes that go unnoticed by the individual, but without intervention, can increase, causing pain and potentially impacting activities of daily living, affecting balance and increasing the risk of falls.

Objective: To provide a 3-monthly drop-in posture clinic offering measurement and an optional posture-orientated session of education, advice, exercises & stretches. The primary aim was to encourage individuals to be aware of, and responsible for, maintaining & improving their posture.

Method: Individuals who attended for physiotherapy assessment &/or review at the Parkinson's Specialist Assessment & Rehabilitation Centre, were offered information with dates for Drop-in clinics (no appointment necessary). Five clinics were offered over a 15 month period. Each clinic lasted one hour with posture measurement using Tragus-to-Wall (TtW) on arrival, and an optional posture-orientated session of education, advice, exercises and stretches. Ten individuals (8 men, 2 women) attended with one attending every clinic (5 clinics), one attended 4, three attended 2 and five came to 1. Ages ranged from 60 to 80 years and time since diagnosis from 2–16 years.

Results: Of the 10 subjects, posture improved in 5 after the initial clinic attended, 1 deteriorated and there was no subsequent data for the 4 who only came to 1. However, one of those 4 attended an individual physiotherapy review 2 months after initial clinic and posture had improved by 11cm (right & left). Posture improved in those who attended either 4 or 5 times although in the individual attending 4, it initially deteriorated by 2cms but then improved by the next clinic with this maintained at subsequent clinics. Of those attending twice, 2 improved during a 3 month period (one by 6cm on right TtW) and 1 showed a deterioration (1cm on right TtW). In feedback, individuals reported that clinics were useful because they "remind you about your posture" and "when you are maintaining or improving previous posture measurements it encourages you to keep going and do the exercises & stretches".

Conclusion: Although small numbers were involved, a drop-in clinic provides an opportunity & encouragement for individuals to focus on maintenance and improvement of posture. Further clinics are planned and future data should involve larger numbers, a control group & blinded assessment.

P33.40

Assessment of function and cognition in patients with mild to moderate stage Parkinson's disease participating in a high intensity training program

Dawn Lucier, David Lowell, Linda Melillo, Heather Merrill, Dorian Robinson
Spaulding Rehabilitation Hospital Cape Cod, East Sandwich, MA, USA

Objective: We investigated whether participation in a structured program of high intensity exercises improved function and cognition in people with mild-moderate stage Parkinson disease (PD).

Methods: Retrospective data analysis of 18 people living with PD who participated in Spaulding Cape Cod's High Intensity Training for Parkinson's Disease (HIT-PD) program. Outcome measures: 5x Sit to Stand (S2S), Mini-Balance Evaluation Systems Test(Mini), 6 Minute Walk Test (Walk), Montreal Cognitive Assessment (MoCA),

Fatigue Severity Scale (FSS), Visual Analog Fatigue Assessment (VAFA) and Activities Balance Confidence Scale (ABC). Assessments were completed at the beginning and end of the program by licensed physical therapists who structured and ran the HIT-PD program which was held twice weekly, 1.5 hours each session, for 6 weeks and consisted of large amplitude whole body movements, agility work, spinal flexibility, cardio-vascular training, high effort/ rate progressive strengthening and dual task training.

Results: All 18 participants completed pre and post testing for most outcome measures. A paired samples t-test was performed to test the hypothesis that participation in the HIT-PD program would result in no significant differences in each of the seven measures. The mean improvement in the MoCA (M=1.89, SD=2.85) was significantly greater than zero, two-tailed p=.012. The mean improvement in the timed Walk test (M =92.75, SD=175.49) was significantly greater than zero, two-tailed p=.039. The mean reduction in the time to complete the S2S (M=-1.37, SD=1.36) was significantly greater than zero, two-tailed p=.001, and the mean improvement in the Mini (M =2.00, SD=1.97) was significantly greater than zero, two-tailed p<.000. No significant differences were identified in the ABC, FSS or VAFA. Of note, all measures tied to objective performance tests were significantly different from pretest to posttest, yet none of the subjective measures related to patient reported outcomes reached significance.

Conclusion: Our data suggests that participation in a high intensity training program has a positive effect on balance (Mini), strength (S2S), endurance (Walk) and cognition (MoCA) in mild-moderate stage PD. Though the participants' objective measures demonstrated statistically significant improvements, participants' perception of balance confidence and fatigue did not significantly improve with this intervention. Sample size is a limitation of this study.

Paired Samples Test

	Mean Pre/Post	Paired Differences					t	df	Significance (p-value)
		Mean Change	SD	Std. Error Mean	95% CI				
					Lower	Upper			
Pair 1 MOCA1 Pre MOCA1 Post	24.78 26.67	1.889	2.847	.671	3.305	.473	2.815	17	.012
Pair 2 Walk Pre Walk Post	1655.92 1748.67	92.750	175.492	41.364	180.020	5.480	2.242	17	.039
Pair 3 S2S Pre S2S Post	10.330 8.965	-1.365	1.357	.3291	-.6677	-2.0629	-4.149	16	.001
Pair 4 Mini1 Pre Mini1 Post	24.56 26.56	2.000	1.970	.464	2.980	1.020	4.306	17	.000
Pair 5 ABC Pre ABC Post	90.7165 88.7982	-1.918	5.566	1.3500	.9437	-4.78022	-1.421	16	.175
Pair 6 Fatigue Pre Fatigue Post	34.41 33.59	-.824	14.297	3.468	6.527	-8.174	-.237	16	.815
Pair 7 Visual Pre Visual Post	6.65 6.88	.235	2.905	.705	1.729	-1.259	.334	16	.743

Limitations include N=18 participants.

P33.41

Effects of a home-based brisk walking program in improving activity volume and walking capacity in people with Parkinson's disease

Margaret Mak¹, Wingson Chan², Mandy Auyeung³, Anne Chan⁴, Nelson Cheung⁵, Vincent Mok⁴

¹ Department of Rehabilitation Sciences, Hong Kong, Hong Kong, Hong Kong

² Physiotherapy Department, Haven of Hope Hospital, Hong Kong, Hong Kong, Hong Kong

³ Pamela Yonde Nethesole Eastern Hospital, Hong Kong, Hong Kong, Hong Kong

⁴ Prince of Wales Hospital, Hong Kong, Hong Kong, Hong Kong

⁵ Queen Elizabeth Hospital, Hong Kong, Hong Kong, Hong Kong

Background: Physical deterioration and decrease in activity volume of Parkinson's disease (PD) patients begin at early stages. It is important to improve PD individuals' activity volume in order to deter the degenerative process. Previous findings support the efficacy of home-based exercise in enhancing motor performance and walking endurance in PD individuals.

Objectives: To examine whether a 6-week home-based brisk walking program is safe and effective to improve the daily step count and walking endurance in people with PD.

Methods: Eligible subjects were randomly assigned to experimental (EXP) and control (CON) group using sealed envelopes. The EXP group received one training session of brisk walking followed by 6 weeks of home-based training for a frequency of 3 times/week. CON group received facial and mobility exercises at the same frequency as that of the EXP group. The outcome measures were daily step count taken by a pedometer and 6-minute walk distance. Subjects were assessed baseline (Pre), end of 6-week training (Post), and 6 weeks after treatment completion (Post6wk). Adverse effects and fall incidence were recorded.

Results: Thirty-seven subjects completed the study (EXP=19, CON=18, Hoehn and Yahr stage=1.8±0.5). There was no between-group difference for the demographic data or disease severity. Results of 2-way repeated measure ANOVA indicated group x time interactions for the daily step count ($p=0.006$) and 6-minute walk distance ($p=0.088$). For the daily step count, only EXP group significantly increased (by 21%, $P<0.01$) at Post and EXP group also had a greater number of daily step count than CON group (by 35%, $p<0.05$). For the 6-minute walk distance, only EXP group had significant increases at Post (by 10%, $p<0.001$) and Post6wk (by 10%, $p<0.01$) when compared with the baseline. EXP group also had greater increase in 6MW distance than the CON group at both Post (by 14%, $p<0.05$) and Post6wk (by 16%, $p<0.05$). There was no adverse effect or fall incidence.

Conclusion: The 6-week home-based brisk walking program increased the activity volume and walking capacity in individuals with early-stage PD. Positive findings of the study suggest home-based training is feasible and safe for this PD population.

P33.42

Changes in voice onset time and consonant spirantization following the Lee Silverman Voice Treatment in dysarthric speakers with Parkinson's disease

Vincent Martel-Sauvageau, Cléo Guillemette
Universite Laval, Quebec City, Quebec, Canada

Objective: Hypokinetic dysarthria, a speech disorder frequently associated with Parkinson's Disease (PD), is characterized by impairments in phonation, articulation and the timing between these two components. The Lee Silverman Voice Treatment (LSVT) is an intensive speech therapy program focusing on loud speech, designed to reduce the symptoms of hypokinetic dysarthria. In past studies, this treatment has been proven effective at improving multiple aspects of dysarthric speech in PD such as intensity, vowel articulation, coarticulation and overall intelligibility. Due to the nature of the treatment, it may also have an impact on phonation-articulation timing and consonant articulation. These acoustic variables are of particular interest because they are known to contribute directly to speech intelligibility and they have not been studied in a systematic way.

Methods: The present study was designed to 1) investigate the impact of LSVT on 1) phonation-articulation timing using the Voice Onset Time metric (VOT) and 2) consonant articulation looking at spirantization rates. We report the acoustic data of 10 PD subjects

with moderate hypokinetic dysarthria, before, immediately after, then one and two months after receiving the LSVT program. VOT and spirantization rates were measured in stop-vowel sequences (/b/ /d/ /g/ /p/ /t/ /k/) and compared, pre- and post-treatment.

Results: Results showed no clear change in VOT with the treatment. On the other hand, spirantization rates of the stops were significantly reduced after the treatment. This improvement was mainly observed on the bilabial stops (/p/ and /b/). Since spirantization is commonly caused by hypokinesia and/or weakness in PD, these results suggest that the LSVT could improve the range of movement and the strength of the lips. These results further demonstrate the effects of this treatment of segmental aspects of dysarthric speech in PD.

P33.43

The effect of assistive devices on gait patterns in Parkinson's disease: a pilot study

Inês Martins¹, Josefa Domingos², Joaquim J. Ferreira³, Catarina Godinho⁴

¹ Escola Superior de Saúde Egas Moniz, Monte da Caparica, Portugal, Lisbon, Portugal

² Clinical Pharmacological Unit, Instituto de Medicina Molecular, Lisbon, Portugal. Campus Neurológico Sénior (CNS), Portugal., Lisbon, Portugal

³ Clinical Pharmacological Unit, Instituto de Medicina Molecular, Lisbon, Portugal. Campus Neurológico Sénior (CNS), Portugal. Laboratory of Clinical Pharmacology and Therapeutics, Faculty of Medicine, University of Lisbon, Portugal., Lisbon, Portugal

⁴ Clinical Pharmacological Unit, Instituto de Medicina Molecular, Lisbon, Portugal. Campus Neurológico Sénior (CNS), Portugal. Center for Interdisciplinary Research Egas Moniz (CiiEM), Instituto Superior de Ciências da Saúde Egas Moniz, Monte de Caparica, Portugal., Lisbon, Portugal

Objective: To assess the influence of six different assistive devices (ADs) on gait patterns in people with idiopathic Parkinson's Disease.

Methods: Prospective, single-center pilot study involving people with Parkinson's disease (PwPs). Participants were instructed to walk on a comfortable, self-selected, walking speed across the 2' by 16' Zeno walkway (ProtoKinetics, Havertown, PA), with a 16-level pressure sensing mat sampling at 60Hz. Spatiotemporal gait measures were collected when participants walked with and without different ADs: an aluminium straight cane (Cane); a tripod cane (TCane); a pair of Nordic walking sticks (NWS); a standard walker (StW); a two-wheeled walker (2WW) with fixed wheels and a four-wheeled walker (4WW) with front wheels casters. Participants' postural stability was assessed and rated accordingly to the item 3.12 of the MDS-UPDRS. Gait parameters were analysed including: stride length; stride time; stance period; swing period; double support time; velocity; cadence; CISP anterior/posterior and medial/lateral. Since PwPs have abnormal gait patterns compared to healthy individuals, each participants' no assistive device condition ('no AD') was considered the baseline for comparison with each AD in Wilcoxon analysis.

Results: Fifteen PwPs were included with a mean age of 65.2±7.9 years old. There was no impact in gait parameters when using a 4WW device as the StW showed the highest variability with differences in all gait measures ($p<0.05$). Using 2WW reflected on differences in stride length, stance and swing period, double support time and cadence ($p<0.05$). Walking with a Cane showed differences in double support time, gait speed and cadence while TCane differed in stride time, stance and swing period ($p<0.05$). Finally, the use of NWS resulted in different stride time, velocity and cadence ($p<0.05$). None of the ADs used in the present study had impact in weight transfer parameters.

Conclusion: With 4WW PwPs experienced rapid improvements in gait performance and quality. Walking with a 4WW produced a similar gait pattern to when PwPs walking with 'no AD'. Weight transfer does not seem to interfere with the use of ADs. The impact of different ADs in gait patterns should be considered when prescribing ADs to PwPs. Further research is being carried out to expand these finds.

P33.44

Application of the dual task taxonomy: Parkinson's disease and freezing of gait – a case study

Tara McIsaac¹, Lisa Muratori²

¹ A.T. Still University – ASHS, Mesa, AZ, USA

² Stony Brook University, Stony Brook, NY, USA

This presentation reviews the dual task taxonomy recently proposed by McIsaac, Lamberg and Muratori (2015) and discusses the application of this framework to people with Parkinson's disease (PD), specifically with freezing of gait (FOG). The study of dual task interference and its cost to performance of everyday activities has gained increasing attention in the rehabilitation literature, but has evolved across disciplines without clear and common terminology or consistency in experimental methodology. The dual task taxonomy was proposed with an operational definition of dual task, distinguishing it from a complex single task. This taxonomy classifies cognitive and motor modes of interference in dual task behaviors, linking traditional concepts of learning and principles of motor control with multitasking analyses currently used. Five mechanisms underlying FOG have been proposed, two of which involve cognitive issues of visuospatial deficits and frontal executive dysfunction (Nutt et al. 2011). Dual tasking, with its greater cognitive requirement, increases the likelihood of freezing in people with PD. Indeed, dual task-related neural connectivity has been shown recently to be altered in PD and was correlated with worse dual task performance in freezers compared with non-freezers (Vervoort et al. 2016). Dual task training, either an integrated or consecutive approach, may improve dual task abilities in people with PD (Strouwen et al. 2015). We present through case study on results of a 10-week intervention with a freezer with PD with whom we applied the progression framework based on the dual task taxonomy.

P33.45

Quantity and intensity of physical activity in people with Parkinson's disease during exercise interventions

Marie E. McNeely, Ryan P. Duncan, Gammon M. Earhart

Washington University in St. Louis School of Medicine, St. Louis, MO, USA

Background: Studies on the impact of exercise, particularly dance, on motor function in people with Parkinson's disease (PD) typically do not include objective measures of the amount and intensity of activity. Optimizing parameters of exercise interventions may help maximize or better target benefits in PD.

Objective: Examine the amount and intensity of physical activity performed by people with PD during group exercise classes.

Methods: A subset of people with mild to moderate PD participating in 12-week, twice weekly 1-hour tango (n=6) or Dance for Parkinson's (D4PD, n=6) interventions wore activity monitors on the dominant ankle during classes. We compared the amount (steps, acceleration vector magnitude) and intensity (sedentary, light, moderate, vigorous, and very vigorous activity time) of activity between classes. Baseline and post-intervention balance (Mini-Balance Evaluation Systems Test (MBT), Activities-Specific Balance Confidence (ABC)) and mobility measures (timed-up-and-go (TUG),

6-minute walk test (6MWT)) were collected. We assessed the relationships between participants' activity during class and their baseline performance and changes in performance.

Results: Minimal vigorous and very vigorous activity occurred, so these were excluded. Sedentary time was higher in the D4PD (p=0.003) class. Light activity (p=0.007) and steps (p=0.017) were higher in the tango classes. ABC improvements were associated with less sedentary time (r=-0.631, p=0.037) and more steps (r=0.737, p=0.006) in class. MBT improvements were associated with more light activity in class (p=0.598, p=0.040). Better baseline ABC (r=0.649, p=0.022), TUG (r=-0.624, p=0.030), and MBT (p=0.664, p=0.018) were associated with higher vector magnitudes in class. Better TUG (r=-0.624, p=0.030), 6MWT (r=0.755, p=0.004), and MBT (p=0.671, p=0.017) at baseline were associated with higher moderate activity in class.

Discussion: Though dance improves motor performance in PD, it is unclear whether certain forms of dance are more helpful and how benefits from dance compare to other exercise interventions. Activity during the tango and D4PD interventions differed, and neither involved vigorous exertion. Preliminary outcomes suggest amount and intensity of activity during dance may be related to extent of improvement in balance and balance confidence. However, baseline levels of balance and mobility likely impact how active a participant is during an intervention.

P33.46

Housing accessibility problems in people with Parkinson's disease

Maria H Nilsson¹, Susanne Iwarsson², Jorge Alegre Ayala³, Björn Slaug²

¹ Department of Health Sciences, Faculty of Medicine, Lund University; Memory Clinic, Skåne University Hospital, Malmö, Lund, Sweden

² Department of Health Sciences, Faculty of Medicine, Lund University, Lund, Sweden

³ Department of Physiotherapy, Occupational Therapy, Rehabilitation and Physical Medicine, Faculty of Health Sciences, Universidad Rey Juan Carlos, Alcorcón, Lund, Sweden

Background: Housing accessibility problems are high on the political agenda. Accessibility, or person-environment fit, problems arise as a function of functional limitations and physical environmental barriers. There is however limited knowledge regarding housing accessibility problems in people with Parkinson's disease (PD).

Objective: To investigate housing accessibility problems among people with PD in relation to different disease stages.

Methods: This study included 253 (61% men) participants with PD. Their mean (SD, min-max) age was 70 (9.2, 45–93) years; the median (q1-q3, min-max) PD duration was 8 (5-13, 1–43) years. Accessibility problems were assessed by using the Housing Enabler (HE) instrument, which is administered in 3 steps: 1) assessment of functional limitations and dependence on mobility devices (personal component), 2) assessment (according to national standards and guidelines) of physical environmental barriers in the home and close exterior surrounding (environmental component), 3) calculation of an accessibility problem score, generated by the personal and environmental component data (Steps 1 and 2). Disease severity was assessed by using the Hoehn and Yahr I-V stages ("on state"; higher scores = "worse").

Results: In the total sample, the top two items of the personal component that contributed the most to accessibility problems were poor balance followed by dependence on walking aids. Balance problems explained 22% and walking aids 17% of the magnitude of accessibility problems (HE scores). Physical environmental barriers contributed to the accessibility score to a lesser extent than the

personal component. The top two environmental barriers were “no grab bar at shower/bath/toilet” (3.7%) and “wall-mounted cupboards and shelves placed high” (3.6%). The median (q1–q3) HE-scores ranged from 122 (56–198) in HY stage I to 328 (240–384) in HY stages IV–V. Accessibility scores differed significantly ($p < 0.001$, Kruskal Wallis) in relation to HY stages. Subsequent comparisons (Mann Whitney U test) showed statistical differences between all HY stages but between stages I and II, i.e. even if correcting for multiple comparisons.

Conclusions: The results suggest that actions targeting balance problems and dependence on mobility devices would have the greatest potential for reducing housing accessibility problems in people with PD.

P33.47

Three-dimensional evaluation of postural stability in Parkinson's disease with mobile technology

Sarah Ozinga, Mandy Koop, Susan Linder, Tanujit Dey, Jay Alberts
Cleveland Clinic, Cleveland, Ohio, USA

Background: Postural instability is a hallmark of PD and is often refractory to medication and deep brain stimulation. Objective metrics, that can be easily gathered and calculated, to characterize postural stability are necessary for the development of effective fall risk stratification models and treatment algorithms to more aid in the management of declines in balance.

Objective: To validate a mobile device evaluation platform and resultant three dimensional balance metric that objectively and quantitatively characterizes PD posture stability.

Methods: An iPad/iPhone mobile Application was developed, in which biomechanical data from the embedded accelerometer and gyroscope were automatically processed to characterize movement of the center of mass in the medial-lateral (ML) and anterior-posterior (AP) planes and trunk rotation (TR). Twenty-seven mild to moderate individuals with PD and 27 age-matched controls completed balance tasks in which the support surface, stance, and vision were altered. A postural stability metric quantifying the maximum and minimum range (peak-to-peak; P2P) of sway acceleration in each movement direction (i.e. ML, AP, and TR) was compared between the PD and control groups. The P2P value in each direction for each individual with PD across all trials was expressed as a normalized value of the control data in order to identify individuals with PD with severe postural instability (percentile value of postural instability greater than 95th percentile of controls). Lastly, the normalized P2P data in all three directions were then combined to create a balance metric, Cleveland Clinic-Postural Stability Index (CC-PSI), to quantify postural instability across all movement directions.

Results: Patients with PD showed significantly greater postural instability compared to the control group across all balance conditions shown by the CC-PSI metric ($p < 0.01$ for all tests). Additionally, within the PD group, postural instability increased across all sway directions as sensorimotor integration became more challenging as the difficulty of the postural stability task increased.

Conclusions: Overall, the CC-PSI, which can be rapidly derived using a mobile device, provides an unbiased and systematic metric for the quantification of postural stability in PD patients. The ease of data acquisition and processing make the CC-PSI ideally suited to better understand specific postural stability declines in PD patients and assisting in its treatment.

P33.48

Prosodic improvement in persons with Parkinson's disease undergoing “SPEAK-OUT!®” voice therapy

Eunsun Park¹, Christina Santos², Justin Dvorak¹, Frank Boutsen¹

¹ University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, USA

² INTEGRIS Jim Thorpe Rehabilitation Center, Oklahoma City, Oklahoma, USA

Background: Parkinson's disease (PD) is a progressive neurodegenerative disorder affecting 1 in 100 adults over the age of 60. A majority of persons with PD manifest hypokinetic dysarthria, which is characterized by reduced loudness, breathy voice, mono-pitch, and voice tremor, intermittent rapid rushes of speech. SPEAK-OUT!® is a voice therapy program to improve functional communicative ability, stressing “speaking with intent” to increase amplitude. This program has total 12 sessions, 3 sessions per week for 4 weeks.

Purpose: Using readings of the “My Grandfather” passage (GP), vowel prolongation, diadochokinetic tests, and conversational speech samples, this study evaluated the efficacy of the SPEAK-OUT!® program in terms of prosody changes such as speech intensity, rate and pitch range for persons with idiopathic PD and evaluated their perceptual vocal handicap pre and post treatment.

Methods: Data have been collected on 13 participants (10 M, 3 F; mean age 70.9±7.2 yrs, mean duration of PD 8.4±10.0 yrs). Data included participants' scores on the Voice Handicap Index (VHI) and Voice-Related Quality of Life (V-RQOL) questionnaires, audio recordings, and demographic data such as age, gender, ethnicity, handedness, diagnosis, onset of PD, and current Parkinson's medication(s). Participants were asked to read the GP, produce a sustained vowel sound (/ah/), produce repetitions of the syllables /pə/, /tə/, and /kə/, produce diadochokinetic (DDK) syllables /pətəkə/ for a duration of 10 seconds, and produce conversational speech. Computation of pre/post amplitude and pitch differences was carried out with custom routines developed in MATLAB®, followed by paired t-tests, linear regression, exact sign tests and bootstrap regression.

Results: Participants gained an average of 7.7±2.5 dB SPL ($p < 0.0001$) in conversational speech and 8.9±3.4 dB SPL ($p < 0.0001$) in the GP reading. Participants' pitch range expanded by an average of 10.5 Hz (95% CI: 4.5–10.7) ($p = 0.0001$). Post-therapy VHI score was significantly lower than pre-treatment ($p = 0.0187$). Speech rate during the GP reading was marginally slower ($p = 0.0886$), having been reduced by an average of 0.3±0.5 syll/sec.

Conclusion: Participants achieved a statistically and clinically significant increase in speech intensity and pitch range after SPEAK-OUT!® training, consistent with self-report voice scores. Speak-out therefore is a viable treatment alternative to Lee Silverman Voice Treatment.

P33.49

Alterations in upper and lower extremity kinematics in Parkinson's disease during dual-task conditions

Amanda Penko, Anson Rosenfeldt, Tanujit Dey, Andrew Bazyk,

Matthew Streicher, Jay Alberts

Cleveland Clinic, Cleveland, Oh, USA

Introduction: Gait dysfunction is a hallmark of Parkinson's disease (PD). Alterations in PD gait are more pronounced during dual-task conditions which a cognitive or motor task is paired with gait. It is unclear what specific aspects of executive function may be compromised that contributes to greater declines in gait dysfunction under dual-task conditions. This project aimed to systematically evaluate gait during the performance of cognitive tasks requiring different aspects of executive function.

Methods: Twenty three participants with idiopathic PD walked on a self-paced treadmill while performing the following cognitive tasks: N- back (working memory), Serial 7's (attention and problem solving) Digit recall (attention and verbal memory), Verbal fluency (semantic memory and fluency), and Stroop test (information processing speed and visuospatial processing). Upper and lower extremity kinematic and kinetic outcomes were gathered and evaluated with the Computer Assisted Rehabilitation Environment (CAREN) virtual reality system.

Results: All participants were Hoehn-Yahr I-III and mean UPDRS Motor III was 33.0 ± 13 . DT resulted in declines ($p < .005$) in gait velocity (0.16 ± 0.04 m/s) and step length variability ($.014 \pm .003$) for all cognitive tasks when compared to walking alone. All cognitive task results in two or greater deficits in the following spatiotemporal gait parameters: gait velocity, step cadence, step length, arm swing arc length, stance time and step length variability. Serial 7's resulted in the largest number of significant ($p < .005$) gait parameter changes, with decreases in arm swing arc length ($.12 \pm .03$ m), gait velocity ($.23 \pm .04$ m/s), step cadence (8.04 ± 1.42 steps/min), step length ($.09 \pm .02$ m), stance time ($.06 \pm .01$ sec), and an increase in step length variability ($.015 \pm .003$).

Conclusions: Gait dysfunction becomes more apparent during DT conditions regardless of the cognitive task, however, Serial 7's resulted in the greatest number of spatiotemporal gait parameter declines, while the Stroop test resulted in the least amount number of spatiotemporal gait parameter declines when compared to walking alone.

P33.50

Anticipatory postural adjustments to internal and external perturbations in people who do and do not experience freezing of gait

Daniel Peterson¹, Christian Schlenstedt², Fay Horak³

¹ Arizona State University, Phoenix, Arizona, USA

² University of Kiel, Germany

³ Oregon Health & Science University, Portland, OR, USA

Introduction: Anticipatory postural adjustments (APAs) prior to voluntary stepping are important to facilitate large and effective steps. However, APAs prior to protective stepping, which occurs after an external perturbation such as a slip or a trip, may be detrimental, delaying step initiation. Indeed, delays in stepping after large external perturbations are closely related to falls. Previous investigations suggest that people with PD who freeze (FR) exhibit APAs prior to protective steps that are larger than healthy adults (HC), and may contribute to delayed stepping. However, it is unknown whether people with PD who do not experience freezing (NF) also exhibit abnormally large APAs prior to protective stepping. Given the relationship between APAs, step latency, and falls, characterizing the APAs prior to protective stepping in people with PD may inform fall prevention interventions.

Methods: Thirteen FR, 15 NF, and 12 healthy adults participated. FR and NF groups were matched for age and disease severity. Participants completed cued normal stepping, in response to a small proprioceptive cue, and protective stepping, in response to a quick movement of the support surface (15cm, 56cm/s). Force-plates captured center of pressure (COP) movements and step latency prior to cued and protective stepping.

Results: During cued stepping, no differences in APAs were observed across groups. However, during reactive stepping, FR exhibited larger APAs than both NF ($p = 0.036$) and healthy adults ($p = 0.010$). APAs in NF were similar to HC ($p = 0.150$). Further, APA size was directly correlated to step latency in FR ($p = 0.01$), but not NF ($p = 0.259$) groups.

Conclusions: Despite similar disease severity, and similar APAs during cued stepping, FR exhibited larger APAs prior to protective

stepping than NF, and these APAs were directly related to worse outcomes (delayed step onset). These results suggest that FR, but not NF, exhibit large APAs prior to protective stepping which may contribute to worse stepping outcomes. Future work should investigate ways to improve APAs prior to protective stepping in this population.

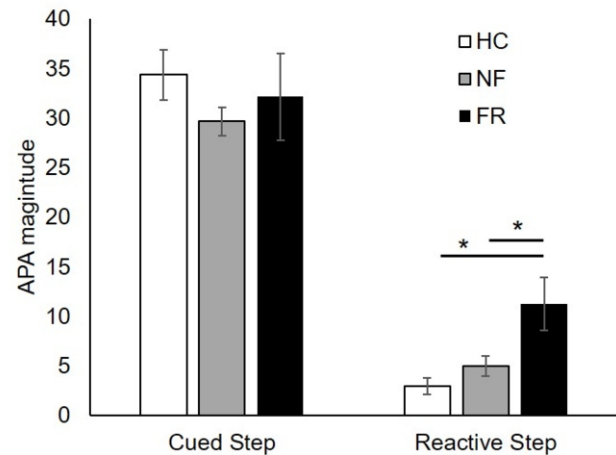


Figure 1. Mean and standard error of anticipatory postural response (APA) magnitudes prior to cued and reactive stepping in healthy adults (HC), people with PD who do not freeze (NF), and people with PD who do freeze (FR). *designates a significance of $p < 0.05$

P33.51

Action observation therapy in Parkinson's disease patients: review and suggestions for application protocol in physiotherapy.

Mai Pham, Sylvie Nadeau
Montreal, Quebec, Canada

Problematic: Parkinson's disease (PD) is a chronic, complex neurodegenerative disorder characterized by progressive deterioration of mobility (gait, balance...) and decrease of activities in daily living such as transfers, bed mobility, ... Conventional physical therapy interventions are considered as an adjuvant to pharmacological treatment in PD patients, but it provide only small and short-lasting clinical benefits. Action observation therapy (AOT) is proposed as an innovative cognitive tool in the rehabilitation of PD. The neurophysiological basis of AOT is the "mirror neuron system". Patients were asked first to observe the motor act described on the video-clip and then practice the observed task in order to restore or recruit the corticospinal circuits normally activated in the brain.

Objectives:

- Review of the literature about AOT.
- Establish some suggestions for application protocols of AOT as treatment in PD patients in physiotherapy.

Method: Literature review with key terms: action observation therapy, Parkinson's disease, physiotherapy was used to search on Pubmed, Embase, Cochrane databases.

Results: Reviews of the existing studies up to date have suggested that AOT could induce improvements of motor performance such as reducing bradykinesia, freezing of gait episodes in PD patients. However, the application of AOT was heterogenous.

Conclusions: AOT is a novel approach in neurorehabilitation that physiotherapists should learn to optimize their interventions on PD

patients. Some guidelines were found to define the best way to apply AOT in clinical practice. Video-clips of other functional.

P33.52

Enhancing adherence to a community-based movement disorders exercise program through follow-up phone conversations

Robert Phillips, Abbey Schory, Hillary Markel, Natalie Swartz, Jeremy Klaserner, Jennifer Reneker
USA

Background: Research has shown that exercise can slow disease progression in individuals with movement disorders. Motivation is essential for participation in an exercise program and telecommunication is an inexpensive way to motivate individuals. No research exists on the effects of telecommunication in combination with motivational interviewing techniques (MIT) for this population. The purpose of this study was to analyze participant adherence to a community-based movement disorders exercise program: Do individuals 1) who receive weekly telephone conversations using MIT show better adherence than individuals not receiving MIT? 2) who receive MIT have improved participation during their sessions? 3) have better performance on standardized outcome measures of physical function and quality of life (QOL) after receiving follow-up phone calls using MIT?

Methods: 30-individuals (16 idiopathic PD) with movement impairments participating in a community-based movement disorders clinic for 12 weeks. A single-blinded, between-group design was utilized. Half of the participants received motivational support.

Results: Comparing the attendance between groups using an independent-samples t-test and there was no difference between control (14.50±6.29) and MIT (15.81±5.64; $p=0.551$) groups. There was no significant difference between groups for SIRAS questioning: Scores for the control and MIT groups were 3.97±0.56 and 4.01±0.56, $p=0.844$ for Question 1; 3.93±0.56 and 4.25±0.32, $p=0.060$ for Question 2; and 4.46±0.45 and 4.57±0.38, $p=0.492$ for Question 3, respectively. A repeated-measures ANOVA was performed for functional outcome measures and QOL with no observed interaction ($p=0.862$): 91.7% all participants scored better or stayed the same on both the TUG and FGA, 78.6% on the WHO-QOL Brief, and 100% of scored better on the Four Square Step Test.

Limitations: Many participants had previous experience and were bias towards the benefits of group exercise. A sample of convenience was used limiting the size of the participant pool. Researchers were not trained to administer MIT through phone conversation.

Conclusions: Individuals with movement disorders benefit from group exercise in a community-based clinic. Function and QOL are improved after 12-weeks of group exercise. MIT through phone conversations led to increased attendance and better performance during workouts. Questions Pending Analysis: What are some of the determinants affecting adherence?

P33.53

World Health Organization's International Classification of Functioning, Disability, and Health (ICF) as model to guide the interprofessional care for Parkinson's Disease

Maria Elisa Pimentel Piemonte¹, Michelle Tosin², Giovana Diaferia², Katia O. Pinto², Leticia Mansur², Maria H Morgani², Erika Okamoto², Erica Guelfi², Tamine Capato², Carlos Rieder²

¹ Sao Paulo, Brazil

² Brazil

Aim: To verify the effectiveness of the World Health Organization's International Classification of Functioning, Disability, and Health (ICF) as model to guide the interprofessional care for Parkinson Disease (ICPD).

Background: Despite the empirical evidence about the positive effects ICPD, there is a limited scientific evidences confirming it. Considering that PD has consequences on a variety of levels including physically, mentally, emotionally, and socially, there is needed to adopt a framework which allows a broad analysis about all of these consequences in order to make possible to integrate the information and determine relationships between levels thus helping professionals to fully understand how PD affects the individuals and/or their family. ICF may be a useful framework for ICPD.

Method: Three patients with PD were included in this study: the first of them was a woman, 57 years old, married, in 1 H&Y stage, referring as the main complain a slowness and weakness in the upper limb movements; the second was a man, 69 years old, married, in 2,5 H&Y stage, referring as the main complain a progressive worsening in the balance associated to falls; and finally, the third patient was a woman, 62 years old, married, in stage 4 H&Y stage, referring as the main complain a drooling, deficit in the gait associated to frequent falls and loss of independence in daily living activities. All patients were evaluated for a neurologist specialized in Movement Disorders, Physiotherapists, Nurses; Occupational therapists, Speech language pathologists, and Psychologists. After the conclusion of evaluations, the cases were discussed by ICPD following the ICF model in order to establish the best interprofessional care for each of patients.

Results: The results from all evaluations were organized into the three ICF domains: Body structure and Function, Activity level and Participation level. This facilitated the integration of information from different professional areas, allowing a broad analysis of consequences of PD on all aspects of patient's life. As consequence, an integrative interprofessional care program for each patient was established.

Conclusion: ICF can be consider a useful model to guide the ICPD which allows the integrative analysis of the consequences of PD and facilitate the elaboration of a more effective interprofessional care program.

P33.54

The effects of Nintendo Wii balance board training on walking, quality of life and depression in Parkinson's disease patients – pilot study

Sabina Posar Budimlic¹, Robert Rajnar², Lidija Kambic², Jelka Janša², Rok Koritnik², Klara Trpkov², Lidija Ocepek², Nina Zupancic Križnar², Aleš Pražnikar², Zvezdan Pirtošek², Maja Trošič²

¹ Lukovica, Slovenia, Slovenia

² Slovenia

Objective: The aim of this pilot study was to evaluate effectiveness of Nintendo Wii balance board training in Parkinson's Disease (PD) patients on walking, depression and quality of life.

Background: PD with motor and nonmotor symptoms influences patient's quality of life. The changes in walking patterns, slowness and freezing of gait are among most clinical features of PD. Some PD patients additionally experience nonmotor symptoms, depression being particularly common. Physical exercise has been proven to have a positive effect on PD patients' daily life. We explored the effectiveness of the virtual reality exercises by using Nintendo Wii.

Methods: Seven randomly chosen PD patients underwent 10 training sessions with Nintendo Wii Balance board. They exercised 3 times per week for 30 minutes. Assessment and training were performed in patient's ON phase and PD-related medication has been stable at least 2 weeks before and throughout the study. For

the description of the situation of patient's disease, patients were assessed by Hoehn&Yahr Staging and Mini Mental State Examination (MMSE) before they underwent 10 training sessions. Patients were assessed before and after 10 training sessions as well as two months later by the following assessment tools: 10 Meter Walk Test (time and the number of steps), HiMAT (walk backwards, walk over obstacle), PDQ-39 and Beck Depression Inventory (BDI).

Results: 5 male and 2 female patients, aged 66.8±SD years, disease duration 8.6±SD years, Hoehn&Yahr 2.4±SD and MMSE 27.1±SD. After 10 treatment sessions there was an improvement in Timed 10 meters Walking Test and in the number of steps (in 10 meters). This improvement however did not last for 2 months. Walking backwards and walk over obstacle did not improve (HiMAT). PDQ-39 showed improvement after 10 sessions as well as at 2 months follow-up. BDI showed improvement after 10 sessions, but not any more at 2 months follow up. The results did not reach statistically significant level.

Conclusions: Nintendo Wii Balance Board has improved walking ability, mood and general quality of life in PD patients. This finding is in agreement with the growing evidence of the beneficial effect of patients' physical activity on their wellbeing. Additional studies on higher number of patients are needed to further clarify the effect of this training.

P33.55

A comparison of the effect of multi-modal sensorimotor agility training on functional outcomes measures in individuals with atypical Parkinsonism versus idiopathic Parkinson's disease: A retrospective observational case-control study.

Catherine Printz¹, Carter McElroy¹, Eric Rhoden¹, J. Vincent Filoteo^{2,3}, Irene Litvan³

¹ Department of Rehabilitation Services, University of California, San Diego, La Jolla, California, USA

² Department of Psychiatry, University of California, San Diego; La Jolla, California, USA

³ Department of Neurosciences, University of California, San Diego, La Jolla, California, USA

Background: Sensorimotor agility training improves functional tests and measures in individuals with idiopathic Parkinson's disease (IPD). There is very little evidence, however, to support whether this approach improves mobility outcomes in patients with atypical parkinsonism (AP).

Objective: To compare multi-modal sensorimotor agility training effects on functional outcomes measures in individuals with IPD versus AP.

Methods/Design: Twenty-three patients with IPD were compared to 9 patients with AP, including corticobasal degeneration, multiple system atrophy, or progressive supranuclear palsy. Study included movement disorder patients seen from February 2013 to April 2015 if they had the following evaluations at baseline and discharge: Mini Balance Evaluation Systems Test (Mini BESTest), Timed Up and Go (TUG) and Timed Up and Go Cognitive (TUG-C). Treatment included some component of progressive sensorimotor agility training that either (1) reduced the patient's base of support, (2) changed the surface compliance, (3) increased the speed or resistance of the activity, (4) increased the cognitive demand, or (4) limited the visual input to force the body to use multiple balance systems.

Separate 2 X 2 repeated measures ANOVAs were completed with group (IPD versus AP) and time (baseline and discharge) as factors for all three dependent measures (Mini BESTest, TUG, and TUG-C).

Results: At baseline, the patients with IPD scored an average of 14.23 seconds on the TUG, 16.98 seconds on the TUG-C, and a 69.4% on the Mini BESTest. The patients with AP scored an

average of 13.89 seconds on the TUG, 17.53 seconds on the TUG-C, and a 59.0% on the Mini BESTest. At discharge, the patients with IPD scored an average of 9.89 seconds on the TUG, 11.91 seconds on the TUG-C, and a 81.2% on the Mini BESTest. The patients with AP scored an average of 11.91 seconds on the TUG, 14.64 seconds on the TUG-C, and a 69.0% on the Mini BESTest. The 2 X 2 ANOVAs demonstrated that both groups benefited equally from the intervention for the Mini BESTest, TUG and TUG-C variables.

Conclusion: Patients with IPD and AP benefited equally from progressive sensorimotor agility physical therapy training, as evidenced by improvements in functional outcomes measures including the TUG, TUG-C, and Mini BESTest.

P33.56

Evaluating dexterity in people with Parkinson's disease: construct validity of the Nine Hole Peg Test and Purdue Pegboard Test.

Elizabeth Proud¹, Belinda Bilney¹, Kimberly Miller², Meg Morris³, Jennifer McGinley¹

¹ The University of Melbourne, Parkville, Victoria, Australia

² University of British Columbia, Vancouver, British Columbia, Canada

³ La Trobe University and Healthscope Australia, Bundoora, Victoria, Australia

Objectives: Clinicians and researchers regularly use the Nine Hole Peg Test (NHPT) and Purdue Pegboard Test (PPT) to quantify dexterity in people with Parkinson's disease (PD), yet the validity of these tools is largely untested in this group. We investigated the convergent validity of the NHPT and PPT in a sample of Australians with PD.

Methods: Participants were 30 volunteers with idiopathic PD on daily oral levodopa. The NHPT and PPT were administered in the 'on' phase of the medication cycle, and participants completed the Manual Ability Measure-36 (MAM-36), a manual activity questionnaire (1). Moderate relationships ($r=0.50$) were hypothesised between variables. Participant characteristics were reported with means and standard deviations or median scores, and Pearson's Correlation Coefficients examined relationships between dexterity measures and self-reported manual performance.

Results: Participants had a mean age of 67.1 years, mean disease duration of 6.4 years, and median HY Stage of 2. Moderate negative linear relationships existed between MAM-36 and NHPT scores (dominant $r=-0.37$; nondominant $r=-0.37$), and stronger positive linear associations were observed between the MAM-36 and PPT subtests (dominant $r=0.31$; nondominant $r=0.49$; bimanual $r=0.45$; combined $r=0.44$; assembly $r=0.51$). In an analysis based on the laterality of motor signs, MAM-36 scores were more strongly associated with NHPT and PPT more affected hand scores than with dominant hand scores (NHPT $r=-0.46$; PPT $r=0.47$).

Conclusion: NHPT and PPT scores were moderately correlated with self-reported manual performance in this group with mild to moderate PD, and difficulties carrying out daily manual tasks were more strongly associated with dexterity in the more affected hand than the dominant hand. Lower than hypothesised correlations may be partly due to differences in constructs measured by the pegboards and MAM-36, that is, the ability to complete standardised dexterity tests in a controlled setting and performance of dextrous activities in the home environment. This study provides new evidence to support the continued use of the NHPT and PPT in clinical practice, but further evidence of construct validity is needed in people in HY Stages I to IV, who may be candidates for physiotherapy interventions.

[1] Chen, C.C. and R.K. Bode, Psychometric Validation of the Manual Ability Measure-36 (MAM-36) in Patients With Neurologic and Musculoskeletal Disorders. *Arch Phys Med Rehabil*, 2010. 91: p. 414-420.

P33.57

Allied health utilization variability and outcomes for people with Parkinson's disease: National Parkinson Foundation Quality Improvement Initiative (NPF-QII) data

Miriam Rafferty¹, Angela Roberts², Peter Schmidt³, Sheng Luo⁴, Kan Li⁴

¹ Northwestern University, Chicago, IL, USA

² Roxelyn and Richard Pepper Department of Communication Sciences and Disorders, Evanston, IL, USA

³ National Parkinson Foundation, Miami, FL, USA

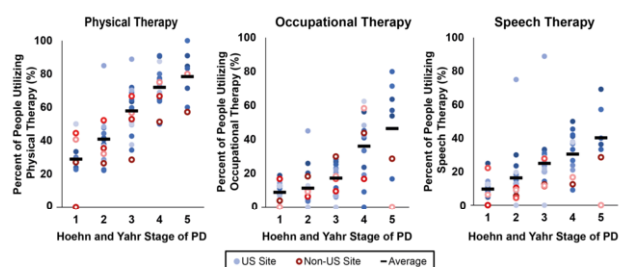
⁴ Department of Biostatistics, University of Texas Health Science Center at Houston, Houston, TX, USA

Background and Objective: Rehabilitation interventions, including the allied health services of physical therapy (PT), occupational therapy (OT), and speech therapy (ST), are well-supported for people with Parkinson's disease (PD). The objectives of this study were to (1) describe allied health utilization in people with PD across expert clinics in the USA (US) and abroad, and to (2) examine the association between allied health utilization and patient outcomes.

Methods: The National Parkinson Foundation Quality Improvement Initiative (NPF-QII) is a prospective, longitudinal, observational study of people with Parkinson's disease cared for at National Parkinson Foundation Centers of Excellence. The goal of the NPF-QII is to identify potential best clinical practices for people with PD based on quality of life, mobility, cognition, hospitalizations, and caregiver strain measures. Participants were included in this data query if they had been enrolled in the NPF-QII study for at least 2 visits (n=4976 from 20 clinics in 4 countries). We describe self-reported utilization of PT, OT, and ST in the past year for participants in each stage of PD. Then, we rank site performance in the top and bottom 50% based on a combined global outcome measure z-score, and compare utilization rates at higher and lower performing sites.

Results: Average utilization of PT, OT, and ST were 40.7%, 12.0%, and 14.4%, respectively. Utilization increased with increased disease severity for all disciplines (p<0.0001), but was highly variable across sites. Controlling for clinic size and case mix, the top performing sites had higher rates of PT utilization than the lower performing sites (PT: 40.8% to 37.0%, p=0.007). The sites with lower performance had increased utilization of OT (10.1% to 14.4%, p<0.0001). The relationship between greater PT utilization and better outcomes was strongest in early and moderate PD.

Conclusions: Greater allied health utilization in advanced PD suggests a prevalence of reactive, rather than preventive referrals. Better outcomes at sites with higher rates of PT utilization, particularly in early PD, suggest that early or preventive PT referrals could improve global outcomes.



P33.58

Global implementation of efficacious voice treatment for Parkinson's disease: LSVT LOUD: Germany®

Lorraine Ramig¹, Thomas Brauer², Heike Penner³, Petra Benecke⁴, Cynthia Fox⁵

¹ University of Colorado-Boulder and LSVT Global-Tucson, New York, New York, USA

² Universitaetmedizin, Mainz, Germany

³ Agaplesion-Bethanien-Krankenhaus, Heidelberg, Germany

⁴ Paracelsus-Elena-Klinik, Kassel, Germany

⁵ LSVT Global, Inc., Tucson, Arizona, USA

Objective: This project was designed to evaluate the implementation of an efficacious voice treatment (LSVT LOUD) developed in the USA and designed to improve speech and voice disorders in Parkinson disease (PD) into scope of clinical speech practice in Germany.

Background: Implementation science is the study of methods that influence the integration of evidence-based interventions into real world practice settings (Center for Research in Implementation Science and Prevention (CRISP), 2015). This presentation will describe the implementation of LSVT LOUD, an efficacious voice treatment for PD, with three Randomized Control Trials (RCTs) documenting the short and long-term efficacy in the USA, into the clinical speech practice in Germany. As summarized by CRISP, the translation pathway of research lab efficacy into practice includes: "clinicians adopting the program and successfully implementing it into their setting and culture, the sustainability of the fidelity of the intervention and patients and payment agencies adopting the treatment as well".

Methods: The translation pathway recommended by CRISP was followed, with emphasis on treatment fidelity. Thus a key element in the implementation process was training of speech clinicians.

Results: In collaboration with Deutscher Bundesverband fuer Logopaedie, 14 LSVT LOUD Training and Certification Workshops were held throughout Germany since 2000. As a result, today, there are over 1,300 LSVT LOUD Certified clinicians in Germany. With an estimate of over 15,000 patients in Germany having received LSVT LOUD. The LSVT Companion Software System (Funded by the National Institutes of Health (NIH) and the M. J. Fox Foundation) has been translated into German and is being used by over 100 German clinicians in treatment and nearly 100 German patients in independent home practice. Clinical outcome data will be presented. Today LSVT LOUD is named as a treatment within the guidelines for neurologists who prescribe treatment (Deutschen Gesellschaft fur Neurologie (DGN). Health insurance reimburses the costs of LSVT LOUD.

Conclusions: LSVT LOUD has been implemented successfully into scope of clinical speech practice in Germany. Follow-up groups (LOUD for LIFE) are being initiated. This successful implementation model provides a road map for other countries where LSVT LOUD clinicians are trained (over 15,000 LSVT LOUD clinicians in 60 countries).

P33.59

The therapeutic effects of singing for individuals with Parkinson's disease

Kelly Richardson, Lisa Sommers

University of Massachusetts Amherst, Amherst, MA, USA

Purpose: The purpose of the current study was to investigate the effects of choral singing on speech and voice characteristics and quality of life in individuals with idiopathic Parkinson's disease. Methods: Ten individuals with mild to moderate hypophonia, secondary to idiopathic Parkinson's disease, were studied. Patients

participated in an 11-week choral singing group that met weekly for 90 minutes. The speech and choral singing activities were directed by two speech-language pathologists and a vocal instructor. Outcome measures were collected two weeks pre-treatment and one week post-treatment. Outcome data included acoustic metrics of speech and voice function, listener ratings of speech intelligibility, and a self-reported inventory for quality of life. Results: Group data showed that individuals with idiopathic Parkinson's disease significantly increased maximum cued sound pressure level, fundamental frequency range, and vowel space area in response to treatment. No significant changes were observed post-treatment for maximum phonation time. Listener ratings of speech intelligibility were also significantly higher post-treatment. Participant ratings of quality of life significantly improved post-treatment in the subcategories of coping and independent living. Conclusions: The present results suggest that choral singing may improve speech and voice characteristics for individuals with Parkinson's disease. In addition, choral singing may be an effective means for improving quality of life and communicative effectiveness in this clinical population. A randomized controlled trial is warranted to investigate the clinical utility of implementing choral singing as a stand-alone or complementary therapy program.

P33.60

Dynamic cycling improves motor symptoms and mobility in individuals with PD

Angela Ridgel, Dana Ault

Kent State University, Kent, OH, USA

Focus: Parkinson's disease (PD) affects more than one million people in the US and this number is expected to double by 2040. PD is a progressive neurodegenerative disease that leads to difficulties in performing activities of daily living, such as balance and walking. Dynamic high cadence cycling is a unique rehabilitation modality that has been shown to improve motor function in individuals with idiopathic PD. However it is not known if multiple bouts of dynamic cycling lead to improvements in gait and balance. Purpose: To assess if six bouts of dynamic cycling, on a motorized recumbent cycle, improves motor function, gait and balance in individuals with PD. Method: Individuals were randomized to either a dynamic cycling or a stretching group. Dynamic cycling consisted of a 5 minute warm-up at 50 revolutions per minute (rpm), 30 minutes of dynamic high cadence cycling between 75-85 rpm, and a 5 minute cool down. Motor function, balance and gait were assessed after every cycling bout using the UPDRS Motor III scale, Kinesia One, Timed up and Go (TUG), and the Modified Clinical Test of Sensory Interaction in Balance (mCTSIB). Results: Six bouts of dynamic cycling significantly improved UPDRS III scores ($F=5.814$, $P=.030$), kinetic tremor ($F=15.58$, $P=.001$), hand movement amplitude ($F=10.32$, $P=.006$), rapid alternating hand movement speed ($F=16.58$, $P=.001$), gait ($F=11.504$, $P=.004$), and TUG time ($F=8.313$, $P=.012$) from baseline testing to end of treatment. There was a 17% improvement in UPDRS scores from baseline testing to end of treatment. However, dynamic cycling did not improve balance. Conclusion: Six bouts of dynamic cycling improves motor symptoms, overall motor function and mobility but does not alter balance capabilities in individuals with PD. These findings suggest that dynamic cycling could be a valuable rehabilitation modality in this population.

P33.61

The profile of individuals with Parkinson's disease referred for allied health services: National Parkinson Foundation (NPF) QII Study

Angela Roberts¹, Samuel Wu², Miriam Rafferty³, Peter Schmidt⁴, Kristin Larsen⁵, Tanya Simuni⁶

¹ Northwestern University, Roxelyn and Richard Pepper Department of Communication Sciences and Disorders, Evanston, Illinois, USA

² Department of Biostatistics, University of Florida, Gainesville, Florida, USA

³ Center for Education in Health Sciences, Northwestern University, Chicago, Illinois, USA

⁴ National Parkinson Foundation, Miami, Florida, USA

⁵ Department of Speech Language Pathology, Northwestern Memorial Hospital, Chicago, Illinois, USA

⁶ Department of Neurology, Northwestern University, Chicago, Illinois, USA

Introduction: Allied health services (AHS) are integral to Parkinson's disease (PD) care guidelines, yet little is known about AHS utilization by expert care centers.

Objectives: This study explores AHS utilization in PD expert care centers and describes demographic and clinical differences in individuals referred vs. not referred for AHS.

Method: Data from the NPF-QII Study (a prospective, observational study of people with PD) were queried to collect AHS utilization, demographic, and clinical data. Data from 5,191 participants from 19 expert movement disorders neurology clinics from 4 countries were analyzed. Only participants with a diagnosis of idiopathic PD and an established (≥ 1 year) care relationship with an expert care center were included.

Primary Outcomes: Participants referred to AHS during study-visit two (a regular clinic visit).

Results: AHS utilization increased with increased disease severity. Rates for monodiscipline referrals were 18.3%, 26.7% and 32.4% and for multidiscipline referrals 5.4%, 11.0% and 14.6% for early (1-2), middle (3) and late (4-5) Hoehn & Yahr stages, respectively. There were significant differences across centers in both types of referrals, for all three levels of disease severity. Interestingly, SLP-only referrals diverged from this pattern, demonstrating middle stage referral peaks. AHS-referred were: significantly older; more likely to have ≥ 2 co-morbid diagnoses; more likely to have a recent history of falls; more likely to have recently visited a hospital/emergency room; and more likely to have been prescribed psychoactive medications than AHS-not-referred (all $p=0.001$). AHS-referred also had significantly ($p=0.0001$) more impaired cognition (i.e., MoCA scores), more impaired HrQoL (i.e., PDQ-39 summary index and domain scores – except stigma), and greater caregiver burden (i.e., Modified Caregiver Strain Index).

Conclusions: AHS utilization was greater in advanced PD stages, suggesting 'problem-driven' service utilization. Importantly, these data highlight both discipline-specific and mono vs. multidiscipline utilization differences that inform policies and practices for optimizing AHS access across the continuum of PD. These data reveal potential key indicators for AHS, beyond disease severity. This is an important first step in elucidating the predictive value of key AHS indicators relative to intervention studies, screening for AHS needs, and advocating for AHS resources in PD.

P33.62

Global postural reeducation versus aquatic physical therapy on respiratory muscle strength in Parkinson's disease

Larissa Salgado de Oliveira Rocha¹, Dayse Danielle de Oliveira Silva², Luciane Lobato Sobral Silva³, Rodrigo Santiago Barbosa

Rocha³, Anderson Antunes da Costa Moraes⁴, Rosana Macher Teodori⁵

¹ Physical therapist, Sciences Program of Human Movement by UNIMEP, Amazon University, Belém, Pará, Brazil

² Physical therapist, Universidade Nove de Julho, Belém, Pará, Brazil

³ Physical therapist, Program of Human Movement by UNIMEP, Amazon University, Belém, Pará, Brazil

⁴ Physical therapist, Resident Physical Therapy program in Emergency Department Trauma. Universidade Federal do Pará, Belém, Pará, Brazil

⁶ Physical therapist and Biologist. Doctor in Biology and Bucco-Dental Pathology, UNICAMP. Professor of the Graduate Program in Human Movement Sciences at UNIMEP, Belém, Pará, Brazil

Introduction: Muscle skeletal changes on the Parkinson's Disease (PD) compromise respiratory dynamics which makes the functional activities. Among the physiotherapy resources Global Postural Reeducation (GPR) and aquatic physiotherapy show promise in minimizing flexed posture with consequent improvement of chest expansion and respiratory muscle strength, as it works the active breathing and postural awareness. **Objective:** To compare the influence of the use of aquatic physical therapy protocol and RPG on the inspiratory and expiratory muscle strength in patients with Parkinson's disease. **METHOD:** We selected 20 subjects with clinical diagnosis of PD, lying on the Hoehn and Yahr scale from 2 to 3, of both genders, mean age 60.8±8.9 years, divided into two groups (n=10): Group aquatic physical therapy (GFA)- subjected to a special aquatic physical therapy protocol divided into four stages: heating, stretching, training, and relaxation in the swimming pool heated to 34±6 °C, and Group global postural reeducation (GRPG): individually subjected to treatment with the RPG method, using the frog postures on the floor and ballet dancer, both held three times a week, lasting 60 minutes, totaling 24 sessions, which they were evaluated before and after treatment by the force of the inspiratory and expiratory muscles through pressure investigation. We used the Shapiro-Wilk test and the chi-square test for comparing pre and post – treatment groups (p=0.05). **Results:** The intergroup evaluation was noted for variable maximum inspiratory and expiratory pressure in the pretreatment statistical difference (p=0,0001) between RPG treatments (pi=-111,5; pe=83) and aquatic therapy (IP=-99,5; EP=79), as well as post- treatment compared to the variable maximum inspiratory pressure (IP: -155,5; IP=-103, p=0,0001), respectively. There was no significant difference in the variable maximal expiratory pressure after intergroup comparison. (p=0,08). **Conclusion:** In the present study may be noted that the RPG protocol provided more evident improvement in inspiratory muscle strength in patients with Parkinson's disease, because the need for active breathing control patient for the advancement of positions in relation to aquatic therapy.

