ABSTRACT BOOK
OF THE

5th World PARKINSON CONGRESS
Kyoto, Japan

JUNE 4–7, 2019

Hosted and designed by the

World Parkinson Coalition

New York, NY, USA
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CONTENTS

SPEAKER SESSIONS

POSTER SESSIONS (P)

LATE-BREAKING POSTERS (LBP)

INDEX

Journal of Parkinson's Disease 9 (2019) 3-278
DOI 10.3233/JPD-199900
IOS Press

5th WORLD PARKINSON CONGRESS ABSTRACTS

Pre-Congress Courses

PCO1

Advocacy pyramid: Patient engagement and communication

*Soania Mathur**
Designing A Cure, Ajax, ON, Canada

The advocacy pyramid initially described by Cure Parkinson Trust founder, Tom Isaacs, serves as a framework for understanding the journey a patient takes from the time of initial diagnosis to advocacy and engagement. Recognizing that the end result, patient involvement, is necessary and vital in the search for a cure for this disease.
The emotional journey that every patient advocate experience begins at the time of diagnosis. The natural progression leads to the stage of shock, anger and denial. Once hopefully transcended, this stage is followed by communication, acceptance and education, then engagement and participation. An effective patient advocate is ultimately able to share their insight, passion and engagement to effectively influence the future care and treatment of people with Parkinson's disease.
This talk will further explore the advocacy pyramid and elaborate on the details of each psychological stage a patient experiences on this sometimes arduous, journey from diagnosis to advocacy and influence and how barriers to this progression, may be overcome.

PCO2

What causes PD?

*Barry Snow**
Auckland City Hospital, Auckland, New Zealand

The cause of Parkinson's disease remains elusive. The discovery of the dopamine deficiency in the basal ganglia and the response to dopamine treatment meant that for many years the focus was on a primary dopamine lesion. The appreciation that the disorder probably starts around two decades before motor symptoms and involves non-dopamine systems such as smell, sleep and bowel function has changed that thinking. Previous emphasis on environmental causes driven by twin studies and the MPTP experience was replaced by a focus on genetic causes. The genetic cause has now been modified in light of the new understanding of epigenetics, and now it is likely that Parkinson's disease is caused by a complex interaction between different degrees of genetic and environmental influences and possibly a degree of random events. This combination appears to start a self-sustaining process of accumulation of abnormal protein that spreads gradually through the nervous system. The rate and location of that spread is likely the reason for the marked difference between individuals with Parkinson's disease.

PCO3

What are the clinical features of PD?

*Shen Yang Lim**
Division of Neurology, University of Malaya, Kuala Lumpur, Malaysia

In this talk, I will give a broad overview of the movement problems that occur in Parkinson's. These include the "core" motor features such as slowness of movements (bradykinesia), stiffness (rigidity), shakes (tremor) and walking difficulty. Currently, the diagnosis of Parkinson's relies on the presence of a combination of these features. In addition, as the disease progresses some patients experience motor fluctuations ("OFF" and "ON" periods) and dyskinesias (involuntary movements occurring after levodopa intake).
In addition, although currently the diagnosis of Parkinson's rests primarily on the presence of core motor features, a wide range of non-motor symptoms (NMS) also occur, with almost all patients having at least one – and most patients several – NMS. In fact, it is now recognized that in some patients, NMS (e.g., dream-enacting behaviours during sleep, impaired sense of smell, or constipation) can occur as prodromal symptoms preceding the onset of motor symptoms. I will present a framework for thinking about NMS under the "neuropsychiatric", "sleep", "autonomic", and "sensory" categories.
It is evident that there is substantial variation between individuals with Parkinson's, and attempts to understand why this is so is currently an active area of research.
The underlying neurobiological basis for these features will be discussed which provides some understanding of the genesis of these symptoms and a rationale for therapies.
The presentation will be accompanied by many visuals to aid understanding of the material, including figures and videos.

PCO4

How has medical & surgical treatment evolved over time?

*Genko Oyama**
Department of Neurology, Juntendo University Faculty of Medicine, Tokyo, Japan

Since the first description of the disease by Dr. James Parkinson, many discoveries and advances have occurred regarding symptomatic treatments. Before the introduction of stereotactic surgery in the 1950s, there were only a few medications such as anticholinergics and its effectiveness was limited. Surgical treatments such as thalamotomy and pallidotomy resulted in excellent outcomes but it also brought serious adverse events such as gait problem. Since then, two big milestones in the treatment for Parkinson's disease have been achieved.
The first milestone was a discovery of levodopa. It provided a bright future for people with Parkinson (PwP), but levodopa-induced motor

complications were recognized several years after the introduction of levodopa. Wearing off and dyskinesia limited the benefit of levodopa. Subsequently, development of dopamine agonists and MAO-B rfinhibitors started with the hope of preventing motor fluctuation and disease progression, followed by the development of several formulations of dopamine agonist including long-acting and sustained-release type. The recent challenge to overcome motor fluctuation includes continuous delivery of medications using a pump, such as continuous subcutaneous apomorphine pump, and levodopa/carbidopa intestinal gel (LCIG).
The second milestone was the development of deep brain stimulation (DBS). This technique could modulate brain circuit and result in a tremendous symptomatic benefit for PwP. With the accumulation of large-scale studies, DBS of the subthalamic nucleus and globus pallidus interna have been established the firm position as a treatment for the advanced Parkinson's disease. Recent advancement of magnetic resonance-guided focused ultrasound therapy has shed a light on the old-fashioned lesioning surgery again.
In this session, the history of the development of these medical and surgical evolvements and current status of potential future treatment will be discussed.

PCO5

What's new in research?
*Ryosuke Takahashi**
Kyoto University Graduate School of Medicine, Kyoto, Japan

I would like to talk about the updates of the research on newly emerging therapies, especially induced pluripotent stem cell or iPS cell-derived dopamine cell transplantation therapy. Induced pluripotent stem cells or iPS cells were established by introducing a small number of genes into ordinary human somatic (differentiated) cells. These pluripotent cells can differentiate into any type of cell in the body and proliferate indefinitely in culture. iPS cells were first generated by Professor Shinya Yamanaka's group at Kyoto University. Mesencephalic dopamine neurons, which are lost in the brain of the people with Parkinson, can also be differentiated from iPS cells and used for the resource for transplantation. Fetal midbrain tissue has been used for transplantation since 1980's and occasionally showed excellent effect on motor symptoms of PD. However there are ethical controversies over using fetal tissues that are obtained from artificial abortion. Moreover the number of the dopamine cells obtained from a fetus is limited. In contrast, there is little ethical problems in the usage of iPS cells and theoretically unlimited number of cells can be obtained from iPS cells. The major challenge of iPS cell-based transplantation therapy is tumor formation by contaminated undifferentiated iPS cells. Dopamine cell sorting technology using Corin antibody can eliminate undifferentiated cells and overcome the challenge. A clinical trial to examine the safely and efficacy of iPS cell-derived dopamine cell transplantation therapy has been launched at Kyoto University Hospital with close collaboration with Professor Jun Takahashi's team at Center for iPS cell research and application (CiRA), Kyoto University in 2018. The subjects are seven people with Parkinson. They will be followed up for 24 months for clinical evaluation.

PCO6

Tips and tricks for living with Parkinson's that go beyond medication – Speech and swallowing
*Hanneke Kalf**
Rdaboud University medical center, Nijmegen, The Netherlands

Parkinson's generally has consequences for all motor functions, including speech and swallowing, which both can also become soft and slow. Usually problems with speech and swallowing occur in the later stages of the disease, but others experience changes in speaking and eating or drinking in an earlier stage.
Speech problems may reduce intelligibility which sooner or later can have a negative impact on social interaction with family or in professional relations. Anti-parkinson medication does its work, but generally does not generate normal speech. However, exercise can help to regain intelligible speech. Obviously the best tip is to find a skilled speech therapist, but in this presentation we will share some other tricks for both people with Parkinson's and their caregiver.
Chewing and swallowing food and liquids almost seems to go automatically, because that is how we can focus on tasting and enjoying drinking and eating. Until it goes wrong or eating and drinking slows down. As in speech, parkinsonian swallowing problems are compensated or improved optimally when people with parkinson's and their caregivers understand when to worry and when swallowing is only slow, but no reason to worry.

PCO7

Tips and tricks for living with Parkinson's that go beyond medication – Balance and gait
*Lynn Rochester**
Newcastle University, Newcastle upon Tyne, United Kingdom

Parkinson's present the individual with multiple challenges in order to maintain a high level of functionality. Gait and balance are fundamental aspects, however, optimal management goes beyond targeted intervention aimed as these two features. Staying active is critical throughout, and an understanding of why this is important and how to achieve this is important. Maintaining optimal mobility and function of the upper limb supports independence around daily care. Addressing other critical mobility difficulties that impede everyday activities is also imperative, for example, getting in and out of a chair or bed. This presentation will highlight the breadth of areas that are important to focus on and present simple solutions to aid independent mobility.