P33.63

Biomechanical gait analysis of the Two Minute Walk Test during single and dual task conditions in individuals with Parkinson's disease

Anson Rosenfeldt¹, Amanda Penko¹, Tanujit Dey², Andrew Bazyk¹, Matthew Streicher¹, Jay Alberts³

¹ Department of Biomedical Engineering, Cleveland Clinic, Cleveland, OH, USA

² Quantitative Health Sciences, Cleveland Clinic, Cleveland, Ohio, Cleveland, OH, USA

³ Department of Biomedical Engineering, Center for Neurological Restoration, Cleveland Clinic, Cleveland, Ohio, Cleveland, OH, USA

Introduction: Individuals with Parkinson's disease (PD) have difficulty performing dual task (DT) activities, or activities that require

execution of a motor and cognitive task simultaneously. Consequently, DT conditions result in greater number of falls in those with PD compared to their healthy peers. The purpose of this study was: 1) To compare the distance covered in an over ground Two Minute Walk Test (2MWT) under single task (ST) and DT conditions in individuals with PD; 2) To characterize changes in gait parameters observed during ST and DT conditions using a three-dimensional biomechanical gait analysis.

Methods: Individuals with idiopathic PD performed the 2MWT under the following conditions: 1) Over ground walking alone (2MWT-ST); 2) Serial 7s (2MWT-COG); 3) Holding a cup of water (2MWT-MOTOR). The 2MWT-ST and 2MWT-COG were then performed on the Computer Assisted Rehabilitation Environment system, a virtual reality system with a fully integrated three-dimensional motion capture and a self-paced treadmill system.

Results: Twenty-three participants completed the study. The mean UPDRS score was 33.0±13.1 with Hoehn and Yahr scores ranging between I-III. There was a significant difference in over ground distance walked between the 2MWT-ST (518.7±85.2 ft.) and 2MWT-COG (432.3±98.2 ft.) (p<0.001) and between the 2MWT-ST and 2MWT-MOTOR (467.7±76.4 ft.) (p=0.002). During the 2MWT-COG, individuals displayed a significant decrease in arm swing, velocity, cadence, step length, and a significant increase step width (p<0.05).

Discussion: Individuals walked a significantly shorter distance during the 2MWT under DT conditions. The difference can be attributed to changes in velocity, cadence, and step length. By identifying gait parameters that are associated with DT losses, therapists may be able to provide more targeted treatments to improve gait performance.

This study was funded by the Davis Phinney Foundation.

P33.64

A pilot, randomized, double-blind, sham-controlled trial of transcranial direct current stimulation to enhance dual-task gait training in people with Parkinson's disease

Siobhan Schabrun¹, Robyn Lamont², Sandra Brauer²

¹ School of Science and Health, University of Western Sydney, Sydney, NSW, Australia

² School of Health and Rehabilitation Sciences, The University of Queensland, Brisbane, Qld, Australia

Background and aim: Transcranial direct current stimulation (tDCS) has been shown to boost the effect of physical gait training in people with Parkinson's disease (PD). Greater improvements in gait velocity are realized when tDCS and physical training are combined than when either therapy is applied alone. The aim of this preliminary study was to investigate whether the addition of anodal tDCS over the motor cortex (M1) would improve gait performance and motor function beyond that of dual-task gait training alone in people with PD.

Methods: A pilot, randomized, double-blind, sham-controlled trial with 12 week follow-up was undertaken. Sixteen participants diagnosed with idiopathic PD were randomized into a dual-task gait training group with active tDCS and a dual-task gait training group with sham tDCS. Training occurred across nine, 20 minute sessions over three weeks. The primary outcome was gait speed when walking over an 8m GAITRite mat and undertaking one of three concurrent cognitive tasks (word lists, counting, conversation). Secondary measures included step length and cadence over 8m, the Timed Up and Go (TUG) test under single and dual task conditions, bradykinesia and motor speed. Two-way ANOVAs were performed to determine differences between groups and across timepoints.

Results: Overall, there was a significant improvement in gait speed (p<0.035), step length (p<0.045) and cadence (p<0.22) under all dual-task conditions from pre to post with training which was

maintained at follow-up. There was no difference in improvement between the active and sham tDCS groups. There was no change in TUG walking performance over time or between groups, but the active tDCS group improved in their concurrent cognitive task correct response rate post training, whereas the sham group did not. There was an improvement in bradykinesia after training in both groups, but no change in motor speed between groups or over time.

Conclusions: Three weeks of dual-task gait training improved gait performance while concurrently performing cognitive tasks, and bradykinesia, immediately following training and at 12 weeks follow-up. Only one parameter was enhanced by anodal tDCS: the number of correct responses provided while performing the TUG under dual-task conditions. Anodal tDCS applied to M1 may not be an effective adjunct to dual task gait training in PD.

P33.65

Correlation between functional capacity and vital capacity for individual Parkinsonian

Dayse Danielle de Oliveira Silva¹, Mariana dos Anjos Furtado Sá¹, Valeria Ferreira Marques Normando¹, Erik Artur Cortinhas Alves¹, Renata Amanajás de Melo¹, Nayan Leonardo Sousa Lopes², Flávia Lobato Maciel², Fernanda Ishida Corrêa³, João Carlos Ferrari Corrêa³

¹ Universidade do Estado do Pará, Belém, Pará, Brazil

² Universidade da Amazônia, Belém, Pará, Brazil

³ Universidade Nove de Julho, São Paulo, São Paulo, Brazil

Objective: To correlate sedentary individuals Parkinsonian nonsmokers' functional capacity and vital capacity. **Methods:** We selected 13 volunteers, 2 females and 11 males, aged 50–80 years, diagnosed with Parkinson's Disease (PD). The collection of survey data was conducted on resistance exercises Laboratory and Health (you read) of the University of Pará (UEPA) in Belem, Brazil. To evaluate the functional capacity of these individuals was used ADL Glittre Test and for the analysis of CV was used portable spirometer SPIROTEST brand (Germany-ALE). Data were analyzed by SPSS20 package, a significance value of $p < 0.05$. **Conclusion:** The vital capacity of individuals with PD, does not influence on the ADL Glittre Test time.

P33.66

Effects of a physical rehabilitation program with cognitive challenge for freezing of gait – a pilot study

Katrijn Smulders¹, Martina Mancini¹, Natassja Pal², Graham Harker², Brett W. Fling², Patricia Carlson-Kuhta², Fay B. Horak², Laurie King²

¹ Oregon Health & Science University, Portland, Oregon, USA

² USA

Introduction: Parkinsonian gait and balance impairments have been associated with cognitive deficits. This correlation seems to be even stronger in people with Parkinson's disease (PD) with freezing of gait (FoG). Hence, it may be helpful to integrate cognitive challenges into mobility training. The objective of this pilot study was to evaluate effects of a novel, cognitively challenging mobility rehabilitation program in people with PD and FoG, and to explore which clinical characteristics are related to success of this program.

Methods: Ten subjects with PD and self-reported FoG participated in this cross-over controlled intervention study, consisting of 6 weeks of Agility Boot Camp exercises with increasing cognitive challenge (C-ABC) and 6 weeks of education (control). Participants had moderate to severe PD (MDS-UPDRS-III, NFOG-Q), were aged between 59–88 and were all men. The main outcome measure was severity of FoG measured as an objective Freezing Ratio during 360° turns in place. Secondary outcome measures were scores on the New Freezing of Gait Questionnaire (NFOG-Q), the

MiniBESTest, and gait and turning parameters during a 2 min walk. Inertial sensors were used to quantify gait and turning performance. All tests were performed in the "OFF" state.

Results: No changes in the Freezing Ratio or NFOG-Q were observed following either intervention. The performance on the MiniBESTest did not show changes after the C-ABC program or after education. Objective measures of the 2 min walk showed an improvement of arm swing amplitude after exercise (29° to 35°, $p = .037$), but no other changes related to gait or turn parameters were observed. A reduction in arm swing velocity was however noted from pre- to post-education (162 to 148 °/s, $p = .028$). Higher severity of FoG at baseline was associated with less beneficial changes after C-ABC in turn duration ($Rho = .712$, $p = .031$), and tended to associate with less beneficial changes after C-ABC in stride length ($Rho = -.627$, $p = .071$) and arm swing ($Rho = -.644$, $p = .061$). None of the other disease severity measures at baseline associated with changes after C-ABC.

Conclusion: The results indicated that severity of motor symptoms, particularly FoG, might be an indicator for rehabilitation success. Specifically, participants with severe gait impairments were less likely to benefit from this intervention.

P33.67

Repetitive TMS for Parkinson's disease rehabilitation: differential clinical outcomes from a randomized trial

Katherine Sticklor¹, Milton Biagioni², Shashank Agarwal², Jamika Singleton-Garvin², Franziska Battenberg², Pawan Kumar², Andre Y Son², Geraldine Dacapano², Rebecca Gilbert², Alessandro DiRocco²

¹ Weill Cornell Medicine, New York, NY, USA

² NYU Langone Medical Center, New York, NY, USA

Objective: To compare changes in clinical outcomes after weekly low-frequency (LF) repetitive transcranial magnetic stimulation (rTMS) sessions over one vs. two pre-motor cortex (preMC) areas in Parkinson's disease (PD).

Background: The preMC is a key component in the complex system responsible for motor execution. Particularly, dorsal preMC (PMd) and supplementary motor area (SMA) are critically involved in PD pathogenesis due to their broad anatomical and functional connectivity with the basal ganglia and motor cortex (Buhmann et al, 2004; Shirota et al, 2013). Weekly rTMS over SMA has been determined as an effective add-on therapy for PD motor symptoms (Shirota et al, 2013). Nevertheless, the therapeutic potential of combining different premotor targets has never been tested. We designed an active controlled study to explore potential additive effects of rTMS over both SMA and PMd as compared to SMA alone.

Methods: Eighteen PD patients with H&Y scores 2 and 3 participated in a parallel double-blind randomized study of four weekly sessions of LF rTMS. Outcomes were assessed at baseline and 4 weeks post-treatment completion. Stimulation arms were rTMS over SMA or rTMS over both PMd and SMA (PMd+SMA). Clinical outcomes were total UPDRS-III and axial, tremor, rigidity, and bradykinesia subsets during ON time.

Results: Baseline demographic and clinical characteristics did not differ between groups. Fourteen patients, 6 SMA-alone and 8 PMd+SMA, completed all study visits. Both interventions, SMA-alone and PMd+SMA, significantly decreased UPDRS-III ($z = -2.21$, $p = 0.027$; $z = -2.53$, $p = 0.011$, respectively). Subset analyses showed SMA-alone significantly decreased only bradykinesia subset ($z = -2.21$, $p = 0.027$) while PMd+SMA decreased both bradykinesia and axial subsets (AxS) ($z = -1.98$, $p = 0.048$; $z = -2.39$, $p = 0.017$, respectively). Comparison between arms showed that only PMd+SMA significantly improved AxS ($U = 5.5$, $p = 0.013$). [figure 1] There were no significant differences in changes in total UPDRS-III or any other subset.

Conclusions: Both rTMS interventions were well-tolerated and improved UPDRS-III total motor scores and bradykinesia. However, improvement in AxS was seen only in the PMd+SMA group, suggesting that LF rTMS over combined preMC areas could be an effective therapy to improve axial symptoms. Larger placebo-controlled studies need to be conducted to corroborate these findings.

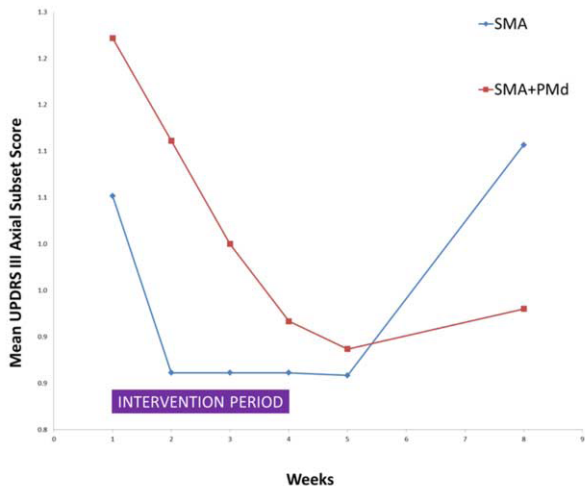


Fig 2. UPDRS-III Axial Subset Score at different study time points in the two groups

P33.68

Visuo-cognition in gait in Parkinson's disease: response to visual cues

Sam Stuart¹, Brook Galna¹, Sue Lord², Lynn Rochester¹

¹ Newcastle University, Newcastle upon Tyne, United Kingdom

² Newcastle University, Newcastle upon Tyne, Uzbekistan

Background: Gait impairment is a core feature of Parkinson's disease (PD) with implications for falls risk. Visual cues improve gait in PD but the underlying mechanisms are unclear. Evidence suggests that cognitive (attention) and visual processes may play an important role but this has not been previously examined. Cognition and vision are interrelated (termed visuo-cognition), which confounds interpretation. Understanding visuo-cognitive response to cues is key to developing effective therapeutics.

Objective: This study examined visuo-cognition during gait in PD in response to a visual cue. We studied; 1) saccade (fast eye movement) frequency under cued and dual task conditions; and 2) relationship between visual function, attention, saccade frequency and gait in PD.

Methods: Saccade frequency (SF: a proxy for visuo-cognition) was measured during walking in 55 PD and 32 age-matched control participants using a mobile eye-tracker. Participants walked straight with and without a visual cue under single and dual task (number repetition). Vision and attention assessments were conducted. SF response to visual cue and dual task were assessed using repeat measure ANOVAs. Relationships between SF, visual function, attention and gait (velocity) were explored using bivariate and multivariate analysis (e.g. structural equation modelling (SEM)).

Results: Attention and visual functions were significantly impaired in PD. SF was reduced in PD during non-cued gait compared to controls. For both groups SF increased with a visual cue ($p < .001$) and was maintained under dual task ($p = .008$) irrespective of group, with greater increase in PD.

Attention and visual function related to SF response in PD, but SEM with hypothesised interrelationships showed that visual function only related indirectly to SF through attention ($\beta = -.12$, $p = .008$). Attention related to SF, visual function and cued-gait ($\beta = -.37$, $p = .036$) in PD but not controls. SF was associated with cued-gait in PD but not controls. SEM showed that attention facilitated indirect relationships whereby SF ($\beta = .10$, $p = .031$) and visual function ($\beta = -.17$, $p = .031$) were both associated with cued-gait in PD.

Conclusion: This novel data indicates the pivotal role that attention plays in facilitating response to cues in PD. These results have implications for future research which must consider the role of attention, and for clinicians using cues to improve performance. Understanding these complex features will help inform intervention development.

P33.69

Perceptual problems in PD affect measurement of vocal QOL: recall of feedback from others is a more effective measure than self-perception of voice/speech improvement in people with PD.

Merrill Tanner

Glenrose Rehabilitation Hospital, Edmonton, Alberta, Canada

Difficulty matching effort level with kinesthetic feedback, including the required effort to make audible speech is a perceptual problem associated with PD (1,3,4,7). People with PD have to learn that the feedback they receive from their body is not accurate. The author's pilot study on a vocal strengthening group that involved singing for people with PD, showed three statistically significant improvements in maximum intensity (loudness) range (dB) and average frequency or pitch (Hz) in reading, as well as improved vocal quality of life (QOL) (8). Two "vocal quality of life measures," the Voice Related Quality of Life (V-RQOL) the Self Intelligibility Inventory: Self Assessment Form (SII) were completed by participants before and after the treatment period (5,6). The V-RQOL has 10 questions that ask about participants' own perception of their communication effectiveness. The SII has 21 questions and asks how well participants feel they are understood by others in different circumstances. Only the SII, measuring self-assessed intelligibility based on feedback that people with PD received from others, was statistically significant (with the correction for multiple variables). This finding suggests that the information received from others about intelligibility showed a significant change and that people with PD noticed that this change had taken place. However, the lack of significance in the V-RQOL suggests that this information did not change their perception of their own voices. The longer length of the SII questionnaire perhaps makes it a more effective measure. This is unlikely as the shorter V-RQOL is commonly used in voice studies and has been deemed to be the most sensitive for research purposes (2) and its reliability, validity, responsiveness and low burden have been well established (5). It seems that the two questionnaires actually measure two different aspects of vocal QOL. The SII measures what others tell me about my intelligibility or how easy I am to understand. The V-RQOL measures how I feel about my voice. Due to the perceptual disconnect experienced by people with PD, the two questionnaires may be less closely related than with other populations. If this is the case, then the SII questionnaire may be uniquely well suited to the study of PD. Since it relies on other people's perceptions as told to those with PD, results may also have implications for how we evaluate quality of life for these patients. Further research is needed.

P33.70

Medication management in women and men with Parkinson's disease: challenges and strategies

Linda Tickle-Degnen¹, Haley Bliss², Marie Saint-Hilaire³, Cathi Thomas³

¹ Tufts University, Medford, Massachusetts, USA

² USA

³ Boston Medical Center, Boston, MA, USA

Background: Management of Parkinson's disease (PD), a chronic movement disorder, involves a complex medication regimen, requiring increasing daily doses as the disease progresses. The majority of PD patients fail to adhere completely to their medication regimens, and this suboptimal adherence can be detrimental. Underuse of antiparkinsonian medications can cause bradykinesia and rigidity, and overuse can cause dyskinesia, confusion, visual hallucinations, and obsessive behavior. Purpose: This study aimed to see what challenges lead to nonadherence, and what strategies people use to effectively manage their medications and organize their medication schedules. Methods: Findings are reported from baseline qualitative interviews from a longitudinal study on social self-management in PD. Interviews from twenty people with PD (10 men, 10 women) were coded using NVivo Qualitative Analysis under the construct of the Person-Environment-Occupation (PEO) model used in occupational therapy practice. Results: Instances of ineffective medication management included forgetting pills, adding extra pills for certain activities, skipping pills, and not taking pills on a consistent schedule. Strategies for effective medication management included person-centered strategies (P) such as using pill boxes and alarms, organizing medications around mealtimes, and using emerging symptoms as a reminder; environment-centered strategies (E) such as strategic placement of pills and water in the home, and having support from a spouse; and occupation-centered strategies (O) such as talking to a healthcare provider to change a medication regimen. Conclusion: Reasons for nonadherence and strategies for effective management were highly varied among participants. Therefore, interventions to improve medication management should be individually targeted to personal characteristics (P), social and physical environments (E), and daily activities (O).

P33.71

Effects of vibrotactile feedback on vocal intensity in individuals with Parkinson's disease – a pilot study

Ramya Konnai, Lonni Schultz, Alice Silbergleit, Edward Peterson USA

Voice therapy may not always be successful in helping the individuals with PD (IwPD) carry over the treatment benefits outside the clinic or in the long-term. Portable voice monitors are available to provide biofeedback in the form of a vibratory signal for IwPD to talk louder. This pilot study is the first to use a portable monitor called the Vocalog2 (VL2; Griffin Labs, Temecula, CA) to determine if vibrotactile feedback helps IwPD talk louder and if they are able to retain the probable benefits over a one month period. Three subjects (2 males and 1 female) with idiopathic PD were enrolled. Mean age range was 57 years. The number of years post-diagnosis varied between 4 and 15. The exclusion criteria was Deep brain stimulation surgery, dementia, other neurological conditions such as stroke. The VL2 consists of a throat microphone with an adjustable neck band and a small data logging device. A 3-day average baseline vocal intensity was obtained for all subjects's conversation at home and the clinic. The clinician then set the target threshold at 4 dB above the baseline. If the subject spoke below the target intensity for 500 ms of continuous phonation, then the VL2 vibrated

as a cue to speak louder. All subjects were instructed to wear the VL2 at home for at least four hours a day, four days a week for four weeks, and monitor the placement of the VL2 on their neck. Vibrotactile feedback was given intermittently during week 1 and week 3. Vocal intensity was also obtained in the clinic and at home during a follow up after one month from week 4. Subjects also completed the Voice Handicap Index (VHI) at baseline and during the one-month follow up. A mixed model analysis revealed that there was no significant difference in vocal intensity with and without vibrotactile feedback ($p=0.46$). Also, the difference between the VHI measurements was also not significant (baseline: mean=65 (SD=5) vs follow-up: mean=60.33 (SD=15.63), $p=0.52$). All 3 subjects reported that the VL2 vibrated frequently and they tended to "ignore" the vibrations overtime. Subjects also reported inconsistencies in vibration during soft speech, vibrating for non-speech sounds such as swallowing, and the device falling off their neck occasionally. Altering the frequency of vibrotactile feedback over time and more secure attachment of the VL2 accelerometer to the neck should be considered for future studies.

CLINICAL SCIENCES: COMPLICATIONS OF THERAPIES

P34.01

Prevalence of vitamin B12 deficiency, hyperhomocystenemia and its association with peripheral neuropathy in Indian patients with idiopathic Parkinson's disease

Rukmini Mridula Kandadai, Neeharika M, Shaik Afshan Jabeen, Meena A Kannan, Rupam Borgohain
Department of Neurology, Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India

Background: Levodopa is the most effective and common medication used for the treatment of idiopathic Parkinson's disease but it can interfere with absorption of Vitamin B12 and cause B12 deficiency and hyperhomocystenemia. In a country like India where the dietary intake of vitamin B12 is low in many sects of the population, this may exacerbate the deficiency and predispose to peripheral neuropathy

Aim: To assess the prevalence of vitamin B12 deficiency, hyperhomocystenemia in Indian PD patients and their association with peripheral neuropathy.

Methods: 93 PD patients and 93 age, sex and diet matched controls who were not on B12 supplementation or didn't have any predisposing condition for B12 deficiency were included in this study at a tertiary care centre in South India. All PD patients were diagnosed based on UKPD brain bank criteria and were assessed for motor and non motor disability. All patients and controls were evaluated for serum B12, homocysteine and folate levels and underwent nerve conduction studies for identification of peripheral neuropathy. All variables were compared between patients and controls. Based on vitamin B12 levels, PD patients were divided into 4 quartiles and the 1st and 4th quartiles were compared.

Results: Most PD patient had moderate disease with mean Hoehn and Yahr score of 2.65(+2.8) and a mean disease duration of 7.39 (+5.12) years. PD patients had significantly lower mean serum vitamin B12 values ($p=0.027$) and higher mean plasma homocysteine levels ($p=0.038$) when compared to controls. But there was no significant difference between the patients and controls in prevalence of vitamin B12 deficiency, hyperhomocystenemia or peripheral neuropathy. On comparison of first & last quartiles based on Vitamin B12 levels, lower B12 was significantly associated with longer disease duration ($p=0.0007$),

higher cumulative levodopa dose ($p=0.04$), higher UPDRS III Off score ($p=0.002$) and higher plasma homocysteine levels ($p=0.0002$) (see table 1).

Conclusions: Although mean B12 levels were lower in PD patients especially those with longer, more severe disease requiring higher levodopa dose, there was no significant difference in the prevalence of B12 deficiency, hyperhomocystenemia and peripheral neuropathy between PD patients and general population.

Table 1: Comparative profile of quartiles in patients' cohort

		Quartile 1 (n=23)	Quartile 2 (n=23)	Quartile 3 (n=23)	Quartile 4 (n=24)	p value (1 st - 4 th quartile)
Age (years)	Mean	57.39	55.30	58	59.62	0.38
	SD	7.71	9.54	9.32	9.40	
Gender (M:F)		19:4	11:12	16:7	19:5	0.76
Disease duration (years)	Mean	8.67	9.76	6.63	4.65	0.0007
	SD	4.30	6.58	4.67	3.02	
UPDRS III On score	Mean	16.65	17.17	15.96	14.25	0.24
	SD	5.64	6.07	6.77	8.09	
UPDRS III Off score	Mean	59.22	58.13	59.22	47.42	0.002
	SD	11.97	10.99	11.97	13.03	
Modified H & Y Score	Mean	2.61	2.89	2.61	2.48	0.43
	SD	0.54	0.77	0.62	0.56	
L-dopa cumulative dose [mg]	Mean	905.43	918.05	787.21	501.03	0.04
	SD	791.04	935.22	715.69	481.85	
Daily L-Dopa dose equivalent	Mean	546.52	454.85	462.13	577.17	0.82
	SD	250.25	263.66	295.67	594.52	
Serum vitamin B 12 [ng/ml]	Mean	193.13	366.61	551.61	1252.71	0.0002
	SD	63.61	62.31	83.26	457.99	
Plasma homocysteine [mg/dl]	Mean	27.43	19.49	16.38	13.15	0.0002
	SD	15.66	6.97	5.05	4.93	
Blood folate (ng/ml)	Mean	8.62	7.25	8.04	11.65	0.11
	SD	6.23	3.84	3.8	6.47	
Peripheral neuropathy	Symmetrical sensory axonal	2	0	0	1	0.14
	Symmetrical sensorimotor axonal	2	2	0	0	
Autonomic dysfunction	Parasympathetic	4	8	4	4	0.67
	Sympathetic & parasympathetic	2	0	1	1	
Dyskinesias	Peak dose	12	9	10	8	0.31
	Diphasic	0	1	0	1	
	Off dystonia	0	0	1	0	

P34.02

Stimulation of sonic hedgehog signaling reduces formation and display of L-dopa induced dyskinesia in models of Parkinson's disease.

Andreas Kottmann¹, Lauren Malave¹, Andres Stucky²

¹ City College of New York, New York, NY, USA

² University of Southern California, Los Angeles, CA, USA

In Parkinson's Disease (PD) acetylcholine (ACh) tone in the striatum rises as dopamine (DA) levels fall due to progressive DA neuron degeneration, which in turn renders the striatum hyper-sensitive to DA. DA substitution therapy ameliorates many but not all symptoms and, worse, induces debilitating, uncontrollable L-Dopa induced dyskinesias (LIDs) leaving open the possibility that DA neurons possess additional means for inter cellular communication. Indeed, in addition to releasing dopamine, DA neurons secrete a number of molecules. The concentration of all of these factors must diminish in the basal ganglia of PD patients due to the progressive degeneration of DA neurons. We previously found that all DA neurons produce sonic hedgehog (Shh), a cell trophic factor, throughout life and release it in the striatum. There Shh activates the G-protein coupled receptor (GPCR) smoothened (Smo), which is expressed by cholinergic (ACh) interneurons in the striatum and regulates the transcription of the dopaminotrophic factor GDNF and the muscarinic autoreceptor M2. Striatal ACh neurons are critically involved in procedural learning. Recent data suggests that a disturbance of the balance of dopaminergic and cholinergic signaling results in aberrant learning processes that contribute to bradykinesia and L-Dopa induced dyskinesias (LIDs) in PD. We hypothesize that reduced or absent Shh signaling in the striatum contributes to disease- and drug- induced functional pathologies in PD.

Here we report that Shh signaling from DA neurons is a critical determinant of the efficacy of procedural learning of a T-maze, motor habit formation and egocentric search strategies. Further, we find that the reduction in Shh signaling from DA neurons facilitates dyskinesia formation and display upon long term DA substitution while increasing Shh signaling reduces and delays dyskinesia formation in murine models of LIDs. DA neuron produced Shh signals selectively to cholinergic and fast spiking gabaergic interneurons located in dorso-lateral striatum among all dopaminergic targets of the striatum. We find that Shh signaling reduces MAP kinase pathway activation selectively in cholinergic neurons and alters glutamatergic synapse architecture on cholinergic neurons. Our results implicate reduced Shh signaling due to the progressive degeneration of DA neurons in the pathophysiology of PD and support the use of Shh agonists as an adjuvant during L-Dopa treatment as a therapeutic strategy.

P34.03

Genetic variants of dopamine receptors and the BDNF gene, the role in dyskinesia and potential consequences for treatment in Parkinson's patients

Cynthia Kusters¹, Kimberly Paul¹, Yvette Bordelon², Jeff Bronstein², Janet Sinsheimer³, Matt Farrer⁴, Beate Ritz¹

¹ UCLA Fielding School of Public Health, Department of Epidemiology, Los Angeles, CA, USA

² UCLA, Department of Neurology, Los Angeles, CA, USA

³ UCLA, Department of Biostatistics, Department of Human Genetics, Los Angeles, CA, USA

⁴ University of British Columbia, Department of Medical Genetics, Centre for Applied Neurogenetics, Djavad Mowafaghian Centre for Brain Health, Vancouver, British Columbia, Canada

Background: Dyskinesia is a known severe side-effect of the treatment of Parkinson's Disease (PD). In this study, we reviewed the association of dyskinesia with haplotypes in the genes of three dopamine receptors (DRD1, DRD2 and DRD3) and of the Brain Derived Neurotrophic Factor (BDNF).

Methods: PD patient data was drawn from a population-based case-control study, the Parkinson's Environment and Gene study. 350 PD patients were included with a confirmed diagnosis by a movement disorder specialist, were using levodopa at the time of assessment, and had a minimal 3 years of disease duration. We analyzed 2 SNPs of the BDNF gene; 5 SNPs of the DRD1; 12 SNPs of the DRD2; and 8 SNPs of the DRD3 genes. Haplotypes were generated using Haploview and Phase. We created 1 haplotype for the DRD1- and BDNF-gene, and 3 haplotype blocks for the DRD2 and DRD3-genes. The first haplotype block of the DRD2-gene was based on the rs10891549, rs1554929, rs2242592, rs112443, and rs2245805; the second on rs1076563, rs1116313, rs2471857, and rs2471854 and the third haplotype block was based on the rs4245146, rs7122454 and rs11214611. Descriptive analysis and logistic regression were performed.

Results: There was no difference in dyskinesia among the haplotypes of the DRD1, DRD3 and the BDNF gene. All three haplotype blocks of the DRD2-gene were associated with dyskinesia. Subjects with the TCAGG haplotype (block 1) had an increased prevalence of dyskinesia (crude OR 1.73 (95% CI: 1.11–2.70, p-value: 0.02), adjusted OR 1.93 (95% CI: 1.19–3.13, p-value: 0.01)). The AATC haplotype (block 2) was associated with an increased prevalence (crude OR 1.65 (95% CI: 1.07–2.56, p-value: 0.02), adjusted OR 1.87 (95% CI: 1.16–3.01, p-value: 0.01)). Finally, subjects with the CGA haplotype (block 3) had an increased odds of developing dyskinesia (crude OR 1.52 (95% CI: 1.04–2.21, p-value: 0.03), adjusted OR 1.47 (95% CI: 1.00–2.18, p-value: 0.05)).

Conclusion: Subjects with variations of the DRD2 gene had a 50 to 90% increase in the odds of developing dyskinesia, making these

subjects more susceptible for developing dyskinesia. The DRD2 gene appears to be involved in the pathomechanism of developing dyskinesia. Follow-up studies reviewing the functional effects of these variations in the DRD2 gene could clarify this association further. In addition, PD patients with these specific haplotype should be prime candidates for any preventative approach to prevent or delay the development of dyskinesia.

P34.04

Levodopa induced dyskinesia in Parkinson's disease

Kelly Lyons¹, Peter Schmidt², Rajesh Pahwa¹

¹ University of Kansas Medical Center, Kansas City, KS, USA

² National Parkinson Foundation, Miami, FL, USA

Objective: To understand the impact of levodopa induced dyskinesia on Parkinson's disease (PD) patient treatment and outcomes.

Background: The introduction of levodopa represented a revolution in PD care, but its use is not without challenges. As PD progresses, the dopamine system becomes increasingly sensitive to changes in the concentration of levodopa. Consequently, long-term use of levodopa is associated with dyskinesia.

Methods: The National Parkinson Foundation Quality Improvement Initiative is a longitudinal clinical study of the natural history of PD in the context of expert care. Currently, the study includes over 8,179 subjects evaluated 20,713 times at 21 expert clinics. The study dataset covers a range of demographic, social, clinical, and treatment variables which were supplemented at the University of Kansas Medical Center expert clinic with data on the presence or absence and daily duration of dyskinesia from chart review. Analysis focused on factors that differentiated participants who experienced a reduction in dyskinesia (RD) from those who reported the same or increasing dyskinesia (CD).

Results: Dyskinesia data were available for 79% of the KUMC cohort (394/500). Average age was 65 (SD:9.9) and disease duration was 7.5 years (SD:5.6 yrs). Subjects had an average of 3.9 evaluations over 3.5 years (range: 2–7 evaluations over 0.9 – 5.5 yrs). Dyskinesia data were available for an average of 2.3 sequential evaluations (range: 1–4). Overall, 188 participants reported no dyskinesia and 206 reported dyskinesia. Of these, 135 reported experiencing dyskinesia at every visit while 54 reported the onset of dyskinesia while participating in the study and in 17 dyskinesia resolved.

There were 55 participants in the RD group and 128 in the CD group. There was no significant difference between groups in age, duration, sex, or comorbidities. Both groups were equally probable to have a history of levodopa and dopamine agonist use; however the RD group was more likely to be started on amantadine ($p < 0.05$). The RD group also had a significantly increased frequency of treatment for mental health problems (depression-RD 62%, CD 44%, $p < 0.01$; psychosis-RD 7.2%, CD 1.1%, $p < 0.05$).

Conclusions: These results suggest that, in the context of expert care, amantadine should be considered to treat dyskinesia. Further, the association between reduction in dyskinesia, use of amantadine and treatment of mental health problems are important topics for further studies.

P34.05

Impact of levodopa induced dyskinesia on quality of life and caregiver burden

Kelly Lyons¹, Peter Schmidt², Rajesh Pahwa¹

¹ University of Kansas Medical Center, Kansas City, KS, USA

² National Parkinson Foundation, Miami, FL, USA

Objective: To understand the impact of levodopa induced dyskinesia on quality of life and caregiver burden in Parkinson's disease (PD) patients.

Background: Although levodopa is the gold standard treatment for PD, prolonged use often results in the development motor complications such as dyskinesia. The impact of dyskinesia on patient quality of life and caregiver burden is not clear.

Methods: As part of the National Parkinson Foundation Quality Improvement Initiative (NPF-QII), 500 PD patients are followed annually at the University of Kansas Medical Center. At each visit, quality of life is assessed with the Parkinson's Disease Questionnaire (PDQ-39) and caregiver burden is assessed with the Modified Caregiver Strain Index (MCSI). In addition, data on the presence of dyskinesia and the daily hours of dyskinesia were obtained from review of patient records collected the same day as the NPF-QII visit data. Subjects were separated into those with and without dyskinesia. For subjects that had no dyskinesia at any visit, for consistency, the most recent visit was selected for analysis and for those with dyskinesia, the visit with the greatest number of hours of dyskinesia per day was analyzed.

Results: PDQ-39 and MCSI data were available for 394 subjects and of these 47% had no dyskinesia and 53% experienced dyskinesia at some point during the follow-up. On average, subjects were followed for 3.5 years, ranging from 1 to 5.5 years. Average age for those without dyskinesia at the last visit was 70 years (range 30–92 years) with a disease duration of 9.6 years (range 1 to 27 years). In the dyskinesia group, average age at the selected visit was 68 years (range 39–96 years) and disease duration was 11.5 years (range 3 to 35 years). PDQ-39 subscores of stigma and bodily discomfort were significantly worse in patients with dyskinesia compared to those without dyskinesia ($p < 0.01$). There were no differences between the two groups on subscores of mobility, ADLs, emotional well-being, social support, cognition or communication subscores of the PDQ-39. In addition, there were no differences in any of the MCSI subscores between the two groups.

Conclusions: These results suggest that dyskinesia significantly impacts quality of life in PD patients by increasing stigma and bodily discomfort. In this cohort, caregiver burden was not affected by dyskinesia.

P34.06

Risk of movement disorders with antipsychotic drugs in patients with schizophrenia or depressive disorders

Maria Veronica Rey¹, Luis Molina², Byron Recinos³, Bezner Paz⁴, Mauricio Rovelo⁴, Arturo Rodriguez Elias⁵, Jose Calderon⁶, Arturo Arellano⁷, Santiago Pomata⁷, Santiago Perez-Lloret⁸

¹ Catholic University, Buenos Aires, Argentina

² Nicaragua

³ Guatemala

⁴ Honduras

⁵ El Salvador

⁶ Panama

⁷ Costa Rica

⁸ Cardiology Research Institute, National Council for Scientific Research, Buenos Aires, Argentina

Antipsychotic drugs (APDs) are well-known causes of movement disorders in schizophrenic patients. APDs are being increasingly used for depressive disorders. It remains unknown to what extent they increase the risk of movement disorders in this population. The objective of this study was to compare the risk of movement disorders with antipsychotic drugs (APDs) in patients suffering from Schizophrenia or Depressive Disorders. In this study, 814 patients with a primary diagnosis of Schizophrenia ($n = 204$) or depressive disorder such as Bipolar Depression ($n = 343$) or Major Depression ($n = 267$) were recruited from psychiatric clinics in Guatemala,

Honduras, El Salvador, Panama and Nicaragua. Presence of parkinsonism, dystonia, tardive dyskinesia, tremor, tics, and akathisia were explored by the Simpson-Angus and UKU scales. Results showed that 61 patients (7.5%) had movement disorders (parkinsonism=10, dystonia=7, dyskinesias=3, tremor=34, tics=12, akathisia=16). Movement disorders were more frequent in Schizophrenia compared to depressive disorders (11% vs 6% respectively, $p<0.05$). As shown in Table 1, only male gender and exposure to typical APDs or lithium were independent and significant predictors of the occurrence of movement disorders. Exposure to typical APDs was related to significantly lower risk of movement disorders in schizophrenic patients compared to depressive ones (OR=3.4 [1.2–9.8] vs 6.1 [2.4–15.3], $p<0.05$). Atypical APDs were not related to an increase in the risk in schizophrenic or depressive patients (OR [95% CI]=0.78 [0.39–1.55] vs 0.51 [0.19–1.35] respectively, $p=0.2$). Finally, lithium increased the risk of movement disorders in schizophrenic and depressive patients to a similar extent (OR [95% CI]=4.2 [1.9–9.3] vs 4.1 [0.9–10.5] respectively, $p=0.3$). In summary, movement disorders were observed both in schizophrenic or depressive patients. Exposure to typical APDs and lithium increased the risk of movement disorders in both groups of patients. Interestingly, the increase in risk associated with exposure to typical drugs was significantly higher in depressive patients.

Table 1. Factors related to Movement Disorders (MDs) in schizophrenic and depressive patients

	No MDs (n=753)	MDs (n=61)	Logistic Regression OR (IC 95%)
Age	42.1±15.6	43.3±17	
Males	266 (35%)	35 (57%)**	2.21 (1.26-3.88)
<i>Clinical Diagnosis</i>			
Schizophrenia	182 (24%)	22 (36%)	1.00 (Ref)
Depression	571 (76%)	39 (64%)*	0.65 (0.35-1.21)
<i>Treatments</i>			
Typical antipsychotics	38 (5%)	13 (21%)**	4.49 (1.19-16.89)
Atypical antipsychotics	299 (40%)	19 (31%)	0.72 (0.15-3.33)
Lithium	45 (6%)	11 (18%)**	4.55 (1.18-17.54)
<i>Quality of Life</i>			
Mobility	1.2±0.4	1.8±0.7**	
Self-care	1.3±0.5	1.6±0.7**	
Daily activities	1.6±0.6	1.9±0.6**	
Pain/Discomfort	1.4±0.6	1.8±0.7**	
Anxiety/depression	2.0±0.8	2.3±0.8**	

P34.07

Higher mortality with antipsychotic medication use in individuals with Parkinson's disease

Peter Schmidt¹, Tanya Simuni²

¹ National Parkinson Foundation, USA

² Northwestern University, Chicago, Illinois, USA

Objective: Analyze mortality in Parkinson's disease (PD) patients receiving antipsychotic medications (APs) versus patients not treated with APs in NPF-QII.

Background: Psychosis is a significant comorbidity in PD and the major cause for nursing home placement. APs are routinely used for management of psychosis despite the black box warning of increased risk of mortality in elderly patients with cognitive impairment however there is little data on mortality associated with appropriate use of APs in expert clinical practice.

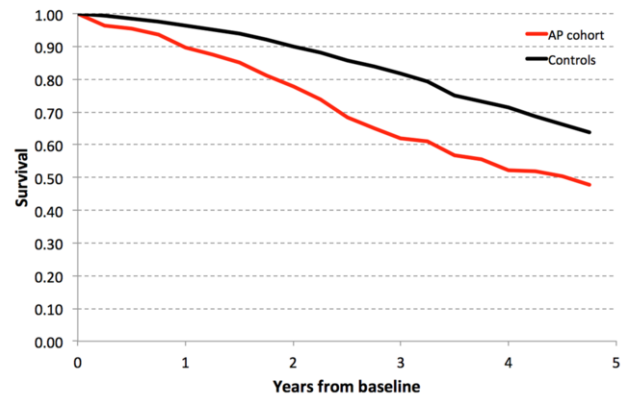
Methods: NPF's Quality Improvement Initiative is a longitudinal clinical study of the natural history of PD in the context of expert care, including 8,179 subjects evaluated 20,713 times at 21 expert clinics. The study dataset covers demographic, social, clinical, and treatment variables. Subjects were divided into two groups: those who were provided APs at some point (AP cohort) and those who

were not (controls). In the AP cohort, time from when APs use was first identified to mortality or most recent follow-up was determined, and for controls, time from recruitment to mortality or most recent follow-up. The survival rate was the quotient of the number of deaths and the total population for each 3 month period through five years from baseline. Survival over time was the product of sequential 3-month survival calculations, accounting for variable follow-up. Comparisons were evaluated using a weighted average of controls was determined using the population frequency in age and duration quintiles for the AP cohort to address population differences.

Results: In total, there were 814 patients in the AP cohort, with average baseline age 70.3 years (SD: 9.0) and duration 11.2 years (SD: 6.5). These were compared to 7,357 controls with average baseline age 67.0 years (SD: 9.9) and PD duration 6.8 years (SD: 5.7). In the AP cohort 129 deaths were recorded and 531 in controls. In the weighted average controls the average age was 70.2 years and average PD duration was 11.0 years. Comparing the AP cohort versus weighted average controls, survival at five years was determined to be 47.8% in the AP cohort and 62.4% in controls (Figure). The odds ratio for mortality was determined to be 1.64.

Conclusions: There is higher mortality in the AP cohort. That likely reflects the combination of symptom burden, more advanced pathology, and iatrogenic effects associated with antipsychotic medication in individuals with PD.

Kaplan Meier survival for AP cohort and controls over five years



CLINICAL SCIENCES: CLINICAL TRIALS: DESIGN, OUTCOMES, RECRUITING ETC.

P35.01

PD TrialTracker: analyzing the Parkinson's disease clinical trial pipeline to facilitate patient collaboration in research

Susan Buff

Sunnyvale, CA, USA

Objective: Parkinson's disease patients and families play an important role in research to understand the causes of the disease and find better treatments and a cure. A centralized, publicly-available tool providing up-to-date visibility into the status of the Parkinson's disease (PD) clinical trial pipeline could enable increased patient collaboration with the research community to help guide priorities, uncover and address roadblocks, and provide recommendations in order to accelerate the path to a cure.

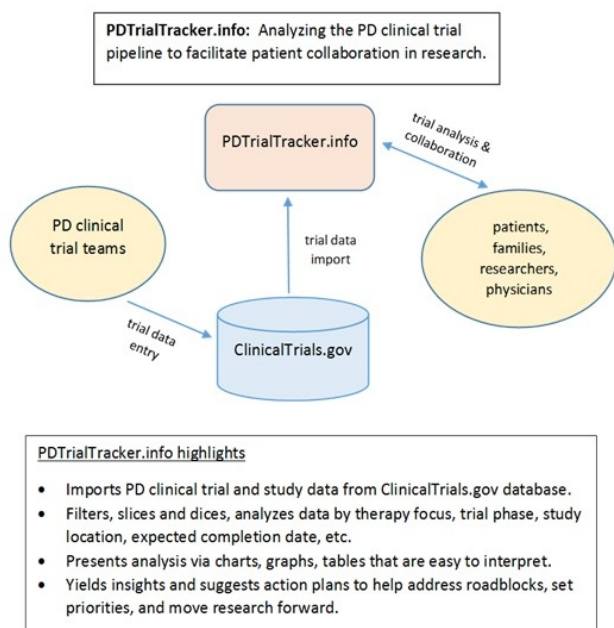
Method: To facilitate patient-researcher collaboration, a web-based tool called PDTrialTracker (www.PDTrialTracker.info) has been developed to provide analysis of ongoing PD clinical trials and studies worldwide for which study data is available on ClinicalTrials.gov. ClinicalTrials.gov is an online, publicly-available service launched in 2000 by the National Institutes of Health, and to date includes information on over 1500 publicly and privately-supported PD studies from around the world, with over 450 of these currently active.

PDTrialTracker analyzes PD trials/studies that are in-progress and filters study data along parameters such as study type (interventional vs. observational), therapy focus, trial phase, study location, and trial target completion dates.

PDTrialTracker analysis is presented in graphical and tabular formats that provide high-level/aggregated views of trial information with the ability to drill down to individual trial specifics in order to help the PD community:

- understand the types of trials underway and where they are in the pipeline.
- highlight the most promising avenues of research (e.g., specific therapies to modify disease progression or treat symptoms).
- uncover roadblocks in the trial process and ways to address them (e.g., improving recruitment methods, enhancing clinical trial best practices).
- promote accurate and timely sharing of trial information for ongoing and completed trials (e.g., within ClinicalTrials.gov, on medical center websites).

Insights derived from analysis of PD clinical trials could suggest action plans and help enable a direct and focused feedback loop between patients and the research community. As a next step in the development of the PDTrialTracker tool, resources can be added to build patient/researcher feedback mechanisms directly within the site.



P35.02

Stable levodopa plasma levels with ND0612 (levodopa/carbidopa for subcutaneous infusion) in Parkinson's disease (PD) patients with motor fluctuations

Nir Giladi¹, Sheila Oren², Yoseph Caraco³, Tanya Gurevich⁴, Ruth Djaldetti⁵, Yael Cohen², Oron Yacoby-Zeevi²

¹ Tel Aviv Medical Center, Tel Aviv University, Tel Aviv, Israel

² NeuroDerm Ltd., Rehovot, Israel

³ Hadassah Medical Center, Jerusalem, Israel

⁴ Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel

⁵ Tel Aviv University, Tel Aviv, Israel

Objective: To assess the safety, tolerability and pharmacokinetics of six dose regimens of ND0612, a novel liquid formulation of levodopa/carbidopa administered subcutaneously through a belt-pump delivery system.

Background/aims: Continuous levodopa/carbidopa administration is considered to be the optimal delivery route for treating PD patients with motor fluctuations, but poor levodopa solubility has prevented the development of a subcutaneously-deliverable formulation. Current infusion systems require gastrointestinal surgery to deliver continuous levodopa directly into the duodenum and are associated with potentially serious complications. ND0612 is a proprietary liquid formulation of levodopa/carbidopa that enables for the first time subcutaneous administration of levodopa/carbidopa to achieve steady levodopa plasma levels.

Methods: Sixteen PD patients currently receiving long-term treatment with oral levodopa/carbidopa and experiencing motor fluctuations were treated with standard oral levodopa on day 1. They were then treated with low-dose ND0612 (ND0612L; n=9) or high-dose ND0612 (ND0612H; n=7) administered with high or low dose carbidopa on days 2 and 3. ND0612H with high dose carbidopa and adjunct oral entacapone was administered on day 4. The levodopa pharmacokinetics of ND0612 were compared to pharmacokinetics of oral levodopa/carbidopa. All patients completed the study.

Results: Fluctuations in levodopa plasma levels were markedly reduced for all ND0612 regimens in comparison to oral levodopa/carbidopa. Levodopa plasma levels were dose proportionate. The levodopa C_{max} was: 528 ng/ml for ND0612L/low dose carbidopa; 477ng/ml for ND0612L/high dose carbidopa; 596ng/ml for ND0612L/high dose carbidopa plus adjunct entacapone; 1333ng/ml for ND0612H/low dose carbidopa; 1436ng/ml for ND0612H/high dose carbidopa; and 1807ng/ml for ND0612L/high dose carbidopa plus adjunct entacapone. Treatment with ND0612 was well tolerated; occasional mild, transient local reactions at the infusion site were noted.

Conclusion: The results from this study demonstrate that ND0612H given subcutaneously with carbidopa (both high and low doses) can reach high levodopa plasma levels that are stably maintained. ND0612H may offer a simple and effective treatment option that will minimize the need for surgical intervention in patients with advanced PD.

P35.03

Rationale and design of the RESTORE study to assess the long-term safety and efficacy of droxidopa for treatment of symptomatic neurogenic orthostatic hypotension

L. Arthur Hewitt¹, Guangbin Peng², Randall Owen², Charles Cram², Gerald J. Rowse², Stephen W. Gorny¹

¹ Lundbeck LLC, Deerfield, IL, USA

² Formerly of Lundbeck LLC, Deerfield, IL, USA

Purpose: Droxidopa is approved in the USA for treatment of symptomatic neurogenic orthostatic hypotension (nOH) caused by primary autonomic failure (Parkinson disease, multiple system

atrophy, pure autonomic failure), dopamine β -hydroxylase deficiency, or nondiabetic autonomic neuropathy. In short-term phase 3 trials, droxidopa improved symptoms of nOH and was well tolerated. Objective data for clinically relevant endpoints of long-term, large-scale, randomized trials are needed to guide the appropriate use of droxidopa for nOH in clinical practice. Here, we describe a time-to-treatment intervention study designed to evaluate the durability of the clinical benefit of droxidopa in patients with symptomatic nOH.

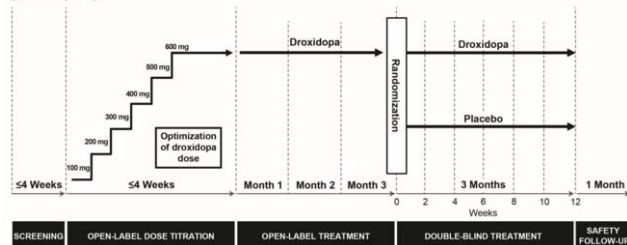
Methods: The placebo-controlled double-blind (DB) RESTORE study (NCT02586623) is being conducted at 125 US sites. The study comprises 5 periods: screening, open-label (OL) droxidopa dose optimization (=4 weeks), OL droxidopa treatment (12 weeks), DB treatment (12 weeks; continued droxidopa or placebo), and safety follow-up (4 weeks; Figure 1). Recruitment (sufficient to ensure ~482 patients in DB treatment phase) is ongoing. Dose optimization will start at droxidopa 100 mg 3 times daily (TID) and will not exceed 600 mg TID, with the last dose administered in the late afternoon to minimize potential drug effects during nighttime sleeping hours. Dose escalation will be stopped if a patient experiences blood pressure \geq 180 mmHg (systolic) or \geq 110 mmHg (diastolic) in a supine, or semirecumbent, position (head and torso elevated 30° from horizontal) ~3 hours after dosing, or if unable to tolerate treatment-related side effects.

Results: The primary outcome of the study is time to treatment intervention during the DB treatment period, defined as (1) worsening of dizziness, lightheadedness, or the "feeling that you are about to black out" (Orthostatic Hypotension Symptom Assessment Item 1) by \geq 2 units or (2) discontinuation because of lack of efficacy. Results will be summarized using the Kaplan-Meier method and compared between treatment groups using a log-rank test. Secondary outcomes will evaluate long-term efficacy (composite Orthostatic Hypotension Questionnaire score, clinician- and patient-reported Clinical Global Impression–Severity scores) and safety.

Conclusions: The scientifically rigorous design of this study will provide information needed to guide long-term clinical use of droxidopa for treatment of symptomatic nOH.

Funding: Lundbeck

Figure 1. Study Design



P35.04

Effect of honda stride management assist device (SMAD) on gait in patients with Parkinson's disease

Noriko Kawashima¹, Michiko Matsuhashi², Tomomi Hamano¹, Kayo Nagami¹, Takako Furukado¹, Masako Iijima¹, Masayo Isogaya¹, Mikiko Komachi¹, Aya Kumon¹, Kumiko Miyashita¹, Atsuko Sato¹, Hasegawa Kazuko³

¹ Japan

² PT, Japan

³ The department of Neurology, National Sakamihara Hospital, Sagamihara, Japan

Objective: To clarify the effect of a wearable exoskeleton stride management assist device (SMAD: Honda R and D Corporation, Japan) on gait in Parkinson's disease (PD) patients. The SMAD increases step length and decreases spatial asymmetry when

walking in post-stroke patients. There are few reports conducted about the effect of SMADs on mobility in PD patients. We studied the direct effect when wearing SMAD and the indirect effect after rehabilitation using SMAD in PD patients. **Methods:** We evaluated two PD patients. Patient 1 (P1) was a 78 year-old female (HY 2.5, disease duration 5 years), only had mild start hesitation and needed Nordic walking poles in 3 minutes walking. Patient 2 (P2) was an 81 year-old female (HY 4, disease duration 22 years), had freezing ON time and needed a walker in 3 minutes walking. In the direct effect study, patients did 10 meters (m) and 3 minutes walking wearing SMAD with and without stride assist six times on separate days and we estimated the velocity, distance, step length and cadence. In the indirect effect study, patients did step and walking rehabilitation 4 times / 3 weeks without SMAD (phase A) and using SMAD (phase B) in addition to the direct study. We evaluated 10 m and 3 minutes of walking without SMAD, Timed Up and Go test (TUG), Berg Balance Scale (BBS), UPDRS part III, Freezing of Gait Questionnaire (FOG-Q) and Parkinson's Disease Questionnaire-39 (PDQ39) at pre-phase A, post-phase A and post-phase B. The study was approved by the ethics committee of the Sagamihara National Hospital. The statistical analysis was done using the paired t-test in the direct study. **Results:** In the direct study, the walking distance for 3 minutes of walking in P1 increased from 135.5 m to 145.0 m ($p=0.013$) and step length at 10 m of walking in P2 also rose from 37.5 cm to 40.3 cm ($p=0.010$). In the indirect study, P1 could walk a longer distance in 3 minutes (pre-phase A 127 m; post-phase A 147 m (+15.7%); post-phase B 156 m (+22.8%)). The changes of TUG, BBS, UPDRS part III, FOG-Q and PDQ39 were not remarkable. P2 could not complete the indirect study due to severe motor fluctuation. **Conclusion:** This study showed that SMAD could increase walking velocity in PD patients without freezing, and step length in PD patients with freezing. The SMAD could be a useful device to increase exercise capacity in PD patients. This study is preliminary and further investigations involving a larger number of subjects are warranted.

P35.05

AFF008A: successful boosting of an existing PD01A-induced immune response. safety & immunological analysis of an AFFITOPE®-based vaccine approach (PD01A) for the treatment of patients with early stage Parkinson's disease

Alexandra Kutzelnigg¹, Dieter Volc², Caroline Thun-Hohenstein³, Jana Zimmermann¹, Vera Buerger¹, Dorian Winter¹, Sabine Schmidhuber¹, Gergana Galabova¹, Achim Schneeberger¹

¹ AFFIRIS AG, Vienna, Austria

² Studycenter of PROSENE, Private Clinic Josefstadt, Vienna, Austria

³ Studycenter of PROSENE, Vienna, Austria

Introduction: Parkinson's disease (PD) is a common progressive neurodegenerative disorder, which prevalence is age-related with a range of up to 4% above the age of 85. The first clinical signs of the disease are movement disorders. However, non-motor symptoms like olfactory deficits, constipation, depression and orthostatic hypotension are also characteristics of disease onset while cognitive impairment to dementia might occur during disease progression. Despite an intensive scientific engagement in understanding the disease's pathogenesis, the currently available treatments are limited to symptomatic ones, but lack disease modifying properties. α -Synuclein (α Syn), and in particular its oligomeric structure, is believed to be a major pathological hallmark of disease pathogenesis, and thus is an attractive target for the development of therapies against PD.

Aim: Development of AFFITOPE®-based vaccines (e.g. PD01A) for the long-lasting treatment or prevention of Parkinson's Disease.

Studies Design and Methods: The Phase I study AFF008A (NCT02216188 – follow-up boost) to assess the immunization with

the peptide-based AFFITOPE® PD01A was patient-blinded, single-center, randomized, controlled, parallel group assessing two "boost" dosages (15µg and 75µg). The study was performed in early stage PD patients. The primary endpoint was tolerability and safety of one s.c. boost injection. Each dosage was tested in patients that have previously received four priming immunizations either with 15µg or 75µg AFFITOPE® PD01A (NCT01568099, AFF008). Secondary endpoint was the immunological response following boosting induced by the two AFFITOPE® PD01A dosing regimens. Moreover, antibody titers of IgG Abs specific for the immunization peptide, KLH (carrier protein), αSyn target sequence were monitored by ELISA.

Results: The boost using two different dosages of PD01A AFFITOPE®-based vaccine was well tolerated. The exploratory efficacy variables showed no deterioration of clinical symptoms in the treated groups compared to the untreated control-arm of the study. The boost vaccination with PD01A leads to the re-activation of a specific immune response one year after the priming immunizations in a dose-dependent manner.

Conclusions: The AFFIRIS PD01 vaccine approach in early PD patients is well tolerated, leads to long-term immune response and is boostable.

P35.06

A phase II, pragmatic, randomized clinical trial on a high-intensity exercise and fall prevention boot camp for Parkinson's disease: feasibility and safety

Merrill Landers¹, James Navalta²

¹ Department of Physical Therapy, University of Nevada, Las Vegas, Las Vegas, Nevada, USA

² Department of Kinesiology and Nutrition Sciences, University of Nevada, Las Vegas, Las Vegas, Nevada, USA

Objective: To test the feasibility and safety of a high-intensity exercise and fall prevention boot camp (HIBC) in people with Parkinson's disease (PD).

Background: Most contemporary exercise programs for people with PD are low to moderate intensity. Recent evidence suggests that older adults can safely tolerate higher intensities and attain more meaningful improvements.

Methods: Participants were randomized into either a high intensity exercise and fall prevention boot camp or a usual care, low intensity usual care boot camp (Fitness Counts Exercise Program (FCEP)). These two boot camps were both for 8 weeks at a frequency of 3 times per week. For feasibility, participant intensity and attendance were collected as well as attainment of Centers for Disease Control (CDC) minimum weekly exercise standards (150 minutes of moderate intensity exercise and strength training the major muscle groups twice). For safety, adverse events, soreness, and falls were monitored. A post treatment questionnaire was also collected (Post-Intrinsic Motivation Inventory (PIMI)).

Results: There were 13 completed participants in the HIBC arm (mean age=63.7±11.3; 9 males, 4 females) and 11 in the FCEP arm (mean age=64.9±6.2; 8 males, 3 female). There were no differences between the groups in age, gender, PD duration, PD medications, Hoehn and Yahr Stage, and fall history (ps>.164). Mean attendance days were close to the goal of 24 days over 8 weeks (HIBC=22.9±3.6; FCEP=20.5±8.8, p=.419). The HIBC was significantly higher for the number of weeks attaining 150 minutes (HIBC=5.0±2.7; FCEP=1.7±2.8, p=.013) and strength training (HIBC=2.1±1.5; FCEP=0.0±0.0, p70% of heart rate maximum per week (HIBC=99.3±44.4; FCEP=7.1±11.8, p.102), or falls (p=.641) during the trial. PIMI results suggest that both groups liked the exercise equally.

Conclusions: HIBC is feasible and safe in PD with good compliance and attainment of high intensity exercise. Compared to the FCEP, there were no differences in the rate of injuries, falls, or

exercise side effects for the high intensity exercise boot camp. These results warrant further investigation in a large scale comparative effectiveness trial.

P35.07

A phase II, pragmatic, randomized clinical trial on a high-intensity exercise and fall prevention boot camp for Parkinson's disease: signal of efficacy

Merrill Landers¹, James Navalta²

¹ Department of Physical Therapy, University of Nevada, Las Vegas, Las Vegas, Nevada, USA

² Department of Kinesiology and Nutrition Sciences, University of Nevada, Las Vegas, Las Vegas, Nevada, USA

Objective: To determine if a high intensity exercise and fall prevention boot camp (HIBC) would produce greater benefit than a low intensity control (Fitness Counts Exercise Program (FCEP)) in Parkinson's disease (PD).

Background: Most exercise programs for older adults are low to moderate in intensity. Recent evidence suggests that higher intensity exercise may be more beneficial. This has not been well vetted in PD.

Methods: Participants with PD were randomized into either an 8-week HIBC or FCEP, supervised by physiotherapists at community exercise gyms. The following were assessed pre and post: 1. balance (mini-Balance Evaluation Systems Test (mini-BESTest)); 2. balance self-efficacy (Activities Specific Balance Confidence Scale (ABC), Falls Efficacy Scale (FES)); 3. physical activity (International Physical Activity Questionnaire (IPAQ)); 4. PD symptoms (Unified Parkinson's Disease Rating Scale (MDS-UDPRS), Parkinson's Disease Questionnaire-39 (PDQ)); 5. fatigue and endurance (6 Minute Walk Test (6MWT), Parkinson Fatigue Scale (PFS)); and, 6. muscle/bone strength (30 second Sit-To-Stand Test (STS)), bone mineral densiometry (BMD)).

Results: There were no differences between the HIBC (n=13, mean age=63.7±11.3; 9 males) and FCEP (n=11, mean age=64.9±6.2; 8 males) on demographics (age, gender, fall history, PD duration/medications, Hoehn and Yahr Stage), ps=.164. The HIBC improved on the miniBESTest on/off medication (ps=.027) while the FEB did not (ps=.140). Both improved on the FES (ps=.022) but not the ABC (ps=.359). The HIBC increased time in moderate physical activity (p=.004) but the FCEP did not (p=.225). MDS-UPDRS Parts I-III decreased on/off in the HIBC (ps=.050) but the FCEP did only for Part I on/off (ps=.046) and Part III on (p=.050). There were no changes for either on the PDQ (ps=.068). The 6MWT improved in the HIBC on/off (p=.050) but only FCEP on (p=.015). The PFS decreased in the HIBC (p=.033) but not in the FCEP (p=.208). STS improved in the FCEP on (p=.026) but not in the HIBC (p=.154). Increased hip density in the HIBC was the only noted BMD change (p=.047).

Conclusions: High intensity exercise compared to low intensity exercise produced greater improvements in balance, physical activity, PD symptoms, endurance, fatigue, and bone health in people with PD.

P35.08

Highly challenging gait and balance training can improve cognitive processing during dual-task conditions in elderly with Parkinson's disease

Niklas Lofgren¹, David Conradsson¹, Linda Rennie², Rolf Moe-Nilssen³, Erika Franzén⁴

¹ Karolinska Institutet, Sweden

² Research Department, Sunnaas Rehabilitation Hospital, Oslo, Norway, Norway

³ University of Bergen, Norway

⁴ Karolinska Institutet; Karolinska University Hospital, Sweden

Introduction: The ability to perform tasks automatically is important for everyday life since it allows for attention to be consciously directed elsewhere. This may be investigated with the dual-task (DT) paradigm by comparing the concurrent performance of two different tasks in relation to the performance of each task separately (i.e. single-task, ST). For people with Parkinson's disease (PwPD), processing is impaired for gait performance and cognitive tasks, indicating limited automaticity. However, it remains unclear if training can help. We aimed to investigate the effects of a challenging training, including DT exercises, on the DT-interference (DTI) of gait and a cognitive task in PwPD.

Methods: 100 PwPD with mild to moderate disease severity were randomized to 10-weeks (3 sessions/week) of gait and balance training or to a control group (care as usual). Gait was performed upon the GaitRITE electronic walkway, at comfortable speed with and without an added task. The added task, entailed reciting alternate letters of the alphabet (following a standardized scheme and) was performed under ST (while seated) and DT conditions, respectively. The outcome measure was absolute DTI (difference between the DT and the ST-condition) for gait, as well as mean performance (%error) and variability of the added task. The Mann-Whitney U test was applied to compare between-group differences (i.e. the difference between the baseline and follow-up assessments). When significant differences were found, the Wilcoxon signed ranks test was used to investigate the within-group differences. Significance level was set to: $p=0.05$.

Results: 87 participants were included. Following the intervention, between-group differences ($p=0.032$) showed that the training group had improved the DTI of both cognitive performance ($p=0.018$) and cognitive performance variability ($p=0.032$). Conversely, the control remained unchanged ($p=0.114$). No significant differences were found between the training and the control group for the DTI of gait ($p=0.084$).

Conclusion: The results indicate that challenging gait and balance training, including DT conditions can improve the DTI of the performance as well as on the variability of the cognitive task in PwPD. On the other hand, training did not affect gait performance, indicating that training induced attention allocation to the cognitive task. Future studies ought to investigate if DT-interventions should target gait, cognitive abilities, or both.

P35.09

Does outpatient palliative care improve patient centered outcomes in Parkinson's disease: study protocol for a multi-center randomized controlled trial

Janis Miyasaki¹, Laura Palmer², Maya Katz³, Nicholas Galifianakis³, Jean Kutner², Benzi Kluger²

¹ University of Alberta, Edmonton, Alberta, Canada

² University of Colorado Denver, Denver, Colorado, USA

³ University of California San Francisco, San Francisco, California, USA

Objective: To present the rationale and study design of a multi-site randomized controlled trial (RCT) of outpatient palliative and supportive care for Parkinson's disease (PD).

Background: Palliative and Supportive Care is a holistic approach to chronic or life-threatening illnesses focusing on physical, psychosocial and spiritual symptom relief and that addresses concerns of both the patient and family. As PD is associated with increased mortality, difficult to manage non-motor symptoms and caregiver distress several centers have begun to offer outpatient palliative care for PD. We present the study design of the first RCT

of palliative care for PD. This study is funded by PCORI (Patient Centered Outcomes Research Institute).

Methods: Neurologists, palliative care specialists and PD patient/caregiver advisors from 3 centers offering Neurologist-led outpatient palliative and supportive care for PD collaborated to create standardized methods for screening patients, assessing patient-centered outcomes and delivering a team-based intervention. Additional collaboration involved experts in palliative medicine and palliative care research.

Results: Patients (and caregivers when present) will be screened using a modified version of the Needs Assessment Tool PD and randomized to palliative care or usual care (including a neurologist). Primary outcome measures include Quality of Life Alzheimer's Disease (QOL-AD) for patients and Zarit Burden Inventory (ZBI) for caregivers. QOL-AD has been used in PD and is validated for proxy reporting and covers major domains affected by palliative care. Planned secondary outcomes include the Edmonton Symptom Assessment Scale PD (ESAS-PD) and patterns of healthcare utilization (e.g. hospitalizations).

Conclusions: While outpatient palliative and supportive care can address gaps in current standards of care for PD, these clinics are time and resource intensive. The presented study design will provide evidence regarding the effectiveness of Palliative and Supportive Care for PD as well as the opportunity to validate scales in an under-investigated patient group, advanced PD.

P35.10

The safety profile of pimavanserin (NUPLAZID™): focus on motor symptoms and extrapyramidal-related adverse events in patients with Parkinson's disease psychosis (PDP)

James Norton, George Demos, Kathy Chi-Burris, Randy Owen
ACADIA Pharmaceuticals Inc., San Diego, CA, USA

Objective: To assess the effects of treatment with 34 mg of pimavanserin on motor symptoms and adverse events of special interest in the Parkinson's disease psychosis population

Background: Parkinson's disease psychosis is a common non-motor symptom, affecting more than 50% of PD patients over the course of their disease. It is associated with institutionalization and increased morbidity and mortality. Pimavanserin is a potent 5-HT_{2A} inverse-agonist developed for the treatment of PDP. It does not bind to dopaminergic (including D₂), histaminergic, adrenergic, or muscarinic receptors that are frequently associated with extrapyramidal symptoms/parkinsonism, sedation, and orthostatic hypotension.

Methods: In an integrated analysis of two, 6-week randomized, controlled clinical trials comparing pimavanserin 34 mg (n=202) and placebo (n=231), adverse events of interest (falls, orthostatic hypotension, extrapyramidal symptoms/parkinsonism, sedation) and UPDRS Parts II (Activities of daily living) and III (Motor examination) were reviewed.

Results: The UPDRS Parts II + III change from baseline was similar across both groups: pimavanserin 34 mg (-2.0) vs placebo (-2.2). When looking solely at the results for UPDRS Part III, the change from baseline was again similar: pimavanserin (-1.4) vs placebo (-1.1), indicating no worsening of motor function for patients on pimavanserin compared to placebo. The incidence of orthostatic hypotension was statistically lower in the pimavanserin group (1.0%) vs placebo (5.2%) ($p<0.05$). Additionally, falls occurred at a lower rate in the pimavanserin group (6.4%) vs placebo (9.1%). Parkinsonian-like events (e.g., gait disturbance, tremor, freezing, etc.) occurred at similar rates: pimavanserin (5%) versus placebo (5.2%); however, gait disturbance itself occurred at a higher rate in the pimavanserin group (2.5%) vs placebo (0.4%). Rates of sedation-related events were also similar: pimavanserin (6.4%) versus placebo (5.2%).

Conclusions: Overall, pimavanserin was well-tolerated and did not have a negative impact on motor control or exacerbate other Parkinsonian-like events during the course of the trial. Additionally, the rates of orthostatic hypotension, falls and sedation were not increased in the pimavanserin group. These events are of particular concern in the PD population where motor control is already compromised, and comorbid disease- and age-related impairments are common.

P35.11

Potential treatments for Lewy body dementia being investigated in three randomized, double-blind, placebo-controlled phase 2 studies of RVT-101 and nelotanserin

Jason Olin, Lawrence Friedhoff, Ilise Lombardo, Warren Wen, Geetha Ramaswamy
Axovant Sciences, Inc., New York, NY, USA

Objective: To evaluate the safety and efficacy of RVT-101 and nelotanserin in Lewy body dementia.

Background: Lewy body dementia (LBD) is a progressive neurodegenerative disease, affecting approximately 1.4 million elderly in the U.S. LBD includes two related disorders: dementia with Lewy bodies (DLB) and Parkinson's disease dementia (PDD). Although cognitive dysfunction is a core component of LBD, approximately 80% of patients also exhibit behavioral disturbances, including visual hallucinations (VH) and REM behavior disorder (RBD). RVT-101, a potent antagonist of the 5-hydroxytryptamine 6 (5-HT₆) receptor, is being evaluated in the HEADWAY-DLB study. Nelotanserin, a highly potent and selective inverse agonist of the 5-HT_{2A} receptor, is currently being evaluated in two phase 2 studies in LBD.

Methods: HEADWAY-DLB is a 24-week, randomized, double-blind, placebo-controlled study of RVT-101 in subjects with a diagnosis of DLB. Key efficacy evaluations will focus on measures of cognition and function. Subjects must have an MMSE score of 14 – 26 (inclusive) at screening. Completing subjects from HEADWAY-DLB will be eligible to enroll in an active extension arm.

The first study of nelotanserin will be in subjects with a diagnosis of DLB or PDD. This is a randomized, double-blind, placebo-controlled, crossover study in subjects experiencing frequent VHS. There will be two 28-day treatment periods separated by a washout period. The second study of nelotanserin is a randomized, double-blind, placebo-controlled study in DLB subjects experiencing frequent episodes of RBD. Subjects will undergo assessments of RBD at baseline and at the end of the treatment period. Completing subjects from both nelotanserin studies will be eligible to enroll in an open-label study.

Each study requires subjects to have a reliable caregiver or study partner.

Results: N/A

Conclusion: Three studies evaluating RVT-101 and nelotanserin in LBD were initiated in early 2016. The studies focus on core symptoms of LBD: cognitive dysfunction, visual hallucinations, and REM behavior disorder.

P35.12

A randomized controlled clinical study to evaluate the efficacy and safety of subcutaneous levodopa/carbidopa (ND0612H) in patients with advanced Parkinson's disease

Sheila Oren¹, Karl Kiebertz², C. Warren Olanow², Yael Cohen¹

¹ NeuroDerm Ltd., Rehovot, Israel

² Clintrex, Rochester, NY, USA

Objective: To evaluate the efficacy of continuous subcutaneous infusion of 2 dosing regimens of ND0612H in reducing daily OFF time

Background: Although levodopa remains the most effective anti-parkinsonian agent, chronic oral treatment is associated with the development of motor complications that limit its clinical utility. Continuous levodopa/carbidopa (LD/CD) administration is considered ideal for PD patients with advanced motor fluctuations, but current infusion systems have to be surgically routed to the duodenum. ND0612 is a proprietary liquid formulation of LD/CD (60/7.5 mg/mL) developed to enable subcutaneous administration for a more convenient, better-tolerated option. Preliminary studies have indicated efficacy in reducing OFF time; however it is unclear whether continuous 24-hour infusion confers benefit over daytime dosing.

Methods: This is a multicenter, parallel-group, randomized clinical study in advanced PD patients taking at least 4 doses/day of LD and experiencing predictable morning OFF episodes and =2.5 hours of OFF time per day. All subjects will undergo 1 day of standard oral LD/CD inpatient dosing followed by 2 days of inpatient treatment with 1 of 2 randomly allocated (1:1) dosing regimens of ND0612H subcutaneous infusion (24 hour dosing = total LD/CD dose of 720/90 mg infused over 24 hours or awake dosing=537.6–614.4/67.2–76.8 mg infused over 14–16 hours plus a supplemental dose of oral LD/CD [150/15mg] in the mornings). Subjects will then continue on a maintenance period of the assigned ND0612H dosing regimen for the next 25 days and in-patient visit on Day 28. Efficacy assessments (Days 1, 2, 3 and 28 as judged by a blinded rater) include: time to full ON in the mornings, assessment of motor states (ON with and without dyskinesia and OFF time), UPDRS subscores, clinical global impression, Parkinson's Disease Sleep Scale and PDQ-39. Safety evaluations include AE reporting as well as assessment of infusion sites, daytime sleepiness, impulse control and suicidal behaviors.

Results: A planned recruitment of 36 subjects (18 per arm) from 10 study sites is due to complete during 2016.

Conclusions: The effective management of motor fluctuations remains a key unmet need. ND0612H is under development as an alternative to surgical intervention in patients with advanced PD.

P35.13

Pharmacokinetic profile of ND0612L (levodopa/carbidopa for subcutaneous infusion) in patients with moderate to severe Parkinson's disease

Sheila Oren¹, Nir Giladi², Yoseph Caraco³, Tanya Gurevich⁴, Ruth Djaldetti⁵, Yael Cohen¹, Oron Yacoby-Zeevi¹

¹ NeuroDerm Ltd., Rehovot, Israel

² Tel Aviv Medical Center, Tel Aviv University, Tel Aviv, Israel

³ Hadassah Medical Center, Jerusalem, Israel

⁴ Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel

⁵ Tel Aviv University, Tel Aviv, Israel

Background: The symptomatic efficacy of continuous levodopa/carbidopa (LD/CD) delivery in PD patients with motor fluctuations is well known. However, intrajejunal infusion systems are associated with tolerability concerns, and poor LD solubility has prevented development as a subcutaneously deliverable formulation. ND0612L is a proprietary liquid formulation of LD/CD that enables subcutaneous administration of LD/CD to achieve steady levodopa plasma levels.

Objective: To characterize the pharmacokinetic profile of ND0612L in PD patients with motor fluctuations.

Methods: This was a Phase II randomized, placebo-controlled, double-blind, two-period study of ND0612L in PD patients with motor response fluctuations. During Period-1 (14 days), 30 patients received their optimized current oral treatment (dose reductions

permitted), and were randomized (2:1) to adjunct ND0612L or placebo. During Period-2 (7 days), 16 patients were offered open-label ND0612L and were randomized to ND0612L monotherapy or ND0612L plus oral entacapone.

Results: Patients treated with adjunct ND0612L had their plasma LD concentrations consistently maintained above a mean (\pm SD) of 800 \pm 570ng/ml, as well as a lower peak-to-trough ratio and fluctuation index vs. placebo. Exploratory efficacy analysis showed that ND0612L treatment reduced OFF time by a mean \pm SD of 2.42 \pm 2.62h and 2.13 \pm 2.24h from baseline according to in-clinic and home diaries, respectively (vs. 0.41 \pm 2.62h and 1.39 \pm 2.33h with placebo). ND0612L also improved sleep quality (17.1 \pm 17.58 improvement in PDSS scores from baseline vs. 0.5 \pm 11.35 with placebo), quality of life (6.6 \pm 10.52 improvement in PDQ-39 scores from baseline vs 1.78 \pm 11.10 with placebo), and global impression (90% of the patients had improved CGI-C scores vs. 36% in placebo). All 16 patients chose to continue to Period-2 in which plasma LD levels were maintained at a mean of 550 \pm 79ng/ml with ND0612L monotherapy and 800 \pm 144ng/ml with ND0612L plus oral entacapone. In these patients, the oral LD intake was reduced by a median of 80%, with 3 of 16 patients completely discontinuing oral LD therapy.

Conclusions: These data suggest that subcutaneous continuous delivery of LD/CD with ND0612L, provides relatively stable LD levels with reduced variability compared with oral LD. Efficacy findings are also promising and warrant further study.

P35.14

Levodopa-carbidopa intestinal gel (LCIG) results in significantly lower variability in levodopa plasma concentrations compared to oral levodopa-carbidopa: pharmacokinetic results from the LCIG Phase 3 trial

Ahmed Othman¹, Matthew Rosebraugh², Krai Chatamra¹, Sandeep Dutta¹

¹ AbbVie, North Chicago, IL, USA

² North Chicago, IL, USA

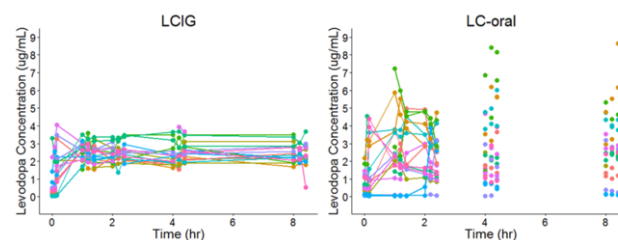
Background: In a double-blind, double-dummy, Phase 3 trial in advanced Parkinson's disease (PD) patients (LCIG Horizon study), Levodopa-Carbidopa Intestinal Gel (LCIG) has been shown to significantly reduce the "Off" time and increase the "On" time without troublesome dyskinesia compared to oral immediate-release levodopa-carbidopa (LC-oral) treatment. This work characterized the comparative pharmacokinetic profiles for LCIG and LC-oral from this Phase 3 trial.

Methods: In this Phase 3 trial (Lancet Neurol 2014; 13: 141–49), 71 PD patients were randomized to receive continuous LCIG infusion plus placebo LC-oral capsules (n=37) or to receive LC-oral capsules plus continuous placebo LCIG infusion (n=34) for 12 weeks. Both groups were titrated to optimal effect. Complete pharmacokinetic profiles, evaluated on Weeks 4 and 12 in 20 patients, were compared for LCIG (n=10) vs LC-oral (n=10) formulations. The inter- and intra-subject variability for levodopa and carbidopa plasma concentrations (Weeks 4, 6 and 12) during the 2- to 16-hour interval relative to start of LCIG infusion or administration of the first morning LC-oral capsules were estimated using a linear mixed-effects model using all available pharmacokinetic data (n=61).

Results: On the pharmacokinetic sampling days, the mean daily levodopa doses were 1004–1284 mg for LCIG and 1211–1417 mg for LC-oral, and carbidopa doses were 251–321 mg for LCIG and 303–354 mg for LC-oral. Patients with intensive pharmacokinetic samples had significantly lower variability and fluctuations in levodopa plasma concentrations for LCIG compared to LC-oral (Figure 1). The intra-subject variability in levodopa and carbidopa concentrations were significantly lower for LCIG (21% and 25%, respectively) compared to LC-oral (67% and 39%, respectively).

Similarly, inter-subject variability in levodopa and carbidopa concentrations was significantly lower for LCIG (35% and 31%, respectively) compared to LC-oral (93% and 70%, respectively).

Conclusions: The lower intra-subject variability of levodopa and carbidopa concentrations with LCIG administration than LC-Oral administration is a result of the continuous infusion and bypassing the impact of intra-subject variability in gastric emptying rate on absorption rate with LCIG administration. The improved pharmacokinetic profile for levodopa with LCIG is consistent with the observed lower "Off" times and higher "On" times without troublesome dyskinesia observed in the study.



P35.15

ADS-5102 (amantadine HCl) extended-release capsules improves activities of daily living (ADLs) in Parkinson's disease (PD) patients by reducing levodopa-induced dyskinesia (LID): a post-hoc analysis from the phase 3 EASE LID study

Rajesh Pahwa¹, Mary Jean Stempien², Caroline Tanner³, Robert Hauser⁴, Rob Howard⁵, Reed Johnson²

¹ University of Kansas Medical Center, Kansas City, KS, USA

² Adamas Pharmaceuticals, Inc., Emeryville, CA, USA

³ University of California San Francisco and San Francisco Veterans Affairs Medical Center, Tampa, CA, USA

⁴ University of South Florida, Tampa, FL, USA

⁵ Veridical Solutions, San Diego, CA, USA

Objective: To characterize the effect of LID on ADLs and to evaluate the treatment effect of ADS-5102 on ADLs utilizing subject-reported data from the Unified Dyskinesia Rating Scale (UDysRS).

Background: LID is a dose-limiting side effect of levodopa therapy. Data are limited on the impact of LID on ADLs in PD patients. EASE LID was a 6-month, placebo-controlled study that evaluated ADS-5102, 340 mg taken once daily at bedtime, for the treatment of LID. The primary efficacy outcome measure was the UDysRS. ADS-5102 demonstrated a statistically significant reduction versus placebo in the UDysRS total score at both Week 12 and Week 24. Part 1B of the UDysRS consists of 10 questions, completed by subjects, focusing on the impact of dyskinesia on ADLs. A score of 2 or 3 for each question indicates mild or moderate impairment, respectively.

Methods: Baseline PD home diary and UDysRS, Part 1B data were used to characterize the impact of LID on ADLs prior to start of study drug treatment. The effect of ADS-5102 treatment on ADLs was assessed by comparing the least square (LS) mean change in the UDysRS, Part 1B score in the ADS-5102 vs placebo groups. For each question in the UDysRS, Part 1B, the percentage of subjects who reported improvement (=1 unit decrease) was compared between treatment groups.

Results: The modified intent to treat population included 121 subjects (63 ADS-5102, 58 placebo). Baseline OFF time and ON time with troublesome dyskinesia was 3.1 hours and 4.6 hours, respectively. At baseline, the percentage of subjects with mild to moderate impairment in each ADL was between 18% and 72%. At Week 24, the LS mean change from baseline for the UDysRS, Part

1B score was -6.2 for the ADS-5102 group and -3.1 for the placebo group ($p=0.035$). For all 10 individual questions within the UDysRS, Part 1B, the difference in the percentage of subjects who improved ($=1$ unit decrease) favored ADS-5102 (difference range: 2%–21%). The most frequent adverse events (AEs) were hallucinations, peripheral edema, dizziness, dry mouth, constipation, and falls. Treatment discontinuation due to AEs occurred in 21% of ADS-5102 subjects vs 7% of placebo subjects.

Conclusion: In this clinical trial PD population, all ADLs were negatively impacted by LID. ADS-5102 improved ADLs as evidenced by a reduction in the UDysRS, Part 1B score. ADS-5102 was generally well tolerated and the types of AEs reported were consistent with the known safety profile of amantadine.

P35.16

Feasibility of galvanic vestibular stimulation for Parkinsonian gait

Bubblepreet Randhaw¹, Claire Hinnell², David Rydz³, Marilyn Araujo³, Lisa Wechzelberger³, Carlo Menon⁴

¹ Fraser Health Authority (FHA) and Simon Fraser University (SFU), DELTA, BRITISH COLUMBIA, Canada

² FHA and University of British Columbia (UBC), Canada

³ FHA, Canada

⁴ SFU, Canada

Purpose: Parkinson's disease (PD) is the second most common neurodegenerative disease and affects seven to ten million people worldwide. The cardinal symptoms of PD include bradykinesia, hypokinesia and postural instability leading to festination and freezing of gait. In this pilot study, we are investigating the effect of galvanic vestibular stimulation (GVS) on gait in people with PD. GVS is a non-invasive, well-established technique that stimulates vestibular afferents in the ear. The primary objective of this pilot study is to test the feasibility and acceptability of GVS by people with PD. The second aim is to obtain the preliminary results on the effects of GVS on the gait of people with PD.

Method: This study employs a randomized, single group cross-over design. Currently, we are recruiting individuals with PD (35-80 years), with festination and freezing of gait. So far we have completed testing on 5 participants. All participants received GVS (Good Vibrations Engineering Ltd, Canada) via 2 cm self-adhesive disk electrodes positioned over the mastoid process, controlled by software programming. Stimulation was given at the same time in each participant's regular medication schedule. After determining cutaneous sensation threshold under electrodes, all participants were required to receive 3 sessions of the bilateral bipolar GVS or no electrical current (sham) for 20-minute duration in sitting. For feasibility of the study, we present acceptability, attrition rate and safety reports from the study. For gait assessment, all participants completed 2 trails of timed up and go (TUG) test before and after GVS application.

Results and Conclusion: We have completed testing on 5 individuals with idiopathic PD (mean age: 75.6 years; range: 64-82), Hoehn and Yahr scores 2-3. All participants were asked to attend 6 sessions to complete the study. 4 out of 5 participants completed all 6 sessions of GVS, whereas 1 participant completed 5 sessions because he was not feeling well during one of the sessions and was unable to come. None of the participants reported any adverse effects from GVS (like pain/burning). Participants did report fatigue after the study (self-report). For TUG results, analysis is underway. The preliminary results of this pilot study suggest that multiple sessions of GVS are feasible in mild to moderately affected people with PD. However, more participants and further analysis is needed to evaluate the efficacy of GVS for Parkinsonian gait.

P35.17

Human factors testing of the levodopa-carbidopa intestinal gel delivery system in advanced Parkinson's disease patients and healthcare providers

Ramon L. Rodriguez¹, Hubert H. Fernandez², Alberto J. Espay³, Rajkumar Conjeevaram⁴, Ji Zhou⁴, Matthew Kuntz⁴, Edward Halpern⁴, Janet Benesh⁴

¹ University of Central Florida, Orlando, Florida, USA

² Center for Neurological Restoration, Cleveland Clinic, Cleveland, Ohio, USA

³ University of Cincinnati Academic Health Center, Cincinnati, Ohio, USA

⁴ AbbVie Inc., North Chicago, Illinois, USA

Objective: To understand the factors that contribute to the safe and effective use of the levodopa-carbidopa intestinal gel (LCIG, known as carbidopa-levodopa enteral suspension in the US) delivery system by advanced Parkinson's disease (PD) patients and healthcare providers (HCPs) and to mitigate potential safety risks.

Background: Human factors (HF) testing is a central component of medical device development that is used to inform device design and training materials. This process is particularly important when designing devices for patient populations whose disease may affect their ability to properly complete tasks with the device. LCIG delivered via percutaneous gastrojejunostomy is a treatment option for advanced PD patients that experience motor fluctuations. The LCIG HF Program utilized the HF testing process to evaluate safe and effective use of the LCIG delivery system.

Methods: Two studies (Study 1 and Study 2) evaluated patient and HCP use errors with the LCIG delivery system. In each study, advanced PD patients (mean age, years=60 [9.4]; mean PD duration, years=9 [4.3]) and HCPs were tested on their ability to complete essential tasks with the LCIG system during scenarios that simulated use in a home environment. Task performance was scored as success, failure, or close call (Table 1). Following completion of Study 1, changes were made to the training materials and instructions for use (IFUs) to address the task failures observed during the original study. Study 2 demonstrated that these changes improved patient and HCP performance. Patients and HCPs were compensated for their participation.

Table 1. Total Events Associated with Task Performance

Use Scenario	Study 1				Study 2			
	Patients (N=25)		HCP (N=25)		Patients (N=18)		HCP (N=20)	
	Task Failures	Close Calls ^a	Task Failures	Close Calls ^a	Task Failures	Close Calls ^a	Task Failures	Close Calls ^a
Morning Procedure	2	3	3	2	1 ^b	0	0	0
Extra Dose	0	0	0	0	0	0	0	0
Evening Procedure	2 ^b	3	3	0	0	0	0	0
Change Cassette	4 ^b	1	2	1	0	0	0	0
Adjust Morning Dose ^c	6 ^b	0	0	0	1	0	0	0
Adjust Continuous Rate ^c	1 ^b	0	0	0	0	0	0	0
Alarms and Messages	0	0	0	0	0	0	0	0
Warnings and Caution	1	0	0	0	0	0	0	0
Pump Programming	Not applicable		3	9 ^b	Not applicable		0	0
Set Lock Level for Patients	Not applicable		0	1	Not applicable		0	0
Change Batteries	1	0	0	0	Not Assessed			
Totals	17 ^b	7	11	13 ^b	2	0	0	0

^a Close calls were cases that involved participants initiating an action that would have resulted in failure but self-corrected before failure occurred.

^b Value includes test artifacts. Test artifacts were events not related to the actual use of the LCIG delivery system but the by-products of errors in administration of simulated use.

^c Patient, N = 15; HCP, N = 10

LCIG = levodopa-carbidopa intestinal gel, HCP = healthcare provider

Results: There were 28 task failures and 20 close calls in Study 1 (Table 1). Task failures were generally caused by inadequate training or participants not following instructions (n=10) and test artifacts (n=9) (Table 1). To address these task failures, changes were made to the patient and HCP IFUs and training process. Following these changes, only 2 task failures, related to minor simulation errors, were observed in Study 2.

Conclusions: By taking a patient and HCP-centered approach, the IFUs and training for the LCI system were optimized for the safe and effective use by advanced PD patients.

P35.18

Transforming drug development for Parkinson's disease: Critical Path for Parkinson's* (CPP) Consortium Modeling & Simulation Approach

Klaus Romero¹, Volker Kern¹, Kuenhi Tsai², Timothy Nicholas³, Diane Stephenson¹, Daniela Conrado¹

¹ Critical Path Institute, Tucson, AZ, USA

² Merck, Groton, PA, USA

³ Pfizer, Groton, CT, USA

Background: Learnings from other sectors, like the aerospace industry, can benefit drug development in Parkinson's disease (PD). In this context, models can be applied that allow drug developers to evaluate and compare advancing new therapies for PD through computer simulations. The Critical Path for Parkinson's (CPP) Consortium, funded primarily by Parkinson's UK is planning the development of several simulators that will optimize drug development in PD. Such simulators will be based on a) a comprehensive disease progression model for early motor PD, and b) a drug-disease-trial model that builds on and incorporates drug effects, placebo effects and other relevant clinical trial design aspects, like dropouts. These tools will help optimize the design of phase II & III clinical trials in PD, maximizing the likelihood of success.

Objectives: The objectives of CPP's modeling and simulation workgroup are to bring drug sponsors, regulators and advocacy groups together to build models that can speed drug development. In the specific case of PD, given the complex nature of the underlying disease, uncertainty in differential diagnosis and the need to understand the clinical outcomes that are typically used for registration, a 'top-down' approach is being used, which initially focuses on the registration end points, taking into account genetics and other patient-specific factors. As such, the initial goal of this group is to develop a longitudinal model for PD disease progression that targets the earliest stages of motor symptom onset.

Work Plan: The team's initial focus is on the completion of a quantitative disease progression and drug-effect model, including a model fitting to three presently available data sets. This effort will be followed by submission of a comprehensive briefing package to regulatory authorities (FDA and EMA). In addition, model development and validation to the satisfaction of key stakeholders will be pursued, including posterior predictive checks as well as with external validation.

Expected Impact: Regulatory evaluation and endorsement of modeling and simulation tools will aid in the design of a more-efficient drug development process. CPP's approach provides the framework for the adoption of an integrated drug development process, incorporating modeling and simulation tools as well as biomarkers that provide useful and significant insights into the nature of disease progression in PD.

P35.19

A 3-month pilot trial of the ketogenic diet for people with Parkinson's disease: program design, implementation, and maintenance

Angela Senders¹, Alar Mirka², Andrew Erlandsen¹, Amy Reiter², Bette Manulik², Heather Zwickey¹, Richard Rosenbaum²

¹ National College of Natural Medicine, Portland, OR, USA

² Legacy Research Institute, Portland, OR, USA

Background: The classic ketogenic diet (KD; 80% fat, 20% protein and carbohydrate) is intensive and requires substantial engagement and collaboration between participants, families, and providers. Several academic medical institutions have KD centers that provide inpatient dietary initiation for pediatric clinical populations. Few outpatient programs have been described for clinical research with adults.

Objective: To safely initiate, monitor, and maintain a 3-month KD in a clinical trial setting.

Participants: Thirteen people with mild to moderate Parkinson's disease were enrolled in the study. Six participants were not the primary preparer of food in their home and were asked to bring that person with them as a study partner. A total of nineteen people (three cohorts) participated in the program.

Methods: The intervention was conducted at the National College of Natural Medicine Helfgott Research Institute. Study staff consisted of 21 nutrition graduate students under the supervision of two naturopathic physician researchers. All research staff ate a ketogenic diet for at least one week in preparation for the trial. Students were paired with participants to provide one-on-one support over the course of the diet. A pre-diet nutritional interview was conducted to assess medical history and potential psychosocial barriers to dietary change. Participants also received 4 hours of education, including history of the diet, menu plans, expectations and potential side effects. Once the diet began, weekly study visits consisted of individual check-in with participant-student pairs, as well as facilitated group meetings with the entire cohort for peer support. Adherence was tracked via MyFitnessPal diet diaries and confirmed by serum beta-hydroxybutyrate levels.

Results: One participant worsened and terminated the diet after 4 weeks; 12 participants completed the trial. Data from diet diaries were 95.74% complete and reflected beta-hydroxybutyrate levels. On average, participants consumed 76% fat, 15% protein, 5% net carbohydrate. Adverse symptoms were safely managed. Participants shared challenges and solutions in group meetings, which established community and reinforced motivation.

Discussion: This program successfully initiated and safely monitored an outpatient ketogenic diet, achieving excellent participant adherence to a challenging protocol.

P35.20

Results of a phase 3 efficacy and safety study of ADS-5102 (amantadine HCl) extended-release capsules in Parkinson's disease patients with levodopa-induced dyskinesia (EASE LID 3)

Mary Jean Stempien¹, Rajesh Pahwa², Caroline Tanner³, Robert Hauser⁴, Wolfgang Oertel⁵, Claudia Trenkwalder⁶, Reinhard Ehret⁷, Jean Paul Azulay⁸, Stuart Isaacson⁹, Larissa Felt¹⁰, April Ruby¹⁰, Natalie McClure¹⁰

¹ Emeryville, California, USA

² University of Kansas Medical Center, Kansas City, Kansas, USA

³ University of California San Francisco and San Francisco Veterans Affairs Medical Center, San Francisco, California, USA

⁴ University of South Florida, Tampa, Florida, USA

⁵ Phillips University, Marburg, Germany

⁶ Paracelsus-Elena-Klinik, Kassel, Germany

⁷ Praxis Neurologie, Berlin, Germany

⁸ Hôpitaux de La Timone, Marseille, France

⁹ Parkinson's Disease and Movement Disorders Center, Boca Raton, Florida, USA

¹⁰ Adamas Pharmaceuticals, Inc., Emeryville, California, USA

Objective: Investigate the efficacy and safety of ADS-5102 (amantadine HCl) extended-release capsules, 340 mg administered once daily at bedtime, for the treatment of levodopa-induced dyskinesia (LID) in a 13-week study.

Background: In two prior placebo-controlled, double-blind studies, ADS-5102 treatment improved LID as demonstrated by a statistically significant reduction in the primary outcome measure, the UDysRS total score.

Methods: This double-blind, placebo-controlled study was conducted at 39 sites in the US and Europe (NCT02274766) in Parkinson's disease (PD) subjects with troublesome LID. Subjects were randomized 1:1 to placebo (pbo) or ADS-5102. The primary efficacy analysis was the least square (LS) mean change from baseline to Week 12 in the UDysRS total score in the ADS-5102 group versus the pbo group. Key secondary efficacy analyses were the LS mean change from baseline to Week 12 in selected 24-hour PD home diary states: ON time without troublesome dyskinesia (TrD) and OFF time. Other secondary outcome measures were other PD home diary states and MDS-UPDRS.

Results: 77 subjects were randomized (38 to ADS-5102 and 39 to pbo). ADS-5102 significantly improved LID as shown by a decrease in the UDysRS total score over 12 wks vs pbo ($p < 0.0001$). The percent reduction in the observed mean UDysRS total score from baseline to week 12 was 50% in the ADS-5102 group and 18% in the pbo group. At 12 weeks daily ON time without TrD increased by 4.0 hrs in the ADS-5102 group and by 2.1 hrs in the pbo group ($p = 0.0168$). Daily OFF time decreased in the ADS-5102 group by 0.5 hrs and increased by 0.6 hrs in the pbo group ($p = 0.0199$). Four patients, all in the ADS-5102 group, experienced serious adverse events. In 1 patient the SAE was considered related to study drug; this patient completed study treatment and did not discontinue participation in the trial. Seven (19%) of ADS-5102 patients vs 3 (8%) of pbo patients discontinued treatment due to adverse events (AEs). The most frequent AEs (occurring in greater than 2 patients in the ADS-5102 group) were dry mouth, nausea, decreased appetite, insomnia, orthostatic hypotension, constipation, fall, and hallucination.

Conclusions: ADS-5102 resulted in statistically significant and clinically meaningful improvement in LID, confirming results from earlier controlled clinical trials. A reduction in daily OFF time was also demonstrated. ADS-5102 was generally well tolerated.

P35.21

A phase II, randomized, double-blinded, placebo-controlled trial of liraglutide in Parkinson's disease

Michele Tagliati, Elliot Hogg, Echo Tan, Konrad Talbot
Cedars-Sinai Medical Center, Los Angeles, California, USA

Background: Reduced glucose tolerance in Parkinson's Disease (PD) is well-known and predates the introduction of levodopa therapy. Impaired glucose tolerance can induce brain insulin resistance and thereby help drive PD pathogenesis. Brain insulin resistance is thus a promising therapeutic target in PD. At present, there are two marketed GLP-1 receptor agonists with good safety profiles, exenatide and liraglutide. These treatments are also well known for their neuroprotective effects in animal models of PD. Exenatide has been tested in a pilot trial on PD patients with encouraging symptomatic results and a possible disease-modifying effect in a long term follow-up analysis. Liraglutide, however, may

prove superior in treating PD as it has been found more effective in reducing body weight and hyperglycemia.

Study Design: Phase II, randomized, double-blinded, placebo-controlled clinical trial to examine the safety and efficacy of liraglutide for Parkinson's Disease. The trial will be held at Cedars-Sinai Medical Center in Los Angeles in partnership with NovoNordisk and the Cure Parkinson's Trust, UK. The primary aim is to test the therapeutic efficacy and safety of liraglutide in patients with idiopathic PD. The secondary aim is to correlate the magnitude of any observed therapeutic effect with the degree of reduction in peripheral insulin resistance, measured by HOMA index, over the course of drug treatment. We plan to randomize 54 patients with a diagnosis of idiopathic PD to receive once daily injections of liraglutide (1.2 or 1.8 mg), or placebo, in a 2:1 study design. The primary outcomes will be the UPDRS part III and non-motor symptoms of PD (assessed by NMSS and MDRS-2) after 52 weeks of treatment. The secondary outcomes will be measures of the association between liraglutide's effects on peripheral insulin resistance, PD symptoms, and safety.

Hypothesis: Motor function and non-motor features, including particularly cognition, will either improve or decline less in the actively treated group, as compared to those treated with placebo, over the one year study period. We also hypothesize that any improvement seen in people with insulin resistance will be proportionate to the improvement of the HOMA index. This study will test a new symptomatic and possibly disease-modifying therapy, while shedding light on the role of insulin resistance in the pathogenesis of PD.

P35.22

Driving patient engagement in Parkinson's clinical research: lessons learned in developing successful partnerships with study sponsors

Veronica Todaro¹, Karlin Schroeder²

¹ USA

² Parkinson's Disease Foundation, New York, New York, USA

Objective: To understand the factors that result in successful patient engagement partnerships between a patient group, patients and study sponsors.

Introduction: The Parkinson's Disease Foundation (PDF) is committed to ensuring that people living with Parkinson's disease are partners throughout the research process. Identifying and operationalizing successful partnerships with study sponsors in government, industry and academia is essential. PDF has initiated as well as has been approached by study sponsors to create formal collaborations so as to ensure that the perspective and experience of people living with Parkinson's is incorporated into research decision-making. These collaborations include a wide range of decision points along the clinical research continuum.

Methods: Administration of an online survey and phone interviews of study sponsors who have engaged in a collaboration with PDF and PDF Research Advocates to examine the: 1. perceived versus actual barriers to patient engagement; 2. the impact of patient engagement within the context of the specific collaboration 2. broader organizational impact of the collaboration.

Results: Results from the administration of the online survey and phone interviews will be analyzed, reported and summarized.

Conclusion: Preliminary findings indicate that factors resulting in successful patient engagement partnerships between a patient group, patients and study sponsors are varied. However, there are common factors such as shared goals, agreement on outcomes and project specificity that lead to positive experience and outputs for all stakeholders.

P35.23

Parkinson's Advocates in Research: a Parkinson's Disease Foundation cutting edge program in patient engagement in research

Veronica Todaro¹, Karlin Schroeder², Linda Morgan², Cliff Ishmael²

¹ United State

² Parkinson's Disease Foundation, New York, New York, USA

Objective: To provide a model of a successful program of patient engagement in research in the Parkinson's community.

Introduction: The PDF Parkinson's Advocates in Research (PAIR) program launched in 2008. This innovative program builds partnerships between people with Parkinson's disease (PD), care partners and research teams to design studies that incorporate community needs and priorities. The PAIR program has trained over 250 Research Advocates, developed best practices for patient engagement and worked with researchers to ensure that expertise and perspective of people touched by Parkinson's is incorporated throughout the research process.

Methods: The PAIR program prepares researchers and people with PD and care partners to work collaboratively in the research process. People with PD and care partners are trained in the PAIR Learning Institute. Researchers are trained through mentoring by, and consulting with, PDF staff on a project basis. Tools, resources, additional training and best practices are available on an ongoing basis. PDF Leadership Awards provide a stipend for researchers to work with Research Advocates on a study that overcomes a barrier to moving research forward.

Impact: Ninety-six (96) percent of attendees reported the 2016 Learning Institute changed the understanding of research advocacy either "moderately" or "very much."

Sixty-eight (68) percent of researchers from a conference on fatigue were likely to include patients in future scientific conversations based on their interactions with Research Advocates. A diagram of how patients can engage in the research process developed by PDF has been repurposed and disseminated nationally and internationally by such organizations as the Clinical Trials Transformation Initiative. Research Advocates have: reviewed grants for the Department of Defense; been awarded grants from the Patient Centered Outcomes Research Institute, served on steering committees and data safety monitoring boards for clinical trials funded by the National Institutes of Health and partnered with pharmaceutical companies to provide input into study protocol and device design.

Conclusions: PDF has a proven track record in leading a cutting edge program (PAIR) in patient engagement in research. PAIR has led to research that better meets community needs and priorities through partnerships between people with Parkinson's, care partners and researchers in academia, industry and government.

P35.24

Multi-system balance training programme enhances comprehensive balance and functional performance in Parkinsonian non-fallers: a randomized controlled trial with one-year follow-up

Irene S. Wong-Yu, Margaret K. Mak

The Hong Kong Polytechnic University, Hong Kong, Hong Kong

Background: Previous studies have demonstrated that exercise interventions can improve balance and functional in people with Parkinson's disease (PD), but most training did not target all balance domains and was conducted mainly indoors. Early intervention for PD non-fallers is essential for improving their postural stability and fall-prone functional performance.

Objectives: Our aim is to investigate the long-term effects of a multi-system balance training programme on enhancing comprehensive balance and fall-prone functional performance in PD non-fallers.

Methods: PD subjects without fall history in past 6 months were randomly assigned to an eight-week (one 2-hour session per week) multi-system balance training programme (BAL, N=32) group or active control (CON, N=36) group supervised by physiotherapists. The BAL subjects underwent training for four weeks indoors, followed by four weeks outdoors. Indoor exercises included multi-system postural control strategies such as postural re-education and flexibility exercises, strength and functional training, Balance Dance, modified Wing Chun and Square Stepping Exercise. Outdoor exercises included perturbation-based training, fall-prone functional tasks and dual-task activities in the community. The CON subjects received 8-week upper limb training in sitting at the same dosage. Both groups were instructed to perform 3 hours of home exercise weekly during training period and for duration of 6 months after treatment completion. The outcome measures included the BESTest total score, functional reach (FR) distance, five-time-sit-to-stand (FTSTS) time, and one-leg-stance (OLS) time. All outcomes were assessed before training (Pre), immediately after 8-week intervention (Post8week), and at 12-month (FU12m) after treatment completion.

Results: Immediately after training, the BAL group showed significantly greater improvements from baseline than CON group for the BESTest total score, FR distance, FTSTS time and OLS time (all $p < 0.05$). At FU12m, the BAL group showed significantly greater improvements from baseline than CON group for the BESTest total score, FR distance, and FTSTS time (all $p < 0.05$).

Conclusion: The BAL subjects outperformed CON subjects for the BESTest total score, FR distance and FTSTS time post-treatment and at 12-month follow-up. Positive findings of this study support the notion of using the multi-system balance training programme to enhance the long-term comprehensive balance and functional performance in PD non-fallers.

CLINICAL SCIENCES: RATING SCALES

P36.01

A Patient-Centered Rating Scale for Parkinsonism

Laurie Mischley

Bastyr University, Kenmore, WA, USA

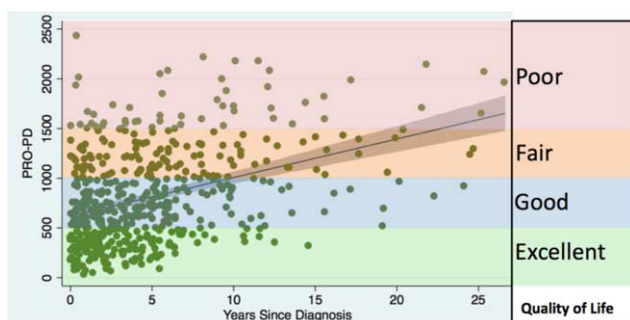
Background: The Patient-Reported Outcomes in Parkinson's Disease (PRO-PD) is an internet-based assessment tool designed to capture PD severity in an inexpensive, clinically relevant, and comprehensive fashion. It was designed to assess patient perception of both motor and non-motor symptoms, and require minimal time and instruction.

Methods: The PRO-PD is a cumulative score of 33 slider bars, each evaluating a common PD symptom. The affected individual is asked to rate symptom severity, on average, over the previous seven days. Thus far, the PRO-PD has been used in three research studies; the baseline data from all available studies was pooled for this cross-sectional analysis.

Results: Three studies provided 902 participants, 58 of who were physically examined. The most frequently reported PD symptoms were impaired handwriting/ typing (91.8%), fatigue (91.2%), slowness (89.8%), daytime sleepiness (89.7%), muscle cramps (88.9%), forgetfulness (87.6%), impaired sense of balance (86.9%), and loss of smell (86.0%). PRO-PD scores increase over time, with higher scores being associated with lower quality of life and worse

outcomes on the Hoehn & Yahr (HY) and Unified Parkinson's Disease Rating Scale (UPDRS).

Conclusions: The most important criteria for a scale capable of quantifying disease progression is that it worsens over time and reflects the patient experience, which was demonstrated here. This scale has potential to be used as a communication tool between patient and provider in telemedicine and clinical care, to both help identify problem areas and set therapeutic goals. The scale has especially attractive for research purposes, in that it correlates with established measures of PD severity, utilizes direct data entry, permits stratification by symptom(s), takes only a few minutes to complete and does not require a trained clinician. Whether therapeutic interventions can stabilize or reverse PRO-PD scores has yet to be determined.



CLINICAL SCIENCES: E-HEALTH AND TECHNOLOGY

P37.01

Objective characterisation of Parkinson's disease motor fluctuations with the Parkinson KinetiGraph – three years experience at a movement disorder clinic

Filip Bergquist¹, Thordis Gudmundsdottir²

¹ University of Gothenburg, Sahlgrenska Academy, Dept of Pharmacology, Gothenburg, Sweden

² Sahlgrenska University Hospital, Dept of Neurology, Gothenburg, Sweden

Background: Assessing motor fluctuations in people with Parkinson's disease (PwP) is tainted by poor recollection and insufficient patient recognition of symptoms of over- and under medication. In 2013 we started to use a commercial accelerometer device (Parkinson KinetiGraph, PKG) to assist the clinical evaluation of motor fluctuations in PwP where fluctuations were suspected or where it was difficult to take up history. We report the outcome of 359 PKG home registrations performed during 6 -10 days in a total of 258 PwP between April 2013 and March 2016.

Method: Patients were recruited from one specialised movement disorder centre and six spoke neurology clinics in west Sweden and the measurements were performed as part of the standard patient assessment as well as during work-up for the initiation of advanced treatment (DBS, LCIG or Apomorphine-infusion). Repeat measurements were made in 75 patients. Outcomes based on normal PKG reference values were compared with visual assessment of the registrations performed by a trained specialist, and was back-referenced to clinical assessments at the regular clinic visits.

Results: PwP tolerated the PKG measurement well and only 8% had problems handling the reminder function or wearing the device.

Although the proportion of registrations that by visual assessment suggested treatment could be optimized was similar to the proportion of PwP registrations where any measurement score was outside the normal inter-quartile range (64% and 60% respectively), the agreement between visual assessment and assessments based on median PKG scores was low (Cohen Kappa 0.11). In particular, the PKG fluctuation dyskinesia score (FDS) identified fewer OFF-fluctuators than visual assessment by a trained specialist as 25% of the population had significantly increased FDS, but visual assessment identified OFF-fluctuations in an additional 45% of the population.

Conclusions: Accelerometer devices are emerging as a new way to collect data about motor fluctuations in PwP. There is no previous gold standard that is reliable enough to bench-mark accelerometer systems against and it is therefore important to report clinical outcomes in relation to objective home measurements to establish the usefulness of unobtrusive accelerometer recordings for identifying patients in need of optimized treatment.

P37.02

Beta testing with Parkinson's patients for a mobile research study

Margaret Daeschler¹, Dana Drutman², Lydia Herron¹, Michal Afek², Eli Cohen², Lauren Bataille¹, Catherine Kopil³

¹ The Michael J. Fox Foundation for Parkinson's Research, New York, NY, USA

² Intel Corporation, Israel

³ Canada

Objective: To establish a system for collecting patient feedback to inform development of a mobile app for Parkinson's disease research and management.

Methods: The Michael J. Fox Foundation and Intel Corporation launched the Fox Insight Wear research study in 2015 to amass a 'big data' set of continuous and longitudinal movement information from people living with Parkinson's disease in their home environment. The study utilizes a wearable smartwatch and custom mobile app (Fox Insight) to gather 24/7 data on participants' movements, medication schedule, and symptoms, and provides real-time reports to users about their activity level, tremor, and medication adherence. To ensure app functionality and ease of use, we have engaged a group of approximately 12 people with PD to serve as Beta testers. A new version of the Fox Insight app is released every two months. Prior to public availability, in-person usability testing is performed to assess features in the early development phase. Beta testers use the app without any guidance or instruction, and challenges they encounter inform modifications to user experience and flow. Secondly, Beta testers use the app at home for 2 weeks and provide recommendations on changes through virtual feedback sessions. Questions about connectivity, battery, measurements, and features are used as a guide to obtain records of participant experiences, which then inform development of the app (table below).

Results: Engaging people with Parkinson's as Beta testers is feasible, requiring about two hours of commitment per user each release. Beta Testers have identified bugs and suggested areas to improve flow and functionality. Many suggestions have been implemented in the app (e.g. changes to the medication reporting tool to allow for easier entry of medication reminders and the logging of previously taken medications). Beta Testers have also looked beyond the scope of the feedback table, providing strategic recommendations for future app functionality, including a step counter, dyskinesia or bradykinesia measures, and a clinician-facing data portal to share at-home experiences with their doctors.

Conclusion: Establishing a systematic Beta Testing program for Fox Insight app development has improved app quality and

functionality, generating a patient-centric user experience, and creating a cohort of engaged and forward thinking users. This systematic approach could be easily adopted for other Parkinson's-based mobile-tech development.

Feedback Table			
Number	Category	Description	Your comments
1	Disconnections	1- Did you face scenarios where the watch and phone disconnected? 2- Did they reconnect automatically? If so, how long did this take? 3- Did you have to do anything to make them reconnect?	
2	Battery	1- How much time did it take for your Pebble's battery to drain? 2- How much time did it take for your phone's battery to drain? 3- How long does it usually take for your phone battery to drain (when not running the Fox Insight app)?	
3	Activity graph	1- Was the activity graph updated over time? 2- Did you have episodes in which the graph wasn't updated and it wasn't clear why? 3- Was the graph reflective of your day to day activity?	
4	Tremor graph	1- Was the tremor graph updated over time? 2- Did you have episodes in which the graph wasn't updated and it wasn't clear why? 3- Was the graph reflective of your tremor activity?	
5	Night graph	1- Was the night graph updated over time? 2- Did you have episodes in which the graph wasn't updated and it wasn't clear why? 3- Was the graph reflective your night time activity?	
6	Medication Reminders	1- How easy was it for you to set medication reminders? 2- Did the reminders appear on time on both your watch and phone? 3- Did you use this tool to record your medication intake and	

P37.03

Building Parkinson's communities of support in virtual worlds

Donna Davis¹, Tom Boellstorff²

¹ University of Oregon, Portland, Oregon, USA

² University of California, Irvine, Irvine, California, USA

Objective: Individuals diagnosed with Parkinson's disease (PD) face significant challenges in obtaining and sustaining peer support. This is particularly the case for those who have early onset PD, live remotely, or face mobility limitations (for instance, not being able to drive). An increasing interest in telehealth and online support groups has resulted in an increasing number of online platforms designed to improve peer support given these challenges. A simple Google search of online PD support groups reveals greater than 350,000 such groups including groups sponsored by the Michael J. Fox Foundation, the Parkinson's Disease Foundation, and a host of universities and medical providers. However, most of these groups work through websites, listservs, or social network sites like Facebook. With regard to PD peer support, what can virtual worlds—with their possibilities for 3D, immersive interaction—do that these other formats cannot?

Method: Our 4-year ethnographic study included extensive virtual-world participant observation with members of a weekly PD support group in the 3D virtual world Second Life, ranging in age from 50 to 89. Fieldwork included everyday activities outside the support group (e.g., shopping, dances, and sightseeing). We also conducted

multiple interviews with members of the group. This resulting corpus of data was coded and analyzed with regard to the themes relevant to our analysis.

Results: Participants report many benefits from participating in the virtual-world support group, perhaps most profoundly in regard to quality of life measures. They report a reduction in depressive symptoms, an increase in social support, and often report a loss of tremor while engaged in the virtual world. Several participants found the virtual world provided an excellent outlet for creativity, often associated with an increase in the "compulsive creativity" that is well-documented in PD research. One participant reported increased confidence in her balance after watching her avatar doing tai chi, resulting in improved physical-world mobility. Further exploration of these reported benefits is warranted.

P37.04

Technology utilization and preferences among people with Parkinson's

John Dean

Davis Phinney Foundation, Boulder, Colorado, USA

Emerging technologies offer many exciting opportunities to improve quality of life among people living with Parkinson's. However, technological adaptation is somewhat slow and inconsistent among this community. This may be the result of demographic elements such as an aging population that is likely less comfortable with technology perhaps it's due to neurological changes associated with Parkinson's that impairs the ability to interact with these tools. In 2015, the Davis Phinney Foundation produced a technology "needs gap" survey that identified core technology utilization characteristics among the community living with Parkinson's (as well as care partners, healthcare providers and others). The survey (n=851) revealed a very high level of computer usage with email being the most commonly used tool and Facebook as the most widely used social media platform. Smart phone use was lower and only about 27% of respondents indicated they made use of wearable technology.