PCO8

Tips and tricks for living with Parkinson's that go beyond medication – Nutrition and constipation
*Laurie Mischley**
Bastyr University Research Institute, Seattle, WA, USA

Constipation is considered a pre-motor symptom of Parkinson's that affects the majority of people with Parkinson's and can start more than a decade before diagnosis. Sluggish bowels affect mood, appetite, nutrient uptake, levodopa availability, and influence the intestinal microbiome. Beyond laxatives, we'll discuss foods to encourage and avoid, options for fiber supplements, and the emerging role of intestinal infections and irritable bowel syndrome in PD pathophysiology.

PCO9

Tips and tricks for living with Parkinson's that go beyond medication – Cognitive training, life hacks, and self-management

*Lissa Kapust**
Beth Israel Deaconess Medical Center, Boston, MA, USA

Those living with Parkinson's know that "beyond the pillbox" approaches are critical for quality of life and mood, This talk highlights strategies and "work arounds" for maintaining quality of life and independence. What are life hacks? They are ways of doing things, shortcuts or tricks, that make life easier in all walks of life. There are practical and psychological hacks. We'll consider both in this discussion. Have you ever heard of the "OHIO" principle to help with organizational and memory problems? If you are curious, this secret will be revealed! This principle demonstrates how simple cognitive and behavioral strategies make a big difference in daily life. We'll consider some gizmos and gadgets that improve daily activities such as managing buttons, getting in and out of cars, moving around in bed. Satin can be your new best friend! Finally, for the PWP and care partners psychological life hacks can improve your life. There's nothing to purchase and no worrisome side effects but will involve some developing new habits and attitudes. Learn new "tricks" and contribute some of your own. In this interactive discussion, everyone is an expert!

PCO10

Tips and tricks for living with Parkinson's that go beyond medication: Facing challenges and overcoming adversity: Family, work, marriage

*Victor McConvey**
Parkinson's Victoria, Melbourne, Victoria, Australia

Being diagnosed with Parkinson's is not straight forward, there is no test or scan and when that news is delivered you may be shocked, angry, relieved or be experiencing all the emotions at once. This news and its subsequent treatment is delivered by medical professionals who will prescribe medication to alleviate symptoms. Increasingly we are becoming aware that the management of Parkinson's goes beyond medication. This presentation will look beyond medication and at what we can do to improve living with Parkinson's and meet the challenge it sometimes provides.
We will explore how we can become experts in our own condition and take control, identify some strategies to manage symptoms that may not be well acknowledged or managed by medical professionals and discuss considerations to take when thinking about using Complementary and Alternative medicine to help manage our Parkinson's.

PCO11

Resilience – Beyond a diagnosis

Kathie Hill, Nancy Peate*
Parkinson's Resources of Oregon, Portland, Oregon, USA

Overall goal: To enhance understanding of the role of resilience in managing chronic disease and wellness.
Can resilience be learned? The authors examine behaviors and attitudes that contribute to living well with Parkinson's disease, including the importance of socialization, group exercise, seeking gratitude and cultivating mindfulness. The relevant current literature about resilience is reviewed and connections to managing life with Parkinson's are discussed. The authors describe their personal stories after the diagnosis of Parkinson's disease in mid-life and their journeys to find resilience. The process of finding community and founding a wellness-focused support group in Portland, Oregon is described. The significance of neuroplasticity and aging are also discussed. Current best practices are presented and methods are described to enhance the ability to find and maintain quality of life.

PCO12

Multidisciplinary and interdisciplinary care and the current state of the evidence

*Julie Carter**
Oregon Health and Science University, Portland, Oregon, USA

Interdisciplinary team care is distinguished from multidisciplinary team care by the fundamental difference of a collaborative care plan. Multidisciplinary teams use their own expertise to develop individual care goals while interdisciplinary teams build on each other's expertise to achieve shared patient care goals. There is a general assumption that interdisciplinary teams improve patient outcomes, increase individualized and patient-centered goals, improve quality care and provide for more efficient care. This talk will explore the evidence for this assumption. The complexity of measuring objective and subjective outcomes for team effectiveness will be discussed.

PCO13

How do I build a multidisciplinary or interdisciplinary center? Challenges we may face in the process

Micheal Okun[1], Genko Oyama*[2]*
[1] Fixel Institute for Neurological Diseases, Gainesville, FL, USA
[2] Department of Neurology, Juntendo University School of Medicine, Tokyo, Japan

Building a multidisciplinary or interdisciplinary Parkinson's disease center can be challenging. In this talk we will review the key elements necessary for success. The first principle is understanding the difference between consultative care, multidisciplinary care and interdisciplinary care. Next, one must understand the geography of the region, the referral patterns and also the resources available from local, regional, state and federal governments. Finally, a multidisciplinary or interdisciplinary care team must be thoughtfully assembled. Most Parkinson's disease care teams are led by a patient coordinator or liaison. Core team members frequently include a movement disorders neurologist, a neurosurgeon, a neuropsychologist, a social worker (or a counseling psychologist), a speech/swallow therapist, an occupational therapist and a physical therapist. Some teams also include a nutritionist, a dentist, an internist and/or a gastrointestinal doctor. One key element for success includes weekly meetings with interdisciplinary discussions focusing on patient care issues. Finally, many successful centers will embed clinical trials and research into the patient experience and include databases to track outcomes. There are several recent examples of interdisciplinary care models including the Dutch ParkinsonNet and the American Service and Science Hub though models should be designed to embed with available local resources. Ideally in a Parkinson's care model, all services can be offered under one roof, outcomes can be tracked and the next generation clinicians can be trained. Additionally, the integration of telemedicine will likely become increasingly important. Many centers will embed within their care teams other processes and care groups including DBS, depression/apathy, gait/balance and brain health among others.

PCO14

Models of care across different regions of the world: What can we learn from each other?

*Bas Bloem**
Department of Neurology, Radboud MC, Nijmegen, The Netherlands

Innovations are needed to create more patient-centered and sustainable models of healthcare. The speed of this reformation could be accelerated by exchanging experiences across different innovations. Presently, many innovations arise independently, and we learn insufficiently from the lessons of failed innovations, nor do we benefit by scaling successful innovations from one area of medicine to another. In my presentation, I will illustrate the opportunities offered by the art of imitating and duplicating successful innovations already proven to be successful in another area of care. Specifically, I will demonstrate this by discussing our own experience in extending a cost-effective network solution – developed in The Netherlands, and initially for persons with Parkinson's disease – to other countries, to other healthcare settings and to other disease populations. Our key experience is that innovations are greatly facilitated by "learning from differences". Moreover, successful innovations can be extended readily to other geographical areas and even to other areas of medicine, but not in a straightforward "copy-paste" fashion, but rather by adjusting the model to local circumstances, existing services and specific needs. My take home message is that, in addition to stimulating innovations, it is equally important to carefully taking stock of existing successful models and to translate their effective ingredients – if needed in adjusted form – to other settings.

PCO15

Deep brain surgery: Differentiating different devices

*Kelly Foote**
University of Florida, Gainesville, USA

Deep brain stimulation (DBS) is the treatment of choice for patients with advanced idiopathic Parkinson's disease (PD) with problematic motor fluctuations on medical therapy, or those with debilitating, medication refractory tremor. For many years, Medtronic was the only manufacturer of implantable DBS hardware, but recently Abbott and Boston Scientific have produced competing DBS systems. Competition in the DBS market is beneficial, and should motivate innovation and drive down costs, but differentiating among the available DBS hardware systems and choosing which DBS device is best suited for a given patient or application is a new challenge faced by DBS practitioners.

The lack of comparative studies among available devices and the absence of published guidelines in this decision process contributes to uncertainty and confusion among providers and patients. Here are several useful factors for clinicians to consider when selecting the appropriate DBS device for patients:

The published primary clinical outcomes across all three devices reveal similar efficacy for improving dyskinesia and motor fluctuations in PD patients. The devices are more similar than they are different. All three devices provide constant current options although the MedtronicTM system allows for more limited programing with constant current. Constant current ensures that changes in tissue impedance will not affect the delivery of a precise amount of electricity. There are major differences in the US FDA approvals for specific devices both in brain target and in brain disease. There are differences in technology, availability, and specifications (Table 1).

Suggested tips for choosing DBS hardware:

Tip #1 Selection of the optimal brain target for a given patient (STN vs. GPI) and the approach (unilateral vs. bilateral) may narrow the choice of device.
Tip #2: Assess access to programming and technical support.
Tip #3: A rechargeable device may not be appropriate for all patients.
Tip #4 Assess the potential need for future full body MR imaging.
Tip #5 Predict the utility of current steering or current shaping.
Tip #6 DBS practitioners' efficiency, comfort, and efficacy using a particular programming platform is an important determinant of DBS outcomes.