A follow-up survey was conducted in 2016 (n=1364) to identify changes in technological use as well as identifying additional information about technology utilization and additional data regarding non-Parkinson's-specific use of apps and technology for tracking exercise, meals and caloric intake among other features. This information was further supplemented with a brief follow-up survey to a small cohort of 168 individuals to identify data regarding exercise habits and other enhanced demographic information. In addition to this small follow-up survey, user interviews were performed with a select group of individuals among various demographics. It was the incorporation of user interviews that provided the most interesting and telling data and components about technology use in Parkinson's. These one-on-one interviews provided telling insights about actual use of a number of technologies. For example, in a number of cases, the "wearable" technology cited by respondents in a survey actually turned out to be single-purpose devices including emergency notification systems and alarms.

The result of this work has been beneficial on numerous levels. On the one hand, it has provided significant relevant information about technology utilization throughout our community as well as some longitudinal data about changes in technology use over the course of a single year. However, the experience of performing user interviews was extremely enlightening and provided value far beyond the surveys alone.

P37.05**Designing technologies alongside the Parkinson's community using principles of user-centered design***John Dean*

Davis Phinney Foundation, Boulder, Colorado, USA

Many emerging technologies offer exciting opportunities to improve diagnosis, assessment and treatment of many aspects of Parkinson's disease. Of particular recent interest are tools that provide opportunities for self-assessment as well as enhancing compliance with medications in addition to increasing physical activity among people living with Parkinson's.

However, there have recently been a number of innovative projects that have failed to engage the person with Parkinson's or other end-user. There appears to be a disconnect between the groups researching and developing and tools and the individuals who will ultimately making use of these tools such as individuals with Parkinson's as well as their care partners and healthcare providers.

Principles of user centered design (UCD) provide a framework for including all key decision-makers throughout the development process. This inclusive approach has become a feature of many prominent organizations and institutions including the Medicine X conference at Stanford with its "Everyone Included™" model of collaboration. The World Parkinson's conference embodies this ethos by bringing together researchers, clinicians and other professionals alongside people living with the disease and their care partners.

This model is even more critical when attempting to design tools for a population with such a highly variable set of symptoms and clinical presentations as those living with Parkinson's. These neurological deficits can impair the ability to interact with smart phones, wearables and other technologies. These neurological changes can impair vision, fine motor control as well as cognitive components necessary for interaction including executive function, memory and even emotional state.

As a result, the traditional approach of getting user response via survey feedback and/or incorporating more traditional models of focus group testing etc. is not a robust enough model for successful development. Incorporating individuals living with Parkinson's into the design process at the outset and maintaining that relationship throughout development process via rapid prototyping with feedback provides a significantly more functional product. It also has the potential to significantly reduce costs later in the development process.

P37.06**Measurement of dyskinesia during a golf activity using a novel putter and the BioMech Swing Analysis System (SAS)***Frank Fornari¹, Gwen Bauer², Vijay Peddinti², John Douglas³, Bridget Bell³, Chris Campanella², Rita Fornari²*¹ Jamestown, RI, USA² BioMech Sensor, Jamestown, RI, USA³ BioMech Sensor, Potomac, MD, USA

Parkinsonian dyskinesia in the upper extremities can prevent affected golfers from continuing to stay active in the sport. The Acculock ACE putter is designed to rest against the inside of the user's leading forearm at a comfortable anatomically efficient forward lean angle. The overlap provides an additional point of attachment, creates a stable triangle with the arms and shoulders and significantly reduces dyskinetic motion. The BioMech Swing Analysis System (SAS), a inertial measurement unit based platform coupled with synchronized video and multi-sensor data capture was used to compare motion in patients with significant dyskinesia during a putting exercise with their traditional putter versus the

AccuLock ACE. Measurements include putting path, face at impact, putting stability, consistency, precise timing, acceleration, overall balance, anatomical orientation, and EMG analysis. Overall results demonstrate that when used, the Acculock ACE putter significantly improved every aspect of the motion. These studies show that when putting performance is restored and enhanced, it improves the patient's activity level and participation, extends the benefits of remaining active during the progression of the disease and demonstrates the utility of monitoring motion with (SAS) in this patient group.

P37.07**Usability of a patient-centered wearable system for continuous monitoring of Parkinson's disease***Natalie Fountas-Davis, Jenna Daghstani, Dustin Heldman, Christopher Pulliam, Joseph Giuffrida*
USA

Objective: The objective was to examine the usability of a wearable sensor-based system for monitoring Parkinson's disease (PD), confirm accurate detection of motor symptoms, and obtain patient feedback on patient-centered features. Clinicians make decisions using direct observation, patient diaries, and clinical rating scales, but may miss fluctuations or the extent and severity of prolonged symptoms and side effects throughout the day and between visits. Current diagnostic methodologies lack the ability to fully assess the patient's ongoing state of symptom management.

Methods: 31 individuals with PD participated in usability and home-validation studies to investigate a system consisting of two wearable motion sensors, a smartphone app, and clinically validated algorithms for continuous ambulatory monitoring of PD. 13 of the participants set up and used the system in a supervised lab setting so errors during each step could be identified and recorded. The other 18 participants set up and used the system at home during their daily activities for 1–3 days. Self-reported tremor and dyskinesia were compared with symptoms detected by the ambulatory monitoring system. Participants in both studies completed a survey assessing their satisfaction with the system.

Results: Participants rated their experience with the system highly, indicating it was easy to use and comfortable to wear. All participants were able to set up the system with <1 critical error per task per person; which were addressed through design revisions to the UI. Significant differences ($p < 0.05$) were detected by the ambulatory monitoring system when comparing participants who self-reported tremor and/or dyskinesia to those who did not. Patient feedback on the usability of preliminary reports lead to visual patient-facing reports for actionable disease management by the patient. Ongoing surveys indicate a need for remote monitoring of PD symptoms to adequately understand disease progression, medication changes, effects of activities and stressors, and comparisons based on PD demographics.

Conclusions: The wearable monitoring system is easy to use and can accurately and precisely track PD motor symptoms throughout the day. Design elements are conducive for direct symptom tracking by patients with PD.

P37.08**The applicability of a portable electronic falls diary to assess fall frequency in Parkinson's disease***Catarina Godinho¹, Josefa Domingos², John Dean³, Miguel Coelho⁴, Leonor Correia Guedes⁴, Anabela Pinto⁵, Bastiaan Bloem⁶, Joaquim J. Ferreira⁷*¹ Clinical Pharmacological Unit, Instituto de Medicina Molecular and Center for Interdisciplinary Research Egas Moniz (CiiEM), Instituto

Superior de Ciências da Saúde Egas Moniz, Monte de Caparica., Lisboa, Portugal

² Campus Neurológico Sénior and Clinical Pharmacological Unit, Instituto de Medicina Molecular, Lisboa, Portugal

³ Davis Phinney Foundation, USA

⁴ Clinical Pharmacological Unit, Instituto de Medicina Molecular., Lisboa, Portugal

⁵ Department of Rehabilitation, Hospital Santa Maria, Lisboa, Portugal

⁶ Department of Neurology, University Medical Centre St Radboud, Nijmegen, Netherlands

⁷ Campus Neurológico Sénior and Clinical Pharmacological Unit, Instituto de Medicina Molecular and Laboratory of Clinical Pharmacology and Therapeutics, Faculty of Medicine, University of Lisbon., Lisboa, Portugal

Although falling is a frequent occurrence in Parkinson disease, the best method(s) for measurement of falls remains unclear. Paper and electronic "falls diaries" are commonly used in health care and clinical research to assess the frequency and circumstances of falls and near fall events. However, there is a lack of objective documentation of the applicability of such diaries and limitations with respect to their use in both paper and electronic formats, which may ultimately affect the ability of these instruments to assess falls effectively. The aim of our study was to evaluate the applicability of an electronic diary when compared with a paper diary as a clinical measure of frequency of falls and near falls in individuals with Parkinson disease. Eight individuals with a history of falls were asked to complete a paper or an electronic diary at home for 8 weeks, with a crossover of the type of every 2 weeks. Diary applicability was evaluated by questionnaire. Our results showed that most participants were able to complete both types of falls diaries successfully. Compliance for registering entries into both diaries was high and 62.5% (5 in 8) of participants preferred to use electronic diary. Electronic diaries are as good as paper diaries in depicting participant's frequency of falls. In addition, electronic diaries provide an opportunity to control the quantity of data in a manner that is not possible with a paper format. Phone calls and including caregivers may complement diary use and compliance.

P37.09

A randomized controlled trial of telemedicine for Parkinson's disease (Connect.Parkinson) in the USA

Steven Goldenthal¹, Connect.Parkinson Investigational team²

¹ Rochester, NY, USA

² USA

Objective: The Connect.Parkinson study aims to assess the feasibility, efficacy, impact on quality of care, and value to patients and families of home telemedicine visits for Parkinson disease (PD).

Background: Despite the proven benefits of specialist care for PD, access to PD specialists in the U.S. is limited by distance, disability, and distribution of specialists. Preliminary data suggests that receiving specialist care in the home via telemedicine may be feasible, effective, and acceptable for those with PD. This is the first national randomized controlled trial of telemedicine for PD.

Methods: Participants were recruited by a variety of methods: PD community websites, social media outreach, emails to advocacy groups, and outreach to primary care providers in underserved areas. Once enrolled, participants were randomly assigned to usual care (control arm) or usual care and 4 telemedicine visits (treatment arm) with a specialist in their state. Primary outcomes included feasibility, measured by percentage of telemedicine visits completed, and efficacy, measured by change in quality of life.

Results: As of April 2016, approximately 11,000 individuals have visited the study website and over 1,000 indicated interest in study

participation. 210 individuals from 18 states enrolled in the study and 195 were randomized, with 97 individuals in the treatment arm and 98 in the control arm. Participants are mostly Caucasian (96%), college educated (73%), male (53%) with a mean age of 66 years and mean disease duration of 8 years upon enrollment.

To date, 361 virtual visits are completed, with 98% completed as scheduled. On average, these visits lasted 42 minutes, with 35 minutes spent with the Parkinson disease specialist. Participants in the treatment arm preferred virtual visits (91%) to in-person (4%) and the comfort of virtual visits (45%) to in-person (18%) while they preferred the care from in-person visits (36%) to the care from virtual visits (27%). Overall, participants preferred virtual visits (43%) over in-person visits (23%), and 90% of participants reported interest in receiving future care via virtual visits.

Conclusion: Early study results suggest that providing care to individuals with Parkinson disease via telemedicine receives high interest, is feasible, and well received. The last study visit is expected to be completed in the first week of July. Preliminary analysis of the data will be prepared by September.

P37.10

Innovative use of mobile health technology in physical therapy for people with Parkinson's disease

Kathryn Hendron¹, Jim Cavanaugh², Tamara DeAnglelis¹, Nicole Sullivan¹, Lori Goehring³, Cathi Thomas⁴, Marie Saint-Hilare⁴, Nancy K Latham³, Terry Ellis¹

¹ Boston University – Department of Physical Therapy & Athletic Training, Center for Neurorehabilitation, Boston, MA, USA

² Department of Physical Therapy, University of New England, Portland, ME, USA

³ Health and Disability Research Institute, Boston University School of Public Health, Boston, MA, USA

⁴ Boston University Medical Campus – Parkinson's Disease and Movement Disorders Center, Boston, MA, USA

Objective: To evaluate preliminary evidence for a novel physical therapy (PT) intervention using a mobile health (mhealth)-mediated, home-based exercise program to increase physical activity in persons with Parkinson Disease (PD) over one year.

Background: Patients living with PD typically receive PT only periodically and mainly with an acute change in physical functioning. Effective PT service delivery models for promoting routine physical activity as a secondary prevention strategy are lacking. Development of innovative approaches to improve the current PT model may improve activity levels and adherence to exercise programs.

Methods: An innovative model of PT using mhealth technology was implemented in twenty-three individuals with PD. Participants received one to two initial in-person PT clinic sessions to establish a home exercise and walking program using an activity tracker ('fitbit'). Exercise instruction and progression was delivered using a web-based exercise application ('Wellpepper') housed on a tablet or smart phone. Fitbit data were integrated with the Wellpepper platform. Patients accessed their exercise program in the home setting between bouts of PT. Wellpepper allowed the PT to remotely monitor adherence, progress the exercise program, and communicate via two-way text message with participants.

Summary of Use: Twenty-three participants with mild to moderate PD (UPDRS Part III 31.1, ±10.1) used the mhealth technology for 12-months. Fifty-two percent were male and mean age was 64.8±8.8 years. Ninety-six percent lived with family. Eighty-three percent had a college degree or higher. Adherence to using the exercise application was >70% over the 12-months. Significant changes between baseline and 12-months included increased physical activity using the Godin Leisure Time Total (p<0.001), improvement in walking speed using the six-minute walk test (p<0.05), and

improvements in balance using the BriefBest ($p < 0.05$). Eighty-three percent said they would like to continue to use the exercise program. All participants would recommend the program to others and rated their overall satisfaction 8.8/10 (10 = highly satisfied).

Conclusion: Use of mobile health technology in an innovative PT model was found to be safe and acceptable in people with PD. Patients with PD demonstrated an increase in activity levels over the 12-month study. Further research is warranted to understand how to optimize mhealth technology for PT interventions.

P37.11

Perceptions and preferences concerning the use of wearable sensors in Parkinson's disease and epilepsy: a focus group study

Dongni Johansson¹, Anneli Ozanne², Margit Alt Murphy¹, Kristina Malmgren¹, Filip Bergquist³

¹ Department of Clinical Neuroscience and Rehabilitation, Institute of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

² Institute of Health and Care Sciences, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

³ Department of Pharmacology, Institute of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

Objective: The use of garment integrated multimodal sensors for monitoring movement and physiological variables in neurological diseases, such as Parkinson's disease (PD) or epilepsy, is attractive for clinical applications. The aim of this study was to examine facilitators and barriers to wearable technology use as reported by people with PD and epilepsy, as well as health professionals.

Method: Interviews were performed in eight focus groups composed from patients or professionals from either diagnostic group and included men and women (N=40). Each interview explored facilitators and barriers for the use of wearable sensors and the usability of smart garments. Audiotaped and transcribed interviews were analyzed by qualitative content analysis with focus on subject and context to identify similarities and differences across all focus groups.

Result: The main facilitators for using wearable sensors in PD and epilepsy were: the potential for assisting and improving diagnosis and disease management, and also allowing objective continuous long-term out-patient monitoring. Respondents from the PD groups emphasized that data acquired from wearable sensors could be used for dosage regimen adjustments and to assist postural control as well as rehabilitation. The main barriers that concerned all groups were: feeling controlled; uncertainties about the accuracy of the monitoring; hygiene concerns during long-term monitoring and worries about the difficulties of interpreting technical data. The key preferences for using wearables were: system reliability; independence of use; social consequences and availability to contact health professionals. Participants in the PD groups highlighted medication reminder and monitoring of non-motor symptoms like sleep disturbance as wanted functions. Technical features, such as ease of wear, unobtrusive design and battery capacity were prioritized across all groups. Esthetic aspects, issues with type of textile used and the kind of garment planned (tank top, jumper) were also important for patients.

Conclusion: Wearables need to be user-friendly and accessible for patients to fully embrace this innovation. Wearables also need to be functional and attractive and therefore patients have a role in participating in the design of their health monitoring devices. Cross-scientific competence is necessary to develop well-accepted wearables by understanding the relationship between today's wearable technology and the preferences of relevant user-groups.

P37.12

Alleviating freezing of gait in Parkinson's disease: open-loop external cues versus closed-loop biofeedback

Martina Mancini, Graham Harker, Katrijn Smulders, Fay Horak, John Nutt
USA

Background: Accumulating evidence suggests that inadequate integration of sensory information and defective proprioceptive internal maps may underlie abnormal motor control in PD. Interestingly, freezing of gait most frequently occurs during tasks that require control of asymmetric motor tasks, such as turning or gait initiation and depend heavily on integration of proprioceptive information. For these reasons, augmenting somatosensory information with biofeedback during appropriate phases of the gait cycle may improve gait disturbances.

Objective: To compare the effects of open-loop external cues (metronome) and closed-loop tactile biofeedback on freezing of gait (FoG) in Parkinson's disease (PD).

Methods: Twenty subjects with idiopathic PD with FoG (MDS-UPDRS III: 43 ± 11 ; new FoG-questionnaire score: 18 ± 7) performed a turning task, consisting of turning in place for one minute (changing turning direction after each full turn) while off their levodopa medication. Three inertial sensors were mounted on the posterior trunk and on each shin. Turning was compared across 3 randomized conditions: i) baseline (no cues); ii) turning to the beat of a metronome, and iii) turning with phase-dependent tactile biofeedback via light vibration to the wrists every time the ipsilateral foot was in stance phase. For each condition, a Freezing ratio calculated as the power spectral density ratio between high and low frequencies of shin accelerations and the percentage of time spent freezing during the task were measured. This study is in progress and will also examine 20 PD subjects without FoG.

Results: All subjects showed mild-to-moderate FoG during the assessment. At baseline, the Freezing ratio was 2.2 ± 0.4 , and it significantly reduced with both the metronome to 0.8 ± 0.2 ($p < 0.001$), and tactile-biofeedback conditions to 0.8 ± 0.1 ($p = 0.001$; ANOVA $F = 6$, $p = 0.004$). Similarly, the % time spent freezing in the turning task significantly decreased from $45 \pm 5\%$ at baseline to $18 \pm 4\%$ in the metronome ($p < 0.001$) and to $19 \pm 4\%$ in the tactile biofeedback condition ($p = 0.001$; ANOVA $F = 12$, $p = 0.001$).

Conclusions: We observed a significant decrease in freezing of gait while turning in both a biofeedback (closed-loop) and externally-cued condition (metronome, open-loop). These preliminary observations suggest that augmenting somatosensory information with a phase-dependent biofeedback system relying on an unobtrusive modality, might be an effective tool in reducing FoG in everyday life.

P37.13

Quantification of Parkinson's disease motor functions using wearable sensors

Mevludin Memedi¹, Ilias Thomas², Dag Nyholm³, Jerker Westin², Marina Senek³, Somayah Aghanavesi², Alexander Medvedev⁴, Håkan Askmark³, Sten-Magnus Aquilonius³, Filip Bergquist⁸, Radu Constantinescu⁹, Fredrik Ohlsson¹⁰, Jack Spira¹¹, Anders Lycke¹²

¹ Computer Engineering, Dalarna University, Informatics, School of Business, Örebro University, Falun, Örebro, Sweden

² Computer Engineering, Dalarna University, Falun, Sweden, Sweden

³ Neuroscience, Neurology, Uppsala University, Uppsala, Sweden

⁴ Information Technology, Uppsala University, Uppsala, Sweden

⁸ Dept. of Pharmacology, University of Gothenburg, Gothenburg, Sweden

⁹ Dept. of Clinical Neuroscience, University of Gothenburg, Gothenburg, Sweden

¹⁰ Acreo Swedish ICT, Gothenburg, Sweden

¹¹ Sensidose AB, Uppsala, Sweden

¹² Cenvigo AB, Uppsala, Sweden

Objectives: The goal of the study is to investigate whether wrist worn motion sensors are feasible tools to measure motor functions in Parkinson's disease (PD). More specifically, the aim is to construct a sensor-based levodopa-response index (SBLRI) and evaluate its clinimetric properties (convergent validity and internal consistency).

Background: Nineteen advanced PD patients and 22 healthy controls were recruited in a single center, open label, single dose clinical trial in Sweden. The aim of the trial was to assess clinimetric properties of a system consisting of multiple sensors for quantifying motor function in patients experiencing motor fluctuations.

Methods: The subjects performed standardized motor tasks while wearing one sensor on each wrist and one on each ankle. Each sensor unit consisted of three-dimensional accelerometer and gyroscope. The patients were video recorded and the videos were blindly rated by three independent movement disorder specialists. The clinical scores were given using the Treatment Response Scale (TRS) on a scale from -3='Very Off' to 0='On' to +3='Very dyskinetic', based on the overall motor function of the patients. A mean TRS was defined as the mean of three specialists' assessments per time point. The tests were repeated overall several time points following a single levodopa/carbidopa morning dose (50% over normal to induce dyskinesia). Sensor measurements during rapid alternating movements of hands were processed with time series analysis methods to calculate spatiotemporal parameters, which were then used as predictors in a machine learning procedure to produce the SBLRI.

Results: The SBLRI was strongly correlated to mean TRS with a Pearson correlation coefficient of 0.79 (CI: 0.74-0.83, $p < 0.001$). The 95% confidence interval for the mean squared error of SBLRI was from ± 1.62 with a mean value of 0.57. The sensor-based spatiotemporal parameters had good internal consistency with a Cronbach's Alpha coefficient of 0.87 and significantly differed between patients and healthy controls. The mean squared error of SBLRI predictions on healthy controls was 0.27 (CI: -0.73, 1.27). Figure 1 shows two graphs of SBLRI and mean TRS for two patients.

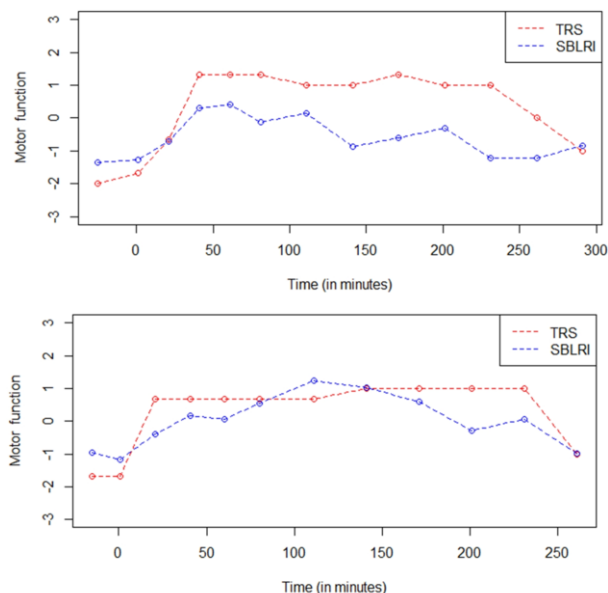


Figure 1. Two representative cases of patients with superimposed mean TRS and SBLIR scores over time.

Conclusions: The results demonstrated that the SBLRI had good clinimetric properties for measuring motor functions (Off and dyskinesia) in PD patients. The SBLRI provides effect-time profiles, which could be useful during therapy individualization.

P37.14

Fine motor spatial and temporal performances of PD patients are more impaired during spiral tests with visual stimuli than during tests without visual stimuli

Mevludin Memedi¹, Dag Nyholm², Dietrich Haubenberger³

¹ Computer Engineering, Dalarna University, Informatics, School of Business, Örebro University, Falun, Örebro, Sweden

² Neuroscience, Neurology, Uppsala University, Uppsala, Sweden

³ Clinical Trials Unit, NINDS Intramural Research Program, National Institutes of Health, Bethesda, MD, USA

Objective: Investigate fine motor spatial and temporal performance of Parkinson's disease (PD) patients in relation to spiral drawing tasks with and without visual stimuli.

Methods: Thirty-three PD patients participated in this study. Seventeen patients (13 males) were clinically stable, early PD patients and 16 patients (13 males) were in their intermediate stage of PD who started to experience motor fluctuations. The patients repeatedly used a touch screen telemetry device in their home environments. On test occasions, patients were instructed to trace a pre-drawn Archimedes spiral with the dominant hand, using a pen stylus. Initially, the patients repeated the test 3 times and were instructed to follow the speed (system-generated) of a moving target (MT) that started moving when the screen was touched followed by 3 more tests without the MT. The raw spiral data was processed and temporal and spatial characteristics of the spirals were quantified by calculating the following parameters: Spiral Impairment Score (SIS), Mean Drawing Speed (MDS), and Temporal Irregularity Score (TIS).

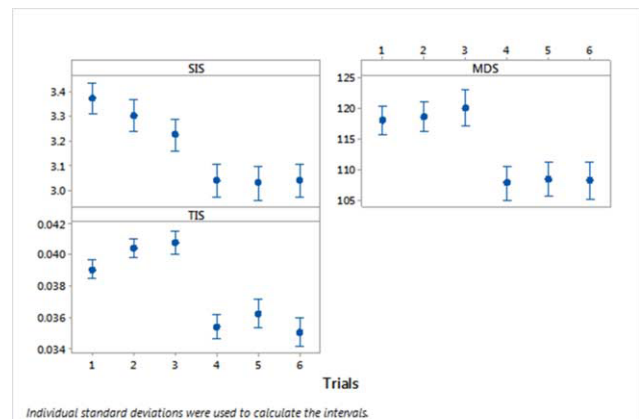


Figure 1. Mean scores of the three parameters over the test trials. The first 3 trials were performed while following a speed of a moving target and the remaining 3 without the moving target. A high score for SIS (Spiral Impairment Score) means severe drawing impairment. A high score for MDS (Mean Drawing Speed) means high speed. A high score for TIS (Temporal Irregularity Score) means high temporal irregularity during drawing. Error bars indicate 95% confidence intervals. Number of occasions: Trial 1 (n=1630), Trial 2 (n=1630), Trial 3 (n=1633), Trial 4 (n=1632), Trial 5 (n=1632), Trial 6 (n=1627).

Results: During tests with MT, patients had more impaired spiral drawing performance with 0.26 [95% CI: 0.22, 0.29] units higher than the performance during tests without MT ($p < 0.001$). Patients also had a higher timing irregularity during tests with MT than during tests without MT with 0.0045 [0.004, 0.005] units difference ($p < 0.001$). However, during tests with MT patients drew the spirals faster than during the tests without MT with 10.6 [8.94, 12.37] units difference ($p < 0.001$). During tests with MT, there were improvements in the parameters suggesting an evidence for a learning effect. There were no observed learning effects in the tests

without MT (Figure 1). The tests without MT had better test-retest reliability than the tests with MT with intra-class correlation coefficients of 0.71 (with MT) and 0.71 (without MT) for SIS, 0.67 and 0.74 for MDS, and 0.43 and 0.65 for TIS.

Conclusions: The main finding of this study is that spiral tests with visual stimuli are associated with impaired drawing performance and temporal irregularity and improved drawing speed as compared to tests without visual stimuli in early and intermediate PD patients.

P37.15

Developing technology-based speech interventions for patients with Parkinson's disease

Juliane Muehlhaus¹, Hendrike Frieg², Kerstin Bilda², Ute Ritterfeld¹

¹ Department of Language and Communication, TU Dortmund University, Dortmund, Germany

² Department of Applied Health Sciences, Hochschule für Gesundheit, Bochum, Germany

Acquired dysarthria is a symptom of Parkinson's disease and poses a substantial risk for social isolation due to unsuccessful communication. Empowerment and autonomy of patients might be supported with well-suited, adaptive technologies that they can use independently from sessions with their speech therapist. The therapist carries responsibility to select, introduce, and monitor the adequate technology to ensure a persistent usage. However, information on technology that has potential for autonomous use is still sparse. Research and development need to address solutions that will be accepted by patients with Parkinson's disease. We therefore propose an approach in which technology design is based on psychological models.

Recently, German engineers for speech signal processing and informatics, media designers, and researchers from the fields of psychology and speech and language pathology were granted a nationally funded R&D project: 'Individualisierte Spracherkennung in der Rehabilitation für Menschen mit Beeinträchtigung in der Sprechverständlichkeit' (ISi-Speech) [individual speech recognition in therapy for people with speech disorders]. The interdisciplinary team joined efforts to develop a digital training system for people suffering from Parkinson's disease. Main goal is to develop an automatic speech recognition system applicable to distorted speech and integrated in a speech therapy application that carries the motivational potential contributing to frequent and autonomous usage. These challenges shall be met within an elaborate and continuous user driven design exemplifying psychological theories such as the self-determination theory.

Our contribution intends to stimulate the discussion about prerequisites that are necessary for a successful usage of technologies in health care. Principles such as autonomy, competence, and relatedness can facilitate activity, engagement, social interaction, and scaffolding, all contributing to potential personal growth in patients with Parkinson's disease. Our R&D project 'ISi-Speech' serves as an example for applying psychological theory into designing technology for speech intervention in patients with Parkinson's disease. We propose that incorporation of a sound motivational model will enhance chances for sustainable usage.

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P37.16

Using a smartphone based self-management platform to support medication adherence and clinical consultation in

Parkinson's disease: results from the SMART-PD randomised controlled trial

Rashmi Narayana¹, Duolao Wang², David Burn³, Ray Chaudhuri⁴, Clare Galtrey⁵, Natalie Valle Guzman⁶, Bruce Hellman⁷, Ben James⁷, Suvankar Pal⁸, Jon Stamford⁹, Malcolm Steiger¹⁰, Simon Stott¹¹, James Teo¹², Roger Barker¹³, Emma Wang¹⁴, Bas Bloem¹⁵, Martijn van der Eijk¹⁵, Lynn Rochester¹⁶, Adrian Williams¹⁷

¹ London, United Kingdom

² Liverpool School of Tropical Medicine, Liverpool, United Kingdom

³ Newcastle-upon-Tyne Hospitals NHS Foundation Trust, London, United Kingdom

⁴ King's College Hospital NHS Foundation Trust, London, United Kingdom

⁵ St George's Healthcare Trust, London, United Kingdom

⁶ John van Geest Centre for Brain Repair, Cambridge, United Kingdom

⁷ uMotif, London, United Kingdom

⁸ NHS Forth Valley, Scotland, United Kingdom

⁹ Cure Parkinson's Trust, London, United Kingdom

¹⁰ The Walton Centre NHS Foundation Trust, Liverpool, United Kingdom

¹¹ John van Geest Centre for Brain Repair, Cambridge, United Kingdom

¹² King's College Hospital NHS Foundation, London, United Kingdom

¹³ John van Geest Centre for Brain Repair & Cambridge University Hospitals NHS Trust, Cambridge, United Kingdom

¹⁴ Queen Mary University of London, London, United Kingdom

¹⁵ Radboud University Medical Center, Netherlands

¹⁶ Newcastle-upon-Tyne Hospitals NHS Foundation Trust, Newcastle-upon-Tyne, United Kingdom

¹⁷ University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom

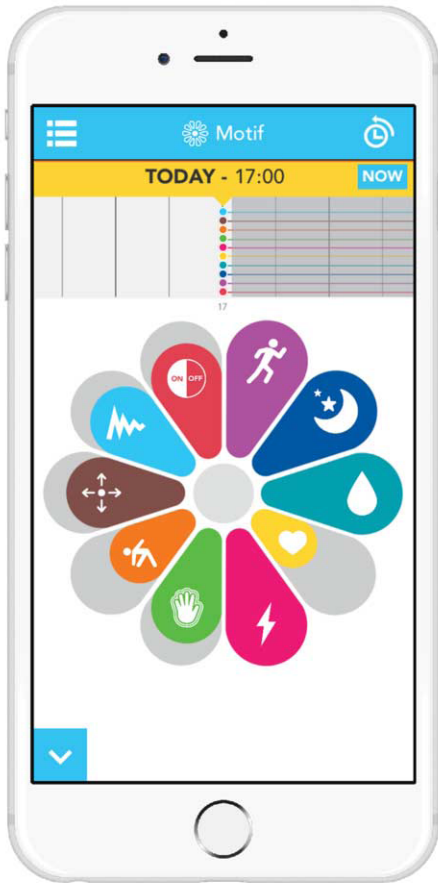
Background: The progressive nature of Parkinson's disease (PD), its complex treatment regimens and the high rates of comorbid conditions make self-management and treatment adherence a challenge. Clinicians have limited face-to-face consultation time with PD patients, making it difficult to comprehensively address non-adherence. A multi-centre (7 centres) randomised controlled trial was conducted in England and Scotland to assess the impact of using a smartphone based Parkinson's Tracker App (PTA) to promote patient self-management, enhance treatment adherence and quality of clinical consultation.

Methods: Eligible PD patients were randomised using a 1:1 ratio according to a computer-generated random sequence, stratified by centre and using blocks of variable size, to intervention (PTA) or control (Treatment as Usual, TAU). Primary outcome was the score of adherence to treatment (Morisky Medication Adherence Scale -8) at 16 weeks. Secondary outcomes were Quality of Life (QoL) (Parkinson's Disease Questionnaire -39), quality of consultation for PD patients (Patient-Centered Questionnaire for PD), impact on non-motor symptoms (Non-Motor Symptoms Questionnaire – NMS Quest), depression and anxiety (Hospital Anxiety and Depression Scale) and beliefs about medication (Beliefs about Medication Questionnaire) at 16 weeks. Primary and secondary endpoints were analysed using a generalised linear model with treatment as the fixed effect and baseline measurement as the covariate.

Results: 156 patients completed the study (PTA=68 and TAU=88). At 16 weeks PTA significantly improved adherence, compared to TAU (mean difference: 0.39, 95%CI 0.04 to 0.74; p=0.0304) with no confounding effects of gender, number of comorbidities and age. Among secondary outcomes PTA significantly improved patients' perception of quality of consultation (0.15, 95%CI 0.03 to 0.27; p=0.0110). There was a borderline significant change in the non-motor symptoms (-0.82, 95%CI -1.75 to 0.10; p=0.0822). 79% of participants in the PTA group continued to use and engage with the application throughout the 16-week trial period.

Conclusions: The PTA can be an effective and novel way of enhancing medication adherence and quality of clinical consultation by supporting self-management in PD.

Keywords: Long-term conditions; mhealth; mobile application; Parkinson's disease; patient centered care; self-management



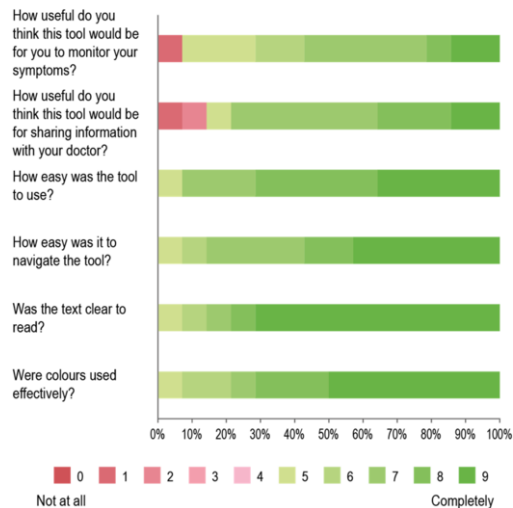
utilisation. A results dashboard allows clinicians to remotely monitor and manage PwP who consent to use P-OLAT.

P-OLAT was presented to UK Parkinson's support groups (Oct 2015–Feb 2016). PwP volunteered to test the tool in their home environment and were given a questionnaire to evaluate its usability and value.

Results: 15 participants completed the questionnaire. 60% were female; 53% aged 70–80 yrs, 27% 60–70 yrs, 13% 80+ yrs. Mean (SD) duration of symptoms related to Parkinson's was 8.7 (6.6) yrs. Most participants accessed the internet at least daily. One participant could not access the tool. For the 14 remaining participants, 50% accessed P-OLAT via desktop computer, 43% laptop, 7% tablet/iPad. 21% required assistance from a family member, 7% from a carer.

Overall, participants rated the tool highly in terms of symptom assessment, sharing information with their clinician, and ease of use (Figure). Participants were generally happy with clinicians using information from online technologies for research or patient care (mean [SD] ratings [0–9 scale; 0=not at all, 9=completely] were: 7.3 [2.1] and 6.7 [2.4], respectively). There appeared to be no association between frequency/method of internet access and these responses. 4 participants experienced minor data entry problems. Qualitative feedback was positive and users were able to provide suggestions for improvement.

Pilot study participant ratings on the usability and value of the Parkinson's online audit tool



P37.17

An online audit tool for people living with Parkinson's: results of a pilot study

Romi Saha¹, Kamal Kishore², Vincenzo Straccia³

¹ Brighton and Sussex University Hospitals NHS Trust, Brighton, United Kingdom

² Health iQ, London, United Kingdom

³ UCB Pharma, Slough, United Kingdom

Objective: Quality of life (QoL) measures and insight into healthcare resource utilisation are important in the management of People with Parkinson's (PwP). This pilot study examines PwP assessment of the utility of an online audit tool which enables clinicians to collect real-time, reliable feedback to improve PwP care.

Methods: An online version of a paper-based audit tool (developed by UCB Pharma) was designed by Health iQ as a browser-based application (not for smartphone use). This tool, P-OLAT, for PwP includes an electronic version of the validated PDQ-39 QoL questionnaire (licensed from ISIS Innovation Ltd), alongside questions on medication compliance and healthcare resource

Conclusion: This pilot study of P-OLAT in a real-life clinical setting indicates that it is intuitive, easy to use, useful for monitoring symptoms, and for sharing this information with treating clinicians. Further assessment of the tool once launched will reveal if real-time data on QoL, health resource utilisation, adherence and overall health could lead to improved care and self-management for PwP.

Funding: UCB Pharma

P37.18

Feasibility of long-term deployment of wearable sensors in Parkinson's disease: the Parkinson@home study

Ana Lúcia Silva de Lima^{1,2,3}, Tim Hahn², Luc Evers², Kariene Hoogeweg², Nienke M de Vries², Bastiaan R Bloem^{1,2}, Marjan J Faber⁴

¹ Radboud university medical center, Donders Institute for Brain, Cognition and Behavior, Nijmegen, the Netherlands

² Radboud university medical center, Department of Neurology, Nijmegen, the Netherlands

³ CAPES Foundation, Ministry of Education of Brazil, Brasília/DF, Brazil

⁴ Radboud university medical center, Radboud Institute for Health Sciences, Scientific Center for Quality of Healthcare, Nijmegen, Netherlands

Background: Wearable devices can collect data about everyday life. In people with Parkinson's disease (PPD), day-to-day information, e.g. physical activity and medication intake, can help healthcare professionals to improve medical management. Here we aim to evaluate the feasibility of using multiple wearable sensors to collect data during PPD lives.

Methods: The Parkinson@home study is a two phase observational study aiming to include 1,000 Dutch PPD. Inclusion criteria were kept broad: diagnosed PPD and age >30 years. To reach potential participants, different strategies, e.g. mass media and personal invitations by physiotherapists, were used. Participants wore a set of sensors (smartwatch and fall detector), and used them in combination with a smartphone app, 24/7, during 13 weeks. The sensors were used to estimate physical activity, tremor, falls and sleep. Medication intake was collected via self-reports in the app. In phase one of the study, we evaluated feasibility and compliance by calculating participation rate, drop-out rate, streaming compliance, and questioning usability.

Results: Within nine months of recruitment the Parkinson@home study received 1,148 applications. Among those invited for phase one (n=345), participation rate was 88%. A total of 42 participants refused to participate mainly due to personal issues (36%; n=15) or the perceived burden of wearing multiple sensors continuously during a prolonged period (19%, n=8). During the follow-up, 12% (n=38) of the participants dropped out, mostly due to personal circumstances (38%, n=12) or experiencing too many technical problems (26%, n=10). Mean streaming compliance was 66% (SD=26%), generating 20,3378 hours of data. The system usability was rated as moderate. From the 108 participants who completed the usability survey, 45% wanted to continue after finishing the follow-up phase. The most important reasons to continue were contributing to science (30%), contributing to further developments (30%), and experiencing usefulness of the sensors for themselves (25%). A smaller percentage (9%) stated they wanted to continue to discuss the measurements with a healthcare professional.

Conclusions: The Parkinson@home trial shows that it is feasible to deploy wearable sensors for PPD. The system, which will be further developed in phase two of the Parkinson@home study, is a promising alternative to overcome the limitations in monitoring disease status and its impact on the lives of PPD.

P37.19

Sensor technology for real-time management of Parkinson's patients' treatment regimen

Yosef Tirat-Gefen

Castel Research Inc., Fairfax, VA, USA

This work evaluates the use of wearable sensors to monitor, collect and analyse health data from Parkinson's patients, with the goal to provide better management of their medication regime and physical therapy and exercise routines. Wearable sensors originally designed to collect performance data from professional athletes in real time are becoming less expensive, and within reach for mass use in clinical scenarios. Current technologies in mobile phones and their apps enable these sensors to be networked with a smart cell phone, which effectively becomes a medical device. The effect of L-Dopa and other Parkinson's medication can be inferred in real-time by measures the body mechanics of the patient: tremors, muscle rigidity, unwanted body movements; in addition to alterations of the voice pitch, and feedback from caregivers. All these measurements

and caregiver's feedback can be easily collected using a smart cell phone linked to wearable network of sensors. We discuss the possibilities of these technologies, available technical solutions being brought to the market, possible algorithms for data fusion of all these measurements, their safety and efficacy in a closed loop mode, i.e. a medical doctor using them to adjust the Parkinson's patient on daily or hourly basis. Even in an open loop configuration, these sensors can give meaningful feedback to medical doctors to adjust the medication for medium or long term, and to physical therapists and Parkinson's savvy fitness trainers to fine tune physical exercise regime on a weekly or monthly basis by providing data about the patients as they go through their activities of daily living and sleep cycles.

P37.20

Tremor severity estimation using Liftware instrumented eating utensil

Sarah Wang¹, Ali Shoeb², Svjetlana Miocinovic¹, Nicole C. Swann¹, Erica S. Swann¹, Anupam Pathak², Jill L. Ostrem¹

¹ University of California San Francisco, San Francisco, CA, USA

² Verily Life Sciences, Mountain View, CA, USA

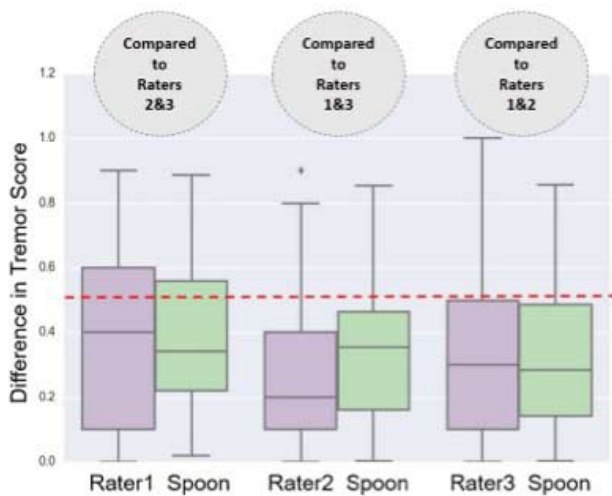
Objective: 1. Demonstrate the feasibility of accurately estimating clinical tremor severity using an eating utensil (Liftware spoon, Verily Life Sciences) capable of measuring and compensating hand tremor. 2. Assess spoon utility based on task performance (food spillage).

Background: Essential tremor (ET) and Parkinson's disease (PD) cause postural and action tremor that can severely limit person's ability to eat and thus significantly decrease quality of life. In current clinical practice, tremor is assessed in the clinic commonly by tremor rating scales and less often with tremor analysis. Tools for assessing symptoms outside the clinic are limited. An eating utensil that compensates for tremor and is capable of accurately estimating tremor severity can provide direct benefit to patients with upper limb tremor, and would allow for practical and daily tremor assessments.

Methods: Thirteen subjects (9M/4F, 8PD/5ET, ages 69±6.5) performed two tasks (moving food from bowl to mouth, and transferring food between two bowls) using a Liftware spoon with tremor-cancellation and motion sensing technology, while tremor-compensating features were on and off. Three movement disorders neurologists reviewed randomized video segments of each trial and rated the hand tremor severity. A machine-learning model that estimates tremor severity using features of the recorded motion signals was trained on neurologist ratings. Each neurologist's performance was compared to the model algorithm. Food spillage as a function of the tremor-compensating feature being on/off was also evaluated.

Results: The average neurologist score was 1.6±0.9 for PD and 2.6±0.8 for ET. The average model score was 1.5±0.7 for PD and 2.7±0.7 for ET. The coefficient of determination (R²) between the model and the average neurologist score was 0.74-0.80. R² between each neurologist and average of the two other neurologists' score was 0.69-0.78. The mean-absolute difference between the model and neurologist scores was comparable for all three raters. Food spillage scores were higher when the spoon was off for eating (2.29±1.38 off; 1.86±1.07 on) and for transferring (1.67±0.82 off; 1.00±0.89 on).

Conclusions: Liftware spoon can compensate for tremor and reduce spillage, and can also accurately estimate clinical tremor severity scores during eating and transferring tasks, which enables daily assessment of tremor and has the potential to enhance clinical care and research study assessments.



P37.21

Development and evaluation of a social robot to assist in a medication management task

Jason Wilson, Linda Tickle-Degnen, Matthias Scheutz
Tufts University, Medford, MA, USA

Background: People with Parkinson's disease (PD) manage a complicated medication regime. Social robotics is an innovative area of assistive technology which occupational therapists (OT) could use to help people with PD participate safely and competently in their daily routines. This study's objective was to begin to design and test a social robot for the purpose of assisting the cognitive performance of a medication sorting task.

Methods: First, four expert OT's evaluated the validity of a standardized medication sorting task as a typical daily life task for PD, and the feasibility of a robot assisting with this task in the home. The OTs watched a video of a two people doing the standardized medication sorting task and examined a task analysis of the performance. They completed a questionnaire, and engaged in a focus group. Data were analyzed quantitatively and qualitatively. Second, based on these findings, we developed a social robot to instruct people in the medication task. University students (N=11) placed pills (candy) on a sorting grid by following the verbal and gestural task instructions of the robot. Each participant then completed a questionnaire to evaluate the robot. Questionnaire items were formed into composites using principal components analysis, and resulting scores were analyzed.

Results: OT experts rated the medication task as an important self-care activity for people with PD. They described robots as potentially valuable for educating clients in medication management. They stated that the complexity of the task would need to be increased to match what would occur in the home. In phase 2, responses by participants who interacted with the robot fell within three components: the robot's ability to (1) perform correctly and reliably; (2) support the person feeling included and responsible for task completion; and (3) support a positive emotional experience. The highest scores were in component 2, suggesting the robot maintained the person's dignity and feelings of competence. The lowest scores were in component 1, indicating the need to improve the robot's performance as a reliable assistant.

Implications: A social robot appears to be feasible for assisting medication self-management. Future development must increase its reliability and its ability to handle complex medication management.

P37.22

Tablet-based application (iMotor) for objective measurement of motor fluctuations in Parkinson's disease

Benjamin Wissel¹, Georgia Mitsi², Alok Dwivedi³, Spyridon Papapetropoulos⁴, Sydney Larkin¹, Ricardo Lopez Castellanos¹, Andrew Duker¹, Ioannis Tsoulos⁵, Athanassios Stavrakoudis⁶, Alberto Espay¹

¹ Gardner Family Center for Parkinson's Disease and Movement Disorders, Department of Neurology, University of Cincinnati, Cincinnati, OH, USA

² Apptomics LLC, Wellesley, MA, USA

³ Division of Biostatistics & Epidemiology, Department of Biomedical Sciences, Texas Tech University Health Sciences Center, El Paso, TX, USA

⁴ Department of Neurology, Massachusetts General Hospital, Boston, MA, USA

⁵ Department of Informatics and Telecommunications, Technological Educational Institute of Epirus, Greece

⁶ Department of Economics, University of Ioannina, Greece

Background: MDS-UPDRS-Part III has been useful for the assessment of motor function in Parkinson's disease (PD). However, its restriction to in-clinic evaluations and variable inter-rater reliability affects its utility. A tablet-based app may complement measurement, reduce noise, and allow for in-home assessments.

Objective: To assess whether the tablet-based iMotor app can objectively and reliably quantify differences in motor performance in PD-associated ON (maximal dopaminergic efficacy) and OFF (reemergence of parkinsonian deficits) medication states.

Methods: Eleven PD patients undergoing ON/OFF assessments for deep-brain stimulation surgery eligibility (age, 60.6±9.0 years; disease duration, 12.8±4.1 years) and 11 healthy age-matched volunteers (age, 62.5±10.5 years) were prospectively enrolled. Patients completed two-target and pronation-supination tests during their ON and OFF states. Total number of taps, tap interval (time [ms] between two consecutive taps) and tap accuracy (distance [pixels] from center of target) were algorithmically calculated for the most affected PD side and dominant hand for controls.

Results: The two-target test showed patients performed significantly better in the ON state in total number of taps (84.2±20.3 vs. 54.9±26.9 taps; p=0.0036) and tap interval (375.3±97.2 vs. 708.2 ms±412.8; p=0.0146), but had poorer tap accuracy (2008.4±995.7 vs. 1111.8±901.3 pixels; p=0.0055) compared to the OFF state. Patients performed significantly better on the pronation-supination test in the ON state in total number of taps (78.1±20.2 vs. 54.9±20.8 taps; p=0.0027) and tap interval (408.6±112.2 vs. 649.9±386.5 ms; p=0.0315). Tap accuracy was not assessed with the pronation-supination test. Tapping test-retest reliability was high (r>0.75). Tapping data moderately correlated with MDS-UPDRS-Part III scores. The satisfaction survey revealed 6 (55%) patients thought iMotor was very easy, 4 (36%) thought it was fairly easy, and 1 (9%) thought it was somewhat easy to use.

Conclusions: iMotor can accurately distinguish between ON and OFF states in PD patients and may discriminate aspects of movement about which the UPDRS is less sensitive.

LIVING WITH PARKINSON'S: PUBLIC EDUCATION OR AWARENESS PROGRAMS

P38.01

#Parkinsons1Day: an experiment in Parkinson's empathy training

Gretchen Church, Michael Church
Movers & Shakers Inc., Naples, FL, USA

Background: #Parkinsons1Day was hosted by Smart Patients, an online community for all types of diseases, with intent of pairing a person with PD & a person without Parkinson's (PWOP) to help them feel what a day in the life was like having to deal with PD. This was the second "Day in the life" Smart Patients had done. The first being Cystic Fibrosis. Smart Patients paired people with PD with people who worked in either the Parkinson's Community/Health Industry that did not have PD. This was done throughout the world.

Aim/Objective:

- Raise awareness and empathy about many issues that people with Parkinson's (PWP) disease face daily.
- Learn from whole body activities, not just verbal descriptions
- Experience the physical limitations that PWP face: tremor, gait issues, limbs not working, freezing, etc.
- Real time communication using email, Twitter, and Skype.
- Show PD is different in all people.
- Make it duplicatable so other groups can do the same in the future

Methods: Smart Patient selected teams of a PWP (teacher) and a PWOP (learner).

- Each team had a pre-#Parkinsons1day meeting via Skype, Phone, or other form of communication to get to know each other.
- A kit was sent to the learner that included ankle weights, and dishwashing gloves
- Some PWP suggested other ways to experience PD.
- Presentation:
- #Parkinsons1day became the hashtag on Twitter that was used throughout the events as a way of communication not only between the teacher/learner but to show followers each teams "Day".
- Facebook & Instagram were also used for communication and sharing of #Parkinsons1Day.

Results:

- Learners had greater understanding/empathy for those battling PD.
- Followers on Social Media gained greater knowledge about PD and differences.
- The outpouring of ideas of how to improve #Parkinsons1day was incredible.

Discussions/Conclusions: The conclusion is that this is something that will be done again. We intend to reach more people and implement more items into the "PDkit". We would like to use it for medical students, first responders, family members, & researchers that often do not see PWP. The WPC will host a Roundtable about #Parkinsons1day, & there will be demonstrations at the WPC welcome table.

P38.02

444 Parkinson's Traveler: example impact of a personal Parkinson's awareness campaign

Marcus Cranston
Las Vegas, NV, USA

Objective: Four years after being diagnosed with Parkinson's disease at the age of 44, I planned a personal travel and running challenge. In addition, I created a social media presence under the title, 444 Parkinson's Traveler. My aim was to leverage publicity garnered by my journey and website writing to raise awareness and funding for Parkinson's disease.

Methods: In 2014, I ran 4 miles in 44 countries in 4 weeks for a quest I titled, Run-the-World 4 Parkinson's. My project, Run-the-Caribbean 4 Parkinson's, involved running 55 miles to cross 5 islands in 5 days in 2015. My current project is Swim-the-Pacific 4 Parkinson's, an attempt to swim 1 mile in 11 remote Pacific island nations. These ventures have been used to raise Parkinson's awareness through social media exposure, print and broadcast media coverage and live presentations delivered to Parkinson's support groups and medical providers.

Results: In two years, April 2014 – April 2016, 444 Parkinson's Traveler's impact on Parkinson's awareness and fund-raising has included:

- Greater than 46,000 page views for the website, 444ParkinsonsTraveler.org
- Over 870 people following the Facebook page, 444 Parkinson's Traveler
- 32 print and online media articles, appearing in 11 countries
- 5 radio and television broadcast segments, appearing in 4 countries
- Live presentations addressing over 1,800 Parkinson's support group members and medical providers in 17 countries
- Over \$4,000 donated to the Michael J Fox Foundation to support Parkinson's research through Team Fox
- \$5,000 donated to support the World Parkinson Congress travel grant program

Conclusion: Personal pursuits, especially physical challenges, have frequently been employed in efforts to raise awareness and/or funding for disease-related programs. The creation of 444 Parkinson's Traveler and utilization of the public attention given to my personal travel and exercise endeavors demonstrates the potential impact of a personal campaign on awareness and funding for Parkinson's disease.

P38.03

A new perspective of Parkinson People – a photographic exhibition

Sandra Elms
Newcastle Parkinson's Support Group. NSW Australia, Newcastle, NSW, Australia

Background: Parkinson's disease is characterised by people stiff, shuffling and shaking with hypomimic faces. This is the image of the general public. But behind these masks lie people actively engaged in artistic, sporting and fitness projects, which belie the stereotypical image of this disease.

Aim: To attract the attention of the general public to types of activities that PD sufferers can and do carry out. To illustrate how people with PD are doing things that was not part of their lives before. To show the strength and courage of these people. To demonstrate to others with PD the range of pursuits that are available. To provide an opportunity for discussion of ways that providers can help with PD. To show by photographic means amusing, inspirational, fitness documentation what people with PD have achieved.

Method: I intend to take photos of people engaged in activities and have already begun, such as Painting, zooming on hands, sculpture, yoga, Pilates, PD Warrior, dancing, singing, tennis and cycling. Photos will be single shots or a collage of an activity. Black and white, presented in same format, aided by Newcastle Tafe. Display card with information of person doing activity (consent

obtained). Exhibits collated by Photography specialist who is also aiding technique. Exhibition held in public space, ie Library, University Gallery.

Publicity – Newspapers, Radio stations ABC/commercial, Posters, Newcastle Hospital, GP surgeries, PD websites and newsletters

Opening Night – local dignitaries, Politicians (State and Federal members of Parliament) Medical people, PD sufferers, general public and people involved in project.

Outcomes: Raise awareness, change stereotype view of PD. Raise funds for activities for PD people so more people can participate. Lobby State and Federal governments for medical funds such as for more Parkinson nurses. Encourage others with PD to participate in activities, shown to have a remarkable effect on the mental and physical health of Parkinson's people.

P38.04

How are we going to tell the children? An overview and review of the children's literature about Parkinson's disease.

Adele Hensley

Clinton, Mississippi, USA

It may seem that Parkinson's disease is far removed from the lives of children, but according to the Parkinson's Disease Foundation 7-10 million people worldwide are living with Parkinson's, and four percent of all of those develop the condition before the age of 50. So with approximately 28,000-400,000 cases of young onset Parkinson's disease, many of whom are in their prime parenting years, some of them are still the parents of children. Add to that the fact that the average age of first onset of Parkinson's is sixty and the fact that in the forty years from 1970 to 2010, the number of households in the USA where grandparents are rearing grandchildren more than doubled from 3% to 7%. Parkinson's has many opportunities to affect the lives of children.

Although a diagnosis of Parkinson's disease in one of as child's primary caregivers can be frightening for children because of their expectations and because the unknown. Even so children are remarkably resilient. A child's ability to comfort him or her self using tools that he or she already knows, such as songs, prayers, and physical exercise, is almost as surprising as the child's ability to offer comfort to others. But first the child needs to know what is wrong with the person he or she loves.

Each book I am including in this annotated bibliography can be a starting point for a conversation about Parkinson's with a child. Some are about more general topics, such as what is parkinson's, or a person's diagnosis. Some are about more specific topics, such as deep brain stimulation surgery, or anxiety. Some are about a child's parents, others about grandparents. Books range from heavily factual to mostly fictional.

Each entry in the list of books will include a recommended age or reading level. Notes on the book itself, such as: Is it a story or more of a reference book? Whether it is for children grandchildren of person living with Parkinson's, and if it is about a topic of special interest, I will include notes about the theme of each book, with suggested points for discussion. I will note which books are readily available for purchase and which are out of print.

P38.05

The Parkinson's disease wellbeing program: translating information into action

Jeremey Home, Megan Campbell, Sue Harkness

Calvary Health Care Kogarah, Kogarah, Sydney, NSW, Australia

Aim: Parkinson's disease (PD) incidence is rising at a rate of 3% per year in Australia, yet remains inadequately serviced by the

health system. Early intervention through a structured group education and exercise program has the potential to enable people with Parkinson's (PwP) to receive timely, multidisciplinary care rather than delayed reactive management. Education and exercise instruction is empowering and the social dynamics of a group setting can contribute to positive outcomes for PwP. Proactive intervention promotes client engagement and aims to maximize health, establish strategies for symptom management and prevent inactivity related decline.

Method: PD clients (Hoehn-Yahr stage 1-3, MMSE >24) were invited to attend a Parkinson's disease Wellbeing program (PWbP). The 5 week multidisciplinary program conducted in a day rehabilitation unit consisted of 2 x 2.5 hour weekly sessions including group education and exercise for 6-8 clients per session. Detailed allied health assessment was conducted at the commencement and completion of the 5 week PWbP and at 12 months.

Results: Results from 135 patients (M:97; F:38); (Age: mean 70; range 30-91) revealed significant improvements (P-value <0.01) in walking endurance, gait speed, sit to stand, timed up and go, balance and grip strength. In addition, a 50% reduction in falls and a 30% increase in planned exercise participation was reported. Psychosocial measures including quality of life (PDQ-39); fatigue (PSF-16) and mood (DASS-21) all improved significantly (P-value <0.01). Clients also improved their knowledge of PD (P-value <0.01). These benefits were being sustained at 12 months post discharge.

Conclusion: The PWbP has conferred significant and sustained benefit in this cohort of PwP in relation to motor function, quality of life, mood and knowledge about their disease. While early information can be confronting, through greater understanding and involvement, PwP can learn to translate information into an active life where they participate, contribute and belong.

Reference:

[1] Deloitte Access Economics, Living with Parkinson's Disease-Update August 2015

P38.06

Benefits of open classes for educating patients with Parkinson's disease and caregivers

Kenichi Kashihara¹, Michio Kitayama², Toshikazu Hamaguchi²

¹ Okayama, Japan

² MD, Okayama, Japan

Parkinson's disease (PD) is a chronic slowly progressive disease that can cause severe disability. Information about this disease may be used to provide patients and caregivers with tips to improve the quality of their lives. In order to facilitate understanding of PD for patients and their caregivers, we have conducted open classes about various aspects of PD, twice a year for more than 10 years.

In order to evaluate the effects of open classes for PD patients and caregivers, we asked attendees if the class was helpful in improving their knowledge of PD and if it facilitated daily exercise at home.

We asked the attendees of an open class, held in August, 2015 in Okayama, to answer several questions on PD. In this open class, there were two lectures and exercise sessions over two hours. Lecture themes were "tips to live with PD" and "recent advances in iPS cell therapy for PD." Around 300 people attended the class.

113 attendees answered the questions. Respondents consisted of 48 men and 65 women, and of 64 patients and 47 caregivers. Regarding motor symptoms, more than a half of respondents answered that tremor, bradykinesia, rigidity, and fall were well known symptoms. On the other hand, they reported learning for the first time in the class that freezing gait, dyskinesia, and wearing-off were symptoms. Among non-motor symptoms, more than a half of the attendants reported constipation, urinary problem, cognitive

impairment, hallucinations, depression, apathy, sleep disturbance, and hypersalivation as symptoms that can emerge in PD. On the other hand, less than a half of participants recognized anosmia, sexual problems, orthostatic hypotension, drenching sweat, disturbed peripheral circulation, leg edema, and excessive daytime sleepiness as possible PD symptoms. In total, 97 patients answered that the open class was satisfactory and 101 attendants reported that the session helped them learn to live with PD. The majority of participants answered that they understood the importance of exercise at home and wished to continue exercising during daily activities. The majority of participants also reported experiencing reduced anxiety about living with PD or caring for PD patients after attending the class.

In conclusion, providing information on PD symptoms and treatment by an open class may be useful to increase understanding of PD and reduce anxiety about living with PD for both PD patients and caregivers.

P38.07

A Learning community for nursing faculty: dissemination and the discovery of caring for people living with Parkinson's disease

Margaret McCormick

Towson University, Towson, Maryland, USA

Background: A community of practice is a group of people who share a common concern, set of problems or a passion about a topic. The members of this community deepen their knowledge and expertise by interacting on an ongoing basis. Members of such a community develop a shared repertoire of experiences, stories, tools and ways of addressing recurring problems that constitute the collective knowledge and memory for the group. Cultivating these connections provide a social context in which educators can share clinical cases, listen, reflect and share an ongoing concern about the state of caring for Parkinson's disease.

Purpose: the aim of this study is to explore how the V.N.F. program promotes the universality of caring in the areas of education, research and practice. The Edmond J. Safra Visiting Nurse Faculty (V.N.F.) Program is an educational program for nursing faculty which serves as a platform to update faculty on the latest research and explores how nursing can take a leadership role in the care of people living with Parkinson's disease.

Methods: Faculty must apply for to participate in the C.E.U. approved program and attend the required didactic sessions, clinical hours, participate in support group sessions and complete an independent project. Following the program, faculty can access the website for the V.N.F. <http://www.parkinsonsnursing.com> which provides access to faculty resources and independent projects completed by the program participants.

Results and conclusions: The importance of well-prepared graduate professional is critically important particularly in those chronic diseases such as Parkinson's disease where nurse patient ratios are often stretched to their limits. A learning community can effectively to add to the overall advancement of nursing science and caring between faculty, students and researchers. Educators can become active elements in the discovery process and dissemination of caring science by increasing their student's ability to engage in thoughtful discourse about Parkinson's disease.

P38.08

Improving nursing education on Parkinson's disease

Gwyn Vernon^{1,2}, Diane Ellis^{1,3}

¹ Edmond J. Safra Visiting Nurse Faculty Program at the Parkinson's Disease Foundation, Villanova, PA, USA

² University of PA Parkinson's Disease and Movement Disorders Center at the Pennsylvania Hospital, Philadelphia, PA, USA

³ Villanova University College of Nursing, Villanova, PA, USA

Traditionally Parkinson's disease (PD) content does not receive the attention it should in nursing school curriculum (unpublished study Vernon and Bunting Perry, 2008). This is changing through the efforts of the Edmond J. Safra Visiting Nurse Faculty Program at the Parkinson's Disease Foundation. Since its inception in 2009, over 200 nurse faculty scholars representing over 100 schools of nursing have integrated Parkinson's disease content into curriculums. They learn from experts in PD, and in turn are teaching over 11,000 nursing students per year. However, the work of these scholars goes beyond the classroom into the general nursing community through their scholarly articles in peer reviewed journals, nursing research projects, and new nursing care models. This presentation will present a sample of highlights of the work of nurse alumni scholars of the Edmond J. Safra Visiting Nurse Faculty Program at the Parkinson's Disease Foundation.

P38.09

The PD Buddy Outreach Program – the student perspective

Sarah Mufti¹, Denise Cumberland¹, Ann Shaw¹, Susan Sawning¹, Erika Branch², Allie Hanson², Kathrin LaFaver¹

¹ University of Louisville, Louisville, KY, USA

² Parkinson Support Center of Kentuckiana (PSCKY), Louisville, KY, USA

Objectives: The PD Buddy Outreach Program is designed to create a community outreach between Parkinson's disease (PD) patients and first year medical students. The objectives of this nine-month intervention are twofold: 1) to impact patients' social connections and decrease the sense of isolation that can occur when a disease affects motors and verbal skills and 2) to improve first-year medical students' knowledge about PD and shift attitudes about patients suffering from PD. This abstract will focus on the student portion of the intervention.

Methods: Twenty-five first-year medical students were recruited from University of Louisville Medical School and paired with PD patients. The program was offered as a community-based volunteering experience. Students completed the following pre-post surveys: 1) a 25-item knowledge test about PD and 2) a modified version of the Geriatric Attitude Scale (GAS). Students and patients met in one-on-one meetings on a monthly basis to engage in shared activities and were asked to reflect about their experiences in a journal. Students also received monthly lectures and mentoring sessions about Parkinson's disease. At the completion of the program, a relationship survey gathered information on the number of times interacted, activities enjoyed, as well as attitudes about their buddy relationship. In addition, three focus groups were used to understand the relationship evolution and how the program could be improved.

Results: Students improved their PD knowledge scores from 14.2 to 19.3/25 points from pre- to post-test (20.5%, $p < 0.05$). Attitude scores towards PD patients were high at baseline and did not improve further. Students and patients were actively engaged throughout the program and rated the experience as overwhelmingly positive on a qualitative level.

Conclusions: The PD Buddy Outreach program is designed as an unique opportunity for first-year medical students to interact with patients suffering from a chronic neurologic disease on a personal level. We have shown that the program improved students' knowledge about PD and provided an enjoyable experience for students and participating patients.

The poster will cover the following:

- Aims of the PD Buddy Outreach Program

- Methodology
- Results: including
 - Pre-post questionnaires (PD knowledge test and GAS)
 - Buddy Program Relationship Survey
 - Student Focus Groups
- Next Steps

P38.10

My PD Journey

Knut-Johan Onarheim¹, Lizzie Graham², Susanna Lindvall²

¹ European Parkinson's Disease Association (EPDA), Sevenoaks, Kent, United Kingdom

² European Parkinson's Disease Association (EPDA), London, United Kingdom

My PD Journey is a pan-European, multi-stakeholder coalition of umbrella patient organisations, key Parkinson's disease specialists and treatment companies, led by the European Parkinson's Disease Association (EPDA).

The objective is to create a sustainable environment that ensures people with Parkinson's (PwP) receive optimal and timely access to diagnosis, treatment and care throughout the progression of their disease.

This has been achieved in part, thanks to the largest piece of qualitative and quantitative research into the needs and views of PwPs ever undertaken in Europe, with almost 1,800 respondents.

This research led to a European Inventory which detailed (a) where gaps in Parkinson's care pathways exist, whilst (b) highlighting examples of good practice which could be replicated elsewhere to address those gaps. These examples were then used to develop European good practice guidelines, which have been supported by patient groups and clinical bodies such as the European branch of the Movement Disorder Society.

At a European level, further solutions to barriers for patients to access treatment, care and support were developed through the creation of a new and easy-to-use composite scale. This is the first time such a scale has been developed and will be useful to clinicians, patients and policy makers in assessing disease severity of PD patients. This innovative composite scale has been created by key PD specialists from across Europe on behalf of the My PD Journey coalition.

Furthermore, this pan-European coalition sought to foster grass-roots actions and has driven the development of national coalitions of patient groups, clinicians, policy makers, payers and treatment companies, with the aim of implementing pilots to address the needs identified in the European research. These pilots will be evaluated and form the basis for the local coalitions to engage in political lobbying at national and European levels to create sustainable change for PwPs. The aim is simple and pragmatic: to present policymakers with evaluated solutions that meet the identified needs of PwPs, rather than focussing solely on the problems. As a result of the European My PD Journey research, national coalitions now exist in 11 European countries.

My PD Journey is a clear example of how bringing different stakeholders together can achieve real and sustainable change to improve the lives of PwPs.

P38.11

Community-based Alexander Technique programming designed and delivered by Parkinson's patient

Paul Recker, AmSAT

Person with Parkinson's, Ellington CT; The Poise Project, Asheville NC, Ellington, Connecticut, USA

Objectives: As a person with Parkinson's disease (PD) and an Alexander Technique (AT) teacher, to lead community-based workshops for others with PD in applying AT principles in their exercise classes and daily activities. To advise in the design of continuing education courses for medical professionals, such as physical therapists, occupational therapists, social workers and neurologists, in how to use the AT principles in their interactions with their PD patients and clients.

Background: I was certified as an AT teacher in 2008, completing a 3-year training program at Alexander Technique School of New England. In 2013, I was diagnosed with Parkinson's disease. Living with PD, I had to make a choice about where to put my limited energy. I now raise awareness in my local health care community about the benefits of AT principles for people with PD to increase their ease, efficiency and confidence in exercise programs, rehab sessions and daily activities.

Methods: AT is a method to teach self-management skills and enhanced self-awareness with greater attention on internal organization and improved spatial awareness. People with PD can learn practical strategies to be more aware when they become anxious and tense, to pause long enough to release and return to balance, and to then keep attention on their coordination while they carry out their exercise program or other activity. I will teach AT to people with PD in existing exercise programs in my region, such as the Rock Steady Boxing affiliate program in East Hartford CT, and I will work with The Poise Project to design AT based courses for people with PD and their care partners, and continuing education courses for medical professionals who work with people with PD. The Poise Project is an initiative to increase the reach of the educational principles of AT to preserve natural poise in youth and restore natural poise in adults. As part of their mission, they create programs adapted for specific populations. They use a coordinated team approach uniting AT professionals, individuals who have benefited from AT, and industry experts.

Conclusion: As a person with Parkinson's and an AT teacher, I am in a unique position to advocate for the benefits of AT to my peers and to advise in the design and implementation of AT principle based programs for people with PD and the professionals who serve them. My presentation will show my current efforts in the field of public awareness of AT for PD within my regional community.

P38.12

What neurologists wish patients with Parkinson's disease knew

Rachel Schwartz, Meghan C. Halley

Palo Alto Medical Foundation Research Institute, Palo Alto, CA, USA

While much attention has been paid to empowering patients to become partners in their healthcare decisions, very few studies have explored, from the physician's perspective, what patient initiatives could enhance healthcare delivery. In this study, we interviewed 15 neurologists across 4 institutions in the San Francisco Bay Area to learn what Parkinson's disease (PD) patients and caregivers can do to improve neurologists' ability to provide optimal care. In this study, we explore neurologists' perspectives on: (a) how patients can learn to distinguish PD symptoms from medication side-effects, and which ones are frequently confused (b) what non-motor symptoms are important for patients to report (c) what treatments may be neuroprotective, and what actions patients can take to become partners in developing a treatment plan (d) cultural and gender differences in patients' experiences of PD, and how patients' awareness of this can influence the clinical interaction and (e) what neurologists wish lay people knew about PD that is not common knowledge. We provide descriptions of tools physicians have devised to help patients track and monitor symptoms, and

communication strategies neurologists feel would improve patients' ability to be appropriately medicated. The interviews provide insight on neurologists' perception of misconceptions about disease progression and treatment options, and offer hope for increased quality of life through better patient education and support services.

P38.13

ParkinsonWISE: Bridging the gap between medical care and community exercise programs for people with Parkinson's disease

Erin Vestal¹, Suketu Khandhar², Nancy Kretz³, Marianne Oliphant³, Jeanine Perry², Christine Shade¹

¹ The Permanente Medical Group, Roseville, CA, USA

² The Permanente Medical Group, Sacramento, CA, USA

³ Parkinson Association of Northern California, Sacramento, CA, USA

Objective: To educate non-medical fitness and wellness experts in the community to provide a continuity of care beyond medical care settings.

Methods: It is fairly well understood that in order to effectively manage motor and non-motor symptoms of Parkinson's disease, a tailored exercise program must complement prescribed medical care. However delivery and maintenance of supervised exercise programs often falls outside the boundaries of what medical care can provide. There often is a drop in compliance after a patient has been discharged from medical physical therapy. Patients then struggle to find appropriate exercise resources in the local community. Through a collaborative effort, a local movement disorders healthcare team, along with the local Parkinson's organization developed a Parkinson's disease educational symposium directed towards non-medical fitness experts in the community. With medical based education, fitness experts in the community can expand their knowledge and ability to assist in exercise programs to improve and maintain quality of life in this patient population. After completion of the course, fitness experts are certified "ParkinsonWISE" and are listed under local exercise resources in an on-line database. Patients, care partners and medical professionals can utilize these local resources to assist in locating and participating in exercise programs close to their neighborhoods.

Results: 45 individuals with various exercise backgrounds including personal trainers, yoga, Pilates, Tai Chi and dance instructors, Rock Steady Boxing coaches, PWR! certified instructors, music teachers and massage therapists participated and will be added to the resource for the Greater Sacramento Area.

Discussion: Although research supports long-term lifestyle exercise programs as beneficial in Parkinson's disease symptom management, the current health-care model faces limitations. Educating fitness professionals about Parkinson's disease and special considerations for exercise program development allows the medical and lay communities to bridge the gap in typical episodic care delivery.

P38.14

This is Parkinson's disease: an awareness campaign promoting the diversity of the diagnosed

Alicia Wrobel, Jean Blake

Parkinson Society British Columbia, Vancouver, BC, Canada

Statistics published from the Ministry of Health in 2014/2015, show there are over 13,300 British Columbians living with Parkinson's disease (PD), a number that is expected to increase 65% by 2031. With every year that passes, the need to draw attention to the incidence and prevalence of PD grows.

One of the first illustrations of Parkinson's disease was published in 1886, and since then, it has been widely understood as a disease that affects only the senior population, primarily characterized by shaking (tremor). This understanding is inaccurate, as PD does not discriminate based on age, gender, ethnicity, religion or sexual orientation. Failure to further educate the public, and change common misperceptions of the disease, may lead to ongoing stigmatization. Furthermore, as the incidence of PD increases, recognition of initial symptoms becomes integral to ensuring a timely diagnosis allowing for one to begin an effective treatment plan.

As a part of Parkinson's Awareness Month, Parkinson Society British Columbia (PSBC) developed a campaign that aimed to reshape the public's understanding of the disease by sharing real-life stories and photos of British Columbians living with PD. The intent was to demonstrate the diversity of the PD community in the belief that it strengthens the network of support.

Drawing inspiration from the "This is Parkinson's" exhibit by Norwegian videographer/photographer Anders Lienes, the Society worked with photographer Noah Asanias and graphic designer Brigitte Stermann to compose a series of posters & ads. Photographs were taken in black and white to assist in standing out from other ads. Furthermore, models were asked to bring "props" that visually demonstrated their varying personalities & interests. The finished pieces utilized simple statements to illustrate that one can live well with Parkinson's.

To distribute posters, PSBC partnered with the following groups: British Columbia Association of Kinesiologists, Physiotherapy Association of British Columbia, facilitators from our network of over 50 support groups across the province, health authorities, clinics and hospital and community centres. PSBC also ran a series of ads on transit in the communities of Vancouver, Kelowna, Victoria & Prince George. By employing the use of transit ads, the Society was able to reach an older demographic that was less likely to be commuting by car or truck, young professionals and school age children.

This is Parkinson's Disease
It doesn't discriminate.

Hope Diamond, 51.
Drag queen.
Corporate management.
Comedian.
Diagnosed with Parkinson's in 2013.

We're in this together.

www.parkinson.bc.ca 1.800.668.3330

Parkinson Society
British Columbia

P38.15**Communication and swallow***Sherri Zelazny, Stacey Dawes*

Parkinson Society BC, Vancouver, BC, Canada

Between 85 and 90% of people with PD will experience voice and speech disorders during the course of their illness, however fewer than 10% pursue treatment. Changes in the ability to communicate and swallow can affect quality of life, social interaction, ability to work, and ability to communicate basic wants and needs. Medication and neurosurgical treatments have had little to no effect on communication and swallowing. External Scientific Evidence has supported using the Lee Silverman Voice Treatment® program for improving hypophonia in people with Parkinson's, as well as rehabilitative approaches for improvement in swallowing. These treatments are included in the standards of practice of licensed speech-language pathologists trained in the rehabilitation of communication and swallowing disorders.

The Medical Services Plan (MSP) of BrC does not provide universal outpatient speech therapy required to evaluate and treat communication and swallowing disorders of PD. However, the Canadian Guidelines on Parkinson's Disease (2012) states that "speech and language therapy should be available for people with PD".

- 12 LSVT® certified SLP's in BC, 4 known public LSVT® programs in the Lower Mainland, serving 13, 300 British Columbians with PD.
- Waiting lists for services are significant, leaving many people at risk for significant impacts to quality of life and increased social isolation.
- Due to geography, distance from qualified practitioners can also be a factor in accessing services.

In response to such trends, PSBC has developed 1 and 2 day Communication and Swallow workshops designed to educate people with PD and their caregivers regarding the identification of symptoms and characteristics of communication and swallow disorders. These workshops are led by a registered speech-language pathologist who is LSVT® certified.

- Their interactive and participatory format allows attendees to practice treatment techniques and gain insight from a registered SLP
- 2015, PSBC held 4 two-day Communication & Swallow Workshops in Burnaby, Kelowna, Langley and Victoria, BC.
- 2016, PSBC has scheduled 7 Communication and Swallow Workshops in the following communities: Kamloops, Coquitlam, Castlegar, Parksville, Cranbrook, Prince George and Vancouver, BC.
- More than 163 people have attended the workshops and learned about voice & swallow disorder challenges and at-home techniques.
- PSBC has created a printed guide to the workshops that is publicly available to all people with PD across Canada.

P38.16**The Parkinson's Disease Wellbeing Program: Putting balance back into the lives of people with Parkinson's disease***Jeremy Home, Megan Campbell, Sue Harkness*

Calvary Health Care Kogarah, Kogarah, Sydney, NSW, Australia

Aim: A goal of the Parkinson's Wellbeing Program (PWbP) is to reduce falls risk by providing a comprehensive education (10 sessions) and exercise program, involving people with Parkinsons (PwP) in their health care from diagnosis. Through increased awareness, early intervention aims to put balance back into the lives of PwP by maximizing their physical, mental and social wellbeing.

Falls may be reduced by teaching strategies to minimize risk, maximize therapy, prevent inactivity-related decline, harness social support and access community health programs. Being proactive and aware may be the difference between having a fall and preventing one.

Method: Idiopathic Parkinson's disease (PD) clients (Hoehn & Yahr stage 1-3, MMSE >24) were surveyed regarding falls and exercise participation 12 months after attending the PWbP.

Results: 124 clients completed a self-report survey. Improvements were reported 12 months post program in falls and exercise participation. There was a 50% reduction in the number of clients who reported falling post-program (pre-61% vs post-30%). Clients participating in regular planned exercise increased 30% (pre-51% vs post-81%). The percentage of multiple fallers reduced from 29% to 16%. Non exercisers were almost twice as likely to fall (47%) compared to those who reported they consistently exercised (25%). Forty-two percent of fallers were less than 4 years post diagnosis. Eighty-seven percent of clients found the falls education beneficial with 79% feeling it had prevented a fall.

Conclusion: In this cohort of PwP, attending the PWbP was reported to reduce falls and increase exercise participation 12 month post program. Central to the success of the program was a combination of early intervention, multidisciplinary education and exercise sessions, social support and long term access to local community health promoting programs. When PwP learn to monitor, manage and maintain their health long term, they are given greater opportunity to achieve life balance, which is essential for living well with PD.

LIVING WITH PARKINSON'S: GOVERNMENT, ADVOCACY, CAMPAIGNS, PUBLIC POLICY

P39.01**Anatomy of The Victory Summit®***Heather Caldwell, Polly Dawkins, John Dean*

Davis Phinney Foundation, Boulder, Colorado, USA

The Davis Phinney Foundation's cornerstone program, The Victory Summit® Symposium is an educational series that gives people with Parkinson's and their families the information and practical tools needed to improve the quality of their lives today. From learning about the latest research and treatment to participating in interactive exercise demonstrations, attendees experience an uplifting day of learning and connection that empowers them to make lasting, positive impact on their wellness.

In order to produce an inspirational event that spurs people to take action around their health, community involvement must exist from the beginning of the planning process.

Regardless of the size of the host city, Parkinson's health care institutions must be willing to come together to serve the greater Parkinson's community. Collaboration is at the core of The Victory Summit's success and ensures that attendees have necessary supports that address the "living well" event theme. Participation in tailoring the agenda to regional needs, exhibiting at the event and sharing expertise increases attendees' familiarity and understanding of how to best access the resources available.

Case Studies

#1 Ireland – In Oct 2014, the Foundation produced an event with Move4Parkinson's, a Dublin-based Parkinson's advocacy nonprofit. To help strengthen the country's Parkinson's community's identity, international speakers shared tips on topics such as how to take

advantage of local resources, how to get the most from your treatment plan and how build a dynamic health care support team. Attendees also had the opportunity to do an interactive Irish Set dancing and voice exercises. To increase available wellness classes, Dance for PD® held a training sessions for local leaders.

#2 Malaysia – In Oct 2015, the Foundation traveled to Ipoh, Malaysia to produce The Victory Summit with the Perak Parkinson's Association. Int'l clinicians provided education about Parkinson's, the role of the care partner and why being active and engaged is crucial to living well with Parkinson's. LSVT Global held a training in Kuala Lumpur for therapists.

Key Takeaways – The Victory Summit continues to be a viable international resource for bringing a unique message focused on improving quality of life for people living with Parkinson's. These programs help unify and organize the local and regional Parkinson's communities in order to help them better serve their respective constituencies.

P39.02

Advocacy is education – developing support for a provincial Parkinson's disease strategy in British Columbia

*Parkinson's Society British Columbia, University of British Columbia Movement Disorders Clinic
Canada*

Background: The current barriers to the proper management of Parkinson's disease (PD) in British Columbia are preventing many people with Parkinson's (PwP) from receiving proper care. These barriers include wait list times of up to 24 months to see a movement disorder specialist; a lack of knowledge of PD in hospitals, clinics, and the allied health professions; and difficulty obtaining alternative treatments for more advanced patients. Achieving systemic change, however, takes significant time, effort, and persistence.

Objectives: Parkinson's Society of B.C. (PSBS) is leading an initiative to establish a provincial Parkinson's disease strategy that will cross some of these barriers in order to improve patient outcomes and reduce costs on the healthcare system. The strategy aims to create a more integrated system by increasing knowledge of PD in the allied health professions, and increasing access to these providers as well as movement disorder specialists. The proposal involves funding for a pilot project that will address these objectives and eventually form a provincial strategy.

Methods: Developing the strategy will be a collaboration between PSBC, movement disorder specialists from University of British Columbia, the Health Authorities in B.C., and members of the Ministry of Health. Obtaining support for developing a strategy involves increasing awareness of the disease, educating about the issues impacting positive patient outcomes, and recommending opportunities to intervene that will also minimize costs. In order to gain political support, representatives from PSBC have gone to legislature to meet with the Minister of Health and other political figures and their recommendations have been crucial in moving forward. PwP are also playing an active role in their advocacy by meeting with their MLA's. The next step involves pairing with a Health Authority to prioritize and implement the strategy in their region.

Discussion: Identification of region-specific barriers to the proper treatment of PD is an important step in working towards large-scale improvement in PD management. Provincial implementation of a strategy that addresses these issues and then requires collaboration between a cross-section of stakeholders is a driving force behind the initiative. System-wide change in the management of neurodegenerative disease is not a trivial endeavour, but can be of crucial importance to ensuring those affected are receiving the care that they deserve.

P39.03

Delivering 'Lee Silverman Voice Treatment' (LSVT) to people with Parkinson's in West Hertfordshire

Richard Windle¹, Sally Pollitt², Anna Farrer³

¹ Patient, St Albans, Hertfordshire, United Kingdom

² Parkinson's UK, Cuffley, Hertfordshire, United Kingdom

³ Parkinson's UK, Hemel Hempstead, Hertfordshire, United Kingdom

Objective: To persuade the local Clinical Commissioning Group (CCG) to examine how LSVT can be delivered as a standard part of the treatment package to everyone with Parkinson's in West Hertfordshire who might benefit from it.

Method: Losing the ability to communicate can be one of the more disabling aspects of Parkinson's. LSVT is available in the UK but this is at the discretion of local CCG's. Although there is a body of evidence pointing to the effectiveness of this therapy the question was how would it be received in West Hertfordshire? In particular take-up, the reasons for non-take-up and the strength of patients' commitment were all unclear at the outset. LSVT is an intensive one-to-one therapy and, if an investment was to be made in the staffing and infrastructure needed to offer the treatment more widely, evidence was required to demonstrate its effectiveness. The local branch of Parkinson's UK took the unusual step of commissioning speech therapists from the National Health Service to teach LSVT to 16 eligible patients. The training was delivered by two LSVT trained clinicians who adhered strictly to the LSVT protocol.

Results: It was found that there were aspects of the current service that could be improved, especially waiting times. Some 26 patients were offered the treatment in order to obtain sixteen who received it. Among those who did not go through with the treatment the main reasons were an inability to commit to the intensity of the programme, moving out of the area and declining the offer of this therapy.

Patient-centred outcome measures were set at the beginning of the programme. These were consistent with the East Kent Output System (EKOS). Both qualitative and quantitative measures were obtained. One client said that his objective was to give the 'father of the bride' speech at his daughter's wedding, which he duly did. Course participants were supported externally by a branch of 'the LOUD Crowd' that was set up by the local Parkinson's group.

Conclusions: Challenges for the programme going forward include how to involve those who are reluctant to commit to the treatment. It was felt that a method of remote delivery over the internet would be the most suitable approach. It was also recommended that careful screening was needed to identify those who would benefit. A business case has been submitted to the West Hertfordshire CCG and we are waiting for this to be approved, thereby making this important treatment more readily available.

LIVING WITH PARKINSON'S: LIVING WELL WITH PD

P40.01

A Parkinson's life – doing well by doing good

Carl Ames

Peoria, AZ, USA

Objective: Illuminate the need and impact of effective Parkinson's role models.

Methods: My diagnosis of Parkinson's disease in February of 2008 didn't strike me with the devastating force that so of the

accompanies the diagnosis. Instead My family and I accepted the challenge to better understand and effectively manage the complexity of organizing care, work, and family that can be overwhelming at times. The opportunities to simply give up and let the disease have its way were there to be taken. Fortunately, my parents, family, and faith inspired me with the determination to fight and the recognition that I could illuminate for others that a life with Parkinson's can be one of vitality, meaning, and promise. For too many, the isolation that Parkinson's often imposes prevents one from gaining the exposure to those who share similar circumstances, yet express a joy and confidence in life. A confidence necessary to summon the will to provide oneself with the permission and expectation to want more from life. My aim is to not only provide a brighter vision of what can be, but to also serve as a beacon for others to play a similar role as a model for others. We are, in the end, a community and that community is lifted and fortified by its collective will to expect more and live life to its fullest. This requires the work of legions of role models. The answer for me was as simple as just showing up. By doing so the doors of opportunity presented themselves. Participating in community events produced by the likes of the Davis Phinney Foundation or the Baehr Challenge, and many others provided the ready means to get engaged and social media enabled me to share the richness of these experiences within our community and a much broader world. These chances to convey a sense of hope, opportunity, control, and peace are gifts that keep on giving. And they are gifts that must be assumed by many more within the Parkinson's community. In the end, I have learned that a vital key to living well with Parkinson's comes from doing good for others.

P40.02

Getting on with your life after being diagnosed with Parkinson's disease or having a loved one diagnosed: getting off your emotional roller coaster, getting over it and stop telling you sob story

John Baumann
Sarasota, FL, USA

I'll end the "out with the bad" section with the most significant edict. Forgiveness. What a powerful word. Who do you need to forgive? Everyone. That includes YOU. Though we should always strive to be, no one is perfect. Sometimes we come down hardest on ourselves. I am not saying forget, but give yourself a break. Learn from mistakes. Learn from failure. As I state on the first page of my website, JohnBaumann.com, "It's through the pain and fear that builds a warrior."

You absolutely can, and must, forgive even if it is something that you will never forget. We need to learn from our experiences, but that does not mean that we cannot forgive. It is totally within your power and control to forgive anyone. The other person does not have to ask for your forgiveness or say that they are sorry for you to forgive them.

Your forgiveness does not entitle them to avoid the consequences of their actions, that is their issue. But you don't have to carry around the anger or other baggage associated with the situation. You have the option of simply forgiving them in your heart. Think back to the people who have wronged you over your lifetime and, one-by-one, forgive them.

I know I sound like a broken record, but, as simple as it sounds, truly forgiving someone, let alone everyone, is also a very difficult thing to do. It takes strength. It takes all kinds of strength, including spiritual strength. "To err is human, to forgive divine." You may question whether you can forgive. What if you were molested? Lost the ability to walk due to the intentional act of another? Had a loved one brutally murdered by someone? Yes. Yes. Yes. And there are many more circumstances, too many to be able to include in this

publication. As monumental as the task, you cannot improve until you have relinquished the anger and pain of your unique past.

P40.03

Is social health associated with Parkinson's disease severity score?

Rachel Bennett, Blake Kovner, Laurie Mischley
Bastyr University, Kenmore, WA, USA

Objective: To determine whether measures of social health are associated with symptom severity in a cohort of patients with Parkinson's disease (PD).

Background: Social health is an often overlooked aspect of PD. Apathy, depression, anxiety, slow movement, walking and cognitive difficulties may all contribute to individuals with PD withdrawing from their social networks and impacting their symptom severity.

Methods: An internet-based natural history study was designed to generate information useful to patients and providers. An assessment tool, the Patient-Reported Outcomes in PD (PRO-PD) scale, was designed to assess PD severity and was validated against the existing measures of disease severity. Disease severity was defined as PRO-PD, adjusted for age, years since diagnosis, and income where the higher the PRO-PD score the worse PD symptom severity. Baseline survey data was used to identify whether individual's self-report of social health and the following comments, "I am lonely" and "I have a lot of friends" were associated with PRO-PD score.

Results: 844 participants were surveyed, with a mean age of 62.8 years and an average 5 years since diagnosis. These subject's PRO-PD score increases 34 points every year since diagnosis. After adjusting for age, years since PD diagnosis, and income, the 17.77% of participants who identified as lonely had an average PRO-PD score 296 points higher than predicted ($P < 0.000$; 95% CI: 220, 372). Conversely, the 64.07% of individuals who identified as having a lot of friends had an average 126 point reduction in PRO-PD score ($P < 0.000$; 95% CI: -188, -65). Participants were asked, "In general, how would you rate your satisfaction with your social activities and relationships?" and in a dose-response fashion, the higher the individual rated his/ her social satisfaction, the lower the PRO-PD score (Fair: -176, $P < 0.028$, 95% CI: -334, -18; Good: -392, $P < 0.000$; 95% CI: -543, -240; Very Good: -576, $P < 0.000$, 95% CI: -706, -406; Excellent: -701, $P < 0.000$, 95% CI: -858, -544).

Conclusion: Building a social network to alleviate loneliness could improve PRO-PD score. The more satisfaction PD patients have with their social activity and relationships the lower the PD symptom severity. This study elucidates the importance of addressing obstacles with PD patients that may prevent them from building strong relationships.

P40.04

The use of web radio station radioparkies.com to entertain and inform people living with Parkinson's

Madonna Brady
Stafford, Qld, Australia

Objectives:

To inform others how to connect and listen to web radio station radioparkies.com

To facilitate people with Parkinson's in sharing their Parkinson's stories via a short talk on my weekly radio show.

To learn from others and connect through music and stories.

Background: People with Parkinson's (PWP) are often searching for connections; the web radio station radioparkies provides information, forums, chat, art, games and translations for over 100

languages. The big social connectors are the DJ's radio shows, which provide entertainment, a friendly voice, local and international information, a different perspective and a sharing of thoughts and ideas. The worldwide availability is part of the appeal of web radio. Music triggers stimulation and can improve mood and responses.

In many parts of Australia, isolation and loneliness are barriers to living well with PD. Isolation and loneliness are often associated with depression. Bringing talks by PWP to the ears of listeners is advocacy, outreach and empowerment in its most simple form.

Methods: This poster/presentation will describe the experiences and outcomes of involvement in the radioparkies community from the perspective of....

Results: The sharing of hobbies, stories, hope and achievements has brought people together from around the world. PWP and associated health professionals and therapists who have participated in talks have reported it being a liberating process. People have been inspired to take on new exercise, write poetry and embrace life. Opportunities for community to connect and promote included recent World Parkinson's Day Awareness events which were talked about on the radio, advertised in the RP calendar with links to the ticketing website and photos of the event.

Future directions: To strengthen the impact of the radio shows, a blog will be developed. The creation of a blog will connect more people to radioparkies and open up avenues for discussion, learning and enjoyment.

Promotion of World Parkinson Congress through radio talks and interviews prior to the event and recorded talks and interviews at the Portland event brings the event into the homes of PWP.

P40.05

The PD Buddy Outreach Program – the patient perspective

Denise Cumberland¹, Erika Branch², Allie Hanson², Sarah Muftic³, Ann Shaw³, Susan Sawning³, Kathrin LaFaver³

¹ USA

² Parkinson Support Center of Kentuckiana, Louisville, KY, USA

³ University of Louisville, Louisville, KY, USA

Objectives: The PD Buddy Outreach Program is designed to create a community outreach between Parkinson's disease (PD) patients with first year medical students. The objectives of this nine-month intervention are twofold: 1) to impact patients' social connections and decrease the sense of isolation that can occur when a disease affects motors and verbal skills and 2) to improve first-year medical students' knowledge about PD and shift attitudes about patients suffering from PD. This abstract will focus on the patient portion of the intervention.

Methods: PD patients were recruited from the UofL Physicians Movement disorder clinic and the Parkinson's Support Center (PSCKY) through outreach efforts. Patients completed the following pre-post surveys: 1) the Geriatric Depression Scale (Short Form) (GDS-SF), and 2) the Parkinson Disease Questionnaire 39 (PDQ-39), which is designed to assess health-related quality of life in PD. Patients and students were matched and met in pairs on a monthly basis to engage in shared activities. At the completion of the program patients were also asked to complete a relationship survey that gathered information on the number of times interacted, activities enjoyed, as well as attitudes about their buddy relationship. Three focus groups were also used to understand the relationship evolution and how the program could be improved.

Results: Indicators from the two patient focus groups held to date indicate the PD patients have enjoyed the relationship and believe they are contributing to the medical students education. One patient commented about the advantage for the students: "There are so many different ways to learn things. This is another way. You can't just sit in the classroom and learn everything you need to know. So, if you want to learn about an illness and how it affects people this is a good idea because it is one on one".

The poster will cover the following:

- Aim of the PD Buddy Outreach Program
- Methodology
- Results: including
 - Pre-post attitude surveys (GDS-SF and PDQ-39)
 - Buddy Program Relationship Survey
 - Patient Focus Groups
- Next Steps

P40.06

Gut bacteria, alphasynuclein, axonal transport via vegus-empirical observations of PWP Curnow. PWP's as "partners in research" more valuable than as "objects of research"

William Charles Curnow¹, Peter Silburn², Tom Borody³, James Aylward²

¹ Life Member Order of Australia Association. Member Australian Institute of Architects, Toowoomba, Queensland, Australia

² Brisbane, Queensland, Australia

³ Sydney, New South Wales, Australia

My busy career was threatened in 2002 with the diagnosis of "Parkinson's". By 2007 I was no longer active, or travelling unaided nationally/internationally. Rather than accepting that I had an incurable condition I decided to read scientific papers and ultimately asked my Neurologist if PD could be caused by bacterial toxins.

Methods/Clinical Incident:

In 2011 I was hospitalised for bowel obstruction and after anti-biotic infusions I noted surprisingly that my PD symptoms virtually disappeared. My notes/drawings before and after treatment graphically illustrated the difference. Silburn (my Neurologist) was surprised when I explained – "Cessation of PD symptoms was like turning off a switch".

Outcome: After discharge PD absence lasted only 2 weeks. If antibiotics suppressed gut bacteria I postulated their toxins caused PD in the brain and connecting nerves must also be implicated. Via literature I located Borody (Gastroenterologist) who administered IV metronidazole + ceftriaxone and PD again disappeared. Effect tapered somewhat after two weeks. This was followed by oral metronidazole and cefaclor which maintained improvement over months but at a reduced efficacy. In 2014 I noted improved motor function immediately after defecation, perhaps due to reduced gut bacterial load and toxins interacting indirectly with gut neuronal axis according to Aylward [CSIRO scientist]. Measured physical performance before and after treatment confirm empirical observations.

Potential Way Forward: Borody previously noted faecal microbiota transplant (FMT) for constipation led to similar results for 2 PWP's, supporting this hypothesis. Arrival of oral capsules for FMT and PWP's observations opens scientifically credible research pathway to better understand the link between gut bacteria, antibiotics, alpha-synuclein, gut-neuronal axis and PD

P40.07

Hourly journaling of events related to diet, medications, exercise and stress and the use of complex event processing to improve "on" time in a Parkinson's disease patient

William Curtis

Bowie, MD, USA

Background: There are a number of interactions related to time of medication, dose, the foods one eats, and exercise, and stress associated with various activities that can effect "on" time. Hourly journaling of food, medication, symptoms, activities, blood glucose levels, and blood D-beta-hydroxybutyrate levels helps to identify

interactions and allows one to make adjustments to achieve a higher percentage of on time.

Objective: Develop a system of hourly journaling that allows one to identify the key events that regulate on time and track the effect of adjustments made to increase on time.

Methods: The author analyzed the data using complex event processing and temporal reasoning, a form of computer artificial intelligence, to discover relevant events. The author experimented with intermittent ketosis, exercise induced ketosis, diet induced ketosis, exogenous methods of raising ketone bodies. The main focus of this poster is hourly journaling and temporal reasoning. The author does endorse journaling. The author does not endorse ketosis or any other treatment.

Results: Off periods were not always predictable. There were times when taking carbidopa/levodopa earlier than scheduled in order to provide a higher dose did not always provide relief. This resistance correlated to prior days without exercise or cumulative number of prior days with "stress". Avoiding protein when taking levodopa significantly lengthened on time as well as reducing the time from taking levodopa until the symptoms were relieved. Taking a full glass of water with levodopa affected how fast it started to work. Foods with high glycemic index correlated with shortened on times, particularly when in a ketogenic state, as measured by blood D-beta-hydroxybutyrate and glucose. Allergy medications had a noted negative effect. The patient was able to increase the number of hours in a day where off time was not perceived within the past hour from 2 to 3 hours a day to 10 to 12 hours a day depending on compliance with best practices identified.

Conclusions: Use of journaling and complex event processing analysis was shown to be an effective tool to increase on time.

P40.08

Using video to explain Alexander Technique to my doctors: an example of patient self-advocacy

Robert Davis¹, Caprice Boisvert²

¹ Board Member, Dancing With Parkinson's Canada; The Poise Project, Asheville NC, Toronto, Ontario, Canada

² The Poise Project, Asheville NC, Toronto, Ontario, Canada

Objective: To present how I discovered an activities-based method to manage my symptoms of Parkinson's disease (PD) and created an informational video about my experience for my doctors.

Background: After my diagnosis in 2008, I took a yoga class with Caprice Boisvert who later introduced me to Pilates, then to Alexander Technique (AT). To this novice, AT was magic: light hands-on guidance that led to a general physical release and ease that stayed with me for significant periods of time. I soon understood there was more to it. AT professionals are not therapists giving treatments, but teachers of skills. AT offered me short-term relief, but then became a reliable long-term strategy as I learned how to apply the knowledge independently. Taking weekly lessons since 2012, I have learned how to move more mindfully and effectively, and how to alleviate tension and stiffness caused by the disease at times when nothing else would work. For example, awakened at night, I am skilled at releasing my whole body and getting back to sleep, gaining 3 or 4 more hours a night. This alone is a huge benefit to my quality of life. Eager to share this with my doctors, and through them, with other PD patients, I spoke with my neurologists and family physician about AT at each medical visit. The doctors were polite, but clearly too busy to go for a lesson. I searched for a different way to get their attention.

Method: I had a brainwave: I would share my experience with my doctors via video. Caprice and I agreed it would be short (under 7 minutes), scientific, straightforward in content and language, and appealing in appearance. It was shot over 2 days with assistance from a photographer friend. I edited the footage in 2 weeks with

feedback from a communications expert, AT teachers and people in the medical field. As I drew people into my project, their positive reactions to the video confirmed my sense that it would be a useful tool in explaining the benefits of AT for people with Parkinson's.

Results: Soon after delivering the video, I received a phone call from my neurologist – who was not normally in the habit of calling. He had shown it at a staff meeting at the hospital's Movement Disorder Clinic, and the staff responded positively. I had succeeded in reaching my medical audience.

Conclusions: As a person with Parkinson's, I am in the best position to assess the benefit of Alexander Technique and to take action to bring awareness of it to other people with Parkinson's.

P40.09

Data sharing: a call to action

Sue Dubman

University of California – San Francisco, CA, Tewksbury, MA, USA

As a person in Cancer Research, I never even considered Parkinson's (PD) as a possibility. Everyone in my family died of Cancer. But, there I was in 2009 getting a diagnosis of a chronic & progressive disease, a diagnosis that was devastating as much for me as my family. After a few years of denial, I knew I needed to do something & believed that my experience as both a patient and as someone in bio-medical research and care (at NIH, UCSF. Bristol-Myers & Sanofi/Genzyme) with strengths in data standards (CDISC, HL7) could be put to good use so that, in the future, others & their families, wouldn't have to suffer like mine. I am a big believer in the power of science. Science is an investment in the future & we need to make sure we have appropriate funding. There is no calling greater than helping people who can't care for themselves. We can't be satisfied that things are okay. We need major change in the way we do research and how patients and providers interact with the healthcare system. While recently there have been more attempts to share data, the data made available to others is often not in a form that is really useful, is stale, is restricted to a small community of researchers and/or it is very difficult and, at times, nearly impossible to combine that data with other data since existing data standards were not used. Furthermore, the current model of care & research is based on tools developed in the time of Gutenberg (1440). If we continue to adhere to this model, our understanding of clinical interventions and our ability to develop new treatments will continue to be limited. 21st Century medicine requires new organizational approaches that embrace our capacity to work digitally. As a patient, I find the lack of data sharing to be a travesty. PD patients need to demand change! We are making progress but way too slowly. This is a call to action. Data sharing, especially given no effective treatments to slow or stop progression, is critical. Science is a community, continually building on one another's ideas. In the era of electronic knowledge exchange, only when data sharing becomes the norm, can we derive its full benefits. Change is challenging, but change we must. What is true for any scientific inquiry is true for improving healthcare: the better the data, the more meaningful the results. The time is now for clinical care, research, and scientific discovery to be connected in a seamless continuum that speeds innovation and benefits patients.

Data Sharing: A Patient's Call to Action

	Where We Are Today	Where We Need to Be
Accuracy	<ul style="list-style-type: none"> Compromising copy-and-paste dependence and multiple data storage locations perpetuate inaccurate, outdated data. 	<ul style="list-style-type: none"> Automated quality checks and verification requirements ensure that data is always accurate and up to date.
Accessibility	<ul style="list-style-type: none"> Key clinical data live in multiple places and is difficult to find. Data is silo-ed and cannot be shared with other systems for both care and research. 	<ul style="list-style-type: none"> Mission critical data is central, succinct: one click away. Standardized and consistent data capture allows information to be transmitted across multiple platforms.
Efficiency	<ul style="list-style-type: none"> Data is entered and abstracted many times; work is duplicated. Cumbersome, time-consuming data entry means less quality time with patients. User interface hampers rather than facilitates clinical care and research workflow. 	<ul style="list-style-type: none"> Data is entered correctly once and persists throughout the patient's care, only needing occasional updates. One-click clinical notes and treatment summaries User-centered design supports workflow rather than hindering it.
Re-usability	<ul style="list-style-type: none"> After collection, data cannot be used in any meaningful, clinically-relevant way. 	<ul style="list-style-type: none"> Captured data can inform care decisions and drive clinical trials, registries, referrals, etc.
User Experience	<ul style="list-style-type: none"> Unfriendly design and usage complexity lead to frustration, low compliance, and decreased completion. Model of ownership does not support effective collaboration. 	<ul style="list-style-type: none"> Intuitive and user-centered design boosts ease of use and completion rate. Information model facilitates a collaborative, "team science" approach to medicine.

"21st Century medicine requires new organizational approaches that embrace our capacity to work digitally." In practice that means:

Patients can:

- Have their key medical information and history accessible to any provider or researcher they choose, freeing them from the burden of requesting records and answering the same questions repeatedly;
- Patients automatic access to the appropriate resources (counseling and preventative services) based on their personal medical information;
- Participate in research more easily with greater access to ongoing trials and without the need to repeat tests and imaging;

Healthcare providers and researchers can:

- Securely and appropriately share high-quality, structured and standards-based data from the authoritative data source, including electronic patient reported outcomes, wearables, devices and more.
- Access and query large collections of high quality clinical data, annotated specimens and images, genetic testing results, and much more;
- Facilitate clinical trial and registry enrollment;
- Identify and isolate disease sub-groups, which can be used to validate biomarkers and risk models;
- Develop personalized, evidence-based innovations in the diagnosis and treatment of cancer and other diseases and allow continuous quality improvement.

Dubman, I. Sue, April 25, 2016

P40.10

Where there's a way there's a way

Daryl Eigen
Portland, OR, USA

Introduction: Parkinson's Disease (PD) usually requires symptom management with a pharmacological solution that could possibly progress to brain surgery. Alternative Therapies (ATs) based in Eastern wisdom traditions have been explored with some success as complementary treatments for PD. ATs include elements of fitness, spiritual practice and healing methods such as Taoist Tai Chi, Yoga, and Ayurveda that are more than 2000 years old. ATs embody some useful PD symptom management techniques; we have tended to interpret a small subset of these traditions as exercise. Modern research has evidence that exercise is effective in slowing the rate of symptom progression. Yet this misses the spirit of the ancient traditions. An analysis of what these ATs have to offer beyond fitness helps us understand the PD symptom management secrets held in ancient wisdom.

Approach: To isolate the effects of the ATs, the most applicable method for a particular symptom is chosen. (See table) ATs may be useful for multiple symptoms. Three aspects that are discussed in the ancient Eastern traditions are stating intent, being present, and expressing will. Determining one's intent or purpose guides the way we practice and thus makes it more efficient in reaching the desired goal. Secondly, being present with what is, both inside (self-awareness) and out, in a focused state brings sharper intellect, calmness, and improved capability. Meditation is an example. Third, expressing will, the degree of motivation, provides the power to decide, choose, and implement an AT. These three steps make one's efforts more on point and thus more effective. These three

aspects are what distinguishes simple exercise from ancient healing methods. Simply stated one must choose a goal, exert effort to do the appropriate AT and be present enough to do it correctly with deep awareness. ATs with the three aspects require clinical and scientific validation to be fully embraced as successful PD remedies. However, there is ample anecdotal, historical precedent, and documented evidence of positive results from these ATs with little associated risk if done correctly. As a student and user of these techniques I can testify to their effectiveness.

Table: Examples of PD symptoms and complementary alternative therapies (ATs)

PD Symptom/Quasi-Symptom	Alternative Therapies	Specific Techniques
Bradykinesia	Ayurveda	Herbs
Postural Instability	Tai Chi	Taoist Sequence
Balance	Yoga	Postures
Gate Freezing	Tai Chi	Taoist Sequence
Stooped Posture	Yoga	Shavasana
Tripping	Tai Chi	Taoist Sequence
Depression	Yoga	Karma Yoga
Fatigue	Ayurveda	Herbs
Slow Digestion	Ayurveda	Herbs
Stiffness	Yoga	Postures

P40.11

PWPs supporting other PWPs in their quest for knowledge

Simon Griffith
United Kingdom

Rationale: PWPs are faced with a bewildering amount of information in the public domain including 'snake oil' sellers, complexity, hearsay and unnecessarily pessimistic, often contradictory or outdated views. This makes it hard for us to make well-informed decisions and wastes precious time.

Objective: From talking with other PWPs I realise there is a need to create a simple, upbeat guide to help people at a critical time in their life. As a prematurely retired information specialist and PWP I want to help improve awareness and empowerment among PWPs so they can rapidly explore what is scientifically and practically worth knowing.

Contents of the document:

- Diagnosis
- Serendipity (pleasant surprises through knowledge networking)
- Exercise
- Nutrition
- Tips and tricks
- Drugs to treat symptoms
- Research into neuroprotection and neurorestoration
- Happiness
- Your own knowledge journey

Method:

Phase 1: A small group of PWPs kindly tested my pilot document. I also shared the concept with different Parkinson's groups through social media.

Phase 2: I am now creating a revised document which I plan to share more widely with PWPs and professionals via a simple website.

Phase 3: Exposure to the WPC would provide invaluable feedback to really make this document useful to PWPs. The poster would contain a link to the website and a sample from the 'nuggets' which the document shares.

Phase 4: I will keep the document up to date with developments on an ongoing basis.

Results to date: Phase 1 has generated a better understanding of the detail required and the topics to be addressed and led to practical mutual help being provided. Outcomes ranged widely from two ladies finding that high heels improved gait to contact being

established for involvement with a trial on the other side of the world.

P40.12

Tips and tools for maintaining improvements in communication, mobility, and activities of daily living following LSVT LOUD® and LSVT BIG®

Laura Guse¹, Cynthia Fox¹, Lorraine Ramig¹, Angela Halpern²

¹ LSVT Global, Inc., Tucson, AZ, USA

² LSVT Global, Inc., Denver, CO, USA

Rehabilitation and exercise regimens are widely recognized for the positive impact they can have on communication, mobility, and potentially brain health in people with Parkinson disease (PD). The LSVT LOUD and LSVT BIG protocols have been developed and scientifically researched over the past 25 years with federal funding. Research on LSVT LOUD has shown that people with PD maintain improvements in loudness and intonation for at least two years post-treatment. LSVT BIG research has documented improvements on the UPDRS motor scale as well as other tests of motor functioning in people with PD.

While these research outcomes are exciting, clinically one of the challenges many people with PD face following therapy is how to maintain treatment effects. Lack of adherence to post-treatment home exercise programs reduces the positive benefits of intensive treatment. This presentation will share key tips and tools that may assist people with PD in maintaining positive treatment effects after LSVT BIG and LSVT LOUD.

1) The LSVT protocols are structured, intensive PT, OT and Speech treatments that adhere to principles of motor learning and neuroplasticity. A key goal during the one month of treatment is to develop a LIFE-LONG habit of daily homework practice so that improvements in voice and movement will become habitual for use in everyday life.

2) Because of the chronic, progressive nature of PD and challenges with long term exercise adherence, tune-up sessions every 6-12 months can motivate continued practice and are recommended to re-calibrate sensory-motor perception of normal voice or movement following LSVT treatments.

3) Select patients respond well to guidance during exercises, thus, the "LSVT LOUD and LSVT BIG Homework Helper" videos of the core exercises are tools that can be used. The LSVT Companion® (an interactive FDA cleared medical device) is another technology tool to support home practice of LSVT LOUD speech exercises.

4) Post-LSVT exercises classes have long been a part of the clinical practice, however, structured programs called BIG for LIFE™ and LOUD for LIFE™ can increase the fidelity of the classes and accessibility for people with PD. These group exercise classes are for those who have already received LSVT BIG/LSVT LOUD.

It is our hope that increasing patient awareness of the need for regular episodes of therapy in combination with daily home exercise practice supported by use of these tools will enable people to live better with PD.

P40.13

Building your best program: making a BIG impact with a SMALL budget

Michelle Haub

Meadowlark Hills Parkinson's Program, Manhattan, KS, USA

The Parkinson's Program of Manhattan at Meadowlark Hills began in 2007 with a multi-disciplinary Core Team of professionals volunteering ~three hours/month and a budget of less than \$2k. Presently, it continues to be lead by the Core Team but has a part-

time director and raises ~\$55k annually. The program serves 75 PWP, and their family and friends within a 75 mile radius of Manhattan, KS. They utilize the FREE services provided by this organization, which is viewed throughout the state as an advocate and leader in the care for those with PD. Although other cities in Kansas are larger than our community of 52k people, Manhattan is the only city providing comprehensive PD support free of charge and led by professionals trained to help manage PD. As an indicator of quality, sustainability and practicality, this program won the 2014 LeadingAge Kansas "Excellence in Social Accountability" award. This program is sustainable so long as those involved stay engaged and the program has resources (director and physical office) to manage it. In a recent survey of those PWP who frequently attend the programs services, 75% of the respondents were diagnosed in the last five years. This demonstrates the the potential for continued growth and sustainability. Being linked with a continued care retirement facility, that is also a non-profit, assists with the sustainability as the program attracts future residents and enhances the quality of life of current residents with PD.

I would be honored to share more about our services, professionals, programs and fundraisers to help others be resources for those in their communities and help businesses look to the future of helping those with PD live life to the fullest.

Parkinson's Program of Manhattan at Meadowlark Hills FREE services for those in the Flint Hills affected by PD

Education <ul style="list-style-type: none"> • Monthly education group meetings • Monthly Young Onset group meetings • Personal Consultations • Bi-Monthly Core Partner Support Group • LSVT-LOUD & BIG therapies 	Exercise <ul style="list-style-type: none"> • Bi-weekly seated/standing exercise classes—Gary Sobol Trained • Weekly Voice Classes • Open access to TheraCycle • Three times/week boxing classes (see below) • Fit 2 Fight PD Boxing—Started in December 2015 following collaborative training between Core Team professionals and a boxer. Classes held at community partners gym one day/week and at Meadowlark Hills two days/week.
Scholarship <ul style="list-style-type: none"> • Free boxing gloves for PWP • Lending Library of books & equipment (i.e. U-Step Walkers, LRVWares, voice amplifiers) • MyID Medical Bands—provided free of charge to any with PD so all participants may have an identification bracelet notifying medical staff of PD, timing of medications needed & contraindications • Paid transportation for individuals wanting to attend activities that do not live on the Meadowlark Campus 	Outreach <ul style="list-style-type: none"> • Monthly PD Partners Luncheons—1x months, meals have been donated by community partners • Pig Out for Parkinson's 2016 is the sixth annual event to raise awareness for PD during National Parkinson's Awareness Month. It is held at local BBQ and has been our best avenue to reaching those with YOP and afraid of gross settings • Speedy PD Race for Parkinson's is in it's eighth year and had over 700 participants in the 5K/10K & 1/2 Mile Family Fun Run/Walk in 2015 and raised over \$41k. In it's first year it had 125 people & raised \$11k. • Mary Roberts Memorial Parkinson's Party—inaugural event in April 2016, provided literature about our free services to doctors & pharmacists to distribute to their patients; had 70 people attend. Nationally acclaimed speaker, John Baumann, present "Positively Un-Shake-able"

P40.14

Partners in Parkinson's: discover the benefits of team

Caitlin Jurman¹, Kat Kennedy¹, Lura Long¹, Blaire Gansman¹, Sohini Chowdhury¹, Dave Iverson¹, Mary Ann Binner-Adams², Blaire Gansman¹

¹ The Michael J. Fox Foundation for Parkinson's Research, New York, NY, USA

² AbbVie, Chicago, IL, USA

Objective: To educate and empower Parkinson's patients and caregivers to build the most effective medical team for their Parkinson's care.

Method: In 2014 the Partners in Parkinson's (PiP) program was created through a partnership between the Michael J. Fox Foundation and AbbVie Pharmaceuticals. Since launch, PiP has hosted 25 local in-person events around the country, a webinar series, and a website that features a movement disorder specialist finder tool and the ability to connect with a PD Advocate. A virtual event experience is planned for later this spring and the footage will be produced into an online educational symposium accessible over time. Each PiP offering includes panel discussions that feature patients, caregivers, loved ones, researchers, clinicians, allied health professionals and community leaders, who are tapped to highlight the important role they play in the care team. In addition, in-person events include a resource fair that exhibits national and local PD organizations, opportunities to get involved in clinical research, allied healthcare providers, local community exercise and support groups.