Table 1. Comparison of DBS Devices

	Medtronic™	Abbott Infinity™	Boston scientific Vercise™
Approved indications	Bilateral STN and GPi DBS for PD Bilateral STN and GPi for dystonia* Unilateral VIM for tremor Bilateral Anterior Limb of the Internal Capsule for refractory OCD *	Bilateral STN for PD Unilateral or Bilateral VIM for ET	Bilateral STN for PD
Directional Lead approval	Not available	(2016) Segmented 1-3-3-1 lead, current steering	(2019) Segmented lead 1-3-3-1, Current shaping and with Multiple Independent Current Control
Sensing capabilities	Advanced sensing platform NEXUS, not yet available commercially	Not available	Not available
System Battery life	Medtronic Activa SC (single chamber) and PC (dual chamber) estimated 3-5 years batery[A] Medtronic Activa RC (rechargeable) 15 years after recent software update.	Abbott Infinity™ (Dual chamber Non-rechargeable) estimated 4-5 years of battery life[A].	Vercise Primary Cell Battery ™ (Dual chamber) estimated 4.5 years of battery life and the Vercise Gevia™ rechargeable systems, estimated 15 years* approval in USA, 25 years in Europe (no shut-off)
MRI Conditionality	Conditional	Conditional	Not Available
Number of stimulation Contacts	8 Contacts (2x4)	16 Contacts (2x8)	16 Contacts (2x8)
Wireless Remote Control	None	1-2 meters in telemetry	91.4 cm (36 in) telemetry
Programming features	Frequency 2-250 Hz Pulse Width 60-450 µs Max Amplitude 10.5 V (voltage mode) / 25.5 mA (current mode)	Frequency 2-240 Hz Pulse Width 20-500 µs Max Amplitude 12.75 mA	Frequency 2-250 Hz Pulse Width 20-450 µs Max Amplitude 12.7 mA per contact (20 mA total)

PCO16

DBS programming with different devices. Advantages of using different devices for optional programming

*Michele Tagliati**
Cedars-Sinai Medical Center, Los Angeles, CA, USA

Motor fluctuations are important determinants of quality of life in Parkinson's disease (PD). When medical strategies fail, patients may be candidates for deep brain stimulation (DBS), a surgical procedure that has become an established treatment for movement disorders and other indications. More than 120,000 patients worldwide have been implanted over the past three decades. DBS can be currently performed using one of at least three different devices, which offer different capabilities, including implantable pulse generators (IPG) able to deliver electrical pulses using single or multiple independent sources at constant voltage or constant current, traditional (cylindrical) or segmented active lead designs. To date, virtually no comparative studies have evaluated the efficacy of the available DBS devices for specific motor problems in advanced PD. As a result, neurologists and neurosurgeons currently lack

guidance as to which device could be most appropriate for a particular PD patient. Current literature for each device will be reviewed, with the intent of identifying clinically relevant variables that may guide the best choice, including type of electrical delivery, current source, lead and pulse generator design, stimulation setting ranges, ease of programming, therapeutic target and device longevity. For each clinical scenario, pragmatic and (when available) evidence-based recommendations will be provided as to which patients could be candidates for either device based on DBS programming features.

PCO17

Infusion and other novel drug therapies in the treatment of PD
*Peter LeWitt**
Departments of Neurology, Henry Ford Hospital and Wayne State University School of Medicine, West Bloomfield, Michigan, USA

Control of Parkinsonian symptoms can be problematic because of irregular and delayed uptake of levodopa (LD), leading to motor fluctuations and exacerbation of dyskinesias. These are primarily problems associated with the pharmacological properties of orally-administered LD, which has a relatively short clearance half-life. Adequate circulating concentrations of LD (needed to maintain an "on" state) are often not achieved from conventional LD formulations. Attempts at improving consistency of LD effect through novel oral formulations have been a topic of research in recent years, with CD-LD products marketed or under development by Impax Laboratories and by Intec Pharma (Accordion Pill®). Alternative route of LD delivery, including prodrugs and pulmonary administration (Inbrija® by Acorda Therapeutics), have undergone clinical testing with some success. Another therapeutic approach has been subcutaneous infusion of solubilized carbidopa (CD)-LD, currently in clinical trials being carried out internationally (ND0612; NeuroDerm Ltd). From investigations of the pharmacology of solubilized CD infusion has been the discovery that it confers a unique LD-enhancing effect not encountered with oral administration.
Two marketed infusion therapies for PD have been available for many years. IN recent years, there has been continuing investigation as to their merits and limitations. One of them, per-gastric jejunal pump infusion of a constant concentration CD-LD micro-suspension of CD-LD (Dudopa®/Duopa®), was created to gain more continuous LD effect by bypassing the irregular release of CD-LD from the stomach occurring with conventional oral administration. Another approach for continuous dopaminergic stimulation has been subcutaneous infusion of the dopaminergic agonist apomorphine as either an adjunct to LD or as a solo therapy. A recent international prospective trial of apomorphine infusion (TOLEDO) provided insight into the effectiveness and limitations of an infusion approach to achieve more continuous "on" time. The next frontier for improving continuity of symptomatic control with LD may involve utilizing gene therapy for enhanced pharmacological actions. Completed and ongoing clinical trials of gene therapy have given insights into how these more invasive approaches can enhance the utility of an old drug very much needing improvement.

PCO18

Potential of immune-based therapies
*Seung Jae Lee**
Seoul National University, Seoul, South Korea

Parkinson disease (PD) is characterized by deposition of α-synuclein aggregates in neuronal inclusion bodies, known as Lewy bodies and Lewy neurites. Several inherited forms of PD have been linked to mutations in SNCA, the gene encoding α-synuclein. Furthermore, common genetic variants of SNCA have been associated with sporadic forms of PD. Collectively, these findings suggest that α-synuclein is critically involved in the pathogenesis of PD and is a leading therapeutic target. Recently, several trials for developing immune-based therapies are underway at different stages, some in clinical trials and others in preclinical stages. In this talk, I will review the ongoing efforts towards immunotherapies targeting α-synuclein. I will also discuss the results from animal and cell studies, which provides insights into the mechanism of action for the α-synuclein-targeted immunotherapies. Finally, Potential targets for PD immunotherapies other than α-synuclein will be discussed.

PCO19

Dizziness and PD, what is it and how can my doctor help? Non-motor autonomic problems of PD and what's their impact?
*Timothy Anderson**
University of Otago, Christchurch, New Zealand

"Dizziness" can mean different things to different people so its critical for both patient and clinician to mutually understand what type of dizziness is present.
The most common cause of dizziness in PD is neurogenic orthostatic hypotension (nOH); low blood pressure on standing) defined as systolic blood pressure decrease of 20 mmHg or more, or a diastolic decrease of 10 mmHg or more, within 3 min after rising from a supine to a standing position, not due to cardiac or low blood volume reasons. Prevalence in PD is 30% and nOH can be a prodromal symptom. Another type of OH is post-prandial OH (i.e. low blood pressure after eating). Whilst frequently asymptomatic 15–20% have symptomatic OH, one of the most debilitating conditions in PD, resulting sometimes in recurrent fainting (syncope), fractures and head trauma. Although nOH is related to autonomic nervous system dysfunction it can be aggravated by anti-parkinsonian medications. Severe OH in the first few years of PD may suggest an alternative (atypical) parkinsonian disorder such as multiple system atrophy (MSA). A simple screening test for autonomic dysfunction is heart rate less than 16 beats per minute in response to standing. Non-pharmacologic treatment of nOH includes reduction of BP-lowering medications, and education to stand slowly and not to remain motionless when standing. Compression stockings and abdominal binders are poorly tolerated but may be useful. Increased daily salt and water intake, and a glass of cold water for transient alleviation may help. Elevation of the bed head by 15–20cm can reduce nocturnal diuresis and retain blood volume. Pharmacologic therapy with fludrocortisone, midodrine and droxidopa can be effective whilst there have been reported benefits from pyridostigmine, ergotamine with caffeine, and octreotide.
Other causes of dizziness in PD to be discussed include benign paroxysmal positional vertigo (BPPV) accounting for 11% of PD patients in one study, hyperventilation related to anxiety, somatic manifestation of depression, or an atypical expression of cognitive impairment.

PCO20

Autonomic challenges and PD
*Shen Yang Lim**
Division of Neurology, University of Malaya, Kuala Lumpur, Malaysia

Autonomic dysfunction can occur many years before a diagnosis of Parkinson's disease (PD) is made, and symptoms are prevalent

even in patients with newly diagnosed, untreated PD. Symptoms of autonomic dysfunction substantially impair health-related quality of life, and some symptoms, such as persistent orthostatic hypotension, may also be a predictor of shorter survival. Recognition of autonomic impairment is important and physicians should actively enquire about, investigate and treat these problems as an integral part of managing PD, since symptomatic treatment is frequently effective.
In this lecture, I will give a broad overview of the autonomic problems that occur in PD. Topics covered include orthostatic hypotension, gastroparesis, constipation, drooling, urinary dysfunction, sexual dysfunction and thermoregulatory dysfunction. I will review aspects of clinical presentation and discuss pharmacological management strategies using a pragmatic and evidence-based approach. Non-pharmacological measures will also be mentioned where appropriate.