Results: Partners in Parkinson's has engaged a community of over 20,000 people across all of its activities. Over 15,000 people have attended a PiP event. On average 53% of event attendees reported it was their first time attending an educational event about PD, and after attending the event 83% of patients felt more motivated to engage in their care. In a recent survey sent to attendees one year after their event attendance, 32% of respondents reported that as a result of attending the event they had pursued involvement in clinical trials. The program has also had a significant impact in the number of patients receiving care from a Movement Disorder Specialist, with 20% more people reporting seeing a MDS a year after attending an event. These findings demonstrate the value of not only the Partners in Parkinson's initiative itself, but the correlation this initiative has had with key calls to action that help patients live better with the disease.

P40.15

Positive attitude and the PwP patient

Mary Killian

Volunteer, Louisville, KY, USA

Objective: Provide information in relationship to how a positive attitude of a PwP can impact their disease and how seminars can impact the Parkinson's community.

Methods: We will start with using surveys of 100 PwP patients that are currently diagnosed with depression. We then separate these surveys into one of 4 categories below:

1. Positive attitude
2. Negative attitude
3. Happy
4. Not happy

We will then take the negative and not happy PwP patient and over a 6 month period educate them on the following:

- How to lower their rate of depression
- How to lower levels of distress
- How to reduce stress levels
- Educate them on better coping skills during hardships and stressful times
- How to be positive during difficult times

Results: Research will show that using positive self-talk, surrounding yourself with positive people, smiling and having humor in your life will lead to a positive attitude and happier life.

P40.16

What can a philosopher with Parkinson's say to fellow sufferers

David Kolb

Bates College, Retired, Eugene, OR, USA

I'm a retired philosophy professor with PD. What can philosophy say to me, to anyone with PD, as we stumble downhill together? What character traits beyond patience and compassion will make a Parkinson life as excellent as it can be? The philosopher Epictetus says "Sickness is a hindrance to the body, but not to your ability to choose, unless that is your choice." Choosing to keep moving, to control my discouragement and resentment of PD, is not just an exercise of sheer willpower. It comes from finding a wider view of myself and my context that makes room for me to pull back from being absorbed in my anger and suffering. Yet as our future darkens we with PD are urged to live more focused on the present moment. There is something right about that advice, but it can lead us astray. For what is "the present moment"? Are we to collect absorbing aesthetic experiences? Cling to isolated golden souvenirs? Find temporary respites along a dismal path? Will fragmenting my

Parkinson life into separate beads on a string make it more meaningful? If we look closely at our experience of time, we see that meaning comes thru connection and contrast. No present moment is isolated or self-contained; it lives by connection, gathering an individual past that opens future possibilities. Even as PD constricts my life I can take up that life and find possibilities where my past intersects our wider context. I live most fully when I discern, explore and act on what that present moment calls me to be. It takes energy and attention to hold my time together within wider horizons. It takes energy to heed possibilities that open up despite, and within, my turmoil and suffering. It is easier to avoid the effort, and just slide from one separate moment/event to another. But we can remember how "forced" physical exercise at a higher pace than a patient is accustomed to works better than a comfortable pace in reducing Parkinson's symptoms. Working to connect moments and keep my horizons wide and open, hearing the call of new possibilities even as I decline, this is the temporal equivalent to spatial forced exercise. If we deepen and widen our present moment, beyond any easy drift, we live more fully and excellently, despite Parkinson's. (The poster would include QR codes leading to fuller discussion and further evidence.)

P40.17

Service dogs for Parkinson's

Renee Le Verrier

Washington, USA

Objective: Define and demonstrate why, when and how mobility service dogs enhance the quality of life for people living with Parkinson's.

Methods: 1) To show why service dogs help people live well with Parkinson's: A comparison of charts illustrates the match between physical deficits from Parkinson's, such as loss of balance and freezing, and physical assistance tasks that service dogs provide. Chart column 1 lists various Parkinson's motor symptoms that affect mobility [1]. Column 2 itemizes ambulatory tasks for which mobility service dogs are trained while column 3 specifies wheelchair-assistance work for which mobility service dogs are trained [2]. 2) To show when service dogs are helpful: A collection of clearly captioned photos portrays mobility service dogs in use with Parkinson's partners and the specific tasks they provide in activities of daily living. 3) To show how service dogs are beneficial: Sidebar notes highlight the application-to-recipient process as well as factors to consider such as care and lifestyle impact. 4) Testimonials from current service dog partners confirm that in addition to improved mobility are increased confidence, self-esteem, social interaction and independence. 5) Personal testimonials and live demonstrations of mobility tasks given by author at poster sessions throughout the Congress. 6) Boxed i with resources on agencies and further information.

Results: Viewers gain useful and relevant information on how a four-legged furry cane can help in the management not only of mobility issues that result from a variety of Parkinson's symptoms but those of dependency and social interaction as well.

[1] Diseases and Conditions: Parkinson's disease symptoms, Mayo Clinic Staff, Mayo Clinic, www.mayoclinic.org

[2] Assistance Dogs International (ADI),

P40.18

From local partnership to national network: the growth of a medically connected, community based Parkinson's wellness program model

Amy Lemen¹, Peter Schmidt², Ruth Hagestuen², Vaughn Edelson², Meghan Sweeney¹, Alessandro Di Rocco¹

¹ Fresco Institute for Parkinson's and Movement Disorders at New York University Langone Medical Center/New York University School of Medicine, New York, New York, USA

² National Parkinson Foundation, Miami, FL, USA

Objective: To increase the scale of a medical and community partnership model for the delivery of comprehensive Parkinson's Wellness programming.

Background: In 2007, the Fresco Institute for Parkinson's and Movement Disorders at NYU Langone Medical Center launched a novel initiative with Jewish Community Center Manhattan to develop a comprehensive wellness program model designed specifically for the needs of individuals, care partners and families living with Parkinson's disease (PD). The program has been in high demand since its inception and has proven popular with patients, families and providers.

Methods: An interdisciplinary team of medical and community professionals was formed to expand the scale of the program nationally. Top PD specialized clinics and high capacity Jewish Community Centers from around the USA were selected and evaluated for participation in program expansion. Multidisciplinary teams comprised of medical and community professionals from the selected locations participated in program training in New York. The program model is comprised of three group-based components—exercise, support, and education—designed to provide proactive tools to enhance well-being, improve quality of life and complement specialized medical care. These tools are provided within a PD educated, community hub with collaborative support from an expert PD clinic. The benefits of exercise and support are well established in Parkinson's disease and have been previously described.

Results: The New York program was adapted first in Boston, MA, and in Rockville, MD, followed by Tampa, FL, and Chicago, IL, in partnership with an expert PD clinic and Jewish Community Center in each location. Enrollment, satisfaction with the program, and impact on social domains of the patients' and caregivers' quality of life are being tracked. Sufficient data on enrollment and impact of the programs are not yet available, but initial feedback is positive.

Discussion: The program model offers multiple domains of potential benefit in the areas of physical and psychosocial health for patients, care partners and families. Preliminary data suggests that the program model is effective in fostering motivation for participation in programs that aid in physical and psychosocial adaptation to PD. Potential further study and expansion of the program is being considered. This poster will demonstrate in graphics and narrative the development and growth of this program model.

P40.19

Forming community partnerships to create a wellness program for people with Parkinson's disease

David LeVan, Lynne Gotham

Parkinson Partners of Northwestern Pennsylvania (USA), Erie, PA, USA

This poster will illustrate the process and practical considerations that were used by a regional non-profit organization to create a wellness program. Parkinson Partners of Northwestern Pennsylvania (USA) is an organization whose mission is to encourage, educate and support those with Parkinson's disease

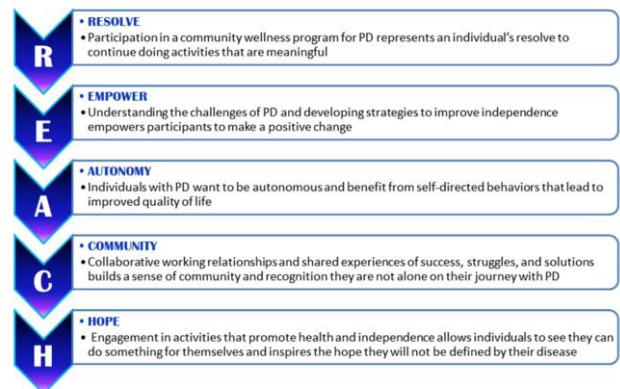
(PD) and their families. As a small non-profit with limited resources, we established key partnerships that served a unique need in the development, implementation, and sustainability of the program. A variety of outreach services and survey methods were used to determine what mattered most to those with PD and their care partners. These findings supported the development of a community program customized to the specific needs of the participants.

The 7th annual PD Purposeful Movement and Wellness Program is a collaborative effort between Parkinson Partners, and community members: UPMC Hamot Medical Center, Hamot Health Foundation, Salvation Army and Gannon University's Occupational and Physical Therapy Programs. This eight week program is offered three times a year and serves approximately 12–15 participants per session. The purpose of this program is to engage participants in evidenced-based exercises and education tailored to people with PD that can be continued at home through a daily routine.

This presentation will highlight several teaching points:

- Understanding what is important and valued in your community forms the framework for development and implementation.
- There are many barriers to exercise participation in public facilities including equipment accessibility, cost, and limited or no awareness of PD.
- PD affects everyone differently and a successful program must be responsive and flexible to the needs of the participants
- The use of graduate OT and PT students provided safety, support, and adaptability
- Engaging in socialization was highly valued by participants
- We developed an approach designed to help participants REACH Wellness:
 - Resolve
 - Empowerment
 - Autonomy
 - Community
 - Hope

In summary, non-profit organizations are uniquely equipped to serve as advocates for improving wellness in the PD community. Working collaboratively with stakeholders can provide needed resources to achieve a common goal of living well with PD.

**Working Together to REACH for Wellness**

P40.20

Long-term effectiveness of Alexander technique lessons for managing symptoms of Parkinson's disease: case studies

Robbin L Marcus¹, Gabrielle Czaja², Rajal G Cohen³, Candace Cox⁴, Monika Gross⁵, Morgan Rysdon⁶

¹ The Poise Project, Asheville NC., Lithonia, Georgia, USA

² Washington Health & Healing, Washington, District of Columbia, US

³ University of Idaho, Moscow, Idaho, USA

⁴ Big Sky Alexander Studio. The Poise Project., Castleton, Ontario, Canada

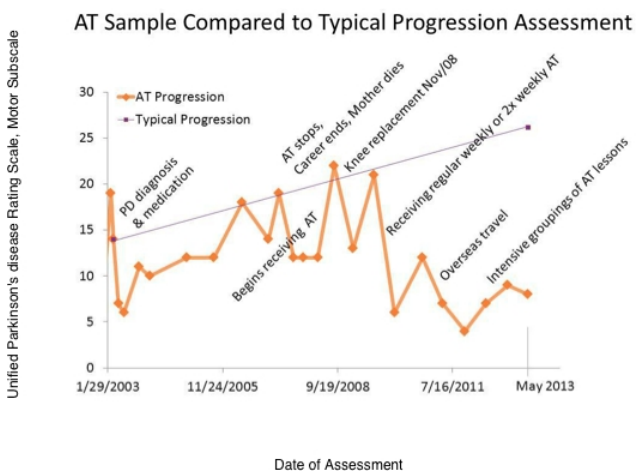
⁵ Form Fitness & Function. The Poise Project., Asheville, North Carolina, USA

⁶ Center Studio LLC. Faculty, The Edmond J Safra Parkinson's Wellness Program – JCC/NYU Langone Hospital, NYC., New York, New York, USA

Objective: To illustrate progression in motor symptoms of idiopathic Parkinson's disease (PD) in individual patients who have had regular Alexander Technique (AT) lessons for at least 3 years.

Background: AT is an educational approach that teaches attention and inhibition to change functional patterns, reduce rigidity, and improve balance and efficiency during exercise and activities of daily living (ADLs). Lessons involve verbal instructions and hands-on guidance to teach self-management strategies that improve and, as much as possible, restore functional movement patterns, enabling the person with PD to participate in ADLs with minimal interference from PD symptoms.

Preliminary data: Candace Cox previously presented a single case study at the 3rd World Parkinson Congress in Montreal in 2013. (Cox, 2013). Diagnosed with PD and prescribed medication in 2003, the patient then had AT lessons for 10 years. Independent, qualified physiotherapists assessed progress of the patient's PD symptoms using the Berg Balance Scale, Timed Up and Go (TUG) and UPDRS III (Motor Subscale) at regular intervals. AT lessons improved range and control of motion and enabled the patient to learn and apply new strategies in sitting, standing, walking, and reaching. Objectively measured symptom severity remained low ten years after diagnosis.



Approach: Using the method of Cox (2013), we will present case studies of 10 PD patients with at least 3 years of AT training. We will compare these to typical progression (as defined by Williams 2012; Mari 2012). Each case study will identify whether the subject initiated AT training before or after diagnosis, and the duration, form (i.e. group or private) and frequency of AT training. Subjective survey responses from subjects, and from their care partners if applicable, will also be presented.

Conclusion: AT shows promise as a long-term self-management approach to reduce PD motor symptoms and maintain an active life.

P40.21

A study on dysphagia, nursing meals, and meal delivery services for patients with Parkinson's disease

Aiko Matsushima¹, Akihisa Matsumoto², Fumio Moriwaka³, Sanae Homma³, Kazunori Ito⁴, Keiko Yamada⁴, Shun Shimohama⁵, Junichi Matsushima⁶, Hirofumi Ohnishi⁵, Mitsuru Mori⁵

¹ Department of Public Health, Sapporo Medical University Graduate School of Medicine, Sapporo, Hokkaido, Japan

² Jyozankei Hospital, Sapporo, Hokkaido, Japan

³ Hokuyukai Neurological Hospital, Sapporo, Hokkaido, Jersey

⁴ Iwamizawa Neurological Medical Clinic, Iwamizawa, Hokkaido, Japan

⁵ Sapporo Medical University School of Medicine, Sapporo, Hokkaido, Japan

⁶ Matsushima Oto-laryngeal and Dizziness Clinic, Sapporo, Hokkaido, Japan

Objective: This study aims to investigate the actual conditions of diets among patients with Parkinson's disease (PD), focusing on the use of nursing meals pre-cooked for the elderly and food delivery services, food processing methods to prevent aspiration pneumonia, and the effectiveness of these.

Methods: Questionnaire surveys were conducted twice at two hospitals and one clinic in Hokkaido, Japan: the first survey period was from February to October of 2013, with 244 PD outpatients participating. The second survey was administered to the same participants in May of 2015 with 209 responding. We performed the Student's t-test to evaluate changes in the dysphasia status. Mean ages at the first and second surveys were 71.2 (+8.4) and 70.3 (+8.3) years old, respectively.

Results: In the second survey, with 209 responses (85.7%), 205 (98.1%) were regarded as valid. The result of the t-test showed a significant deterioration in the dysphasia score between the two surveys (22.8-month interval) ($p < 0.001$). Using nursing meals pre-cooked for the elderly ($n=3$) and food delivery services ($n=18$ including 2 users of the nursing meals pre-cooked for the elderly) was reported as not popular in the second survey. However, the number of users of nursing meals pre-cooked for the elderly and food delivery services doubled as it was only 8 in the first survey. For good points of using care delivery services, participants reported that the services alleviated the burden of the participants (PD patients) and their caregivers for meal preparation, and improved nutritional balance.

Conclusion: Findings suggest that using nursing meals pre-cooked for the elderly and food delivery services to improve diets is one effective option for PD patients to decrease the burden on caregivers that is assumed to increase as the PD and dysphasia become more serious.

Keywords: Parkinson's disease, dysphasia, efforts to improve diets, nursing meals pre-cooked for the elderly, food delivery services

P40.22

"While I dance, I don't have Parkinson's." The perceived impact of arts-based programming for people with Parkinson's

Nancy Mazson
Waltham, MA, USA

Introduction: Medical management of Parkinson's Disease (PD) is only one of the growing challenges as the disease progresses; other challenges, such as decreased social engagement, increased isolation, and decreased physical function, contribute to an overall decrease in quality of life (QoL) for the PWP as well as his/her care partner and family members. In response to the need to support the social and emotional challenges of the disease for all family members affected by PD, the Parkinson's Family Support program

(PFSP) of Jewish Family & Children's Service Boston (JF&CS) has provided arts-based activities for over ten years. These activities include choral singing and therapeutic dance; support groups; and information and referral, which together have resulted in a thriving and supportive local community.

Objective: While the relationship between art and health has been researched for the general population, only a few studies have attempted to measure the perceived impact of arts-based programming on PWP and their care partners. However, in order to meet the increasing demands from nonprofit funders to show impact of our work, as well as an internal desire to better understand the impact of our programs, staff at JF&CS undertook a qualitative exploratory study examining the perceived impact of participation in the dance and singing groups for PWP and their care partners.

Method: Twenty people who participated in weekly choral singing and/or dance programming for at least one year were interviewed in person or by telephone using a semi-structured interview protocol. The interviews were recorded, after which they were transcribed, analyzed and coded for common themes.

Results: As a result of the coding process, several key themes emerged, such as reduction of social isolation, meeting a need in the community, and improvement in quality of life. In addition, we also used a case study approach to examine the personal stories shared with us, such as: "Well I look forward to it, I don't want to miss it. . . . Because when I attend the class, this class, in this environment, I don't even think about Parkinson's." "When I come here I relax, I feel comfortable, I feel that the outside world is leaving me alone and I come in with a group of people that are very welcoming and accepting." Staff of PSFP have used this study to continue to improve the programs as well as to have a means by which to describe the impact of programs to external audiences.

P40.23

Living large with Parkinson's/ hiking the Pacific Crest Trail

Bill Meyer

PasstoPass.org, Spokane, WA, USA

Background: Parkinson's can feel like an incremental yet accelerating loss of participation and dreams. Living large in the world and tackling these limitations in the body and mind created the idea to hike a beautiful and demanding section in Washington State on the Pacific Crest Trail (PCT). The PCT is recognized around the world as an icon of bold and spectacular hiking extending from Mexico to Canada. It symbolizes a challenge requiring strength and courage to dream BIG. Soloing this dream was not an option for one dealing with the advancements of Parkinson's. Sharing a common desire and overcoming adversity together with a community of Parkinson's (PD) folks and other support people became the objective.

Objectives: There are several objective layers to the hike. The physical challenge is to hike 72 miles from Stevens to Snoqualmie Pass on the PCT in the Cascade Mountains as a team of Parkinson's folks and support hikers. We are also increasing awareness of PD through community and organizational outreach by utilizing our website as well as individual communication within our networks. And, through our efforts we are encouraging fundraising opportunities in support of such organizations as APDA, TEAMFOX and NWPF.

Methods: For awareness and fundraising our broad outreach continues months before the actual hike in Aug. 20th – 28th, 2016. Our website; www.passtopass.org provides a platform for explaining our goals while individual communication continues within our various professional and personal communities.

The physical challenge of the hike in wild and remote terrain with roughly 18,000' elevation gain requires additional support by adding pack animals. Every Parkinson's hiker will have 1 support person for

a 1 to 1 ratio of hikers with a maximum of 12 folks. We will hike roughly 9+ miles per day for 8 days with an avg. 2250' elevation gain per day. We will practice 'leave no trace' camping.

Results: Everyone completing the hike with no major injuries or issues is defined as a success. Certainly increasing much needed funding support to help Parkinson's organizations committed to finding a cure or easing the burden is a success. Finally, increasing awareness around the issues of Parkinson's is defended as a success. Perhaps a deeper measure of success, though less tangible, is taken step-by-step. It is the individual's powerful inner courage and determination to say YES to living LARGE and WELL with Parkinson's which offers an example for others.

P40.24

Creating a grassroots non-profit to provide programs and services to improve the quality of life for people living with PD

Mary Neilans

Toronto, ON, Canada

A group of people living with Parkinson's disease (PD) in Toronto came together to address the need to develop an organization that would provide direct programs and services to help people Live Well with Parkinson's. In 2016, the Parkinson's Resource Centre (PRC) was formed to meet this need and to provide resources to improve the quality of life for people with PD. While it's critical to find a cure for Parkinson's, we feel strongly that people living with this disease also need information and resources to live well each and every day.

The initial program offered by the PRC is Rock Steady Boxing Toronto (RSBT), the first Canadian affiliate of the successful Rock Steady Boxing program established in the US in 2006. Rock Steady Boxing is based on a non-contact boxing training regime designed for people with PD. It is also a fun and socially engaging exercise program that provides participants with numerous health benefits that mitigate both the physical and cognitive symptoms of Parkinson's.

Additional programs will include self-management, mindfulness, nutrition, caregiver stress management, financial planning, yoga, dance, and other resources developed based on client-identified needs.

The PRC hopes to serve as an "umbrella" organization to provide information, resources, and a full events calendar to individuals diagnosed with PD, to their families, and to the medical community throughout the Greater Toronto Area (the GTA, with a population of over 4 million, including thousands of people living with PD). While the PRC will provide some programs directly, the organization will perform ongoing community outreach to establish connections with other organizations in the GTA that offer Parkinson's-specific programs and resources. Too often, individuals newly diagnosed with PD are left with more questions than answers. The PRC hopes to fill this gap.

PRC website content will include information and links related to the following categories.

Self-Management and Self-Care

- Exercise and Movement
- Diet and Nutrition
- Attitude and Mental Health
- Rest and Relaxation
- Dealing with Depression and Anxiety
- Support of Others
- Caring for Caregivers

Surviving and Thriving

- Practical suggestions for facing daily challenges
- Working through changes in relationships
- Financial challenges: Facing job loss, insurance issues, retirement and security, disability funding

- Rediscovering yourself: Redefining who you are, your priorities, abilities, what you have to offer the world

P40.25

The lived experience of Parkinson's disease: insights from people living with the condition and those who support them (STEP™ research)

Jared Niedenthal¹, Lizzie Graham², Courtney Lawrence³, Elisabeth Dohin⁴, Patrick Graham³, Dolores Terricabras⁵

¹ UCB Pharma, Smyrna, GA, USA

² European Parkinson's Disease Association, London, United Kingdom

³ Idea Couture Inc, Toronto, Ontario, Canada

⁴ UCB Pharma, Brussels, Belgium

⁵ UCB Pharma, Slough, United Kingdom

Background/Aim: The traditional view of Parkinson's mainly focuses on physical symptoms. The STEP™ program aimed to better understand the full lived experience, and develop solutions for people living with Parkinson's (PwP) and those supporting them.

Methods: Table 1 shows methods/participants. Data were collected using field notes, video/audio, and photographs. Anthropologists and strategists combined observations, categorized findings into themes, and developed 1) key insights, and 2) an experiential Parkinson's journey for PwP and partners/caregivers.

Results:

1) Key insights:

- Clinical definitions of Parkinson's over-simplify the full experience; to truly appreciate challenges of living with the condition, the complex physical, mental, social, and emotional experience must be included.
- Physical loss is not always the hardest; PwP also evaluate Parkinson's impact based on social loss, emotional lows, and sometimes also cognitive impairment.
- Parkinson's is not simply a gradual accumulation of symptoms but a complex transition from a life without Parkinson's to a PwP; this can vary dramatically (throughout day and over-time) depending on medication/lifestyle.
- PwP see the impact on quality-of-life as central, as Parkinson's can challenge mood, sleep, daily activities, and interpersonal relationships.
- PwP become the experts on their version of Parkinson's and rely on a diverse network of experts for support.
- PwP consider themselves host to an "unwelcomed guest", striving for Parkinson's not to become their identity.
- Dedicated to maintaining a pre-Parkinson's lifestyle, PwP develop strategies to manage daily activities; many try to embrace their situation with optimism.
- Parkinson's is a shared disease; progression to advanced stages is difficult to navigate for both PwP and loved ones/caregivers.

2) The Parkinson's journey:

- Medical scales (e.g., Hoehn & Yahr) fail to capture the full experience.
- Parkinson's is first experienced as a lifestyle disease, then as intermittent periods of capability and loss, and finally as a loss of independence.
- While PwP experience a transformation, so do loved ones; partners often transform to caregivers.

Conclusions: The STEP™ research illustrates the unique lived experience of Parkinson's, which can impact a person's life, relationships, and identity. These evidence-based anthropological insights are supporting the development of solutions for PwP addressing the condition's multiple dimensions.

UCB Pharma-funded.

Table 1. Methods and participants of the STEP™ research.

Research methods	Participants ^a (number)	
Methods to glean the experience of Parkinson's directly from PwP and their partner/those providing care and support	Ethnography (empathetic, in-depth study of people and the behaviors, beliefs, attitudes, places, and relationships that form their lives through observation and interviews) ^b	16 (12 PwP and 4 caregivers)
	Context labs (participatory group discussions [3-4 people], where individual experiences are shared openly)	66 (51 PwP and 15 caregivers)
Methods to collect the experience of healthcare professionals (HCPs) and other Parkinson's experts	Expert interviews (in-depth, one-on-one interviews with HCPs and other experts that have frequent interactions with PwP)	18 (5 neurologists, 2 geriatricians, 2 nurse practitioners, 2 physiotherapists, 2 occupational therapists, 1 health transition coach, 1 neuro-psychiatrist, 1 Parkinson's dance program founder, 1 associate at Parkinson's Society of Canada, 1 medical information group associate from UCB Pharma)
	Field immersions (visits to the places and spaces where PwP spend time interacting with HCPs and other experts)	3 (1 physiotherapy/mobility clinic, 1 comprehensive care Parkinson's clinic, 1 Parkinson's dance class)

^aRecruited through patient organisations and a medical recruiting partner in the UK, US, and Canada.

^bParticipants were visited at home, with each visit lasting between 2 and 4 hours. STEP™ is a trademark of UCB group of companies. ©2016 UCB. All rights reserved.

P40.26

Living well by doing [*]; keeping it interesting

Daniel Novak

PDF, Westworth Village, TX, USA

"I keep going because I still find it interesting" (Paul Nitze). See how one person with Parkinson's keeps it [life and PD] interesting through a wide variety of mental and physical activities including continuous learning, challenging work, serving others, social engagement, diverse exercise, and a healthy lifestyle. This PWP has worked to preserve cognitive, motor and social function through consistent use of Wii balance games, musical chairs [homemade vibro-acoustic therapy], recumbent bicycles, boxing workouts, multiple forms of exercise, physical therapy, audio-visual entrainment (AVE), neuro-feedback, demanding work, wearable tracking devices, PD education, standard PD medications, and old-fashioned piddling around. He also had DBS surgery in 2013, but he had it turned completely off in 2015 and only has one side active in 2016, so these activities are not dependent on DBS. These activities and behaviors have a positive effect on autonomic functions, fatigue, sleep, mood, apathy, and social interaction. For example, with a creative boost from Requip in the early days, this PWP customized his recliner into a vibro-acoustic sound machine that plays music and transmits sound waves from any input device including AV receivers, iPods / mobile devices and AVE devices.

He also designed and built custom aluminum bike carriers to transport his 8' long recumbent bicycle and his 9.5' long tandem recumbent bicycle. The carriers are very lightweight and easy to slide into a 2-inch receiving hitch on his SUV. The bikes mount securely with one hand.

Continuous learning keeps it interesting and offers mental and physical challenges. He engages in education about PD and other neurodegenerative issues, along with studying general health and exercise. He engages with graduate students and faculty through full time work.

Healthy behaviors are also an area of focus; healthy eating, vitamins, morning walks, weight management, sleep management and activity tracking.

Will expand upon the concepts shown in the attached pictures with timelines and activities.

Disclosures: No financial or other interests in any of the products or services, no future interests will be accepted. Details of products and designs to be made available [if requested and appropriate] to PWP through a 3rd party website such as PDF.org.

P40.27

Pedaling, living well, seizing the day

Elizabeth Ogren

Mentor, Golden valley, MN, USA

After diagnosis I spent significant time “on the couch”, not moving, as if I could fend off my movement disorder.

My brother proved to me that laying down was not going to help me feel better. He came to my house daily to take me to the health club. After less than three weeks of “forced” exercise, I felt amazingly better. I got back into bicycling—an activity I had neglected since my diagnosis.

Objective

I had to share the secret: Movement is Therapy!

I developed a plan for an annual biking event: Pedal and Roll for Parkinson's, a bike ride for people with Parkinson's, their family and friends.

Method: I shared the Pedal and Roll for Parkinson's plan with my family and my mentor at Park Nicollet Struthers Parkinsons Center. With the support of Struthers and two local bike shops, we borrowed several tricycles and four-wheel, side-by-side tandems to borrow for our event. We attracted 180 people from across Minnesota to come out from behind walkers, to put aside their cane, or to get up from their wheelchair and rediscover the joy of pedaling.

Results: Since 2011 we have held an annual biking/ fundraising event to benefit Struthers Parkinson's Center's exercise and quality of life initiatives. We have evolved into a year-round program of Nordic walking and biking. We have walked and biked with hundreds of people in the greater Twin Cities area. NPFM (National Parkinson Foundation Minnesota) supports excursions to greater Minnesota and cities bordering Minnesota. Our 14 balance- friendly “bicycles” are now available to borrow for free from our storage location on the Minneapolis Greenway. We offer individual “test ride appointments” so we can explain the different styles of bike and make specific comfort adjustments for the unique rider. We have 12 group rides on our summer 2016 schedule.

We provide opportunities for riders to help as “group ride leaders”, “bike mechanics” and “Behind the scenes support”.

Conclusion: In addition to the direct health benefits of cycling, a “club” like Pedal and Roll provides motivating social engagement and opportunities to contribute to others' well- being. All of us benefit with better physical, social, and emotional health. Our knowledge and experience could be used to create a similar program in other areas of the world. Together we pedal, motivate each other and model 'living well' to others. In return, We have a reason to get up in the morning and to seize the day.

P40.28

Our stories: living well with Parkinson's in the early stages of diagnosis

Pamela Paisley

The University of Georgia (on leave – please use home address), Athens, Georgia, USA

This poster session will present the results of a qualitative research study focused on the lived experience of People with Parkinson's (PWP's). The study used qualitative methodology combining structural components and principles from heuristic inquiry and cross-case analysis. The study sought to describe and reflect upon the stories of the researcher (diagnosed in 2010) and 3-5 other People with Parkinson's (PWP's) within one to seven years of diagnosis who “were doing well” as identified through self-report or by referral from their neurologists. The study also limited participation to individuals diagnosed after the age of 50. This exploratory study used a case study approach for each individual story and cross-case analysis to identify common themes. Final themes were determined in collaboration with the participants. The researcher recruited participants through snowball sampling of Parkinson's networks of which the researcher was a member as well as through flyers in two neurologists' offices. The poster session will present common themes identified through participants' stories as well as providing examples of continuing connections between and among participants in empowerment and advocacy initiatives.

P40.29

Overcoming the freezing of gait: a development experience in walking aids (Concepción, CHILE)

Miguel Pino

Concepción, Chile

Background information: Freezing of Gait (FOG) is a common complication of Parkinson Disease, and often is not possible to control them with the medication, which makes this symptom a particularly disabling problem.

Technical Aids are elements used by a person with disabilities to prevent the progression of the disability, or to recover his or her functionality and develop an independent life.

This need in the people with Parkinson Disease, turned into our motivation to develop a new product which easily allows the patient overcoming an acute FOG episode and restore their confidence to walk independently.

Objectives: Develop a new, safe, versatile and efficient walking aid, specifically designed for the PD patient.

Improve the quality of life of the PD patients who currently don't have any kind of technical aid to overcome FOG episodes.

Organize and promote different kinds of activities to educate and motivate PD patients and their families, health care professionals and general community in PD related topics.

Methods:

Our project starts with a review of the medical publications and articles about FOG in Parkinson Disease and strategies to overcome them in therapy and in daily living.

We also did surveys to explore the daily reality of the PD patient and so integrate their experience in the design of the first laser device prototype.

In 2014, we conducted a pilot clinical trial to test the efficacy of the early prototypes in overcoming FOG episodes.

In 2015, we improved the design of the prototypes to develop a commercial viable unit. We also studied the potential market and developed the project official website.

We also did several activities to educate people of our city during two years of constant and committed work.

Results:

The nofreeze laser device for walking aids is now finished and ready for patients use.

The results of the 2014 pilot study demonstrate the efficacy of the nofreeze device, with a significative reduction on the number and the duration of the FOG episodes during walking.

Now our work is recognized in our city of Concepcion as a positive contribution to the quality of life of patients.

Conclusion: With persistent work, we've been able to contribute to the rehabilitation of the Parkinson Disease in a concrete way, by making available for patients in Chile and around the world a new walking aid which gives an answer to the real needs of the patients. NOFREEZE can really help patients become more independent and able to participate for a longer time.

P40.30

Coping strategies: direct insight from people living with Parkinson's disease

Allen Rabinowitz¹, Allison Little², Joe D'Souza², Jesse Fishman², Gregory Cohen², Imane Wild²

¹ Person living with Parkinson's disease, Atlanta, GA, USA

² UCB Pharma, Atlanta, GA, USA

Background: People living with Parkinson's (PwP) have identified coping as a priority area of research that deserves more attention.

Objective: To gain insight from PwP and their caregivers on their most helpful coping strategies, and to share their experiences.

Methods:

1. More than Motion™ Facebook Coping Strategies project – The More than Motion™ Facebook page is an online community enabling PwP, caregivers, and healthcare professionals (HCPs) to connect, receive information, and share experiences. We asked PwP and caregivers to submit their coping strategies. A group within UCB Pharma reviewed all entries and the top nine were shared on the More than Motion™ Facebook page; the community was asked to vote on the strategy that resonated best with them.
2. Coping Strategies focus group – A one day face-to-face meeting (discussions and workshops) held with PwP, caregivers, and HCPs focused on coping strategies, difficulties and unmet needs.

Results:

1. More than Motion™ Facebook project: The 113 received strategies were categorized into different topics: "Exercise/physical activity/physical therapy" (35%), "Attitude/spiritual coping" (35%), "Relaxation techniques" (6%), "Community support" (5%), "Other" (19%). Of the top nine strategies shared on the More than Motion™ Facebook page, the coping strategy that resonated best with the voters was titled "Parkinson Fight Club", a social group of ~480 friends (75% Parkinson Friends and 25% Caregivers) who meet regularly: "Our strategy is SOCIALIZE, EXERCISE, AND COMMUNICATE."
2. Coping strategies focus group: 5 PwP, 2 caregivers, and 3 HCPs (physiotherapist, social worker, nurse) discussed coping strategies and key difficulties/unmet needs; to summarize:
 - PwP have multiple symptoms and none have exactly the same set of symptoms; this can make relating to other PwP challenging.
 - The PwP were frustrated with available information via websites/social media; tends to be general, vague, and rarely describes their symptoms as they experience them.
 - Age appropriate education for family members is a significant unmet need (especially for children).
 - While most of the PwP did not read original research articles, all were interested in having scientific data translated into plain language.

Conclusions: Coping strategies is a key topic in Parkinson's and further initiatives are needed to increase awareness.

Funding: UCB Pharma.

P40.31

From patient to athlete: the development of a novel goal based, interdisciplinary group exercise model for Parkinson's disease

Deanna Rayment¹, Amy Lemen², Meghan Sweeney², Lonnie Nemiroff², Jody Jacob-McVey³

¹ The Marlene and Paolo Fresco Institute for Parkinson's and Movement Disorders at NYU Langone Medical Center, New York, NY, USA

² The Marlene and Paolo Fresco Institute for Parkinson's and Movement Disorders, New York University Langone Medical Center/NYU School of Medicine, New York, NY, USA

³ The Edmond J. Safra Parkinson's Wellness Program-NYC, New York, NY, USA

Objective: To develop and implement a novel, interdisciplinary, community based fitness training program for individuals living with Parkinson's disease (PD) that addresses the physical and psychosocial components of the disease process.

Method: The Edmond J. Safra Parkinson's Wellness Program-NYC Bold Moves Walking Group consists of 8-10 individuals living with PD who train for the 1.4 mile walk at the annual Parkinson's Unity Walk in New York City's Central Park. Bold Moves was designed as a unique model of psychosocial and fitness collaboration co-led by an experienced triathlon trainer and a social worker. The program also includes an educational component by incorporating the training of a master of social work student. This 12-week training program incorporates fitness training education and technology, as well as addresses the emotional needs of participants. Each week participants meet for one 90-minute session, focusing on key components including: body awareness, mobility, strength and aerobic conditioning, confidence building, and group therapeutic support

Results: Reaction to the program has been positive on both physical and psychosocial impact. Participants reported that they became more aware of how PD symptoms affect their daily activities both physically and emotionally. They have reported more confidence, fewer falls, symptom relief, and an overall improved sense of wellbeing in addition to improvements in balance, muscle tone, and body alignment. Participants report a greater frequency of aerobic activity between group sessions. Interdisciplinary collaboration with social work helped participants build a cohesive and supportive network environment. The therapeutic group modality provided support with emotional health, adaptation and management of the feelings that arise in relation to living with PD. Participants report improvements to self-esteem, mood, motivation, and anxiety.

Discussion: This group exercise model motivates participants to exercise, through scheduled, goal-based targets while addressing issues related to the emotional adaption to PD. Participants developed confidence while exercising in a supportive group environment and had an opportunity to redefine their sense of self as athletes rather than patients. Further evaluation and expansion of the program is being considered.

P40.32

Living, learning and laughing with Parkinson's disease

Beverly Ribaudó

Parkinson's Humor, Yuma, AZ, USA

Objective: Teach people about life with Parkinson's disease using humor as both a learning tool and coping mechanism, by Blogging and using Social Media.

Methods: In July of 2011, I started writing my funny stories about my life as a Parkinson's patient in blog form and later on, in book form.

The title of both my blog and book are Parkinson's Humor. The book is available on Amazon worldwide.

Results: My results were amazing. Within a month, I had 1000 visitors from six continents reading my Parkinson's Humor stories. Now my page view counter is at 360,000 and I have readers from 169 different countries. I write about everything and anything Parkinson's, and always try to make it upbeat. I even wrote about my DBS surgery with pictures taken in the operating room. I started a separate blog, My DBS Story which details the process from evaluation to follow up programming. I have a knack of turning confusing medical jargon into user friendly stories that anyone can understand. My stories have been shared by various Parkinson's groups around the globe and on the Michael J Fox website. I run our local Parkinson's support group, help plan local conferences, help educate my local medical community, speak to Medical School students, advocate for more trained therapists and exercise classes. I am active on both Twitter and Facebook and contribute to several Facebook Groups related to Parkinson's.

P40.33

Establishment of InMotion, an independent, fee-free community center for persons with movement disorders

David Riley, Karen Jaffe, Judy Peters

InMotion, Warrensville Heights, Ohio, USA

Objective: To describe the establishment of a community center, InMotion (IM), for persons with movement disorders.

Background: Needs of people with movement disorders grow with expansion of knowledge about motor and non-motor manifestations, and their treatment. The need for lay information guided by knowledgeable parties also grows. However, access and resources for patients have lagged behind. For example, extensive research has shown the value of physical activity for PD, but patients have difficulty finding places where they can safely carry out physicians' recommendations.

Methods: We gathered a group of interested parties consisting of people with PD, a movement disorders specialist, an exercise coach, and philanthropists. We organized a board with varied expertise in nonprofit agencies, law, accounting, and development. We obtained nonprofit status. A Development Committee was charged with fundraising. Using seed money from a major donor, an architectural firm designed a space next to an existing physical fitness facility, including a multipurpose activity room/lecture hall, resource center/library, and meeting rooms.

We drew up a program of targeted exercise, sport (boxing/cycling), dance, tai chi and vocal classes, began two series of monthly lectures, established separate support groups for patients and care partners, and set up a mentorship program for newly diagnosed patients.

All offerings are provided to the community free of charge. Facility operations, administrative salaries, instructor fees and other expenses are fully supported by philanthropy.

Results: In the first 13 months since opening in March 2015, 527 clients registered, with a mean of over 40 new ones per month, raising monthly attendance to over 1,000 visits to our various offerings.

A large grant from a local philanthropic fund allowed us to expand from 3 to 5 days per week. To date, IM has raised over \$1.5 million in pledges, of which over \$1.1 million has been collected.

Conclusions: It is feasible to open/operate a comprehensive community center for persons with movement disorders, independent of existing institutions with other missions and agendas. This model depends on the dedication of many individuals with varying backgrounds to raise funds, set and execute programs, and operate the facility. Nevertheless, our experience with the

enthusiasm and support of our clients and the general community convince us that the effort has been highly worthwhile.

P40.34

Music matters choral initiative: a research and action project involving PD choirs in Philadelphia and Baltimore

Marjorie Samoff

Music Matters International, Philadelphia, PA, USA

Marjorie Samoff, Executive Director, Music Matters International, a non-profit which fosters research on music and the brain and translates that research into evidence-based programs. Choir Directors: Holly Phares, Leo Wanenchak. Scientific Advisors: Allison W. Willis, MD, MS. Associate Professor of Neurology, Perelman School of Medicine, University of Pennsylvania; Alexander Y. Pantelyat, MD. Director, Atypical Parkinsonism Center, Assistant Professor of Neurology, Johns Hopkins University School of Medicine.

This presentation will report on the formation and working methods of Philadelphia's and Baltimore's first Parkinson's choirs, the ParkinSingers and the Parkinsonics, and discuss the status of ongoing research to assess the measurable effects of choral singing on people with Parkinson's at Penn Medicine and Johns Hopkins.

We formed these choirs with a commitment to professional musical leadership, active member engagement in choosing repertoire, and regular public performances so that making music for others would be a central focus in the life of our choirs. This poster will share the experiences of our growing choirs with repertoire, rehearsal techniques, user-friendly at-home practice tools, and building community through choir participation. We will also discuss obstacles that we face, the challenges of conducting research, and solutions we are developing to help form evidence-based PD choirs that are widely available, financially sustainable, and accessible to all.

The Music Matters Choral Initiative seeks to forge a network of PD choirs working in partnership, enabling members to incorporate music-making into their daily lives. The project aims to contribute to the growing research on the impact of choral singing, and to deepen our understanding of the neural underpinnings of how music works in our brains.

The Philadelphia ParkinSingers Choir includes people with PD, care-partners, and community members uniting to make powerful music. Although our conditions vary, we have forged deep bonds and draw strength from group music-making. Members self-report a range of improvements in quality of life, vocal strength, memory, and a positive spirit from being part of a purposeful community.

This "Sung-poster" will present our work and offer WPC attendees a chance to sing with us, so they can experience first-hand the connection between music-making, joy and quality of life. Please join us in song.

P40.35

Spreading smiles and healing through art to those with Parkinson's disease

Saba Shahid

Massasoit Community College, Brockton, MA, USA

People with Parkinson's disease (PD) benefit from engaging in activities that promote creativity, relaxation, and positivity. The Art Cart's Smile Trough Art Workshop is specifically designed to help those with PD explore their creativity by targeting areas that are unique to this population. Our program includes modified equipment (easels, paint brushes, palates, etc.) which has shown to meet the needs of PD participants more successfully than traditional art equipment. For the workshops we design activities that will help this

population combat symptoms of PD such as tremors, rigidity of limbs, micrographia and loss of fine motor control. While our paint dries, we encourage our participants to follow along and participate in exercises that have been developed in conjunction with DopaFit, a Parkinson's disease specific exercise company.

After the culmination of each workshop, participants have the opportunity to provide their feedback regarding the impact the art workshop had on them through a survey. As anticipated, those with PD who participated in our Smile Through Art Workshop left with a heightened level of mood and an increased interest in exploring their creativity. Thus far, nine (9) workshops have been programmed for the PD population in Massachusetts, targeting a total of 24 participants. Six (6) of the nine (9) workshops were offered through a continuous weekend program.

Thus, it is believed that engaging in art and promoting a healthy environment is beneficial and leaves those with PD and their caregivers with a heightened quality of life.

P40.36

Hospitalized patients with Parkinson's disease: using the electronic medical record to reduce medication errors and reinforce staff education at St. Joseph's Hospital and Medical Center and Barrow Neurological Institute

Edie Simpson¹, Matt Baugh², Darolyn O'Donnell³, Julie Ward⁴, Terry Bachman⁵

¹ Muhammad Ali Movement Disorder Center, Phoenix, AZ, USA

² St. Joseph's Hospital and Medical Center and Barrow Neurological Institute, Phoenix, AZ, USA

³ Muhammad Ali Parkinson Center, Phoenix, AZ, USA

⁴ St. Joseph's Hospital and Medical Center, Phoenix, AZ, USA

⁵ Barrow Neurological Institute, Phoenix, AZ, USA

People with Parkinson's Disease are hospitalized more frequently, have longer stays, and poorer outcomes than age related peers. Most problems identified involve a lack of understanding by hospital personnel regarding the complexity of Parkinson's Disease and the medications to treat it.

Four areas were identified to reduce medication errors and improve care: 1) quick identification of PD patients at the time of admission; 2) clear communication between the pharmacy and nursing units regarding the timely administration of medications, based on the at-home schedule; 3) expedited reconciliation of non-formulary medications, and alignment of at-home and inpatient medication schedules; 4) staff education and support.

The electronic medical record (EMR) now replaces written charting and paper references. Therefore, the EMR was felt to be the appropriate tool to address these areas

We have used the EMR as follows: 1) alerts to the Movement Disorder Center and pharmacy when a PD medication is ordered, notifying these areas that a patient with PD has been admitted; 2) notifications have been added to all PD medications of the importance of administering these medications on the same schedule as patients take them at home. If a PD medication is ordered without specific times given, the pharmacy is instructed to contact the nursing unit for the specific times the patient administers this medication at home; 3) for each PD medication there is an associated "reference text" available giving bullet points of information about PD and the particular medication involved, providing consistent reminders for staff, and ; 4) if a medication is ordered that is contraindicated in Parkinson's Disease, a pop up notifies the ordering physician that this medication will make PD worse, and provides the safe alternatives to use.

In addition to use of the EMR, we have provided mini in-services to the nursing units, a 4 CEU class for nurse educators and charge nurses, and in-services for house staff.

Conclusion: We have implemented an EMR based system to minimize medication delivery errors and to alert providers to

contraindicated medication alternatives. Study is being done to assess clinical outcomes and impact on nurses and nursing care.

P40.37

The benefits of therapeutic group singing for PWP in six "Tremble Clefs" chapters in southwestern USA

Karen Skipper¹, James Wong²

¹ Orange County Tremble Clefs, San Juan Capistrano, CA, USA

² Orange County Tremble Clefs, Orange, CA, USA

Summary: People with Parkinson's (PWP) and their caregivers often view fading voice, communication and swallowing difficulties as important contributors to degrading quality of life as the disease progresses. The "Tremble Clefs" use singing to improve voice quality, volume, lung capacity, breath control and swallowing through vocal exercises and songs. Choral singing also provides a supportive and enjoyable activity for people with Parkinson's disease and their care partners in a creative and collegial activity. The six groups surveyed are led by Board Certified Music Therapists (Orange County and Phoenix metro) and a trained, professional choral conductor (San Diego).

Objective: Determine the benefits that participants perceive they are receiving by singing with Tremble Clefs, and the relative importance of each benefit for improving participants' quality of life.

Method: This project surveyed approximately 150 "Tremble Clefs" singers in Southern California (San Diego and Orange Counties) and the Phoenix, Arizona metropolitan area. Each of the three regions has well established chapters that have been active for >10 years. The self-reported survey asked about each singer's perception of the benefits of participation in this program, as well as other demographic data.

Results: Detailed results of the analysis will be presented in the body of the poster. The factors that contribute to building a successful group will also be discussed

P40.38

Meaningful work, a quality of life issue

Gwendoline Spurr

McGill University, Montreal, Quebec, Canada

Objective: After ten years of living with Parkinson's, my functional status is no longer good enough to practice medicine. I describe some of the things I am doing to keep my mind active and perform useful work.

Methods: As unpredictable "off" periods and dyskinesia made it progressively more difficult for me to practice medicine as a hematologist, I have had to retire from practice. The final straw was when the combination of levodopa-induced dyskinesia and microscope-induced travel sickness caused me to vomit in the lab while I was interpreting blood smears.

One of the major contributors to quality of life is useful work, which I have found in demystifying Parkinson's disease for my fellow patients. Each month I review a medical topic related to Parkinson's disease and give my support group a short summary of what is known in the area. It only adds to the challenge that I have to do this in French, which is very much my second language. I have the luxury of being able to spend almost unlimited amounts of time on this. My "students" hang on my every word, and I know that they understand what I tell them by the questions they ask.

At my husband's insistence I have started writing these lectures up (in English) and posting them on my blog: <https://www.bodysoulandparkinsons.blogspot.com>.

Results: This "useful work", in addition to the painting I took up a year before being diagnosed with Parkinson's and the memoirs I am writing, gives meaning to my life.

P40.39**Get Out!™ – intentional regular socialization improves mood, relationships and reduces isolation in people with PD***Judy Talley, Sarah Jones*

Parkinson & Movement Disorder Alliance, Tucson, AZ, USA

Parkinson's disease is a complex disease that requires an extensive amount of time and energy to manage. As a result, individuals with PD and their loved ones quite literally become victims to the disease and it becomes their entire identity. This program helps people with PD and those who love them regain some balance and enhanced quality of life instead of being consumed and diminished by the disease.

Conversations with more than 600 people around Arizona revealed that one of their greatest challenges is the dearth of opportunities to socialize with others with PD without attending support groups.

While PMDAAlliance is passionate about the value of support groups, we learned that many people do not feel support groups are right for them, and as a result do not connect with a support community at all. This is particularly true for young onset individuals and the newly diagnosed. We also know that an enhanced quality of life depends on building community, gaining friends and not feeling alone. These important facets of personal life are even better if they're accomplished in a way that also builds in fun and recreation.

Based in part on the research related to socialization and brain health completed by Stephen Ristau and reported in the Journal of the American Society on Aging, the Get Out!™ program features a monthly social time in a casual, restaurant environment. Educational discussions on topics related to living more fully with PD, including ways to mitigate the impact of PD on daily life are woven into the enjoyment of seeing others in a comfortable, upbeat gathering. By partnering with physicians, movement disorder specialists and other providers to offer the educational component, the format is conversational while meeting its purpose – to build increased socialization as a mechanism of improved brain health.

Quantitative program results demonstrate: 96% improvement in mood at the end of a Get Out! Event. 88% improvement in reduction of the experience of isolation for both people with PD and care partners. Qualitative data includes statements such as, "For the first time in years I felt like PD took the back seat." "We really need this time to just talk and enjoy each other. And if we get a good tip or a good laugh, it's icing on the cake."

P40.40**Parkinson's first hero: King David – the original message of hope for Parkinson's patients***Carl Voyles*

SNS Summerhill, Jackson, MS, USA

Introduction: King David of Goliath fame has recently been identified as the first named person to have had enough symptoms to warrant a diagnosis of Parkinson's disease (PD). Further investigation is appropriate.

Methods: A forensic investigative review of ancient literature provided the information base (literal interpretation of Jewish Scripture and Christian Old Testament).

Results: At an age estimated to be 60-61 years, King David suffered a career-changing sentinel event, narrowly escaping mortal injury from a Philistine giant named Ishbi-Benob. King David's men recognized his documented "weakness and exhaustion" (in retrospect, the alleged earliest recorded signal of his PD); they immediately banned him from the battlefield (2nd Samuel 21:15-17). From that point on, scholars agree that King David's focus shifted to his written legacy (books of Samuel, Psalms, and probably most of Proverbs). With even a cursory view, King David's verses outline (exude/shout) the motor disorder of Parkinson's disease (...like the

feet of a deer... I will not stumble...etc). More importantly for today's new Parkinson patient, the king recorded how his course improved once his despair and depression changed to hope through his faith. In late stage disease, King David's biography recorded further motor disability, social isolation, hypothermia and autonomic dysfunction – all common features in advanced PD.

Discussion/Conclusions: Historical records support the conclusion that King David suffered from a neurodegenerative process very consistent with PD. His positive attitude – attributed by him to his faith – led to a productivity that provides us with his written legacy now 3000 years later.

Club Parkee reflections:

1. Your second career contributions – perhaps unaware to you now – may supersede your first.
2. Creative writing – a function of creative thinking – provides a useful vehicle for negotiating the Parkinson's Trail. Your grandchildren may cherish your writing even after your tremor is gone.
3. King David's despair yielded to hope through Faith.
4. History often hides its secrets in full view. Just look around; you may find one.

P40.41**The benefits of physiotherapy: the experience of the Sibul Parkinson Society, Malaysia***Meng Chuo Wong¹, Hua Hung Song²*¹ Sibul, Malaysia² Sibul Parkinson Society, Sibul, Malaysia

People with Parkinson's (PwPs) live with physical, mental, and social health problems. We wish to share how our community has benefitted from doing group physiotherapy sessions Monday to Saturday.

Aims of the exercises**1. Enhancing flexibility**

We perform useful movements like neck and shoulder rotation, and foot and arm swings in a standing or sitting position. We do stretches, holding them with a hand or using a towel or resistance band. These exercises soften our stiff muscles and help us to relax. We apply heat therapy to reduce muscle stiffness and relieve pain. Following a therapist's instructions, PwPs can do this at home.

2. Improving strength and balance

Weight lifting and gym ball exercises strengthen and vitalize core muscles and other parts of the body. Together with treadmill gait training and other core strengthening techniques, they improve body balance. Colored squares or stripes on the floor help some PwPs to reduce fall and walk more efficiently.

3. Building endurance

Resistance and cycling exercises build up our stamina. Mean time we are introducing dances and Tai Ji to achieve all the above three aims.

Outcome

These activities trigger self-motivated rehabilitation and this shows the wider society how to approach health care in a proactive way. They also allow PwPs to meet in a social gathering that provides important peer support and sharing opportunities. They encourage PwPs to come out of isolation and depression. We believe that, when we consistently continue these exercises, we can experience positive brain changes.

Our society started with a small number of PwPs, but our physiotherapy activities have attracted more members, including non-PwPs and people with depression or other degenerative diseases.

The program is not only of benefit to PwPs; it also helps their relatives and caregivers to gain knowledge. Physiotherapy clearly plays a key role in the holistic care of those with Parkinson's disease.

LIVING WITH PARKINSON'S: ADVANCING RESEARCH VIA FUNDRAISING, TRIALS, EDUCATIONAL CAMPAIGNS

P41.01

Understanding central mechanisms in overactive bladder in patients with Parkinson's disease using BOLD fMRI contrast maps.

Pinky Agarwal¹, Daniel Burdick¹, Arina Madan², Alida Griffith¹

¹ Booth Gardner Parkinson's Center, Kirkland, WA, USA

² Birmingham University, Birmingham, United Kingdom

Objective: To understand central mechanism in overactive bladder in Parkinson's disease (PD) by comparing perfusion activity in the limbic system between subjects with PD and overactive bladder (OAB) and PD only using BOLD fMRI contrast maps. Background: Bladder dysfunction occurs through a complex pathophysiology and the exact cause of OAB in patients with Parkinson's remains known. Several studies show that anxiety and depression increase the risk for OAB in adults. Urgency, the key symptom of OAB, is associated with emotional reactions such as 'fear' of leakage and hypervigilance ('bathroom mapping'). In healthy adults, urgency with bladder filling, a key symptom of OAB, is associated with activation of key region of regions of the brain that process emotion (the limbic system) including the ACC, insula, PFC, amygdala, and basal ganglia. In addition to the traditional nigrostriatal projections, animal studies have implicated the ventral tegmental area (VTA, the A10 cell group)-limbic cortex and the hypothalamic (the A11 cell group)-spinal cord dopaminergic projections in bladder dysfunction. Therefore, OAB in PD may originate from the same brain lesions that involve the prefrontal/medial frontal area and basal ganglia circuit.

Method: Case-control study of 10 adults with PD and OAB and 10 adults with PD only is being conducted. The study consists of two visits. Eligible subjects undergo clinical neurological examination, urine dipstick to rule out urinary tract infection (UTI) and complete study related questionnaires (a single question on lower urinary tract symptoms and Zung's Self-rating Anxiety Scale (SAS)). At the second visit, subjects undergo BOLD fMRI.

Results: 10 patients with Parkinson's disease and overactive bladder and 10 patient with Parkinson's disease only are being evaluated for this study which is ongoing. Overactive bladder in adults with Parkinson's disease may be caused by increased neural activity in the areas of the brain associated with processing emotion, the anterior cingulate cortex, the insula and the prefrontal cortex.

Conclusion: Because the tone of the limbic system can be pharmacologically and behaviorally modulated, identification of active regions of the limbic system that modulate urgency will allow the development of new treatments for OAB in adults with PD.

P41.02

The Parkinson's UK Research Support Network (RSN) – collaborating for a cure

Claire Stephenson¹, Richard Windle², John Telford³, Richard Hill⁴, Anna Smith¹

¹ Parkinson's UK, London, United Kingdom

² Patient, St Albans, Hertfordshire, United Kingdom

³ Leicester, United Kingdom

⁴ Taunton, Somerset, United Kingdom

Objective: To promote interest and awareness in research. To bring together researchers, people with Parkinson's, carers and Parkinson's UK staff in the quest for better treatments and a cure.

Method: The Parkinson's UK RSN was established in 2011 following increasing demand from members asking how they could get involved in research and from researchers requesting support with recruitment. The RSN has since developed into a thriving organisation that works to bring all the stakeholders in Parkinson's research together. It now comprises more than 2,000 members and there are three very specific components to its work:

Participation: The objective is to encourage participation in research, thereby helping to ensure that there are sufficient numbers willing to participate. A formal application process has been developed where researchers can approach Parkinson's UK to work in partnership to maximize the chances of successful recruitment. Resources have been developed to outline the different ways in which the charity can help.