PCO21

Advancing treatment options for PD cognitive impairment
*Daniel Weintraub**
Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, USA

The management of cognitive impairment has benefitted from treatment strategies developed for AD. Despite this, only one large, positive controlled cholinesterase inhibitor (ChEI) randomized controlled trial (RCT) in PDD has been published (100), leading to the FDA approval of rivastigmine as a treatment of PDD, but this was 15 years ago. Statistically significant, but clinically modest, effects for rivastigmine on a range of primary and secondary outcome measures were observed, and ChEI treatment was associated with increased nausea, vomiting, tremor and dizziness. A similar clinical trial of donepezil for PDD produced similar numerical results for cognitive improvement, but due to an outlier site was a negative study based on the primary outcome measure (101). In two RCTs that included both PDD and DLB patients, memantine was found to be partially beneficial for PDD in one (102) but not the other (103), although the latter study showed secondary psychiatric benefit in patients with a DLB diagnosis. The treatment landscape for PD-MCI has been no more promising to date, with failed RCTs for both rasagiline (104) and rivastigmine patch (99), although the latter study showed a secondary, positive effect on a performance-based measure of cognitive functioning.
In terms of PD medications, there is no evidence that choice of the initial PD medication makes a difference in terms of long-term dementia rates (105, 106), but the association between anticholinergic medication use and long-term cognitive decline in PD (107) is a concern given the common use of medications with anticholinergic properties in this population (108). For non-pharmacological approaches, there is preliminary evidence that cognitive (109) and physical (110, 111) training/activity may lead to at least short-term benefit in some cognitive abilities. Given the association between vascular risk factors (42, 112) and pathology (113) and cognitive impairment in PD, and the association between both OH (41) and obstructive sleep apnea (OSA) (114, 115) and cognitive performance in PD, treating other common medical or non-motor symptoms is important as well.

PCO22

Emergency treatment options for PD
*Simon Lewis**
University of Sydney, Sydney, Australia

Most Parkinson's disease (PD) patients who are admitted to hospital as an emergency are generally experiencing another medical problem. Such an admission may (e.g. fractured hip from a fall) or may not (e.g. cardiac stenting) be related to their existing PD. However, a small number of patients will present with an emergency that is directly related to their PD. These problems can occur across motor and non-motor domains and need to be managed swiftly and effectively to avoid further complications. A general approach for dealing with such emergencies is required and will involve an understanding of the potential triggers for the presentation. Clinicians and care givers need to recognise where issues such as infection, metabolic disturbance or changes in medication may have precipitated a sudden change.
This lecture will attempt to summarise the motor and non-motor emergency presentations that need to be recognised and appropriately managed. Motor emergencies can often be divided into those where there is too little (akinetic) or too much (dyskinetic) movement. These may arise from concurrent illnesses, changes in medication (PD and non-PD) or indeed the malfunctioning of a device assisted technology such as Deep Brain Stimulation, Intra-Jejunal Levodopa or Sub-cutaneous Apomorphine infusion. Challenges in the delivery of PD medication, such as peri-operative 'nil by mouth' periods, also present their own challenges that require urgent management. Non-motor emergencies such as psychosis, severe constipation and hypotension will also be briefly covered. It is intended that this presentation will help patients, caregivers and health care professionals identify the red flags that drive these emergencies and hopefully allow swift effective strategies to minimise the harm that might otherwise arise.

PCO23

The future of treatments for dyskinesias
*M. Angela Cenci Nilsson**
Lund University, Lund, Sweden

Dyskinesias continue to be a debilitating complication of dopaminergic therapies for Parkinson's disease (PD). The most common dyskinesias consist of fast ('choreiform') movements that appear when blood and brain levels of dopaminergic medications are relatively high (termed 'peak-dose dyskinesias). This form of dyskinesia can be reproduced in the laboratory by administering relatively high doses of L-DOPA to rodent or monkey models of PD once or twice a day. Thanks to studies performed in these animal models, we have learned a lot about the pervasive changes produced by high doses of L-DOPA in a parkinsonian brain. Thus, animal models of peak-dose L-DOPA-induced dyskinesia (LID) show prominent changes in the activity, molecular structure, and function of both neurons and non-neuronal cells in the striatum and other brain regions. In animal models of peak-dose LID, both the abnormal involuntary movements and the associated brain changes can be suppressed using different categories of drugs. Particularly effective are drugs that interact with glutamate or serotonin receptors. The lecture will present the latest advances made in this area and review ongoing and imminent clinical studies evaluating modulators of glutamate or serotonin receptors in people with PD. Then I will review other forms of PD dyskinesias for which we still lack valid animal models and specific pathophysiological notions. These forms include the so-called "diphasic dyskinesias", "off-period dystonias", and "end-of-day dyskinesias". The latter is a novel form of dyskinesia described in patients receiving continuous dopaminergic stimulation. Although these dyskinesias are less common than the peak-dose variant, they warn us not to underestimate the complexity of dyskinetic phenomena in PD, particularly when developing novel therapeutics. For this reason, the path towards future antidyskinetic therapies goes via personalised options that can be tailored to the needs of individual patients. People with PD can really help scientists and doctors achieve this

goal by carefully reporting their own response to different treatments and life style factors.

PCO24

Roles patients can play in advocacy & activism
*Therese Scott Duncan**
Karolinska Institutet HIC, Health Informatics Centre, Stockholm, Sweden

In the Merriam-Webster dictionary, 'advocacy' is defined as: "the act or process of supporting a cause or proposal". The same source defines 'activism' as: "a doctrine or practice that emphasizes direct vigorous action especially in support of or opposition to one side of a controversial issue". In this pre-congress course the focus will be on the more action-oriented concept of activism. A research-based framework will be used as a basis for discussions throughout the session, see below.
Roles patients play
Research from the Karolinska Institutet in Stockholm, Sweden, has resulted in a framework outlining some of the different roles patients can take when dealing with their health issues. Preliminary results indicate that the framework is helpful for promoting a more nuanced discussion around patient activism, irrespective of diagnosis. A person often takes on several roles at the same time and alters between roles in different situations and/or contexts. The framework currently comprises 12 different roles:

- The Activist – works for changes in policy and practice related to their health and healthcare needs
- The Mentor – shares their knowledge and experiences to teach others
- The Academic – stays updated on the latest scientific articles and evidence
- The Patient Researcher – uses scientific methods to investigate their health issues and/or partners with established academic researchers
- The Self-care Expert – does what they can to learn about their health and wellbeing and works to improve it
- The Communicator – writes and/or speaks about their own health experiences in conferences and meetings and/or articles, blogs and social media
- The Hacker – addresses health issues through the use of technology
- The Tracker – self-monitors health issues
- The Healthcare Partner – creates and manages partnerships with healthcare professionals
- The Innovator – creates or has ideas about new solutions based on their health and healthcare needs
- The Entrepreneur – builds companies or organizations from their experiences with health and healthcare needs
- The Healthcare Coordinator – manages and coordinates multiple healthcare contacts for their health issues

PCO25

A: Research Activism
*Karen Raphael**
New York University, New York, NY, USA

This intermediate-level "Research Activism" session is particularly intended for People with Parkinson's (PwP) who are already familiar with the clinical trials and clinical research process and who may already identify themselves as Research Advocates. It is intended for those who wish to deepen their understanding of inferences that can or cannot be made from a published clinical research paper, science journalism study summary or clinical trial protocol. The intent is to improve participants' abilities to effectively communicate research findings and journalistic research reports in terms of strengths and limitations and applicability to a particular individual with PD. It also intends to improve skills of session participants who work with funding agencies or pharmaceutical companies to go beyond improving recruitment, retention and acceptability of a protocol to PwP. Specifically, it aims to prepare you to advocate for trial designs that are maximally geared toward allowing other PwP to evaluate whether findings from a successful Phase 3 trial indicate that "this new treatment is appropriate for me, given my current clinical situation."

PCO26

B: Wellness Activism
*Tim Hague**
U-Turn Parkinson's, Winnipeg, Manitoba, Canada

'My goal would be to have all my patients become athletes' Dr. Borys a movement disorders neurologist.
The goal of this session is to provide people living with Parkinson's the tools to understand the mindset of a seasoned athlete in the area of Wellness. We will look at wellness from a holistic viewpoint considering all of its spheres. Exploring the mindset of the traditional athlete we will discover what sets that individual apart and how we can incorporate their thinking into our personal plan of action to live well with Parkinson's disease. Key take always will be learning how to craft your plan of action in living well with Parkinson's; gaining POIS2E as you learn a holistic approach to caring for the whole you, and discovering again the 'secret' hiding in plain sight – wellness – what the research has said all along.

PCO27

C: Tools for activism
*Martin Taylor**
Parkinson's Research Advocacy Group, Gorebridge, Edinburgh, United Kingdom

Most PwP consume their research news through social media, in particular the charity social media accounts. It is often apparent from the comments on these news stories that there is a genuine lack of understanding by many of those reading, but also in the level of expectancy, which is often very unrealistic as regard what impact the news will have for the patient community.
The session will look to outline and assess the various tools available to PwP to interact and engage with research activism and further demonstrate how that activism can be leveraged to influence the PD research agenda. Further it will inform as to how these platforms can be used to educate and empower the patient community to have a voice in the work for which they are the ultimate stakeholders. Platforms such as Twitter allow patients to directly opine on research news and ask questions to increase their own and others understanding, it allows us to question the rationale behind research studies and share both positive and negative outcomes from research news stories.

Oral Sessions

O1

What is α-synuclein – The biology

*Ronald Melki**
Institut François Jacob (MIRCen), CEA and Laboratory of Neurodegenerative Diseases, CNRS, Fontenay-aux-Roses, France

The aggregation of proteins within the central nervous system is deleterious and associated to neurodegenerative disorders. The aggregation of the protein α-synuclein is associated to synucleinopathies, in particular Parkinson's disease. How α-synuclein aggregates, how those aggregates traffic between cells, amplify by recruiting endogenous monomeric α-synuclein and cause distinct synucleinopathies is unclear.
I will explain the molecular events that lead to α-synuclein aggregation. I will present data illustrating the propagation propensities of aggregated α-synuclein. I will show how α-synuclein aggregates bind to the cell membranes, what they bind to and the cellular consequences of binding. I will present a quantitative assessment of their uptake, transport and export. I will show data demonstrating that pathogenic α-synuclein aggregates disrupt the endo-lysosomal membranes to reach the cytosol where they amplify. Finally, I will describe how and why different α-synuclein polymorphs cause distinct diseases. Strategies targeting the propagation of aggregated α-synuclein will be presented and discussed.

O2

The pathology of α-synucleinopathies (brain donation)

*Peter Riederer**
University of Würzberg Medical School, Würzberg, Germany

Histological and immunohistological studies demonstrate that Lewy bodies (LB) are the morphological hallmarks of sporadic Parkinsons disease (PD) and dementia with LB (DLB), but can be found also in other neurodegenerative disorders or even in aged subjects. α-synuclein (αSYN) is a major component of LB. There is no doubt, that in αSYN related genetic cases, parkinsonism is the clinical correlate. In sporadic PD, there is also pathological accumulation of αSYN which follows a sequence of pathology in six stages – the Braak stages.
This has been assumed to correlate to respective clinical dysfunctions/symptoms. While some retrospective clinico-pathological studies habe largely confirmed Braaks hypothesis, there is no correlation with clinical severity or duration of PD, duration and severity of motor dysfunction nor to nigral αSYN burden, cell loss and striatal loss of dopamine. According to Jellinger (J. Neurol. 2000) up to 43% follow this pattern. In addition, up to 55% of elderly subjects with LB pathology revealed no neuropsychiatric symptoms or were not classifiable.
In PD with dementia (PDD), LB are predominant in transentorhinal and entorhinal cortices as well as in CA2-3 region of the hippocampus suggesting that dementia in PD follows PD-like pathology in limbic structures and is independent of AD (Bertrand et al 2004). Distribution or load of αSYN pathology do not permit a post mortem diagnosis of extrapyramidal symptoms or cognitive impairment (Parkkinen et al 2005). On the other hand, there have been trials for a diagnostic staging of PD (Przuntek et al 2004), but without further post mortem evaluations.
Therefore, all this clearly indicates the necessity for further clinical-pathological studies and underline the importance of human post mortem brain studies, brain donations and human brain banking. As models are mirroring only selected symptoms of a disease it is of utmost interest to perfom eventually prospective clinical-pathological studies on our own species and in particular on human post mortem tissue.

O3

Patients as living science: The importance of participating in clinical trials

*Soania Mathur**
Designing A Cure, Ajax, ON, Canada

As those of us with Parkinson's know, although we may share some symptoms, most of us experience our own unique version of this disease. We differ in terms of age of onset, symptoms, progression, response to treatment and prognosis. This patient experience can inform researchers, and this data must be captured and recorded, analyzed and studied if we are going to successfully figure out the cause of Parkinson's and develop targeted therapies against this disease. Without our involvement, research cannot progress.
For a new neurologic treatment to get from the lab counter to the pharmacy shelf it can take decades and well over a billion dollars. Approximately half of that time is spent in clinical trials. Yet close to 85% of all clinical trials are delayed due to recruitment difficulties and a shocking 30% fail to recruit a single subject. Any delay a study faces due to difficulty in finding participants, leads to a huge waste of resources, money and most importantly time. It is in our best interests for us as a community to improve involvement in medical research.
In this talk how patients can advance our knowledge of Parkinson's disease and the need for clinical trial participation, will be discussed. Some of the barriers to patient involvement and specific ways to address those factors will also be explored.

O4

Clinical trials and efficacy of clinical trials targeting α-synuclein

*Jesse Cedarbaum**
Biogen, Cambridge, MA, USA

The key role of α-synuclein in the pathogenesis of Parkinson's disease is supported both by pathological findings as well as genetic evidence linking mutations and the presence of extra copies of the α-synuclein gene to the development of autosomal-dominant Parkinson's disease, and evidence from research studies that aggregated α-synuclein can cause cellular dysfunction and degeneration. In the past few years, clinical trials have begun that are testing a variety of approaches to reducing or blocking the pathogenic effects of α-synuclein in the brains of patients with Parkinsonian disorders. Monoclonal antibodies and anti-synuclein vaccines currently being studied in Phase 1 and 2 clinical trials are designed to block the spread of synuclein pathology in the brain, and to neutralize its toxic effects. Small molecules designed to prevent aggregation are also being studied, as are approaches to reducing cells' ability to make α-synuclein as well. Challenges in the design of anti-α-synuclein clinical trials include 1) selecting the right patients, 2) developing assays for biomarkers that can tell us if the drug is actually interacting with and changing α-synuclein levels in the brain, 3) understanding if traditional clinical tests will tell us what we need to know about how well anti-synuclein drugs might be working and 4) the development and application of novel testing methods such as wearable technologies and smartphone apps that can potentially give researchers new and better information about the safety and effectiveness of the new drugs under study and how meaningful any positive effects that might be observed will be in the lives of patients and their families. The development of successful anti-synuclein therapies for Parkinson's disease is an ongoing

collaborative effort requiring participation of pharmaceutical companies, academic researchers, government regulators, advocacy and other not-for-profit organizations, persons with Parkinson's disease and their families.

O5

History of Parkinson's disease research in Japan: Past, present, and future

*Toshiharu Nagatsu**
Fujita Health University School of Medicine, Toyoake, Japan

Parkinson's disease (PD) is a progressive aging-related, and the second most common neurodegenerative disease after Alzheimer's disease. Typical symptoms of PD are tremor, bradykinesia, rigidity, and postural instability, as well as non-motor symptoms such as constipation, insomnia and depression. PD is cause by cell death mainly in catecholamine (dopamine, noradrenaline, and adrenaline) neurons, especially in nigro-striatal dopamine neurons. PD was originally described by James Parkinson in 1817 in London. Research on PD began in Europe in the 1800s and in the early half of the 1900s in the USA and Europe. In Japan, studies on PD have been conducted since the latter half of the 1900s, simultaneously with the continued progress made in the USA and Europe. Several of the studies in Japan have been carried out in collaboration with researchers in USA, Canada, Australia, and other parts of Asia. In this lecture we will present several major achievements in PD research in Japan. The topics include the following subjects: stereotactic neurosurgery, now deep brain stimulation; the molecular changes in enzymes related to dopamine and noradrenaline metabolism such as tyrosine hydroxylase, aromatic L-amino acid decarboxylase, dopamine β-hydroxylase, monoamine oxidase, and in cytokines and growth factors related to cell death and neuroinflammation in post-mortem brains, cerebrospinal fluid and blood in PD; possible endogenous neurotoxins; ER stress and oxidative stress; mitochondrial dysfunction, parkin, mitophagy, and apoptosis; new disease concepts such as Segawa disease (DYT5) caused by GTP cyclohydrolase, which regulates dopamine synthesis as cofactor of tyrosine hydroxylase, as causative gene and Kosaka's Lewy body disease; neural circuitries in movement in PD; MIBG for investigating sympathetic involvement in PD; possible neuroprotective therapies with monoamine oxidase B inhibitors; new drugs such as L-DOPS, Zonisamide, and Istradefylline; genes contributing to sporadic PD; gene therapy; and stem cell therapy by using iPSc-derived dopamine cells, which is now preparing for a clinical trial by Jun Takahashi et al. at Kyoto University. Japan is expected to contribute to development of therapy to prevent, recover or stop the progress of PD, such as regenerative therapy and disease-modifying drugs.

O6

James Parkinson Special Lecture – Mitochondrial energy crisis as a pathogenesis of Parkinson's disease

*Yoshikuni Mizuno**
Department of Neurology, Juntendo University, Tokyo, Japan

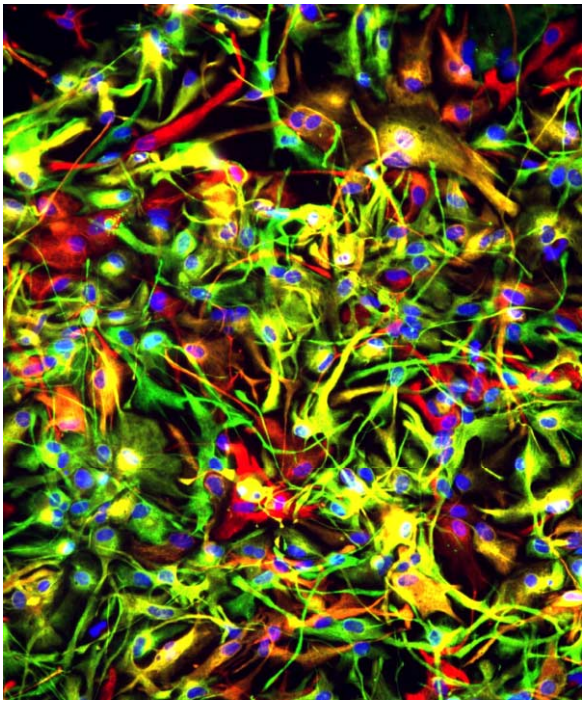
Mitochondrial energy crisis has been raised as an important mechanism in the pathogenesis of Parkinson's disease (PD). In 1986, we found inhibition of mitochondrial complex I by MPTP and MPP+. MPTP is metabolized to MPP+ by the MAOB in the astrocyte and MPP+ is actively taken up into the dopaminergic neurons. Thus selective degeneration of the dopaminergic neurons was explained, but the mechanism of degeneration was not clear. We found inhibition of not only complex I but also inhibiton of the alpha-ketoglutarate dehydrogenase complex of the TCA cycle by MPP+. The alpha-ketoglutarate dehydrogenase complex provides succinate as a substrate for the electron transport system for the ATP synthesis. This dual inhibition of complex I and alpha-ketoglutarate to succinate oxidation would deleteriously impair the ATP synthesis. We examined complex I and alpha-ketoglutarate dehydrogenase complex in 7 persons with PD and 5 controls. All the PD patients showed loss of complex I and alpha-ketoglutarate dehydrogenase complex by immunohistochemistry. In addition, pathogenesis of Park II is a lack of encircling the damaged mitochondria by phagocytes. Furthermore, Devi et al. showed accumulation of α-synuclein in mitochondria of PD to inhibit complex I. Putting these evidences together, mitochondrial energy crisis seems to be an important mechanism in the pathogenesis of PD.