Involvement: The objective is for researchers and patients/carers to work together in the conduct of research projects. Thus far this has involved training a group of fifty members of the RSN to work with researchers on all aspects of the research design, management, data collection, analysis and reporting. The impact of this involvement on Parkinson's research is currently being evaluated.

Local groups: The objective is to stimulate and maintain interest and awareness in research. Local groups provide a focus for the dissemination of information about research in their areas. Their outputs include newsletters, regular meetings and an annual conference. Following this successful model, local groups have been established in Newcastle, South Yorkshire and Wales and are planned in Bristol and Cambridge to supplement those that already exist in Scotland and the East Midlands.

Results: The objectives quoted above combine to raise awareness of research. Over the last two years there has been an increase of 130% in membership with 57% of the RSN participating in research opportunities highlighted in the weekly emails. Our view is that by making research an active collaboration between all the stakeholders increases its effectiveness and speeds the development of new treatments and a cure. At the same time, providing opportunities for people with Parkinson's to engage with the research process helps them to 'take control' of their lives.

P41.03

A new volunteer-led method for looking at drug repurposing

John Telford¹, Richard Hill², Laura Smith³, Peter Sidell⁴, Anna Smith³, Richard Windle⁵

¹ Leicester, United Kingdom

² Taunton, Somerset, United Kingdom

³ Parkinson's UK, London, United Kingdom

⁴ Guildford, Surrey, United Kingdom

⁵ Patient, St Albans, Hertfordshire, United Kingdom

Background: The cost of getting new drugs to market has led to a growing interest in repurposing existing drugs. To date no systematic studies have consulted people with Parkinson's as to what other medications might have affected their condition.

Objective: To gather data from the patient community about non-Parkinson's drugs that they have perceived to have had an impact on their well-being in order to identify possible candidates for drug repurposing. It is noted that only direct experience of the drugs concerned was required (not hearsay).

Methods: Participants from the patient community were recruited via invitations to take part, and through a review of posts in the Parkinson's UK online forum.

Members of the Parkinson's UK Research Support Network (n=2000) were invited via email to submit their experiences of non-Parkinson's drugs that had affected their Parkinson's symptoms. Respondents with relevant experiences were sent a detailed questionnaire designed to capture key information relating to the

drugs cited. Subsequently, Parkinson's UK's quarterly publication 'The Parkinson' (circulation ~40,000) carried an article inviting patients to contribute to the study via a direct link to the questionnaire.

At the same time volunteers carried out a standardised search of thousands of posts in the Parkinson's UK forum for all reports of drugs and other substances having a direct symptomatic effect. Selected topic 'threads' were examined in detail. Where appropriate and possible those forum members were sent the questionnaire to complete.

Results: Several drugs have been cited recurrently in questionnaire responses and forum contributions to date. These include examples of antidepressants, non-steroidal anti-inflammatories, anticonvulsants, tranquilisers and beta blockers. In order to inform potential drug repurposing, more participants will be recruited to the study via forthcoming announcements in relevant publications in the USA.

Conclusions: Given the age-distribution and co-morbidities typical of Parkinson's patients, it is unsurprising that these drug groups are widely prescribed. However, the data raise the question as to whether drugs of these types are being exploited optimally. Next steps are to carry out a structured investigation of clinicians' experience and practice with these drugs in the treatment of Parkinson's and to increase the number of participants to more finely tune the definition of candidates for repurposing.

P41.04

Following a step-by-step process for the creation of a PACT (Partnering Advocates for Clinical Trials) between sponsors and trial participants

Peggy Willocks

Parkinson's Creative Collective, Little Rock, Arkansas, USA

Globally, there is a myriad of needs in successfully making it through the approval process of a clinical trial. To answer many of these needs, this poster will show the step-by-step process for creating a PACT (Partnering Advocates for Clinical Trials) between sponsors and trial participants.

Some of those needs are: recruiting and retaining enough trial participants, creating the informed consent document, consensus agreement in the protocol and/or design used for a specific trial, and legal issues to manage.

Additionally, there are some even greater issues that are at play before a trial is even initiated; such as: finding educated and experienced people to serve as advocates or key players, for responsibilities like serving on the Institutional Review Board of a specific clinical trial, tort management, or collaborative discussions where each one's opinion is of equal value. How or what is lacking in attracting such prime advocates? Most importantly, the answer lies in the building of trust between sponsoring business and industry and acknowledging true empowerment at the grassroots level, or creation of a PACT (Partnering Advocates for Clinical Trials).

This poster will explain how to create a paradigm shift that is long overdue in order to bring about the type of change needed to instill consensus agreement. Although we have come a long way, a lack of trust still exists between trial participants and their caregivers, and trial sponsors and approving agencies – (EMA and FDA). Sponsors, researchers and proven grassroots advocates must work and plan together under the same purpose and goals, removing ambiguity where it is present and replacing it with good training and clearly written protocol. This poster will also show strategies for attracting and retaining such advocates, supplying us with a pool of prescreened participants from which we can speedily draw. Examples of the tools used will be provided.

LIVING WITH PARKINSON'S: OTHER

P42.01

A service evaluation by Parkinson's disease nurse specialists, of Parkinson's Kinetigraph (PKG) movement recording system use in routine clinical care of patients with Parkinson's disease

Jane Price¹, Hannah Martin², Louise Ebenezer³, Patricia Cotton⁴, Julie Shuri⁵, Anne Martin⁶, Anna Sauerbier⁷

¹ Bronllys Hospital, Powys Teaching Health Board, UK, United Kingdom

² University Hospitals Coventry & Warwickshire NHS Trust, United Kingdom

³ Princess of Wales Hospital, Bridgend Abertawe Bro Morgannwg University Health Board, United Kingdom

⁴ Salford Royal NHS Foundation Trust, United Kingdom

⁵ The Royal Wolverhampton Hospitals NHS Trust, United Kingdom

⁶ King's College Hospital NHS Foundation Trust, United Kingdom

⁷ King's College London and King's college Hospital, London, United Kingdom

Background: Parkinson's disease (PD) is a chronic and progressive movement disorder. The main motor symptoms include slowness, stiffness, shaking and postural instability. In advanced stages, patients experience medication-related complications such as fluctuations and dyskinesias. Clinic interview is limited by short observation periods, subjective patient recall related problems, as well as the absence of true evaluation of motor and some non-motor states (such as daytime somnolence) in home circumstances. Parkinson's Kinetigraph™ (PKG™) is a wrist worn medical device that monitors movements and time of intake of medication and allows home evaluation in an objective fashion [1].

Objective: To evaluate the clinical utility of the PKG movement recording system in the routine clinical care of patients with PD within the National Health Service.

Methods: In an ongoing observational project conducted by Parkinson's disease nurse specialists from 6 different UK centers, 120 PD patients in a complex phase of PD, who meet the approved criteria of the PKG will be approached to wear the PKG data logger for 6 days. Each patient will be provided with training on the fitting and use of the PKG data logger. The PKG report will be reviewed and generated by the PD nurse specialist PKG reviewer at each centre who particularly indicates whether the PKG provided new or additional information that drove clinical interventions to improve overall care of the patient.

Results: So far 5 PD patients (40% male, mean disease duration 10.0±3.7 years, mean age at onset 46.0±16.1 years, mean age 56.0±18.1 years, median Hoehn and Yahr 2.5 (range 2-4)) have been included. In the majority the PKG improved the dialogue with the patient and the identification of need for additional tests and treatments, such as the use of nighttime therapies for early morning off or fractionating oral treatment to reduce peak dose dyskinesias which were previously not evident. Overall, patients agreed that the PKG was easy to use and performed as expected.

Conclusion: The preliminary results of this ongoing project highlight that the PKG might be a useful tool in routine clinical care. We are now further expanding the project.

[1] Bergquist F, Horne M. Can Objective Measurements Improve Treatment Outcomes in Parkinson's Disease? *European Neurological Review*. 2014;9:27-30.

P42.02**Parkinson's community transforming service delivery – the UK Parkinson's Excellence Model***Val Buxton, David Burn*

Parkinson's UK, United Kingdom

The UK Parkinson's Excellence Network brings together the passion and expertise of professionals involved in Parkinson's service delivery, the voice of people affected by condition and the strategic leadership and resources of Parkinson's UK. Focused support from Parkinson's UK enables busy clinicians to dedicate time to service improvement.

Background: Health and care services for people living with Parkinson's are not always good quality. We need the whole Parkinson's Community to work together to make access to high quality services the norm. To facilitate this in the UK, the UK Parkinson's Excellence Network was launched in February 2015. Its vision is to transform care by:

- Enabling professionals to work together
- Building an expert workforce
- Equipping professionals to influence services
- Strengthening the voice of people with Parkinson's

To highlight which areas of service delivery need priority, surveys have been carried out to provide the Network with data about the current status across the UK.

The UK Parkinson's Clinical Audit focuses on the effective continuous management of people with Parkinson's within a multidisciplinary team. It addresses the services delivered by consultants, geriatricians, neurologists, Parkinson's specialist nurses, occupational therapists, physiotherapists and speech and language therapists. It uses evidence-based clinical guidelines as the basis for measuring the quality of care.

To gather information from people with Parkinson's, the clinical audit also included a Patient Reported Experience Measure (PREM) survey allowing a 360° picture of each service to be obtained. Concurrently, Parkinson's UK circulated a survey including the PREM questions enabling patients whose service was not in the audit to take part.

Transforming the future

The Network has data from over 18,000 people with Parkinson's and will work to make sure services across the UK:

- Are integrated
- Use standard practice models
- Signpost to information and support from the point of diagnosis
- Provide seamless inpatient care
- Support people in advance decision making

Summary: The UK Parkinson's Excellence Network demonstrates the power in communities coming together. By reducing professional isolation we can facilitate collaboration ensuring that best practice is shared and duplication reduced.

By providing a clear road map to show the starting point that the community can sign up to we can transform care for people with Parkinson's.

P42.03**An interdisciplinary Parkinson's disease case study event for dietetics, education, exercise science, health care administration, nursing and social work students: enhancing effective communication between disciplines***Jennifer DeJong*

Concordia College, Moorhead, MN, USA

Background/Context: From 2001 to present, the Institute of Medicine (IOM) published eight comprehensive reports on education of health professionals to address changes in the health

care delivery system and the changes in the patient/clinician relationship. The Institute of Medicine Committee on Health Professions Education (IOM, 2003) focused on the need for team-based interdisciplinary education strategies as a means to reduce medical error and improve health care quality. In response to these recommendations, faculty arranged three unique experiences for students with majors in the health professions. One of these case studies focused on a patient living with Parkinson's Disease.

Purpose: The purpose of the interdisciplinary case-study event for undergraduate students at a small liberal arts college was to respond to the IOM recommendations and to foster effective communication between the professions of dietetics, education, exercise science, health care administration, nursing and social work in providing evidence-based care for a patient living with Parkinson's Disease.

Methods: Students from each discipline met in a common area to discuss their individualized care plans. Groups consisted of one or two students from each discipline. At the end of the group discussion, faculty members led students in concept mapping to identify priorities. Following the event, students were given ten minutes to complete an anonymous survey consisting of five Likert-scaled statements.

Results: Students reported a greater understanding of other professional roles and the care they would provide to the patient living with Parkinson's Disease following the experience. Students reported that their ability to work with diverse professionals was enhanced by the experience, and the majority of students reported that they agreed "exceptionally" that their role and voice was valued.

Conclusions/Implications: Students going in to the health professions need to be educated to deliver patient-centered care as members of an interdisciplinary team. Students and faculty benefited from developing interdisciplinary case studies that emphasized listening, valuing other professionals' roles, and working as a team to deliver evidence-based, patient-focused care for the patient living with Parkinson's Disease.

P42.04**Group meetings for newly diagnosed Parkinson's disease patients and their spouses: a preliminary experience***Noya Geva¹, Ariela Hillel¹, Yael Manor^{1,2}, Ezra Adi¹, Shira Arad¹, Nir Giladi^{1,2}, Tanya Gurevich^{1,2}*

¹ Movement Disorders Unit, Tel Aviv Sourasky Medical Center, Division of Neurology, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel

² Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel

Background: Parkinson's disease (PD) is a common neurodegenerative disease that is highly stigmatized. The period following diagnosis is inevitably an emotional one for the patient and family which may lead to lack of motivation and poor compliance. Knowledge about various aspects of PD and sharing personal experiences related to PD were proposed to enable better quality of life and coping. In a single 3-hour group meeting, PD patients, all diagnosed within the past year, and their spouses were introduced to the clinical service of our movement disorders unit. The meetings were led by the service's multidisciplinary team, comprised of neurologists, a psychiatrist, a nurse, a speech therapist a social worker (SW) and included 3 parts. Initially, a question was referred to all the participants: "with whom did you share the diagnosis?" followed by an activity with interactive cards "Cope" that aimed to create an emotional bonding by sharing each participant's feeling with the rest of the group members. Finally, the patients and their spouses referred informative questions to the team members.

Objective: To estimate the contribution of a group meeting for newly diagnosed PD patients and their spouses.

Method: A retrospective study, based on a structured telephone survey performed by the SW.

Results: Three individual sessions each 3 hours long were held and included 24 PD patients (7 females, H&Y=2) and 16 spouses (13 females). Thirty-eight participants responded to the questionnaire (23 patients, 7 females, age 54-85 years and 15 spouses, 12 females, age 53-80 years). Twenty-six of them felt that the meetings contributed to the acquaintance with the multidisciplinary team, 30 reported that the meeting helped them feeling welcome at the clinic, 33 felt that the meeting contributed to their ability to discuss the PD diagnosis with friends and relatives, and 4 reported that friendships were formed at the meeting. When asked "what is the most important benefit that you obtained from the meeting?" 21 reported "information", 16 reported "support", 18 reported "getting to know the multidisciplinary team" and 4 reported "friendships"

Conclusion: Most participants felt that these meetings helped them to adjust more easily to the challenges of coping with the recent diagnosis of PD.

P42.05

Promoting physiotherapy specific expertise for people with Parkinson's: a role of the Association of Physiotherapists in Parkinson's Disease Europe (APPDE)

Mariella Graziano¹, Diana Jones², Bhanu Ramaswamy³, Fiona Lindop⁴

¹ President of the Association of Physiotherapists in Parkinson's Disease Europe – APPDE, Esch-sur-Alzette, N/A, Luxembourg

² Faculty of Health and Life Sciences, Northumbria University, Newcastle upon Tyne, United Kingdom

³ Independent Physiotherapy Consultant, Sheffield, United Kingdom

⁴ Derby Hospitals NHS Foundation Trust, Derby, United Kingdom

Objective: To show how a global community of physiotherapists share specific Parkinson's skills and knowledge in clinical practice enhancing services for people with Parkinson's (PWP). Background: The APPDE promotes a PWP centred approach in the context of diverse health care systems worldwide. The Association offers a platform to PWP, carers, members of the multidisciplinary team, including clinicians, researchers and policymakers, to exchange expertise on optimal Parkinson's management choices. Members and friends gain from exchanging and accessing information about variation of practice and experience of receiving physiotherapy in different health care systems. Multimedia resources, especially those drawing on the direct PWP experience, provide powerful learning opportunities.

Methods: The APPDE collaborates with the World Parkinson Coalition and the European Parkinson's Disease Association, both provide first-hand information about how people live with Parkinson's. Links with clinicians are made through interest groups like, the International Neurological Physical Therapy Association, a sub-group of the World Confederation for Physical Therapy, and the Movement Disorders Society(MDS). The APPDE cooperates with the European Guideline for Physiotherapy in Parkinson's project team lead by ParkinsonNET. These exchanges produce and promote physiotherapy material for the benefit of PWP worldwide.

Results: The information is shared as continuing professional development via initiatives like conference participation, mentoring, website (www.appde.eu), Twitter @euPhysioPD, Facebook www.facebook.com/euPhysioPD.

Resources like www.move4parkinsons.com, and an innovative radio station – Radioparkiesandwpc, enable the APPDE to have an insight into the way PWP describe everyday difficulties and the strategies found to overcome them. The APPDE contributed to develop the European Physiotherapy Guideline for Parkinson's (www.appde.eu/EN/european-guideline.asp) published in 2014 and contributes to its implementation internationally,

working closely with ParkinsonNet. It delivers courses since 2007 and contributes to the MDS physiotherapy Allied Health Professional Summer School (the Netherlands 2013, Portugal 2014, Belgium 2016).

Conclusions: The APPDE promotes a research based PWP centred physiotherapy approach. Accessing the experiences of PWP directly, through multimedia or via patient associations provides an important opportunity for continuing development for physiotherapy.

P42.07

A picture is worth a thousand words

Lloyd Jenkins

Auckland, New Zealand

"When you have seen one person with Parkinson's, you've seen precisely that – one person Parkinson's".

This is how Parkinson's was described to me by my neurologist at our first meeting. Parkinson's symptoms vary widely between individuals as do the responses to medication and the underlying progression of the condition. This means establishing and maintaining an appropriate treatment regime is often a case of trial and error in a seemingly endless spiral of symptoms, drugs and side effects.

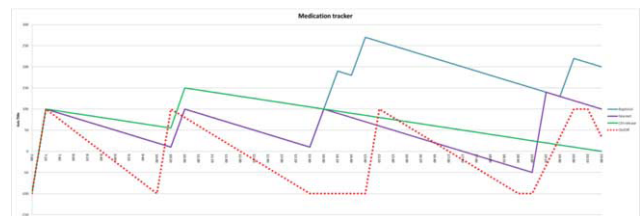
Historically, when I have made changes to my medication I have recorded my progress in a diary. While this has helped to ensure that I have followed the new regime correctly, it has not made it any easier to see patterns in my body's response to the new medication or identify any link to specific drugs. To help me make sense of the data I have developed a graphical model that displays the drugs taken plotted against my physical condition over a "normal" day, see the example below.

The graph has a line for each medication being monitored – in this case there are 3 of them. Each line is a calculation of the dopamine level I would expect that drug to contribute based on how much was taken and when.

The fourth (dotted) line depicts how I felt, physically, during the day. I use a simple binary scale with feeling "on" recorded as positive 100 and feeling "off" is negative 100. These data points are plotted on the graph and connected using linear interpolation.

The result is a graphical representation of the ups and downs of a day in my life with Parkinson's, which I hope will make it easier to spot trends and co-relations in the data. While this is very much a work in progress and the measurements highly subjective but I hope it will take some of the guess work out of adjustments to my medication.

My first steps are a proof of concept using my current medication regime as a base line, against which to compare, future change. If successful I hope to use this tool to review other, non-drug treatments such as exercise, diet and stress.



P42.08

The effects of dysphagia course for speech & language pathologist in Israel on clinical-related knowledge and confidence

Yael Manor¹, Herzel Shabta², Oshrat Sella³

¹ Movement Disorders Unit, Department of Neurology, Tel-Aviv Sourasky Medical Center. Ono Academic College, Faculty of Health Professions, Communication Sciences and Disorders Department, Kiryat Ono, Tel Aviv, Israel

² Movement Disorders Unit, Department of Neurology, Tel-Aviv Sourasky Medical Center, Tel Aviv, Israel

³ University of Haifa, Department of Communication Sciences and Disorders Department. Communication Disorders Rehabilitation Department, Loewenstein Rehabilitation Hospital, Tel Aviv, Israel

Background: Dysphagia management among Parkinson's disease (PD) patients requires specific and comprehensive knowledge on the part of speech and language pathologists (SLPs). Unfortunately, awareness of the nature and management of dysphagia among PD patients is lacking among SLPs and other health professionals.

Objective: We assessed the accuracy of dysphagia management-related knowledge of SLPs in Israel before and after a 60-hour course on dysphagia.

Methods: Structured questionnaires were used to assess change in knowledge between the first and last days of a 10-day course in dysphagia that focused on the anatomy, physiology and biomechanics of swallowing, swallowing impairments, bedside and instrumental evaluations, and management approaches. The questionnaire included multiple-choice items on diagnosis and intervention based on bedside evaluations, videofluoroscopy swallowing studies (VFSSs) and fiberoptic endoscopic examinations of swallowing (FEESs). Four visual analog scales (VASs) were used to evaluate professional confidence in fulfilling tasks related to therapy, supervising students, lecturing and presenting a case study.

Results: Twenty-five out of 35 SLPs (age 33.4±9.3 years, clinical experience 8.2±9 years, 10 males) who attended the course filled-in the questionnaires before and after taking the course. The McNamer analysis revealed a significant increase in correct answers in knowledge related to VFSS interpretation in 3/4 questions ($p=0.016$, $p<0.001$, $p=0.002$). Knowledge related to BSE interpretation and FEES analysis was low and remained unchanged (BSE $p=0.15$; FEES $p=0.11$). The VASs were tested using paired t-tests and showed significant increases in confidence following the course (therapy $p<0.001$, supervising students $p=0.004$, lecturing $p<0.001$, case study presentation $p<0.001$).

Conclusions: Short-term dysphagia courses can improve basic skills, however, more intensive training with hands-on experience under supervision is required to provide SLPs with sufficient tools for confident and knowledgeable case management and decision-making in PD patients with dysphagia.

P42.09

Impact of allied team training for Parkinson's on enhancing services for patients and families in southeastern Washington

Laura Molu, Jennifer Davis

Kadlec Regional Medical Center, Richland, WA, USA

Objective: People with Parkinson's can present with a wide range of motor and non-motor symptoms that require comprehensive inter-professional care. Prior to attending the Allied Team Training for Parkinson, the model of care was a multidisciplinary team approach. Following the Allied Team Training for Parkinson, the clinicians that attended the training from our organization were inspired to lead

improvements in the quality of care and the number of services available to people with Parkinson's and their families in this region.

Methods: Improving the quality of care for people with Parkinson's and their families was achieved in a variety of ways: 1) Implementing monthly Parkinson's meetings with managers to develop the Parkinson's program; 2) Team members obtaining certifications in several evidenced-based treatment programs; 3) Training of additional staff members within our organization by clinicians from the Oregon Health Science University Parkinson's Clinic; 4) Coordinating with the Neurologic Resource Center to enhance services for people with Parkinson's and their families; 5) Completion of the Healthplex and Planetree.

Results: The quality of care provided to people with Parkinson's and their families in southeastern Washington has been greatly enhanced due to the information provided to our team following the Allied Team Training for Parkinson. Care is now available using an inter-professional model by conducting several evaluations on the same day (Physical Therapist, Occupational Therapist and Speech-Language Pathologist) followed by a team meeting to share findings and to determine the best plan of care to meet the needs of the person with Parkinson's and their family. Team clinicians are now certified in programs such as: LSVT LOUD, LSVT BIG, PWR! Moves and SPEAK OUT! Team members further their education by attending annual Parkinson's courses through Oregon Health Science University. Local neurologists are updated periodically about the Parkinson's clinic and the types of evidenced-based therapies that are available. There are many services offered at the Healthplex, including: monthly speech therapy groups following completion of the individual therapy; various exercise and wellness classes; support groups, educational conferences and a resource library offering books and DVD's about Parkinson's (available through the Neurological Resource Center for patients and families to increase their knowledge in self-management of their condition).

P42.10

Risk of Parkinson's disease in the users of non-steroidal anti-inflammatory drugs – a meta analysis of observational studies

Amarnath Mullapudi, Chandra Sekhar Boya, Dipika Bansal

Department of Pharmacy Practice, National Institute of Pharmaceutical Education and Research, Mohali, Punjab, India

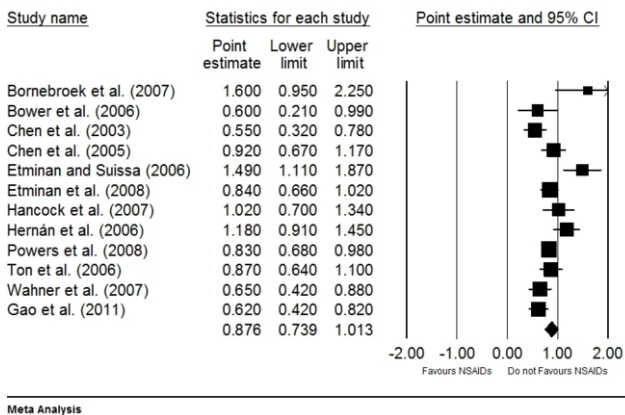
Background: Several epidemiological studies suggested that use of NSAIDs may decrease the risk of Parkinson's disease (PD). However, studies found an association between the use of NSAIDs and the risk remains uncertain. We conducted a meta-analysis to investigate relationship between use of NSAIDs and PD risk. This study aimed to examine the association between NSAID use and risk of PD.

Methods: Literature search was performed in PubMed, EMBASE and PsycInfo databases till January 2016. Observational studies evaluating the association between uses of NSAIDs like aspirin, Non-aspirin, Ibuprofen, acetaminophen and risk of PD were included. Pooled Risk Ratios (RR) and 95% confidence intervals (CIs) were calculated using random-effects model. Subgroup and sensitivity analyses were also performed.

Results: Fourteen relevant studies (9 case control and 5 cohort studies) were included. A significant association was observed between overall use of any NSAIDs (RR 0.87 95% CI=0.73–1.01). There was a significant heterogeneity ($I^2=71\%$) and no publication bias (Begg's test $P=0.2$) was observed. Similarly, use of Non-aspirin NSAIDs showed a significant risk reduction of PD (RR 0.87 95% CI=0.77–0.97). There was significant association was found in the users of Acetaminophen and Ibuprofen, whereas increased risk of PD was observed in the users of aspirin (RR 1.10 95% CI=0.94–1.09)

Conclusion: The present analysis supports the hypothesis that overall use of NSAIDs may decrease the risk of PD. It was found that use of non-aspirin NSAIDs may reduce the risk of PD, whereas aspirin use may increase the risk.

NSAIDs and Risk of PD



P42.11

Caregivers of PDP patients have an increased risk of developing emotional and social distress that is decreased when PDP is treated with pimavanserin

James Norton¹, Dag Aarsland², Kathy Chi-Burris³, Clive Ballard⁴

¹ San Diego, CA, USA

² Stavanger, Norway

³ ACADIA Pharmaceuticals Inc., San Diego, CA, USA

⁴ Newcastle, USA

Objective: To determine the effect on caregiver distress of treating Parkinson's disease psychosis (PDP) patients with pimavanserin.

Background: Parkinson's disease psychosis is associated with functional and mental decline, morbidity and mortality, and increased caregiver burden. The hallmark symptoms of the condition are hallucinations and delusions. Physical, emotional, and social aspects of caregiver quality of life deteriorate as these symptoms worsen. A randomized, controlled clinical trial was conducted to evaluate a unique antipsychotic, pimavanserin (NUPLAZID™), for reducing PDP symptoms. During this study patients demonstrated reduced hallucinations and delusions, improved nighttime sleep and daytime wakefulness, and caregivers reported reduced distress.

Methods: In a 6-week, randomized, double-blind, placebo-controlled study, 185 PDP patients received either pimavanserin 34 mg (N=95) or placebo (N=90). Caregivers of these patients who agreed to participate completed the Zarit 22-item caregiver burden scale (CBS), which was designed to measure the impact of the patient's disabilities on the caregiver's life and reflect the stresses experienced by caregivers. Caregivers were typically either spouses or other family members.

Results: Mean baseline (pretreatment) CBS scores were 30.7 for the caregivers whose relative received placebo and 28.7 for those who received pimavanserin 34 mg. A significant difference in burden was observed for the pimavanserin group (3.9 point improvement) over placebo (0.4 point worsening) after 6 weeks of treatment (p=0.002). Individual items of the CBS that showed statistical improvement included: feeling embarrassed by the patient's behavior, negative effects on their relationship, feeling strained around relative, suffering caregiver health, lack of privacy, suffering social life, and inability to care for the relative much longer.

Conclusions: Caregiver health is deeply impacted by the mental status of the PD patient. Stressors may cause them to make decisions around care for the patient, such as placement into a nursing home, due to their perceived inability to care for the patient. A significant change in caregiver burden scores from this study implies that PDP patient treatment with NUPLAZID (pimavanserin) can positively impact the caregiver feelings of distress.

P42.12

Multidisciplinary group program integrating voice and dance movement therapy for Parkinson's disease patients: a preliminary experience

Roni Peled¹, Dina Shpunt¹, Yael Manor^{1,2}, Marina Brozgal³, Adi Ezra¹, Neomi Hezi¹, Rivka Hen Simon¹, Jeff Hausdorff^{3,4}, Tanya Gurevich¹

¹ Movement Disorders Unit, Dept of Neurology, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel

² Ono Academic College, Faculty of Health Professions, Communication Sciences and Disorders Department, Kiryat Ono Center, Tel Aviv, Israel

³ Center for the Study of Movement, Cognition, and Mobility, Department of Neurology, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel

⁴ Sackler School of Medicine and Sagol School of Neuroscience, Tel Aviv University, Tel Aviv, Israel

Background: Physical exercise and speech therapy are effective treatments for Parkinson's disease (PD). The "Voice in Motion" group activity is led by movement and speech therapists. It encourages patients to perform speech drills based on LSVT-LOUD and spontaneous speech and dance movement therapy (DMT), while at the same time emphasizing posture, balance and lively interactions within the group. Measurements of cognition, speech, voice, gait and quality of life (QOL) were assessed in clinical follow-up.

Objective: To examine the effects of "Voice in Motion" group therapy on movement, speech and QOL of PD patients.

Method: The parameters of volume of vowel prolongation of /aaa/ in a habitual (VVPPh) and loud (VVPI) voice in spontaneous speech (VVSS), gait speed and stride length and responding to questionnaires voice handicapped index (VHI), Visual Analog Scale (VAS), gait parameters and Quality of Life (PDQ-39) were compared before and after 27 weekly sessions in this pilot retrospective report.

Results: Six patients (2 males), mean age 64.5±7.8, Hoehn and Yahr 2.5±0.6; disease duration 3.7±2.7 and Montreal Cognitive Assessment (MoCA) 26.8±1.7 participated in 27 weekly sessions. A positive trend towards improvement was noted in all measurements: VVPH, VVPI and VVSS (T1 68.2±10.5dB, T2 80.8±4.9dB, P=0.068; T1 89.5±5.4dB, T2 96±6.6dB, P=0.279; T1 60.3±4.8dB, T2 65.2±5.4dB, P=0.131, respectively), and gait speed (T1 0.16±1.01 m/sec, T2 1.06±0.3 m/sec; P=0.73). The VHI, emotional category (T1 7±8.3, T2 4.2±2, P=0.197) PDQ-39, stigma parameter (T1 3.2±2.7, T2 2.7±2.3, P=1.000) Patients reported: "The group gave me self-confidence to discuss the disease with family and friends. No falls and adverse events were reported.

Conclusions: Therapy that combines speech and movement is appeared to be safe and feasible. Initial results suggest that integrating voice and dance movement therapy that focuses on expanding the use of bodily expression and social communication can maintain and improve speech, movements and communication abilities and well-being of PD patients.

P42.13

Top 10 priority areas for improving everyday life with Parkinson's

Stacey Storey
United Kingdom

Summary: Parkinson's UK drives better care, treatments and quality of life. Everything we do is shaped by people affected by Parkinson's.

Our number one research priority is to develop new and better treatments. We also champion research to improve the quality of life. To help researchers focus on the most important quality of life issues, we asked people with direct experience of the condition to come up with 10 priority areas for improving everyday life.

Setting the priorities

To identify the top 10 priority areas, Parkinson's UK commissioned a Priority Setting Partnership. Through an online and paper survey people living with Parkinson's, carers, family members and health and social care professionals were asked 'what questions they would like to see answered by research?' in the areas of symptoms, treatments and day to day life.

- 1000 (60% PwP) participants provided over 4000 responses. From this 94 unique unanswered research questions were identified.
- 475 (72% PwP) prioritised the long list producing 26 questions to go forward to the next stage
- 27 stakeholders (37% PwP) came together to prioritise the Top 10 from the shortlist of 26 questions

The top 10 areas identified were:

1. Balance and Falls
2. Stress and Anxiety
3. Uncontrolled Movements
4. Personalised Treatments
5. Dementia
6. Mild Thinking and Memory Problems
7. Monitoring Symptoms
8. Sleep
9. Dexterity
10. Urinary Problems

Conclusion: The Top 10 priority areas can help inform and guide future Parkinson's research not just in the UK, but across the world.

Parkinson's UK is also:

- Making survey data available for researchers to use to support funding applications and research design
- Bringing researchers and people affected by Parkinson's together via focus groups, consultations and themed workshops to accelerate high quality research in the areas
- Helping the research community to have access to people affected by Parkinson's increasing participation in trials
- Working with other organisations that have commissioned priority setting partnerships for their condition to collaborate on shared priorities

P42.14

Treatment patterns of Parkinson's disease in the USA: a retrospective claims database analysis

Francis Vekeman¹, Alexander Niyazov², Amy Guo², Eric Wu¹, Susan Criswell³

¹ Analysis Group, Inc., Montréal, Canada

² Acorda Therapeutics, Inc., USA

³ Washington University in St. Louis, USA

Objective: This retrospective claims analysis aims to assess patient characteristics and treatment patterns for Parkinson's disease (PD),

including the utilization of oral levodopa and other antiparkinson drugs (APDs) that are used in current clinical practice.

Methods: A retrospective analysis of the Truven Health Analytics MarketScan® Research Databases (Q1 2010–Q4 2014) was conducted. Patients with ≥2 diagnoses of PD (ICD-9:332.0) and ≥2 successive fills of the same APD after a PD diagnosis were eligible. The index date (1st observed therapy) was defined as the first observed APD fill date between 2010 and 2014. APD fills prior to the index date were not assessed. The study period spanned from the 1st APD index date until the end of insurance coverage, or data cut-off date. Treatment patterns were evaluated over 3 observed sequential therapies (mono- or combination). An observed therapy was defined as the initiation of a new APD class or reinitiation of the same APD class after a 90-day gap. The duration of each therapy was assessed. The prevalence of mono- and combination therapies were reported for each observed therapy. Stratified analyses by provider (neurologist; non-neurologist) and by age group (<65; ≥65 years) were also conducted.

Results: 76,602 patients met the eligibility criteria: mean±SD age was 71.5±11.5 years; 59.4% were male. At index, 30.7% were <65 years of age; 40.7% were treated by a neurologist. Of the prescribers, neurologists tend to prescribe combination therapies compared with non-neurologists (30.4% vs 25.7% at index). The use of combination therapies was common among younger patients relative to those older; 37.0% vs 23.0% at index, 83.7% vs 71.1% and 88.4% vs 79.1% at the 2nd and 3rd observed therapy, respectively. At index, 72.7% had monotherapy and 27.3% had combination therapy with ≥2APDs (Table). Use of levodopa was prevalent at index (74.9%): 51.3% had levodopa monotherapy; 23.6% had a levodopa combination therapy. Of the index cohort, 42.1% had a 2nd observed therapy, and 15.8%, a 3rd observed therapy (Table). Levodopa utilization increased with each subsequent therapy: 81.4% at the 2nd observed therapy and 85.7% at the 3rd observed therapy.

Antiparkinson Therapies	Observed therapy		
	1 st observed therapy	2 nd observed therapy	3 rd observed therapy
Number of patients, n (% of study cohort)	76,602 (100.0)	32,266 (42.1)	12,133 (15.8)
Duration of therapy in months, median	9.7	10.5	9.6
Monotherapy, n (% of line)	55,694 (72.7)	7,767 (24.1)	2,041 (16.8)
Levodopa	39,271 (51.3)	5,300 (16.4)	1,315 (10.8)
Dopamine agonists	9,025 (11.8)	1,382 (4.3)	395 (3.3)
MAO-B inhibitors	4,695 (6.1)	512 (1.6)	146 (1.2)
Amantadine	1,525 (2.0)	348 (1.1)	113 (0.9)
Anticholinergics	1,128 (1.5)	215 (0.7)	71 (0.6)
Other dopaminergics	50 (0.1)	10 (0.0)	1 (0.0)
Combination therapy with 2 APD classes, n (% of line)	15,519 (20.3)	16,898 (52.4)	4,558 (37.6)
Levodopa-based	12,975 (16.9)	13,765 (42.7)	3866 (31.9)
Non-levodopa-based	2,544 (3.3)	3,133 (9.7)	692 (5.7)
Combination therapy with more than 2 APD classes, n (% of line)	5,389 (7.0)	7,601 (23.6)	5,534 (45.6)
Levodopa-based	5,117 (6.7)	7,200 (22.3)	5,212 (43.0)
Non-levodopa-based	272 (0.4)	401 (1.2)	322 (2.7)
All levodopa-based therapy, n (% of line)	57,363 (74.9)	26,265 (81.4)	10,393 (85.7)

APD, antiparkinson drug; MAO-B, monoamine oxidase B.

Conclusions: Findings showed that of the APDs evaluated, levodopa was the most frequently utilized agent. A third of the patient population was within working age. The high rate of therapy changes highlights unmet needs in the management of PD. Supported by Acorda Therapeutics.

Late-Breaking Poster Presentations

BASIC SCIENCE: ETIOLOGY, GENETICS, EPIDEMIOLOGY AND TOXICANTS

LBP1

Olfactory Dysfunction in Parkinson's and Other Neurological Diseases: Identification of a Common Pathological Substrate

Richard Doty

University of Pennsylvania Smell & Taste Center, Philadelphia, Pennsylvania, USA

The sense of smell, i.e. Cranial Nerve I, is frequently overlooked and rarely tested by neurologists and other medical practitioners. This is in spite of its importance to the patient and the fact that olfactory dysfunction is an early biomarker of a number of neurological diseases, including Parkinson's disease (PD) and Alzheimer's disease (AD). In contrast to PD and AD, such neurodegenerative diseases as progressive supranuclear palsy, amyotrophic lateral sclerosis, and essential tremor have comparatively little olfactory dysfunction, making olfactory testing useful in differential diagnosis. Given the marked similarity between the olfactory losses observed in PD, AD, and such seemingly unrelated diseases as Korsakoff psychosis, myasthenia gravis, and Chaga's disease, the question arises as to whether a common neuropathological substrate underlies the olfactory disturbances that, in some cases, precedes the development of archetypal pathognomonic disease markers. Such a harbinger could, in fact, provide new clues as to the earliest 'preclinical' determinants responsible for the neuropathology of a wide range of neurological diseases. In this presentation I provide behavioural, neuropathological, and physiological evidence supporting the view that damage to the forebrain cholinergic system is responsible for differences in olfactory function found among a wide range of seemingly disparate neurological disorders.

LBP2

Association between tobacco smoking and serum haptoglobin concentration in Parkinson disease cases and controls: effect modification by haptoglobin phenotype

Paola Costa-Mallen¹, Cyrus Parse Zabetian², Shu-Ching Hu³, Pinky Agarwal⁴, Dora Yearout², Harvey Checkoway⁵

¹ Bastyr University Research Institute, Kenmore, WA, USA

² Veteran Affairs Puget Sound Health Care System, Seattle, WA, USA

³ University of Washington, Department of Neurology, Seattle, WA, USA

⁴ Evergreen Health, Booth Gardner Parkinson's Care Center, Kirkland, WA, USA

⁵ University of California San Diego, Department of Family & Public Health, La Jolla, CA, USA

Tobacco smoking is an environmental factor that has been consistently associated with inverse association with the risk of developing Parkinson disease (PD), however the mechanisms for this apparent protective effect of smoking on PD risk have not been elucidated. The hemoglobin-binding protein haptoglobin (Hp) displays a functional polymorphism in the population, and the Hp 2-2 phenotype of haptoglobin has been previously observed to be associated with lower risk of PD as compared to the Hp 2-1

phenotype. Haptoglobin is an antioxidant and with its hemoglobin-scavenging activity it can exert neuroprotective effects. In this study we tested whether tobacco smoking was associated with changes in serum haptoglobin and iron-binding proteins that depended on the Hp phenotype to shed light on possible mechanisms for the inverse association between tobacco smoking and PD risk. Blood iron parameters, including serum haptoglobin concentration and serum ferritin, and the haptoglobin phenotype, were determined in 106 PD patients and 238 age-matched controls. Smoking habits, including ever/never smoking status, current smoking, number of cigarettes smoked/day, years smoked, pack-years of smoking, were collected by questionnaire. Pack-years of smoking was associated with a significant increase in serum haptoglobin concentration in the overall study population (Standardized beta coefficient of regression =0.157, p=0.003). The increase in serum haptoglobin concentration associated with smoking was present most strongly for subjects of Hp 2-2 phenotype (St. beta=0.324, p=0.001), and was less pronounced for subjects of Hp 2-1 (St. beta=0.134, p=0.064), and Hp 1-1 phenotype (St. beta=0.144, p=0.380). When considering PD cases and controls separately, packyears was not associated with increased haptoglobin concentration among PD patients, while the increase in Hp concentration was significant among controls (St. beta=0.188, p=0.002) and especially among controls of Hp 2-2 phenotype (St. beta=0.446, p<0.001). Given the potential neuroprotective effect of haptoglobin, the increase in haptoglobin concentration associated with smoking, especially for subjects of Hp 2-2 phenotype (previously shown to have lower risk of PD) may be a contributor for the inverse association between smoking and PD risk.

BASIC SCIENCE: CELL DEATH, NEUROPROTECTION AND TROPHIC FACTORS

LBP3

Melanoma-linked MC1R supports dopaminergic neuron survival

Xiqun Chen¹, Hongxiang Chen², Michael Maguire², Waijiao Cai², Fuxing Zuo², Robert Logan², Maryam Rahimian², Ketey Robinson², Charles Vanderburg³, Yang Yu², Yinsheng Wang², David Fisher², Michael Schwarzschild²

¹ Massachusetts General Hospital, Charlestown, MA, USA

² USA

Objective: Individuals with Parkinson's disease are more likely to develop melanoma, and melanoma patients are reciprocally at higher risk of developing Parkinson's disease. Melanoma is strongly tied to red hair/fair skin, a phenotype of loss-of-function polymorphisms in the MC1R (melanocortin 1 receptor) gene. Loss-of-function variants of MC1R have also been linked to increased risk of Parkinson's disease. The present study is to investigate the role of MC1R in dopaminergic neurons in vivo.

Methods: Genetic and pharmacological approaches were employed to manipulate MC1R, and nigrostriatal dopaminergic integrity was determined by comprehensive behavioral, neurochemical and neuropathological measures.

Results: MC1R^{re/e} mice, which carry an inactivating mutation of MC1R and mimic the human redhead phenotype, had compromised nigrostriatal dopaminergic neuronal integrity and they are more susceptible to dopaminergic neuron toxins 6-hydroxydopamine and MPTP. Furthermore, a selective MC1R agonist protects against MPTP-induced dopaminergic neurotoxicity.

Conclusions: Our findings reveal a protective role of MC1R in nigral dopaminergic neurons and they provide a rationale for MC1R as a potential therapeutic target for Parkinson's disease. Together with its established role in melanoma, MC1R may represent a common pathogenic pathway for melanoma and Parkinson's disease.

BASIC SCIENCE: PROTEIN MISFOLDING AND HANDLING

LBP4

Structural Heterogeneity and Metal Binding of α -Synuclein Amyloid Fibrils.

Altaira D. Dearborn¹, Joseph S. Wall², Brian A. Huang¹, Alasdair C. Steven¹

¹ Laboratory of Structural Biology Research, National Institute of Arthritis Musculoskeletal and Skin Diseases, Bethesda, MD, USA

² Department of Biology, Brookhaven National Laboratory, Upton, NY, USA

Parkinson disease (PD) is characterized by dopaminergic neuronal cell death and the presence of Lewy bodies, whose main component is α -Synuclein (aS) amyloid fibrils. Metals are also associated with aS fibrils [1] and Lewy Bodies, and metal dyshomeostasis may contribute to the progression of PD. aS is a 140-residue protein, with alternative conformations. In its fibrillar form, the central 70 or so residues form a β -sheet-rich amyloid core with the terminal regions remaining unstructured. Soluble aS is unfolded but binds one cupric ion with nanomolar affinity, though several more can be bound non-specifically at higher concentrations, increasing the kinetics of fibrillation. To investigate the effect of copper in aS fibril morphology, fibrils were observed by Cryo-Electron Microscopy (cryo-EM) and their mass-per-length measured by dark-field Scanning Transmission Electron Microscopy (STEM); copper content was assayed by Inductively Coupled Plasma Mass Spectrometry (ICP-MS).

aS amyloid fibrils are known to be polymorphic. To ascertain whether copper changes or selectively destabilizes particular morphotypes, a sample of in vitro-assembled, recombinant aS fibrils was incubated with excess CuCl₂ and then dialyzed to remove unbound cupric ions. The fibrils retained a significant excess of copper, which was visible in STEM micrographs as pairs of very thin (~5 Å), high-density threads running along fibrils. The presence of threads correlated with fibril morphotype: thin, wavy fibrils lacked threads while thicker, non-twisting fibrils embody a protein fold that is capable of binding copper. To test whether copper affects polymorphism during fibrillation, recombinant aS was polymerized in the presence of equimolar CuCl₂. These fibrils were structurally different from fibrils formed in the absence of copper, being thinner and having a narrower distribution of lower mass-per-length values. Since coordination of cupric ions limited fibril polymorphism, but only when presented prior to fibrillation, the effect must occur during nucleation. These observations suggest that the pathogenic effects of copper and other metals that correlate with Lewy Body formation and neurodegeneration in PD are expressed at the molecular level in their effects on the nucleation and structure of aS amyloid fibrils.

[1] Dearborn et al. J. Biol. Chem. 291:2310 (2016).

BASIC SCIENCE: MITOCHONDRIA, OXIDATIVE STRESS, INFLAMMATION, PATHOGEN

LBP5

Fibrillar but not monomeric α -synuclein induces pro-inflammatory phenotypes but both conformers increase phagocytosis via the TREM2 receptor in microglial cells

Jonathan Wilson¹, Balagopalakrishna Chavali¹, Hong Wang¹, Teri Belecky-Adams², Kalpana Merchant³

¹ Eli Lilly and Company, Indianapolis, IN, USA

² Indiana University-Purdue University Indianapolis, Indianapolis, IN, USA

³ TransThera Consulting Company, Indianapolis, IN, USA

Background: Several lines of evidence indicate that microgliosis and associated neuroinflammation are major pathophysiologies of Parkinson's disease (PD) that may contribute to the progressive neurodegeneration. Genetic and pathology studies have implicated α -synuclein (a-synuclein), the most abundant protein in the hallmark Lewy pathology of PD, as a major contributor to PD pathogenesis. Hence, a number of studies have been undertaken to study the effects of a-synuclein on microglial cells. However, the literature has many inconsistencies regarding the role of monomeric versus aggregated a-synuclein on microglial activation and phagocytic capacity. The present study was undertaken to systematically evaluate the effects of monomeric and fibrillar a-synuclein on a murine microglial cell line as well as primary microglia using morphological, molecular and functional end-points.

Methods: We examined phenotypic states and functional effects of BV-2 microglia and primary microglia following concentration and time-response treatment of a-synuclein. Phagocytic capacity of BV-2 or primary microglia vs Trem2 knock-out microglia was examined by an engulfment assay following treatment of a-synuclein.

Results: Fibrillar, but not monomeric, a-synuclein induced classical activation of BV-2 and primary microglia in a concentration- and time-dependent manner. This was evident by the induction of all M1 markers examined concurrently with a decrease in markers of alternative activation state. Fibrillar a-synuclein also significantly reduced the levels of Trem2 and Tyrobp mRNA in BV-2 microglia. However, treatment with both monomeric and fibrillar a-synuclein increased phagocytosis of bioparticles in BV-2 microglia and primary microglia. Interestingly, the a-synuclein induced increase in phagocytosis was abolished in Trem2-null primary microglia.

Conclusions: Through concentration- and time-response studies with robust controls, the data generated demonstrated convincingly that fibrillar a-synuclein, but not monomeric a-synuclein, shifts the activation state of BV-2 and primary microglia towards the proinflammatory, M1-like state. This effect could contribute to the chronic neuroinflammatory pathophysiology and progressive neurodegeneration in PD brains. On the other hand, the phagocytic function of microglia is induced similarly by monomeric and fibrillar a-synuclein and is mediated by TREM2 receptors. Thus Trem2 gene variants could modify the pathology in synucleinopathies.

LBP6

Design and synthesis of a mitochondrially-targeted glutathione derivative: a potential therapy for Parkinson's Disease?

Pamela Beilby, Nicholas Thomas, Lillian Padgett-Cobb, Samuel Bradford, Tory Hagen, Joseph Beckman

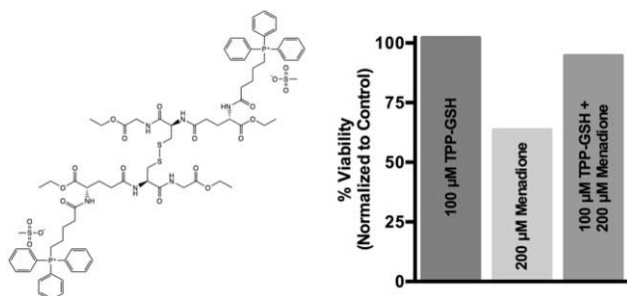
Oregon State University, USA

Background: Glutathione (GSH) is the most abundant non-protein thiol and cellular antioxidant in the substantia nigra (SN). GSH depletion is considered an early event in presymptomatic Parkinson's Disease (PD), and the degree of GSH loss correlates with disease severity and progression. In particular, the mitochondrial GSH (mGSH) pool appears to be the most adversely affected in PD and also in pharmacological-induced models of the disease. mGSH is a slow-reacting pool, distinct from the rest of the cell; no GSH synthesis occurs in the mitochondria and it must be transported into the organelle. Thus, therapies (e.g., n-acetylcysteine) that would sustainably mitigate GSH loss in other cell compartments by rapid induction of GSH synthesis are not effective in limiting mitochondrial GSH loss-associated SN neuron death in PD.

Objective: The goals of the present work are to i). design and synthesize a GSH derivative that can be effectively delivered to the mitochondrial matrix; and ii). examine its effectiveness to replete mitochondrial GSH equivalents and limit neuronal cell loss in an experimental model of PD.

Methods: A synthetic scheme was developed where the GSH reactive carboxylate groups were first esterified to facilitate intact GSH uptake into cells. The carboxyethyl derivative was then conjugated to triphenylphosphonium via a pentyl linker to achieve a final product.

Results: NMR, mass spectrometry and HPLC analysis show that we have achieved a triphenylphosphonium glutathione product (TPP-glutathione) that is >95% pure and contains a free thiolate group. Preliminary testing with TPP-glutathione indicates that the compound is taken up by energized mitochondria and capable of undergoing thiol redox reactions similar to authentic GSH. Additionally, TPP-glutathione ameliorates oxidative stress-induced toxicity experienced by cells exposed to menadione, a redox cycling agent that is known to rapidly deplete mGSH. This result and the structure for the stable GSSG derivative are shown in the figure. Thus, we have a novel analog of GSH that can now be used both to test the role of mitochondrial GSH in PD progression as well as a potential therapy to limit SN loss.



BASIC SCIENCE: ANIMAL & CELLULAR MODELS OF PARKINSON'S DISEASE & PARKINSONISMS

LBP7

The role of adenosine deficiency in Parkinson's disease

Adriana Rocha¹, Letisha Wyatt¹, Eleonora Aronica^{2,3}, Detlev Boison¹, Hai-Yang Shen¹

¹ Robert Stone Dow Neurobiology Laboratories, Legacy Research Institute, Portland, OR, USA

² Department of (Neuro)Pathology, Academic Medical Center/Swammerdam Institute for Life Sciences, Center for Neuroscience, University of Amsterdam, The Netherlands

³ SEIN – Stichting Epilepsie Instellingen Nederland, Heemstede, The Netherlands

Several lines of evidence suggest that the purine ribonucleotide adenosine plays a role in the pathogenesis and pathophysiology of Parkinson's disease (PD): (i) Adenosine is an endogenous neuroprotectant; (ii) Caffeine, an adenosine receptor antagonist, is considered to be of therapeutic value for the protection of PD; (iii) Adenosine receptors control motor function through interaction with dopamine receptors. Therefore, here we investigate the role of the key adenosine-removing enzyme, adenosine kinase (ADK), which is primarily expressed in astrocytes.

First, we demonstrate significant overexpression of ADK in conjunction with astrogliosis in postmortem specimen from PD patients. In line with these human data the a-synuclein transgenic mice displayed astrogliosis and similar pathological increases in ADK expression. These data imply that adenosine deficiency is a pathological hallmark of PD. To delineate a functional role of adenosine deficiency for PD pathology we created an adenosine deficient mouse line by overexpression of ADK in the brain. These mice are characterized by resistance to dopaminergic stimulation and a reduced number of tyrosine hydroxylase (TH)-positive neurons in the substantia nigra. To test the hypothesis that overexpression of ADK in astrocytes of the substantia nigra is sufficient to cause PD-like pathology, we overexpressed ADK in astrocytes of substantia nigra using an adeno associate virus (AAV)-based expression system. Four weeks after AAV-ADK virus injection we found prominent loss of TH neurons in the substantia nigra, and eight weeks after AAV-ADK virus injection animals showed reduced motor response to psychostimulant challenge.

We conclude that glial activation and overexpression of ADK might be a contributing factor for the development of PD.

LBP8

Synaptic alterations in cortico-striatal cocultures from LRRK2 G2019S transgenic mice.

Naila Kuhlmann¹, Austen Milnerwood², Matthew Farrer²

¹ University of British Columbia, Vancouver, BC, Canada

² Canada

Striatal synaptic plasticity and dendritic spine morphology are implicated in numerous psychiatric and neurodegenerative disorders, including Parkinson's Disease (PD). While studying how PD-linked gene mutations alter cellular mechanisms has become an important research area, the role these play in the plasticity of striatal neurons has not been elucidated. We previously reported that mutations in the leucine rich repeat kinase 2 (LRRK2) protein alter synaptic activity of cortical neurons in cultures from LRRK2 G2019S knock-in mice: glutamatergic transmission was increased, and the phosphorylation status of presynaptic proteins was reduced. Here, we first developed assays to examine NMDAR-dependent long-term potentiation (LTP) and mGluR1/5 dependent long-term depression (LTD) in cortico-striatal co-cultures from non-transgenic mice. We quantified striatal spiny projection neuron (SPN) spine morphology and density by confocal microscopy to examine the activity-dependence of structural plasticity, measured changes in synaptic proteins, and used whole-cell patch clamp electrophysiology to examine functional changes. In neurons from non-transgenic mice, chemical LTP increased spine density and increased AMPA-type glutamate receptor subunit expression, as well as causing changes in other synaptic proteins and electrophysiological measures. The reverse was observed for chemical LTD, most markedly in synaptic protein expression. We then extended these findings into co-cultures from G2019S knock-in

mice to first determine how the previously observed changes in cortical neurons may be altered by the presence of striatal neurons, and then to examine how LRRK2 regulates cortico-striatal plasticity and morphology. This study provides a launching point and the necessary assays to further investigate striatal plasticity in genetic models of PD, and how this may contribute to PD pathology.

LBP9

LRRK2 G2019S Knock in Mice: A tool for studying Pre-Synaptic Dopamine Dysfunction in Parkinsonism

Mei Yue¹, Peter Bauer², Ayman Farooq², Heather Melrose²

¹ University of British Columbia, USA

² USA

Leucine Rich Repeat Kinase 2 (LRRK2) is one of, if not the most, promising drug target for Parkinson's disease (PD). Much remains to be understood regarding LRRK2 pathogenicity, but a major recent advance in LRRK2 biology discovered that in vivo, mutant LRRK2 deregulates Rab GTPase homeostasis. Data we have generated from our LRRK2 G2019S knock in (KI) mice has demonstrated that striatal dopamine release is impaired, with onset around 12 months in of age (REF). Our G2019S model also develops profound striatal mitochondrial morphological abnormalities, which are accompanied by altered localization/levels of mitochondrial fission GTPase Drp1. Given the lack of neuronal loss, we believe our model mimics pre-clinical PD at the axonopathy stage. Characterizing these early events holds promise for pharmacodynamic and disease biomarkers, as well as strategies for disease intervention.

Our general hypothesis is that aberrant LRRK2 kinase activity induces synaptic failure and the focus of our current work is to 1) figure out how mitochondrial dysfunction fits in and 2) determine if LRRK2 kinase inhibition rescues synaptic deficits observed in this G2019S model

We present data showing that mitochondrial respiratory function is impaired in the striatal mitochondria of G2019S mice, with similar findings in patient fibroblasts. We also demonstrate that acute LRRK2 kinase inhibition can restore striatal dopamine release in homozygous G2019S mice, but not heterozygous mice, suggesting that the structure and mutant versus wild type preference of the compound is an important consideration for activity in vivo. The work has implications for developing effective therapies for LRRK2 patients since most are heterozygous.

BASIC SCIENCE: BRAIN PHYSIOLOGY AND CIRCUITRY

LBP10

M4 muscarinic receptor activity opposes D1 dopamine receptor-evoked GABA release and motor activity in the SNr: Implications for M4 antagonists as a treatment for movement disorders

Mark Moehle¹, Tristano Pancani², Nellie Byun², Zixiu Xiang², Jurgen Wess³, Jerri Rook², Craig Lindsley², Colleen Niswender⁴, Carrie Jones⁴, Jeffrey Conn⁴

¹ Vanderbilt University, Nashville, TN, USA

² Vanderbilt Ctr. for Neurosci. Drug Discovery and Department of Pharmacology, Nashville, TN, USA

³ NIDDK, National Institutes of Health, Bethesda, MD, USA

⁴ Vanderbilt Ctr. for Neurosci. Drug Discovery and Department of Pharmacology, and Vanderbilt Kennedy Center, Nashville, TN, USA

Objective: Dysregulation of dopamine (DA) within the basal ganglia from midbrain dopaminergic neurons of the substantia nigra pars compacta (SNpc) is a central pathology to several movement disorders. Within the basal ganglia, DA plays a critical role in regulating striatal function by actions on two separate non-overlapping pathways, the direct and indirect pathway. Because of the critical modulatory role of DA, a great effort has been placed on understanding both how DA modulates the basal ganglia direct and indirect pathways and how other neurotransmitter systems, such as muscarinic acetylcholine receptors, regulate DA signaling.