O7

Patient-derived cells to study Parkinson's disease: Are astrocytes passive or active players of the disease?

Kaspar Russ[1], Teku Gabriel[1], Luc Bousset[2], Mauno Vihinen[1], Ronald Melki[2], Laurent Roybon[,1]*
[1] Lund University, Lund, Sweden
[2] Institut François Jacob (MIRCen), Fontenay-Aux-Roses, France

α-synuclein (αSYN) protein misfolding and aggregation is a hallmark of synucleinopathies including Parkinson's disease (PD). However, it is unclear if different species of αSYN that form in the brain of patients can influence cellular behavior. Since recent evidence suggests involvement of astrocytes in PD pathogenesis, we examined the cellular changes triggered by αSYN monomers and assemblies, in astrocytes derived from induced pluripotent stem cells generated from healthy individuals and people with idiopathic and familial PD. Our data provide evidence for astrocytic involvement in PD pathogenesis by showing that astrocytes with certain familial PD backgrounds have exacerbated cellular responses to αSYN species, which could reduce their ability to properly execute their supportive functions in the brain of patients. Astrocytic changes include, but are not limited to, release of pro-inflammatory cytokines, impaired mitochondria function, and αSYN clearance.



O8

Making authentic midbrain dopamine neurons – The challenges

*Agnete Kirkeby**
NNF Center for Stem Cell Biology (DanStem), University of Copenhagen, Copenhagen, Denmark

The treatment of Parkinson's disease (PD) has for >50 years relied mainly on dopaminergic therapies that are highly effective in the early years of the condition, but are ultimately limited by the development of side effects relating to the nonphysiological stimulation of dopamine receptors in the brain. Targeted regenerative therapies designed to restore specifically the lost dopaminergic innervation of the striatum would therefore represent a major advancement in the treatment of PD. Transplantation of human fetal ventral midbrain tissue to the striatum of PD patients has provided proof-of-principle that such an approach can provide long-term clinical benefits with a reduced dependency on oral dopaminergic agents. However, fetal tissue is associated with several ethical and logistical problems and therefore does not represent a realistic route to the clinical treatment of PD, and alternative cell sources are needed for future regenerative strategies in PD

Methods for producing authentic midbrain dopaminergic neurons from pluripotent cells have now advanced to a stage which makes it possible to efficiently and reproducibly produce dopaminergic progenitors at a much higher purity than can be obtained from human fetal tissue. A stem cell-based therapy for PD therefore has the potential to circumvent many of the problems which have been associated with fetal tissue grafting. Here, we describe the strategies pursued in our European effort to bring a human embryonic stem cell (hESC)-derived dopamine cell product to clinical trial for PD. We have developed efficient protocols for production of authentic midbrain dopaminergic progenitors, and with this protocol we expect to be able to produce cell therapies for thousands of PD patients at a relatively small tissue culture scale. The preclinical work in this project has involved transplantation of thousands of animals for assessment of safety and efficacy, identification of predictive markers for in vivo efficacy, GMP adaptation of the hESC differentiation protocol and development of cryopreservation strategies and QC assays. Based on this work we expect to initiate Phase I/II trials in 2020.

O9

Clinical application of stem cell transplantation therapy

*Asuka Morizane**
Kyoto University, Kyoto, Japan

The innovation of induced pluripotent stem cells (iPSCs) and previous embryonic stem cell (ESC) technologies are drawing attention to their application for regenerative medicine. Parkinson's disease is one of the most promising target diseases based on the history of fetal nigral transplantation in clinics. Although pharmacological treatments for PD, such as L-dopa, show good response in the early phase, patient outcomes over the long term are unsatisfactory. As an additional treatment, cell therapy with aborted fetal tissues has been performed since 1980's. The limited supply of donor source and the unstable quality of the cells prevent this therapy with fetal tissue from becoming standard. The technology of iPSCs offers a limitless and more advantageous donor source. One of the advantages is possibility of preparing immunologically compatible donor cells from self-derived or allogeneic iPSCs. Our group has successfully established a protocol for donor induction with clinically compatible grade. The preclinical studies transplanted these donor neurons into PD models of mice, rats, and cynomolgus monkeys, showing graft survival with functional recovery. Based on these preclinical results, Kyoto University has started a clinical trial for Parkinson's disease that transplants dopaminergic progenitors generated from iPSCs; Kyoto Trial to Evaluate the Safety and Efficacy of iPSC-derived dopaminergic progenitors in the treatment of Parkinson's disease (Phase I/II). The trial is designed to evaluate the safety and efficacy of transplanting human iPSC-derived dopaminergic progenitors into the putamen of PD patients. The original donor source is iPSCs prepared at the iPS Cell Stock for Regenerative Medicine at CiRA, derived from third-party donor blood cells, meaning the transplantations are allogeneic. The subject will be observed for two years post transplantation. The presentation will include the recent results of our research and their clinical application.

O10

Cognitive deficits in Parkinson's disease: Clinical features, diagnosis, and evolution

*Caroline Williams-Gray**
University of Cambridge, Cambridge, United Kingdom

People with PD are around 2.5 times more likely to develop dementia than other people of a similar age, and nearly half will have developed dementia by 10 years into their illness. This has a major impact on quality of life, care requirements, and survival. Milder cognitive problems occur earlier in the disease, with one quarter to one third having 'mild cognitive impairment'. Subtle cognitive deficits have even been reported to occur in some 'prodromal' PD cases, before movement problems emerge.

Several different domains of cognitive function can be affected, including executive function (which includes planning and organisational abilities), memory, and visuospatial function. In more advanced PD, cognitive problems can be associated with behavioural changes and visual hallucinations. Diagnostic criteria for PD-Dementia have been established by the Movement Disorder Society, which are based on neuropsychological test scores, evidence of progressive decline, and impairment of day-to-day functioning due to cognitive deficits. Diagnostic criteria have also been developed for PD-associated Mild Cognitive Impairment (PD-MCI). However, there has been some debate about whether this is a useful diagnosis, as early cognitive impairment in PD is highly variable and not all patients with 'PD-MCI' will go on to develop a dementia.

Through studying a population-representative cohort of Parkinson's patients from diagnosis over time (the CamPaIGN study), we have demonstrated that there are distinct cognitive syndromes in PD which evolve differently. In particular, early problems with semantic memory and visuospatial function are predictive of developing a dementia, whereas problems with executive function are not necessarily predictive of dementia, and can even improve over time. We have used genetic and brain imaging studies to demonstrate that these syndromes have distinct underlying biological bases: semantic/visuospatial problems reflect a posterior cortically-based process which is influenced by ageing and genetic variants promoting formation of protein aggregates in the brain; in contrast, executive problems reflect dysfunction in frontostriatal dopamine networks and are influenced by genetic variants affecting dopamine breakdown, and by dopaminergic medication. Through better defining and understanding these separate cognitive syndromes, we can give more accurate prognostic information to patients, and target these different syndromes with more tailored therapies.

O11

Neuropathology of cognitive deficits in PD and its insights into therapeutic interventions

*Thomas Montine**
Stanford University, Stanford, CA, USA

Motor impairments are the hallmark of Parkinson's disease. In part because of interventions that effectively mitigate motor symptoms, recently there has been heightened interest in so-called non-motor symptoms of PD, especially cognitive impairment, a prevalent manifestation at the time of initial diagnosis that eventually afflicts the vast majority of people with Parkinson's disease. Cognitive impairment and dementia in PD have major impacts on quality of life including significant disability, loss of employment, patient institutionalization, caregiver stress and fatigue, increased cost to health systems, and decreased survival. Here I will review current knowledge on the genetic risk, disease mechanisms, clinical manifestations, and experimental interventions for cognitive impairment and dementia in Parkinson's disease.
Dr. Montine is the Stanford Medicine Endowed Professor and Chair of the Department of Pathology. The focus of the Montine Laboratory is on the structural and molecular bases of cognitive impairment with the goal of defining key pathogenic steps and thereby new therapeutic targets. The Montine Laboratory addresses these prevalent, unmet medical needs through a combination of neuropathology, biomarker development and application early in the course of disease, and experimental studies that test hypotheses concerning specific mechanisms of neuron injury and approaches to neuroprotection.

O12

Therapeutic programs for cognitive health in PD – interventions and preventions

*Atsushi Takeda**
National Hospital Organization, Sendai-Nishitaga Hospital, Sendai, Japan

Cognitive declines in Parkinson disease (PD) are shown to be mainly mediated by fronto-striatal dopaminergic dysfunction, frontal noradrenergic dysfunction and frontal cholinergic dysfunction. Among them, activation of cholinergic pathway is established to be able to alleviate cognitive impairments in PD. However, their efficacy is not so high in later stages of dementia and it is often too late to start therapeutic interventions after the apparent manifestation of dementia, thus limiting the efficacy of cholinesterase inhibitors. In addition, there are not a few PDD cases in which dopamine replacement therapy must be restricted and motor function sacrificed due to accompanying psychiatric symptoms such as hallucinations and delusions, which can further worsen prognoses of PDD cases. Although the appropriate timing for therapeutic intervention has not been established yet, early intervention with cholinesterase inhibitors for PD has been recently proposed. For examples, activation of the cholinergic system has been suggested to improve motor function in PD, based on a recent report of reduced risk of falling and improvement of walking-speed following the use of cholinesterase inhibitors in PD patients without dementia. From these backgrounds, we think that it may be possible to improve PD prognosis by intervening with cholinesterase inhibitors prior to the onset of PDD. In the previous study, we showed that severe hyposmia could predict later PDD development within several years. Therefore, we planned and finished a therapeutic intervention study using cholinesterase inhibitor in the non-demented PD group that showed severe hyposmia, one of the strongest predictors of cognitive decline in PD. Although the data of this study are under analyses at present, the result will be presented in this session. In addition to such medication-based therapies, the efficacy of cognitive training has been recently suggested to improve cognitive decline in PD. This topic will also be introduced.

O13

An overview of sleep disorders in Parkinson's disease

*Isabelle Arnulf**
Sorbonne University, Paris, France

The whole gamut of sleep disorders may be seen in PD, occasionally in the same patient. Insomnia, particularly the inability to maintain the state of sleep, is extremely common. There are numerous potential causes for poor quality nocturnal sleep in PD including significant difficulties in moving around the bed during nocturnal awakenings, as well as pain, anxiety, severe dystonia and dopamine dysregulation syndrome. Daytime sleepiness can be the result of poor overnight sleep, but is also caused by the underlying neurodegenerative process itself, with potential contribution of melatonin insufficiency. It may not be reported by patients who often seem unaware of the extent of their somnolence. Parasomnias, particularly REM sleep behavior disorder, and prolonged confusional episodes with or without hallucinations are also a significant issue for many patients and carers alike. Eventually, sleep apnea occurs also in PD (especially those sleeping on their back because of bradykinesia, although its effects and the benefit of treating apnea are debated. A specific sleep problem in multiple system atrophy is stridor, which may be managed with various ventilation modes, depending on whether it is or not associated with apnea.

O14

The restorative function of sleep

*David Breen**
Centre for Clinical Brain Sciences, University of Edinburgh, Edinburgh, Scotland, United Kingdom

Most of us spend around one-third of our lives asleep, with sleep being crucial for a multitude of brain functions (including learning and memory). Sleep dysfunction is well recognised as a consequence of some brain diseases (such as Parkinson's). However, it has recently been suggested that sleep and circadian disruption in healthy individuals may even cause or contribute to age-related neuropathology. Animal and human studies have shown that sleep restriction can lead to the accumulation of Alzheimer's-type pathology (due to increased formation and reduced clearance of amyloid-beta via the glymphatic system), as well as being detrimental to the brain in other ways. Epidemiological studies have also begun to show that poor sleep may be linked to the development of later-life neurodegenerative diseases (including Alzheimer's and Parkinson's). Further research is needed to determine whether this relationship is causal, or whether sleep disruption reflects an early prodromal marker of these conditions. This could open up new avenues for therapeutic interventions.

O15

Tips and tricks to managing sleep disorders in Parkinson's

*Aleksandar Videnovic**
Massachusetts General Hospital/Harvard Medical School, Boston, MA, USA

Parkinson's disease (PD) is the second most common neurodegenerative disorder. Sleep dysfunction is one of the most

common non-motor manifestations of PD that has gained significant interest over the past two decades due to its impact on the daily lives of PD patients, poorly understood mechanisms, and limited treatment options. The etiology of impaired sleep-wake cycle in PD is multifactorial and encompasses medication side effects, nocturnal PD motor symptoms, and presence of co-existent sleep and neuropsychiatric disorders. The primary neurodegenerative process of PD involves brain regions that regulate the sleep-wake cycle. Sleep disorders in PD include insomnia, REM sleep behavior disorder (RBD), sleep disordered breathing (SDB), restless legs syndrome (RLS), and circadian disruption. Despite its high prevalence in the PD population, there is a paucity of clinical studies that have investigated treatment of sleep dysfunction associated with PD. Evidence supporting the efficacy of pharmacological and non-pharmacological treatment strategies in PD is limited. There is thus a great need but also opportunity for development of well-designed clinical trials for impaired sleep and alertness in PD. Providing education about sleep hygiene and strategies for its implementation represents the initial step in management. Prompt diagnosis and treatment of co-existent primary sleep and psychiatric disorders are critical, as this may significantly improve sleep and alertness. While the optimal treatment for insomnia in PD has not been established, available strategies include cognitive-behavioral therapy, medications with soporific properties, and light therapy. Safety measures, clonazepam, and melatonin are the mainstay of treatment for RBD. Continuous positive airway pressure is an effective treatment for SDB in PD. The treatment algorithm for RLS associated with PD mirrors that used for idiopathic RLS. Circadian disruption has emerged as an important etiology of impaired sleep-wake cycles in PD, and circadian-based interventions hold promise for novel treatment approaches. We are at the opportune time to advance our understanding of sleep dysfunction in PD, which will hopefully lead to mechanisms-driven interventions for better sleep and allow us to approach sleep as a modifiable therapeutic target for other non-motor and motor manifestations in PD.

O16

Developmental genes lay the foundation for neurodegeneration in PD

*Ernest Arenas**
Karolinska Institute, Stockholm, Sweden

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by the loss of midbrain dopaminergic neurons (mDANs), the cell type controlling several of the motor motor functions altered in this disease. The cause of PD is largely unknown, but it is currently though that PD emerges from the interaction of both genetic and environmental factors.
We have previously performed single-cell RNA-sequencing (scRNA-seq) of the developing human midbrain. We are now examining whether such developmental genes are also involved in PD by analyzing adult control and PD postmortem samples, as well as PD-iPS cells and PD-GWAS data. Our analyses have allowed the identification of cell types as well as uniquely expressed genes and networks in development and in PD. Functional analysis of some of these genes has provided novel insights into the molecular mechanisms operating in mDANs. For instance, we have previously found that the transcription factor Pre-B-cell Leukemia homeobox (PBX1) is required not only for the generation of mDANs, but also for their maintenance by controlling the expression of antioxidant genes such as Nfe2l1. Reduction of NFE2L1 levels increased damage by oxidative stress in human midbrain cells. Moreover, analysis of postmortem midbrain samples revealed that both PBX1 and NFE2L1 levels are drastically reduced in mDANs of the substantia nigra of PD patients. We suggest that genes important for midbrain development may also play a previously unrecognized role in PD.

O17

The role of cellular thresholds in driving the selective neuronal vulnerability of PD

*David Sulzer**
Columbia University, New York City, NY, USA

While adult human neurons are not typically antigen presenting cells, many substantia nigra dopamine neurons express MHC-I. The death of these neurons causes the motor disorders of Parkinson's, and in mouse substantia nigra neurons, the appropriate combination of neuronally presented antigen and T cell causes cell death. In blood of ~40% of Parkinson's patients and few age matched controls, CD4+ and CD8+ T cells are present that respond to two regions in α-synuclein, a protein misprocessed in the disorder. As degradation of α-synuclein and other proteins by lysosomes changes with disease, changes in cytosolic dopamine, and age, it is possible that autoimmune response to neoepitopes play roles in neurodegenerative and other aging related disorders.