Methods: Using a wide range of behavioral, electrophysiological, optogenetic, pharmacological, and imaging techniques, we directly test how D1 Dopamine Receptor (D1) agonists modulate the basal ganglia and how the M4 muscarinic acetylcholine receptor (M4) activation regulates this signaling.

Results: Here, we report that D1 agonists can induce hyperlocomotion, and that this effect can be blocked by M4 activation. We found that D1 activation robustly induces GABA release from direct pathway spiny projection neurons onto cells of the substantia nigra pars compacta (SNr) and that this is attenuated with M4 activation at the level of the SNr, likely through a cAMP-dependent mechanism. Additionally, we also observed that M4 activity may tonically inhibit D1 activity and GABA release in the direct pathway.

Conclusion: Our data suggest that DA release and D1 activation, as well as acetylcholine release, in the SNr are equally important to produce and regulate movement as their counterparts in the striatum, extending the current model of DA regulation of basal ganglia processing. These data provide initial pre-clinical evidence for the efficacy of M4 antagonists in the treatment of movement disorders.

CARE DELIVERY & QUALITY OF LIFE: FITNESS, WELLNESS, NUTRITION

LBP11

Mindfulness Based Stress Reduction in People with Parkinson's: A Pilot Study with Focus Group Analysis and Quality of Life Measures

Barbara Pickut¹, Susan Hoppough², Susan Woolner¹, Genevieve Barrett², Lynn Cherney², Kasey McCollum³

¹ Hauenstien Neurosciences Mercy Health Saint Mary's, Michigan State University, Grand Rapids, MI, USA

² Mercy Health Saint Mary's, Grand Rapids, MI, USA

³ Grand Valley State University, Department of Public Health, Grand Rapids, MI, USA

Objective: Converging evidence suggests that mindfulness training may have an impact on a number of disease specific symptoms such as cognitive changes, depression, pain and anxiety all of which may present as non-motor symptoms in People with Parkinson's (PwP). The aim of the current study is to investigate the effects of mindfulness training on the quality of life of PwP.

Methods: Five self-report questionnaires were administered for pre- and post-testing to 10 PwP (5 female) who participated in the study. Pre- and post-test scores for each self-report questionnaire were analyzed using paired Student t-tests. Tests were compared using a p-value threshold of 0.05 for significance determination and are presented with 95% confidence intervals. All statistical analyses were conducted in SPSS version 20.

The Focus Group recording was transcribed and reviewed individually by three members of the research team who sought

after topics of spirituality, empowerment, and coping then triangulated their findings.

Results: Statistical analysis from the self-report questionnaires found significant improvements in the Parkinson's Disease Quality of Life (PDQ-39) improvements in emotional wellbeing, and social support ($p=0.022$, $p=0.05$, respectively), the Five Facet Mindfulness Questionnaire non-judgmental element facet ($p=0.022$), and the Beck Depression Inventory-II score decrease by 5.2 ($p=0.058$). The Focus Group analysis indicated strong support for topics of spirituality, empowerment, and coping as well as an unexpected fourth, the group effect.

Conclusions: Significant improvements in emotional wellbeing, and social support were evident on the Parkinson's disease Quality of Life (PDQ-39) questionnaire indicating that mindfulness training is associated with improving a person's sense of emotional wellbeing and increasing the perception of social support. Analysis from the Five Facet Mindfulness Questionnaire revealed a significant difference in the non-judgmental facet indicating that participants experienced an increase in the ability to not judge their own inner experience. Analysis from the Beck Depression Inventory-II found a marginally significant difference in the level of depression experienced potentially enough to change to a lower, more mild depression category. Finally, there was strong support for topics of spirituality, empowerment, and coping as well as an unexpected fourth, the group effect.

CARE DELIVERY & QUALITY OF LIFE: CREATIVITY & ALTERNATIVE OR COMPLEMENTARY THERAPIES

LBP12

Brain, Breath and Emotion: The Resurrection of the Voice

Ruthanna Metzgar
WA, USA

The human voice is a signature in sound, a strong source of identity. Those dealing with loss of voice due to Parkinson's, other neurological disorders and aging are challenged physically, mentally, and emotionally. The inability to be heard or understood through speech, no longer having voice identity, leaves a neurologically challenged person questioning, "Who am I?"

Because the human voice is imbedded in body, mind, and spirit an interdisciplinary holistic approach engaging brain, breath and emotion for voice recovery will be reviewed. An analysis of the ways in which each of the following has an effect on voice restoration will be described: physical awareness and relaxation, diaphragmatic/costal breathing, vocalises, group singing, speech, diction and use of articulators, creative drama and role playing, emotional expression exercises, play, spontaneity, and the power of creative imagination. In Muhammad Ali's words, "The man who has no imagination has no wings."

Initial work began in 2006 at the request of Eisenhower Medical Center in Rancho Mirage, CA for use with Parkinson's patients, but now includes stroke, essential tremor, Meige Syndrome, Bulbar Palsy, other speech related neurological disorders, and aging voices. The program, an adjunct to speech therapy, offers opportunity for patients whose Medicare or insurance benefits are expended to continue with needed therapy at minimal cost, and it is fun for the participant. Many students come at the recommendation of neurologists, speech therapists, or as a result of hearing about the efficacy of the program at various support groups.

These are comments from the participants on the first day of class.

"I don't know who I am when I hear my voice."

"My husband says he can't understand me."

"I am ashamed to go out in public and speak to others."

"I no longer talk on the phone."

"I feel like I am shouting when people say they can hear me."

After very few classes these are the comments:

"They can hear me now! They can hear me!"

"I just have to realize that I'm still me in spite of PD."

"Now I talk on the phone all the time!"

"This class is awesome! I can hardly wait to come back next week."

Empirical and scientific information concerning the brain and the benefits of an integrated approach that yields sustainable results will be presented through power point, video, and audience participation.

CARE DELIVERY & QUALITY OF LIFE: SHARED DECISION-MAKING: PWP – CAREGIVER – DOCTOR

LBP13

Navigating Multidimensional Difficulties of Young-Onset PD - A Five-Year Longitudinal Case Study

Elizabeth Teeling, Nikkiel LeFebvre, Melody Rasmor
Washington State University, Vancouver, WA, USA

Parkinson's disease (PD) is the second most common neurodegenerative disease worldwide and its incidence continues to rise. The emotional and physical strain PD inflicts on the patient and caregiver requires sensitivity from medical professionals (MP). PD is a horrifying, anxiety producing diagnosis that many patients describe as having an intact mind with an uncooperative body. The emotions experienced are similar to Kubler-Ross stages of grief model including: Denial, anger, fear, frustration, sadness and bargaining. Additionally, the medical community has its own set of rules and a complicated culture that is difficult for the layperson to navigate. It is imperative that MP's recognize that the ramifications of diagnosis are multifaceted. PD patients may exhibit knowledge-seeking behaviors, difficulty with compulsions, cognitive problems, financial strain, role ambiguity and caretaker strain. It is important for MP's to set aside cultural bias and make efforts to listen to and understand the patient and caregivers' concerns. Providing competent patient and family-centered care allows the MP to encourage treatment adherence, positive attitudes toward diagnosis and strength. The differentiation between the attitudes of MP's will influence whether or not the care provider is a valuable resource who influences patient well-being and quality of life; or a contributor to devastation by hindering the patient and family's ability to maintain quality of life. A skilled MP will implement care with sensitivity, empathy, and knowledge of late-breaking treatments. Furthermore, practitioners must be informed of the disability application process so they can partner with individuals and families to relieve financial strain. In an effort to better inform MP's of how to be an advocate and partner in PD therapy, a longitudinal case study of one young-onset PD patient and one spouse's perspective was undertaken over a five-year time period.

CARE DELIVERY & QUALITY OF LIFE: SELF-MANAGEMENT, EMPOWERMENT, COPING STRATEGIES

LBP14

What motivates People with Parkinson (PwP) for exercise and self-management strategies?

Audun Myskja

Norwegian Parkinson Union, Ski, Norway

Objective: A 5 year followup study sought to evaluate factors that improve and decrease motivation for exercise. Participants followed a structured training program developed empirically through evaluating research on preexisting exercise programs for PwP, and was adjusted through interaction with the training group.

Background: There is general agreement on the importance of exercise for the long term management of PD, and a growing number of specific training programs. However, there is a lack of knowledge of what strengthens motivation for self-management, especially long-term.

Methods: PwP (n=20) were recruited in a Norwegian region, with patients on waiting list (n=16) as controls. The group followed a structured exercises program once a week, led by physiotherapist. The mean age was 62.4 (SD 7.3) years and the mean disease duration was 8 (SD 5.2) years. Participants were investigated once a year using a purposive, qualitative design over the 5 year training period, applying multiperspectival, semistructured interviews and thematic analysis.

Results: Thematic analysis revealed that fear of falling, insecurity, lack of knowledge of what may help, depression and social isolation impede motivation for exercise and other forms of self-management. The thematic analysis of the structured interviews emphasized the value of group training and the importance of collaboration with participant needs. Specific instructions in movements, rhythm and performance of exercises strengthen motivation, as do group training, regular supportive followup instruction and dialogue. Interview data suggest that a higher rate of follow-up on home training would further improve results.

Conclusions: A 5 year study of factors influencing motivation in a group. The present study supports the importance of penetrating the factors that strengthen motivation for exercise and other forms of self-management over time.

LBP15

Evaluation of a 5 year relaxation exercise program for people with Parkinson (PwP)

Audun Myskja

Norwegian Parkinson Union, Ski, Norway

Objective: To evaluate a structured training program using a series of relaxation exercises for a group of people with Parkinson (PwP). The exercise program has been developed empirically through evaluating research on preexisting exercise programs, and was adjusted through interaction with the training group.

Background: There is increasing interest in the potential benefit of systematic relaxation techniques in the management of symptoms that afflict PwP. However, there is still insufficient knowledge about what type of relaxation exercises may be most beneficial, for which symptoms, and how relaxation exercise programs may be best applied to aid PwP.

Methods: PwP (n=20) were recruited in a Norwegian region, with patients on waiting list (n=16) as controls. The group followed a structured program with relaxation exercises once a week, led by physiotherapist. The mean age was 62.4 (SD 7.3) years and the

mean disease duration was 8 (SD 5.2) years. Participants were evaluated by UPDRS, PDQ-39, Hoehn & Yahr, Senior Fitness, Time Up and go, Montgomery-Aasberg depression rating scale and Herth Hope Index before project start, and once yearly through the study period. Quality of life issues were evaluated by multiperspectival, semistructured interviews applying thematic analysis before project start, and once yearly through the study period.

Results: Functional tests showed stability in the relaxation group compared to control group (findings will be discussed in the presentation). Depression measures showed low values for depression compared to control group. Structured interviews emphasized the value of group training and the importance of collaboration with participant needs. Interview data suggest that a higher rate of follow-up on home training would further improve results.

Conclusions: Our data suggest benefit of a relaxation exercise program developed in collaboration with participants, effects becoming more marked over time. Further research to specify benefits of structured relaxation is recommended.

The presentation will be illustrated by video clips and comparative tables and figures.

CLINICAL SCIENCES: SYMPTOMS, SIGNS, FEATURES & NON-MOTOR MANIFESTATIONS

LBP18

Detection of Prodromal Parkinson's Disease for Primary Care Providers

Melody Rasmor¹, Nikkiel LeFebvre², Elizabeth Teeling¹

¹ WSU, Vancouver, WA, USA

² WSU MSN student, Troutdale, OR, USA

Parkinson's disease (PD) is the second most common neurodegenerative disease worldwide and the incidence of PD is on the rise. Currently diagnosis of PD is determined through a history and physical examination that focuses on the presence of motor symptoms to include: bradykinesia, muscular rigidity, resting tremor and postural instability. Unfortunately, by the time these symptoms appear it is estimated that 50–60 percent of the nigrostriatal neurons affected by PD are already lost. Due to this phenomenon increased emphasis is being placed on earlier detection and diagnosis of PD in an effort to improve treatment outcomes. Existing mainstays of PD treatment involve symptom management, and slowing disease progression via neuroprotective therapies. Neuroprotective therapies are most beneficial when PD is identified prior to significant neuronal loss; which poses a problem and limits therapeutic options for patients who already have advanced neuronal loss at the time of diagnosis. It is suspected that the key to early detection may lie in the prodromal phase of PD where premotor symptoms are present with the absence of motor disease. These symptoms include: functional somatic complaints, REM sleep disorders, constipation, depression, anosmia and fatigue. Many studies assert patients who are diagnosed with PD present to their primary care provider with premotor complaints 5-10 years preceding diagnosis. Therefore, Primary Care Providers (PCP) are uniquely poised to identify non-motor PD sequelae prior to significant neuronal loss. In an effort to improve outcomes and prolong quality of life for PD patients and their families a literature review was undertaken to determine the most comprehensive method to identify premotor symptoms that will aid PCP's in identifying patients who are in the preclinical stages of PD.

LBP20

Breaking the News: An Ethical Approach to Telling Family, Friends, and Co-workers About Your PD Diagnosis

Lisa Garvey

San Jose, CA, USA

If you can hide your Parkinson's symptoms with medication, should you tell people? How much information do we owe our employers and co-workers about our new status as Parkinson's patients? Do we now have to check the "Disabled" box when applying to a job? If you decide to take the leap, what's the etiquette for informing your friends, family, neighbors, boss, and teammates about your recent admission to this special "club" of newly diagnosed PD patients? What are the risks of announcing on social media sites like Facebook and LinkedIn?

We'll look at the ethical and practical implications of the questions above, using several real-life patient examples, including my own story and my personal choice to "go big." (See story: http://www.mercurynews.com/scott-herhold/ci_27858175/herhold-going-public-parkinsons) I'll discuss the impact of that decision, both positive and negative, on my daily life.

Whether you have Parkinson's or care for someone who lives with the unrelenting symptoms, the decision about openness is a very relevant topic.

Speaker bio: Lisa Garvey is a 46-year-old marketing director in Silicon Valley who was diagnosed with Young Onset Parkinson's Disease at the age of 41. In addition to her day job, she is the marketing chair of Moving Day Silicon Valley, an annual event sponsored by the National Parkinson Foundation (NPF). For the last two years, Lisa has been one of the top fundraisers nationally for Moving Day, and has rallied 50-person walking teams to participate in the event. Despite holding a B.A. in Philosophy, Lisa has been consistently employed for over 20 years, and she has spoken at high-tech industry events on a range of topics, including web analytics, branding, and content localization. She lives in San Jose, CA, with her husband, two teenage sons, two dogs, two cats, and the occasional ill-timed hamster.

CLINICAL SCIENCES: DIAGNOSIS (DIFFERENTIAL, ACCURACY)

LBP21

Defining 'Advanced' Parkinson's Disease in Clinical Practice: Results from the OBSERVE-PD Study, a Cross-sectional Observational Study of 2615 Patients

Alfonso Fasano¹, Leonardo Lopiano², Bulent Elibo³, Irina Smolentseva⁴, Klaus Seppi⁵, Annamária Takáts⁶, Koray Onuk⁷, Juan Carlos Parra⁷, Lars Bergmann⁷, Ashley Yegin⁷, Zvezdan Pirtosek⁸

¹ Morton and Gloria Shulman Movement Disorders Clinic and the Edmond J. Safra Program in Parkinson's Disease, Movement Disorders Centre – Toronto Western Hospital, UHN, Division of Neurology, University of Toronto and Krembil Research Institute, Toronto, Ontario, Canada

² Department of Neuroscience, University of Turin, Turin, Italy

³ Department of Neurology, Hacettepe University Hospitals, Ankara, Turkey

⁴ Department of Neurology, Russian Postgraduate Medical Academy, Moscow, Russia

⁵ Department of Neurology, Medical University Innsbruck, Innsbruck, Austria

⁶ Parkinson's Disease and Movement Disorders Clinic, Semmelweis University, Budapest, Hungary

⁷ AbbVie, Inc., North Chicago, IL, USA

⁸ University Medical Center Ljubljana, Ljubljana, Slovenia

Background: The majority of advanced Parkinson's disease (PD) patients are treated at specialized movement disorder centers. However, there is no consensus on the clinical and non-clinical features defining the advanced stage.

Objective: To characterize the clinical and non-clinical features and treatments (including invasive device-aided options) in a population of PD patients who are "advanced" according to the treating movement disorder specialists.

Methods: A cross-sectional, observational, multi-center, multi-country study was conducted at movement disorder centers offering at least one invasive, device-aided PD treatment option. The primary endpoint was the proportion of PD patients identified by their physician as advanced. The clinical and non-clinical characteristics of advanced PD patients, consideration of invasive treatment, and referral practices were compared to non-advanced PD patients using descriptive statistics. Physicians' assessment of advanced PD was compared to a Delphi-criteria-based classification.

Results: 2615 PD patients at 128 movement disorder centers in 18 countries completed the study. According to the physicians' judgment, 51.3% of PD patients overall were considered advanced, but varied among countries. There was a moderate correlation between the physician's judgment and the Delphi-consensus-based criteria for advanced PD. Advanced and non-advanced PD patients were similar regarding age, gender, and living situation, but differed in terms of severity of motor symptoms (Unified Parkinson's Disease Rating Scale [UPDRS] Part III mean score), motor fluctuations (% with motor fluctuations present, UPDRS Part IV Q32 and Q39), non-motor symptoms (Non-motor Symptom Scale mean total score), quality of life (8-item Parkinson's Disease Questionnaire mean total score) and caregiver support status (Table). Of the 1342 advanced PD patients, physicians considered 882 (66%) eligible for invasive treatment, and 548 (41%) had an ongoing invasive treatment or were about to start.

Conclusions: This cross-sectional multi-country study demonstrated that physicians judged that more than half of the PD patients in movement disorder centers across 18 countries as advanced, with distinct characteristics regarding motor fluctuations, non-motor symptoms and quality of life.

Table: Characteristics of Advanced and Non-advanced Parkinson Disease Patients

Characteristics	Advanced PD, N=1342		Non-advanced PD, N=1273	
	n/N (%)	Mean [SD]	n/N (%)	Mean [SD]
Age, years		67.6 [9.4]		66.4 [10.3]
Sex, male	817/1342 (61)		734/1273 (58)	
Living at home	1304/1342 (97)		1264/1273 (99)	
Caregiver support, yes	917/1327 (69)		328/1270 (26)	
Time since diagnosis, years		11.0 [5.8]		4.3 [3.7]
Motor fluctuations present, yes	1167/1342 (87)		295/1273 (23)	
Duration of motor fluctuations, years*		4.9 [3.9]		2.3 [2.1]
UPDRS II (ADL), score ^b		16.5 [8.3] ***		8.4 [5.4] ***
UPDRS III (motor), score ^b		30.2 [14.7] ***		21.1 [11.0] ***
UPDRS IV Q32, dyskinesia, none	501/1338 (37)		1097/1268 (87)	
UPDRS IV Q39, off time, none	271/1336 (20)		931/1259 (74)	
UPDRS V: Modified Hoehn & Yahr, score ^d		2.9 [0.8] ***		2.0 [0.6] ***
NMSS, total score ^e		58.6 [43.0] ***		34.4 [30.9] ***
PDQ-8, total score ^f		36.6 [19.3] ***		20.7 [16.4] ***
Eligible for invasive treatment options, yes	882/1342 (66)		127/1272 (10)	
Status of invasive treatment for eligible patients				
Ongoing	384/882 (44)		15/127 (12)	
Decided at visit to start	164/882 (19)		17/127 (13)	
No	332/882 (38)		91/127 (72)	
Missing	2/882 (0.2)		4/127 (3.1)	

N for advanced PD, non-advanced PD: a. 1151, 272; b. 1341, 1270; c. 1341, 1272; d. 1342, 1272; e. 1070, 1018; f. 1326, 1262.

The UPDRS was measured in the "on" state. Statistical significance based on a t-test between the Advanced and non-advanced PD patients are indicated at the P<0.0001 (***). All proportions except for the invasive treatment status included patients with non-missing data. UPDRS = Unified Parkinson's Disease Rating Scale; NMSS = Non-motor Symptom Scale; PDQ-8 = 8-Item Parkinson's Disease Questionnaire

LBP22

Tremor: Is it Parkinson's or something else?Patricia Cox¹, Melody Rasmor²¹ University of Portland, Portland, OR, USA² Washington State University, Vancouver, WA, USA

Tremor of a body part is the most common movement disorder in the general population. But it can be difficult to determine if the tremor is benign or a symptom of an underlying disease such as Parkinson's. This poster will discuss the differential diagnosis of tremor and the clinical clues that can aid the primary care clinician in making a diagnosis. Is it Parkinson's disease (PD) or something else? PD affects close to six million persons globally and one million in the United States. PD is a progressive and chronic neurodegenerative disease with symptoms worsening over time. The disease has a severe effect on persons with PD causing disability and a decreased quality of life. A common early feature of PD is tremor. Either due to embarrassment or fear of a diagnosis of PD individuals may not seek evaluation right away and this may hinder appropriate treatment. Careful attention to the history and physical examination can determine if the patient has PD or another neurological disorder. Nurse Practitioners (NP) in primary will be challenged with assessing and diagnosing PD as the population ages. Recognizing tremors and other characteristics of PD will increase the NP's confidence to assess and manage patients appropriately. This poster is provided to aid in the differentiation of a PD tremor from an essential tremor, the two most common movement disorders seen in older populations.

CLINICAL SCIENCES: BIOMARKERS AND NEUROIMAGING

LBP23

Gender difference in age- and disease progression- associated changes in blood iron parameters in Parkinson diseasePaola Costa-Mallen¹, Cyrus Parse Zabetian², Shu-Ching Hu³, Pinky Agarwal⁴, Dora Yearout², Kris Ronnie¹, Masa Sasagawa¹, Harvey Checkoway⁵¹ Bastyr University Research Institute, Kenmore, WA, USA² Veterans Affairs Puget Sound Health Care System, Seattle, WA, USA³ University of Washington, Department of Neurology, Seattle, WA, USA⁴ Evergreen Health, Booth Gardner Parkinson's Care Center, Kirkland, WA, USA⁵ University of California San Diego, Department of Family & Public Health, La Jolla, CA, USA

While an increase in free iron levels in the Substantia Nigra of the brain is generally considered a contributor to oxidative stress and neurodegeneration in Parkinson disease, there is emerging evidence that blood iron and blood iron-binding protein levels may be lower in PD cases than controls, and low iron levels and anemia may contribute to increased risk of PD. Gender affects both iron metabolism and risk of PD, given that women have lower risk of PD, but they tend to have lower blood iron levels than men during fertile years. How blood iron related parameters associate with stages of Parkinson disease progression has not been completely established. Changes in blood iron and iron-binding protein parameters occur with normal aging in the general population and the differences between age-associated changes in iron-binding proteins levels between PD patients and normal controls has not been well characterized. In this study, we measured iron-

metabolism related parameters, including hemoglobin (Hb), total serum iron, ferritin, uric acid, transferrin (Tf), transferrin % saturation (Tf% sat), and soluble transferrin receptor (sTfR) levels in 99 PD patients (54 men and 45 women) and 206 controls (88 men and 118 women). Correlations were calculated between Hoehn & Yahr stage and blood iron-related parameters in PD patients, and between age and blood iron-related parameters in both PD cases and controls, and after stratification by gender. Blood Hb levels resulted to decrease with age in men, significantly among PD patients (Standardized beta coefficient of regression=-.398, p=0.007), and not significantly among controls (beta=-0.126, p=0.246). Blood Hb levels did not significantly change with age among women, in both PD patients (beta=-0.060, p=0.693), and controls (beta=-0.011, p=0.908). Hb levels decreased significantly with the Hoehn & Yahr stage of PD in women (age-adjusted p=0.013), but not in men (age-adjusted p=0.939). sTfR levels resulted inversely correlated with serum iron levels, and increased significantly with the Hoehn & Yahr PD stage in both men and women. Differences between men and women in association between Hoehn & Yahr PD stage and uric acid levels were also observed. These results highlight the presence of gender differences in peripheral iron metabolism abnormalities that occur with aging and disease progression in PD patients.

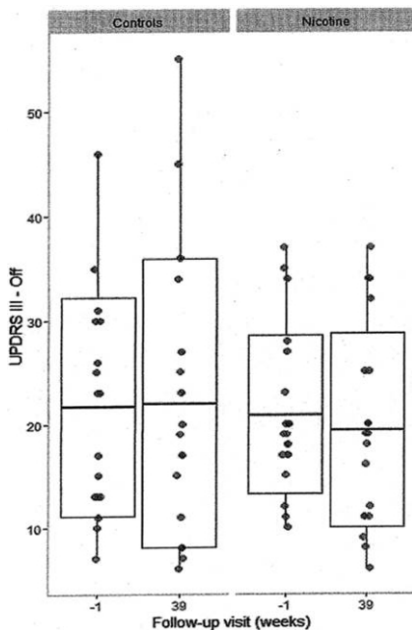
CLINICAL SCIENCES: PHARMACOLOGICAL THERAPY

LBP24

Effect of transdermal nicotine on motor symptoms in advanced Parkinson's disease: results of the Nicopark2 Study.Gabriel Villafane¹, Claire Thiriez², Michel Audureau³, Florence Cormier⁴, Axel Van der Gucht⁵, Céline Straczek³, Philippe Kerschen⁶, Jean-Marc Gurruchaga⁷, Morgane Quéré-Carne³, Eva Evangelista⁵, Pierre Cesaro⁸, Gilles Defer⁹, Philippe Damier¹⁰, Philippe Remy¹¹, Emmanuel Itti⁵, Gilles Fénélon¹²¹ CHU Henri Mondor, Créteil, France² Centre Expert Parkinson, Neurologie, Créteil, France³ URC, CHU Henri Mondor, Créteil, France⁴ ICM, CHU Pitié-Salpêtrière, Paris, France⁵ Médecine Nucléaire, CHU Henri Mondor, Créteil, France⁶ Neurologie, CHU Henri Mondor, Créteil, France⁷ Neurochirurgie, CHU Henri Mondor, Créteil, France⁸ Centre Expert Parkinson, Neurologie, CHU Henri Mondor, Créteil, France⁹ Neurologie, CHRU Cote de Nacre, Caen, France¹⁰ Neurologie, CHRU Nantes, Nante, France¹¹ Centre Expert Parkinson, Neurologie, Créteil Cedex, France¹² Centre Expert Parkinson, Neurologie, CHU Henri Mondor, Créteil, France

Objective: To evaluate the efficacy of transdermal nicotine on motor symptoms in advanced PD.

Background: Effect of nicotine on motor symptoms in PD is controversial. Four of the 5 open-label studies of nicotine in PD suggested motor improvement while 3 placebo-controlled studies were negative. We investigated the efficacy and tolerability of higher doses of nicotine.



Methods: Forty patients were randomly assigned to a treated and an untreated arm in an open-label study. Treated patients received increasing doses of nicotine to reach 90 mg in 20 weeks. This dosage was maintained 19 weeks (W39) then progressively reduced over 6 weeks. A final evaluation was performed after a 6 weeks-washout (W50). The patients were non-smokers, had PD according to UK-PD Brain Bank criteria and had been on L-Dopa for at least 3 years (Dopa equivalent daily doses were 599±270 and 541±303 mg/d in the nicotine and no-nicotine groups, respectively). The main outcome measure was the off-dopa UPDRS motor score measured on video recordings by raters blinded to the nicotine and ON/OFF status of the patients.

Results: No statistically significant difference for off-dopa UPDRS motor scores was observed between the nicotine-treated and non treated groups, neither at W39 (19.4±9.3 vs. 21.9±9.3) nor considering W39 differences from baseline (-1.5±12.1 vs. +0.3±11.2). PDQ-39 scores decreased in nicotine-treated patients (-6.2±21.2) and increased in non-treated patients (+3.9±14.3) but the difference did not reach statistical significance (p=0.11). Overall tolerability was good, and 12 treated patients (60%) reached the maximal 90mg dosage.

Conclusions: High doses of transdermal nicotine were tolerated but failed to demonstrate significant improvement in UPDRS motor score after 39 weeks of treatment.

LBP25

Effects of age and disease duration on quality of life outcomes in advanced Parkinson's disease patients treated with levodopa-carbidopa intestinal gel infusions: a post-hoc analysis from the GLORIA registry

Angelo Antonini¹, Weining Robieson², Lars Bergmann², Ashley Yegin², Werner Poewe³

¹ Institute of Neurology, IRCCS San Camillo, Venice, Italy

² AbbVie Inc., USA

³ Medical University of Innsbruck, Innsbruck, Austria

Objective: To evaluate the influence of baseline (BL) clinical characteristics on preservation of quality of life (QoL) and Activities of Daily Living (ADL) in advanced PD patients treated with

levodopa-carbidopa intestinal gel (LCIG, carbidopa-levodopa enteral suspension in the US) over 2 years.

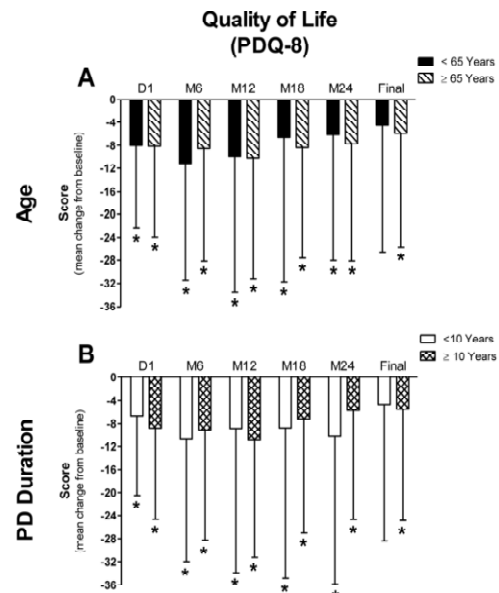
Background: LCIG delivered via percutaneous gastrojejunostomy (PEG-J) significantly improved QoL measures in this registry over 24 months (24M) of treatment; however, the influence of different BL characteristics, such as age and PD duration, on QoL and ADL preservation in patients treated with LCIG has not been reported.

Methods: LCIG was titrated via nasojunal tube and delivered over 24M via PEG-J. For this post-hoc analysis, patients were allocated into subgroups based on BL age (<65 [N=122] and ≥65 [N=207] years), disease duration (<10 [N=111] and ≥10 [N=217] years), OFF time (<3 [N=28], 3–6 [N=96], and >6 [N=87] hours/day), and Levodopa Equivalent Dose (LED) (<800 [N=54], 800–1200 [N=101], and >1200 [N=172] mg/day). The mean 8-item Parkinson's Disease Questionnaire (PDQ-8) (QoL) Summary Index and Unified Parkinson's Disease Rating Scale (UPDRS) part II (ADL) scores were assessed for each subgroup. Adverse Drug Reactions were monitored.

Results: Sustained improvements in PDQ-8 total scores were observed at 24M across all age (mean [SD] <65 years=-6.2 [21.9], P=0.030; ≥65 years=-7.7 [20.4], P<0.001) and PD duration subgroups (<10 years=-10.2 [25.6], P=0.013; ≥10 years=-5.8 [18.8], P=0.002). Sustained improvements in PDQ-8 scores were also observed in patients =3 hours of "Off" time at BL (18M: 3–6 hours =-10.95 [22.8], P 6 hours=-11.14 [23.599], p 1200 mg/day=-8.0 [22.6], P<0.002). Decreased UPDRS II scores were observed across all subgroups during treatment. These improvements from BL were significant at 18M in patients <65 years old (-3.02 [8.4], P=0.004) and those with 3–6 hours of "Off time at BL (-2.56 [9.0], P=0.033) and at 24M in patients <10 years since PD diagnosis (-3.0 [8.6], P=0.025) and in those with a BL LED >1200 mg/day (-3.1 [9.1], P=0.002).

Conclusions: LCIG led to consistent and sustained improvements in QoL irrespective of patient age and disease duration. Notably, improvements in ADL were greater and more sustained in patients treated with LCIG earlier in life and after shorter disease duration.

Figure 1. Mean Change from Baseline in PDQ-8 Total Score



Asterisks indicate statistical significance compared to baseline in a paired t-test at the P<0.05 (*) level. PDQ-8 = Parkinson's Disease Questionnaire 8-item; D1 = first day of LCIG infusion via PEG-J after titration via nasojunal

CLINICAL SCIENCES: SURGICAL THERAPY, INCLUDING CELL AND GENE THERAPY

LBP26

Long-term outcome of subthalamic deep brain stimulation for Parkinson's disease between general and local anesthesia

ShengTzung Tsai¹, Shin-Yuan Chen²

¹ Massachusetts General Hospital, Boston, MA, USA

² China

Background/Aims: Most subthalamic nucleus deep brain stimulation (STN-DBS) for Parkinson's disease (PD) is performed under local anesthesia (LA). Given the advancement of imaging and microelectrode recording, STN-DBS under general anesthesia (GA) is an alternative choice. However, long-term outcome of direct comparison between GA and LA for STN-DBS is lacking. The authors compared five years outcome of STN-DBS for PD between GA and LA.

Methods: 36 consecutive PD with similar motor disabilities underwent either GA (n=22) or LA (n=14) for their STN-DBS. Microelectrode recordings were performed in all patients for STN localization and surgical outcomes evaluation included Unified Parkinson's Disease Rating Scales, Mini-mental status examination, Beck Depression Inventory and surgical characteristics were recorded as well.

Results: Both groups acquired similar benefits from long-term STN-DBS and did not show any significant difference in neuropsychiatric outcome analysis. In terms of stimulation parameters, these all show comparable results. Most adverse effects analysis did not show higher incidences in GA group.

Conclusions: Long-term benefits (five years analysis) confirmed the equal effectiveness and safety of STN-DBS under GA when it compared to LA. STN-DBS under GA should be considered for patients whom are not suitable for electrode implantation under LA.

LBP27

Factors influencing on motor improvement in the off-medication condition after GPi DBS in patients with Parkinson's disease

Eun Jung Lee, Sang Ryong Jeon

Korea, South

Objective: The aim of this study was to evaluate the factors predicting motor improvement in patients with Parkinson's disease (PD) who underwent deep brain stimulation (DBS) on globus pallidus internus (GPi). We particularly focused on the effect of electrode location on the relative motor improvement (MI %).

Methods: A retrospective analysis was performed for 27 patients with PD (mean age, 58.6 years; mean duration of disease, 10 years) who underwent bilateral GPi DBS from August 2012 to April 2015. The end point was change from baseline to one-year in the severity of parkinsonian motor symptoms without medication, as assessed with the use of the Unified Parkinson's Disease Rating Scale, part III (UPDRS-III). Localizations of electrode tips were derived from postoperative MRI-data following anatomical normalization into the standard Montreal Neurological Institute (MNI) stereotactic space. The MIs 1 year after GPi DBS were allocated to low- (<30%, n=5), intermediate- (=30%; <60%; n=12), or high-MI (=60%, n=10) and the factors associated with high-MI were analyzed using logistic regression model. Euclidean distances between coordinates of the electrode tips and the geometric center of the high-MI cluster were calculated.

Results: UPDRS-III in the off-medication condition was improved by 45.7±25.2% after GPi DBS compared to baseline. The extent of motor response to levodopa challenge test at baseline was only predictors of high MI (P=0.046), and it linearly correlated with MI (%) (Pearson coefficient, 0.471, P=0.013). The location of electrode tips of high-MI group in the standard MNI coordinate system were: x=23.05±1.38 mm, y=-11.60±2.27 mm, z=-6.1±1.79 mm for right side and x=-20.78±2.33 mm, y=-10.67±2.60 mm, and z=-5.3±1.80 mm for the left side. The coordinates of electrode tips of low- and intermediate-MI group were similar to those of high-MI group, which were clustered in the posterolateroventral area of the pallidum. Euclidean distances between electrode tip and the center of the high-MI cluster were neither different across the groups nor associated with MI (%).

Conclusions: Preoperative excellent motor response to levodopa medication predicts the higher improvement of motor signs in the off-medication state after GPi DBS. The effects of DBS on motor signs in the off-medication condition are similar so long as the electrode tips are located within the posterolateroventral area of the GPi.

CLINICAL SCIENCES: REHABILITATION SCIENCES (PT, OT, SLP)

LBP29

Community boxing for adults with Parkinson's Disease – a feasibility study

Linda Denney, Cynthia C. Ivy, Kristen Bennett, Megan Jerome, Patricia S. Pohl

Northern Arizona University, Phoenix, AZ, USA

There is strong evidence supporting the value of exercise for adults with Parkinson's Disease (PD), however there is no consensus about the type or intensity of exercise that should be recommended. Programs that are likely to be the most successful are those that are appealing to the participant and available to anyone living in the community. Boxing is an exercise that is gaining popularity among those with and without PD. Recent studies using fitness programs that include boxing movements have shown promising results in ameliorating mobility deficits for those with PD. These programs included 90-minute sessions with only a short time dedicated to boxing, and attrition rates were high (Combs et al., 2011, 2013). It is not known if the training typical of that in a community boxing gym is effective for adults with PD. The purpose of this study is to determine the feasibility of a community-based, bi-weekly (30 minute training sessions) 6-week boxing program. The 6 participants have Hoehn & Yahr scores of 1-2 and range in age from 62 to 76 years. All are living in the community, have normal scores on the Montreal Cognitive Assessment, and are independent walking in the community without an assistive device. Training consists of individualized one-on-one 30-minute boxing sessions with a certified boxing coach. The training includes combinations, heavy bag and focus mitt drills. Participants wear hand wraps and boxing gloves, however no sparring is involved. Intermittent standing rests are provided, and an occupational or physical therapist (PT) or PT student lead brief warm-up and cool-down exercises; they also oversee each boxing session. Outcome measures for balance, mobility, and upper limb performance measures are taken at baseline, after 4-weeks, and at 6-weeks. To date, 4 of the 6 participants have completed 4-weeks of the program. Monitoring during training reveals that participants are achieving 60-80% of their target heart rate. There have been no adverse events. Participants are enthusiastic and have attended every session. They report improvements in symptoms and "feeling

better". Descriptive data of outcome measures will be presented. The results of this study to date suggest that a community-based boxing program is feasible for adults with PD. Further analysis of the full cohort by the date of the conference will provide insight into functional changes associated with the training, and guide future studies.

CLINICAL SCIENCES: CLINICAL TRIALS: DESIGN, OUTCOMES, RECRUITING ETC.

LBP32

Inhibition of glucosylceramide synthase alleviates aberrations in synucleinopathy models: Link to GBA-related Parkinson's disease

S. Pablo Sardi, Catherine Viel, Jennifer Clarke, Hyejung Park, James Dodge, John Marshall, Bing Wang, Seng Cheng, Lamya Shihabuddin
USA

Mutations in GBA, the gene encoding glucocerebrosidase, are associated with an enhanced risk of developing synucleinopathies such as Parkinson's disease (PD). Recent studies have also demonstrated that genetic variation in GBA can impact the progression of PD. Patients harboring mutations in GBA present higher prevalence and severity of motor and non-motor symptoms. However, the precise mechanisms by which mutations in GBA increase PD risk and exacerbate its progression remain unclear. Here, we investigated the merits of glucosylceramide synthase (GCS) inhibition as a potential treatment for synucleinopathies. A Gaucher-related synucleinopathy mouse model (GbaD409V/D409V) was treated with an orally available brain-penetrant GCS inhibitor, Genz-667161 for 8 months. This intervention prevented CNS substrate lipid accumulation. Most notably, treatment with the GCS inhibitor slowed the accumulation of hippocampal aggregates of α -synuclein, ubiquitin and tau, and improved the associated memory deficits. The effects of the GCS inhibitor were also studied in a mouse model overexpressing α -synuclein, PrP-A53T-SNCA, and harboring wild type alleles of GBA. Treatment of PrP-A53T-SNCA mice with Genz-667161 for 6.5 months reduced membrane-associated α -synuclein in the CNS and ameliorated cognitive deficits. Collectively, the data indicate that inhibition of GCS can modulate processing of α -synuclein and reduce various α -synuclein entities, thereby reducing the progression of synucleinopathies in mice with and without mutations in GBA. The present studies support the imminent initiation of clinical studies of a CNS penetrant GCS inhibitor in early GBA-related PD.

LIVING WITH PARKINSON'S: PUBLIC EDUCATION OR AWARENESS PROGRAMS

LBP33

The auditory cortex changes across learning choreography with Parkinson's Disease: fMRI changes across 8 months and a documentary – SYNAPSE DANCE

Vanessa Harrar¹, Joe DeSouza², Rachel Bar³
¹ University of Montreal, Montreal, QC, Canada

² Centre for Vision Research, Toronto, ON, Canada

³ Canada's National Ballet School, Toronto, ON, Canada

Objective: To examine the functional brain changes that occur in the auditory cortex through to the frontal cortex while a participant with Parkinson's disease learns the choreography of a novel dance sequence. This research was the main subject in a recent documentary called SYNAPSE DANCE (2016 – Directed by Karen Suzuki) just released exploring the benefits of dance to people with Parkinson's disease (<https://www.youtube.com/watch?v=q4yXyZjmWMI>).

Background: There are very few neuroimaging studies that examine real dance choreography (Bar & DeSouza, 2016; Di Nota et al 2016) and none that examine the people learning a choreographed dance. Here we present our initial case study examining people with PD learning to move to music.

Methods: One individual with PD participated in 8 months of weekly 1.25-hr dance classes with the Dance with Parkinson's program at the Canada's National Ballet School (NBS). The participant learned choreography and performed it at two venue's outside of NBS (City Hall & Sharing Dance at Yonge & Dundas square). Using a 3T MRI scanner, his fMRI neural activity was recorded using the same scanning protocol as in Bar and DeSouza (2016 DOI:10.1371/journal.pone.0147731). Briefly, the subject was scanned four times during the eight months of weekly dance classes. Before learning the choreography (Sept), while learning it (December and January) and then again at the end of April. In each scan the subject listened to 1-minute of the music from the choreographed dance and asked to visualize dancing to it within the scanner. This 1-minute was repeated 5 times in a typical block design, with 3-seconds between each, for a total scan time of 7.5 minutes.

Results: Using task-based analysis, we examined auditory cortex, insular and supplementary motor cortex (SMA) regions using the GLM (Bonf <0.05; cluster threshold of 44) as focussed on in the documentary SYNAPSE DANCE (2016). In addition, we observed brain activation in premotor cortex and parietal cortex.

Conclusions: To our knowledge, this is the first case study of a person with PD learning dance choreography over 8 months and the associated brain activation patterns in areas of interest previously described in Bar and DeSouza (2016) for professional dancers. Within the documentary, SYNAPSE DANCE (2016), the subject describes how dance has begun to increase his quality of life and ability to deal with Parkinson's disease partly because of changes in motor cortex associated with learning the dance.

LIVING WITH PARKINSON'S: GOVERNMENT, ADVOCACY, CAMPAIGNS, PUBLIC POLICY

LBP34

In Case of Adverse Events: Just Compensation for US Human Volunteers Injured in Clinical Trials

Jean Burns
Sun Lakes, AZ, USA

Background: Unlike most civilized countries, the US does not care for its injured human clinical trial volunteers. At government sites (including NIH), the Informed Consents (IC) say if injured in a clinical trial, the human would get 30 days in hospital. And you can sue the federal government. Two years ago, Jean Burns began to talk about this issue and to advocate for change. Elizabeth Pike wrote an article for no fault insurance to offer fair compensation. Jean

spoke at the NIH Bioethics Grand Round on the topic of No Compensation for Injured Clinical Trial Participants. And she was the first (and so far only) Patient to present at a Bioethics Grand Round. Jean has called and emailed leaders in PD community. The overwhelming response she has received is "It would be so expensive." Recently a USNEWS & World Report reporter has written about this topic. Jean continues to tweet and blog and advocate on behalf of clinical trial participants. A few years ago, Elizabeth Pike, formerly at the NIH Bioethics committee, wrote a proposal for "No Fault Insurance" It has since been published in various journals – an excellent idea! a novel and necessary no-fault compensation system, grounded in the ethical notion of compensatory justice. This first-of-its-kind concrete proposal aims to treat like cases alike, offer fair compensation, and disburse compensation with maximum efficiency and minimum administrative cost. It also harmonizes national and international approaches—an increasingly important goal as research becomes more globalized, multi-site trials grow in number, and institutions and sponsors in the United States move to single-IRB review.

Objective: Change this policy in the US. Publicize this issue. Get the support of the 3000+ attendees of WPC 2016 in Portland, and present a petition for legislation to Senate and House of Representatives. Convince PD org leadership that treating patients better will increase numbers of clinical trial volunteers. Support legislation for No Fault Compensation. If pwp and leadership of PD orgs were to join together to support of No Fault Compensation, we would be on our way to making a change in US policy.

Method: Create petitions; speak at welcome booth; poster presentation; hot topic talk;

Results: Large group willing to lobby their legislators to provide compensation for Just Compensation increases the likelihood we will have change, and protect our clinical trial volunteers.

LIVING WITH PARKINSON'S: LIVING WELL WITH PD

LBP35

Encouragement Angel

Isabell Senft-Daniel
Knoxville, Tennessee, USA

How can one help Parkinsonians to overcome obstacles associated with the disease? This concept is built on a new support group activity creating angels of encouragement and giving them out to group members and families who are home bound or have other difficulties in their life. A considerable higher portion of support group individuals than in the general population suffer from depression and anxiety. As such, it was found that creating the angels had a very positive impact on individual's life. Active group members creating angels further the project and develop encouragement and engagement through buying supplies and woodworking. Parkinsonians with active tremor receive assistance from other group members and everybody can contribute with a task suited to their abilities. Sharing their story with other group members in a smaller group setting helps overcoming anxiety and depression. It enables therapy in its simplest form as following: (1) psychosocial: anxiety, depression, and apathy; (2) occupational therapy: fine motor skills, ADL; (3) physical therapy: bradykinesia, tremor, dyskinesia, rigidity, (4) speech: soft voice, drooling, slurred speech. It covers motor and non-motor Symptoms.

Home bound group members and widows of Parkinsonians receive their handmade angel with a branded encouragement on the bottom delivered by the sunshine team.

The feedback on this activity from family members and other therapists is very positive and health related effects are visible such, that this concept is shared in this poster to encourage other support groups to develop similarly simple projects which can make a big difference in the life of a person suffering from Parkinson's disease and their families.

LBP36

Imagine yourself then, imagine yourself now with Parkinson's disease

Frank Church
University of North Carolina School of Medicine, Chapel Hill, NC, USA

~50,000–60,000 new cases of Parkinson's disease are diagnosed each year in the United States, adding to the one million people who currently have Parkinson's. It has been estimated that 7–10 million people worldwide are living with Parkinson's. My Parkinson's treatment strategy involves traditional drugs, complementary and alternative medicine (CAM), and exercise: Dopamine agonists: For the past two years I've been taking the dopamine agonist Ropinirole. Recently, we decided to add the Neupro transdermal patch, which is another dopamine agonist (Rotigotine). By using the dopamine agonist patch, the thought is to normalize the amount of dopamine agonist in my body throughout the day (i.e., smooth out the peaks and valleys). Isradipine: An FDA-approved calcium-channel blocker (CCB) named Isradipine penetrates the blood brain barrier to block calcium channels and potentially preserve dopamine-making cells. Isradipine may slow the progression of Parkinson's. Complementary and Alternative Medicine (CAM): "Complementary and alternative medicine (CAM) is the term for medical products and practices that are not part of standard medical care." My CAM strategy for treating Parkinson's goes as follows: compounds (reportedly) able to penetrate the blood brain barrier; compounds (possibly) able to slow progression of the disorder; compounds that are anti-oxidative and anti-inflammatory; compounds that don't adversely alter dopamine synthesis/activity; and compounds that support general brain/nervous system health. - Exercise: Exercise improves flexibility, builds muscle mass, aids sleep, and reduces stress. Exercise is neuroprotective in Parkinson's. My strategy is relatively simple, make time in each day to exercise (it's that important): stretch every couple of hours (the exercises in LSVT BIG are fantastic); and try to exercise every day for 30–60 minutes (playing/walking 18 holes of golf takes ~4–5 hr). I do a lot of exercises with range of motion sports like golf and boxing on a reflex bag (more tennis this summer). Most importantly, I do exercises that I really enjoy doing and it brings a lot of enjoyment to the way my body feels. For those of us with Parkinson's, we remain hopeful for new treatments, advances and one day ahead, a cure. But for now, we use courage and determination, mixed with a will to survive, and all held together by glue we call hope. Overall, I'm doing my best navigating life with Parkinson's.

Strategy For Treating My Parkinson's*



Medical:
Dopamine agonist
Isradipine (experimental)

CAM:
Vitamin B Complex
Vitamin C
Vitamin D₃
Vitamin E
Multiple Daily Vitamin
N-Acetyl Cysteine (NAC)
Grape Seed Extract
trans-Resveratrol
Probiotic Complex with
Acidophilus
Melatonin before sleep

Exercise:
Stretch (hourly if able)
Exercise daily (if possible)

*Please note that these views expressed here are my own. Content presented here is not meant as medical advice. Consult with your physician before taking any type of supplements.

LBP37**Parkinsonline – PON, the friendly Parkinson's support group**

Gerald Ganglbauer
Stattegg, Styria, Austria

We are people living with Parkinson's and we enjoy a get-together in support groups, however, some of us are not always able to actually attend meetings, while others are out of town, so Gerald Ganglbauer created virtual support groups. These private meeting points are open 24/7 and run on free Skype Instant Messaging. Virtual (and real) Support Groups for People with Parkinson's disease

With Parkinsonline, Gerald Ganglbauer, Parkinson's Ambassador and co-founder of the Ultimo Support Group, introduces a new "virtual" support group social network. He's put it all in the name: The group's topic is Parkinson's, everyone is online and shares the line with a small group of other people with Parkinson's who are on (not off...) for a chat at home or on the road, day or night.

How does it work?

Parkinsonline virtual support groups run with Skype Instant Messaging Software and apps on all computers, tablets and smartphones, like Macintosh, Windows, Linux, iPad, iPhone, Android, Windows phone, and more, for free! Joining is easy.

Where are these groups?

Skype Groups are so far running in Australia, Austria, and Germany.

LBP38**Promoting awareness of Parkinson's disease(PD) and helping people with Parkinson's(PWP) in Ipoh, Perak, Malaysia**

Lam Swee Yeoh
Malaysia

Objectives:

1. To provide professional help and emotional support to people with Parkinson's(PWP) and their family to improve their quality of life.
2. To promote awareness of Parkinson's disease(PD) and enhance the skills of health professionals and caregivers.

Methods: Ipoh, the capital of Perak with a population of 757,892 (2010) could have 2,804 PWP based on the extrapolation of 0.37% prevalence rate on Western countries. Many of these cases are probably undiagnosed due to few neurologists specializing in PD in Malaysia. Hence many PWP are suffering in silence and they live

out their lives without treatment in misery. Perak Parkinson's Association (PPA) was established on December 3, 2012 after an overwhelming response from the 1st PD forum held in Syuen Hotel, Ipoh on October 13, 2012 with encouragement given by the Malaysian Parkinson's Disease Association (MPDA). PPA is a non profit, charitable NGO which relies on donations and is run by a dedicated team of volunteers. A centre was set up at 128 Hala Wah Keong, Taman Mirindy, 31400 Ipoh. Activities conducted by volunteers include dance movement sessions on Mondays, circuit exercise on Tuesdays, physiotherapy exercises on Wednesdays, karaoke on Thursdays, Tai Chi and Chinese dance on Fridays and Yoga on Sundays. The activities are free with PWP paying only US\$6 yearly membership fees. PPA also held food fairs, cycling events and talks with other organizations to promote awareness and raise funds. Events held in Ipoh by overseas experts include Parkinson's Awareness and Fundraising Open Day on March 30, 2014 and Davis Phinney Victory Summit on October 11, 2015.

Results: Membership grew from 106 with 37 PWP in 2013 to 283 with 105 PWP as of June 2016. Consistent and growing attendance of up to 25 people for some activities in the centre proves that PWP benefited from them. Many look forward to them to enjoy good fellowship, moral support with some making significant improvements. Moreover, a huge turnout of over 800 people at the Davis Phinney Victory Summit proves that we are reaching out to PWP, health professionals, caregivers and the public. Furthermore, a good response from fundraising activities show that we have succeeded in promoting awareness. PD has robbed the sunshine from PWP and PPA seeks to get worldwide support from corporations, organizations and individuals to organize more activities to put back this sunshine for PWP.

swee86@yahoo.com.sg,

<https://www.facebook.com/perakparkinsonsassociation>

LBP39**Quality of Life Group: Maintaining our mental, physical, emotional and spiritual wellbeing**

Alison Williams, William Wright
Parkinson's UK Edinburgh Branch, Scotland, United Kingdom

Why we started a Quality of life group for PWPs only, what the QL group is, how it runs, and its impact.

Why

A PD diagnosis can be a devastating experience, with emotional trauma (we don't use the word lightly) in the moment. Few people in that first meeting can calmly discuss the diagnosis' implications with their physician, so in the following days and weeks they format their own prognosis, usually negatively.

In this all too familiar scenario the PWP is left knowing they have an incurable neurodegenerative disease. Where do they go from there? What is their place in the world? Who should they tell, if anyone? These, and 101 other questions, can be debilitating. While there is medical help, there is little emotional support, so how do PWPs maintain their mental, physical, emotional and spiritual wellbeing?

Researcher Sara Houston (2015:31) observes: "there [is] little to help people address the issue of what constitutes wellbeing and renewal within life as experienced with a chronic condition (Goering 2002)", particularly if there is no cure, quoting Frank (2013:7) "The central problem is how to avoid living a life that is diminished, whether by the disease itself or by others' responses to it".

What & How

The Edinburgh QL Group lets PWPs share experiences, concerns, triumphs and ANYTHING about their quality of life. Long-term PWPs give hope and encouragement to newbies, who in their turn energise the others.

The QL philosophy echoes poet Robin Morgan: "I am not diminished by Parkinson's, I am distilled by it; and I very much like the [person] I am distilling into".

In the safe space of QL monthly meetings PWP's can freely express thoughts and feelings, laugh and cry, free from judgement, criticism, advice or embarrassment. Simple agreements keep everyone safe: MEMBERS: PWP's ONLY

CONFIDENTIALITY: Outside the meeting we can share WHAT was said, but not WHO said it

RESPECT: Everyone's input matters, listen without interrupting

GROWTH: The group and individuals grow when we share our own unique experience of living with PD.

Impact

"... a joyous gathering, sharing our experiences and building trust in such a healing atmosphere."

"The feeling of understanding and companionship was heart-warming. My quality of life has already gone up!"

"It is great to talk about PD without fear of boring or worrying anyone!"

Anecdotally, numbers of people attending other groups (exercise, dance, Pilates) have gone up.

LBP40

Education/Outreach Program: Get Excited and Move (GEM) Savannah

Michael Cohen¹, Sarah Bernzott²

¹ Savannah State University, Savannah, Georgia, USA

² Savannah Parkinson Support Group, Savannah, Georgia, USA

Parkinson disease (PD) which is progressive and neurodegenerative, affects millions of people worldwide each year. As the PD population grows, research indicates that aerobic and learning-based exercise is vital to controlling PD symptoms, which are caused by damage to the dopaminergic neurons of the brain. In six trials, repeated multi-faceted combinations of aerobic and anaerobic exercises, designed for the needs of the damaged brain, have assisted in strengthening the PD body and mind. These combinations of skills and exercises have improved abilities weakened or lost to PD progression, and assist in improving overall quality of life.

Get Excited and Move (GEM)-Savannah is a multi-dimensional exercise program designed and developed by Olympian Michael Cohen. As the USA Paralympic Basketball Strength and Conditioning Coach, Cohen understands that employing a variety of sports (Olympic weightlifting, stretching, agility training and boxing) encourages athletes struggling to maintain a consistent focus on rebuilding lost or underdeveloped skills. Cohen and his team applied this concept to GEM, developing a levelled and ongoing exercise program for PD participants. GEM varies participant workouts while providing necessary, repeated practice of underdeveloped skills.

GEM is designed specifically for the PD brain, encouraging physical and mental improvements. GEM's core exercises and activities allow coaches to easily incorporate a variety of appropriate multi-faceted training into a short workout. GEM also focuses on providing its participants with multiple sustained opportunities to cooperatively learn and independently master smaller, isolated and controlled movements through repeated modelling and practice. Those movements are combined into a variety of larger, multi-faceted exercises, geared to improving underdeveloped or lost skills. GEM participants utilize mastered movements to help develop needed "life" skills such as balance, coordination, fluid muscle movement, executive and motor planning.

GEM also incorporates the caregiver as an active program participant, encouraging positive interaction and support. As a result, both participants report improvements in physical and mental health and social interactions. Spouses cheer each other loudly and

siblings describe successful activities with pride. GEM allows families to rebuild relationships, resulting in a more positive home environment, improving overall quality of life for the entire family.

LBP41

Mindfulness interventions for management of anxiety to improve daily function in Parkinson's Disease

Julia Wood

Dan Aaron Parkinson's Rehabilitation Center, Bala Cynwyd, PA, USA

Anxiety is a common non-motor symptom of Parkinson's disease that can impact quality of life and optimal participation in daily activities. Mindfulness interventions offer potential strategies for management of anxiety to improve occupational participation for people with Parkinson's disease. Two female patients with Parkinson's disease and anxiety completed 10 individual sessions of mindfulness training in an outpatient occupational therapy setting to address difficulties in daily tasks. Improvements in the Hospital Anxiety and Depression Scale (HADS), Patient Specific Functional (PSFS), and the Saint Louis Mental Status Examination (SLUMS) will be discussed in regards to increased participation in sleep, temporal organization, and cooking tasks.

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