O18

The role of neural circuits in PD

*James Surmeier**
Feinberg School of Medicine, Northwestern University, Chicago, IL, USA

The prevailing model of the motor symptoms in Parkinson's disease (PD) posits that symptoms arise from an imbalance in the excitability of so-called direct and indirect basal ganglia networks that stems from the differential expression of D1 and D2 dopamine receptors by striatal spiny projection neurons that anchor these two pathways. This model has been of tremendous heuristic value and has served as the conceptual framework for hundreds of studies and for clinical management of PD symptoms. However, key features of model have never been formally tested. Perhaps the most significant untested tenet of the model is that the motor symptoms of PD arise solely from the loss of dopamine release in the striatum. This assumption is clinically important as it has focused dopamine restorative therapies (e.g., transplant therapies) on the striatum, rather than other parts of the basal ganglia. But testing this tenet has been difficult, as virtually all of our animal models of PD are not progressive and do not produce regionally-selective loss of dopamine release. Recently, this has changed. Using a genetic strategy, the loss of mitochondrial complex I (MCI) function in dopaminergic neurons characteristic of idiopathic PD was mimicked in a mouse. Within months of loss of MCI function, the axons of dopaminergic neurons innervating the striatum were lost, but the cell bodies of these neurons were not. Moreover, dopamine release from these cell bodies was maintained. At this point in time, these mice had severe motor learning deficits but were not overtly parkinsonian. Later, dopamine release from cell bodies was lost. At this point, mice manifested a levodopa-responsive parkinsonism. The observations from this progressive mouse model of PD argue that the classical conceptual framework explaining the motor symptoms of PD needs fundamental revision. Loss of striatal dopaminergic signaling is not sufficient to trigger parkinsonism. Rather, loss of dopaminergic control of basal ganglia output appears to be critical. This shift in our framework has broad therapeutic implications for PD patients.

O19

State of the art of wearable devices in Parkinson's disease
*Joaquim Ferreira**
Lisbon Medicine University, Lisbon, Portugal

There is a growing interest in the quantitative assessment of Parkinson's disease (PD) features. These includes the use of wearable technology that may allow for objective, continuous, unobtrusive and ecologically collected data. These devices allow for multiple time-point evaluations recorded in clinic and home environments.
A critical appraisal of the characteristics and validity of the identified wearable devices for the assessment of PD found different clinimetric properties and clinical validation processes. Another relevant problem associated with the use of wearable devices in PD is the low compliance.
Wearable devices have potential for improving the clinical management and clinical research in PD. However, their development and validation should follow the same steps as a non-technology tool or outcome.

O20

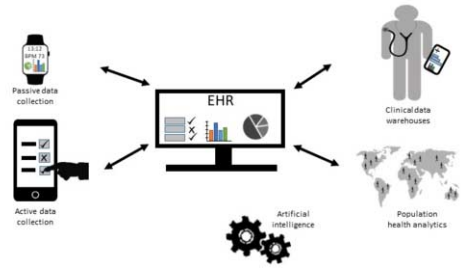
Applications of wearable devices in clincal trials
*Tanya Simuni**
Northwestern University, Chicago, IL, USA

Digital health technologies (DHTs) are rapidly entering the field of medicine. DHTs refer to smartphones, smart watches and body worn censors. Telemedicine is another technology-based platform for remote assessment of patients. Parkinson's disease (PD) lands well to application of DHTs both in clinical care and specifically in clinical research. DHTs have a number of advantages over the traditional clinical rating scales. They offer precision of data acquisition, opportunity to collect data repeatedly in the real life environment and potentially detect early signs of the disease. Additionally smartphone apps allow study participants to input patient reported outcomes (PROs) in real life.
There are sufficient data on the feasibility of utilization of DHTs in PD clinical research. While significant progress has been made in collecting data on correlation of DHTs derived data with the clinical outcome measures, a number of questions remain to be addressed before DHT derived measures are accepted as the standard outcome measures n PD clinical trials. While there will be variety if the DHTs, there should be standardization of the data analysis algorithms and data sharing that will allow comparison between the studies. DHT derived outcomes should not simply perform as well as traditional outcome measures but exceed them and offer novel and more sensitive and reliable ways of data collection. The tremendous amounts of data outputs should be reduced to global measures that can be applied across studies. The DHT based outcomes have to be accepted by the regulatory authorities as acceptable primary outcomes for the registration trials.
In conclusion, while a significant progress has been made, there are a number of unmet needs and challenges that have to be addressed prior to acceptance of DHT derived outcome measures in PD clinical research. The filed is rapidly developing and a number of on-going clinical trials are already including DHT derived data as exploratory outcome measures. In order to be successful in implementation of DHT derived outcomes in PD there should be close communication between all stakeholders including people with PD, academia, industry and regulatory authorities. Patient advocacy organizations are instrumental in on going dialogue between all stakeholders.

O21

"Wearables" for monitoring PD and its treatment
*Walter Maetzler**
University Hospital Schleswig-Holstein, Kiel, Kiel, Germany

The digital future in medicine includes the electronical health record, clinical data warehouses, population health analytics and novel "self-learning" analysis technologies. In addition, massive amounts of digital data will be produced by the patients themselves, e.g. with mobile technology, so-called "wearables". This technique is worn on the body. Its use in medicine has especially been accelerated by collaborations with the health and fitness sector industry. Such wearables allow for the detection of very subtle changes in human activity and disease-associated symptoms and signs. They can thus complement -or even substitute- traditional measurements, such as in-clinic assessments and patient-reported diaries and questionnaires. Based on these characteristics, wearables are attractive options to be included as outcome measures in routine diagnostics and clinical trials investigating symptomatic and disease-modulating treatments. Due to the nature of Parkinson's disease, which is associated with a chronic and progressive course and with predominantly motor symptoms including mobility limitations, falls, and sleep problems, this disease is a "target disease" for the assessment of mobile technology-derived measures. This talk will discuss the enormous potential of wearables for the assessment of Parkinson disease and its treatments in particular and of digital medicine in general, and what does this mean for persons living with the condition and for medical professionals.



The future of digital medicine will include passive (e.g., "wearables") and active data collection devices used by the person that is affected by a condition such as Parkinson's disease. These devices will continuously feed data into the electronical health record (EHR). Analysis strategies within and across databases will be mainly based on artificial intelligence algorithms. Adapted from www.neurologie.uni-kiel.de/en/neurogeriatrics/research.

O22

The history of levodopa and dopamine agonists – Benefits and myths
*Stanley Fahn**
Columbia University Medical Center, New York, NY, USA

Levodopa and dopamine agonists (DAg's) are effective agents in treating most motor symptoms of PD, such as slowness, stiffness, tremor, gait, mobility and dexterity. Both provide this benefit because they activate the dopamine receptors in the striatum, which had become inactive in PD due to loss of dopamine. Levodopa was adopted first as a treatment. In 1957 Arvid Carlsson (Sweden) found that the chemical reserpine depletes dopamine in brain causing drug-induced parkinsonism in animals, and that levodopa restores brain dopamine and eliminates the parkinsonism. In humans, early use of levodopa resulted in nausea and vomiting (N&V), preventing adequate, effective doses. But in 1967, George Cotzias (New York) found a way to avoid N&V, achieving high doses that could dramatically improve PwP. Subsequently, drugs (carbidopa,

benserazide) were developed that could block N&V and allow more levodopa to enter the brain.
DAg's are drugs that directly act on the dopamine receptors. They are the second most powerful drugs to improve the motor symptoms of PD. The first recognized DAg, apomorphine, was synthesized from morphine in the 19th century. In 1951, injections into PwP resulted in transient improvement. In 1970 its beneficial effects were rediscovered. Because it needed to be injected, and its action was short-lived, it was not widely accepted. Derivatives of ergot were soon found to have dopaminergic properties. Bromocriptine was the first ergot tested in PwP. Lisuride and pergolide soon followed. Because of ergot's side effects, non-ergot agents (pramipexole, ropinirole, rotigotine) were tested and developed and became widely used in PD. Apomorphine became utilized as a continuous subcutaneous infusion to treat motor complications of levodopa, and then became available as a single injection to rescue a PwP from a deep OFF state. Sublingual apomorphine is undergoing clinical trials.
If levodopa is superior in efficacy, why even consider DAg's? The answer lies in the side effect profiles of the two. Levodopa can cause dyskinesias and the wearing-off effect; DAg's don't. However, DAg's have their own side effects; the worst are hallucinations, falling asleep without warning (sleep attacks) and impulse control disorders (ICDs), rendering DAg's less suitable and less utilized today.

O23

Learn how to recognize and manage L-dopa induced dyskinesias

*Masahiko Tomiyama**
Department of Neurology, Aomori Prefectural Central Hospital, Aomori, Japan

Long-term L-dopa treatment can be complicated by the development of wearing-off and then L-dopa induced dyskinesia (LID). It is important for patients and their family members to understand LID because they sometimes misunderstand LID as involuntary movements like tremor observed when L-dopa efficacy is lost. A picture is worth a thousand words. I will show typical videos of LID. LID includes chorea, dystonia and ballism. Chorea, meaning "dance", refers to wiggling movements. Dystonia, meaning "bad tone", is characterized by twisting movements. Ballism, meaning "throw", is the movement like flinging whole arm or leg. Furthermore, three patterns of expression of LID are described based on the timing of their appearance in relation to the ON-OFF cycles of L-dopa efficacy. The first, Peak-Dose Dyskinesia is the most common subtype, occurring at the time of best ON response to L-dopa. It is often characterized by mixture of chorea and dystonia. The second, Off-Period Dystonia usually occurs in the early morning when L-dopa efficacy is lost. The manifestation includes foot inversion and painful flexion of toes. The third, Biphasic Dyskinesia, mixture of dystonia and ballism, occurs when patients feel appearance or disappearance of L-dopa efficacy. This predominantly affects the lower limbs. Once LID has developed, management becomes complex. While mild dyskinesia, often unnoticed by patients, may not necessarily require changes in medication, physicians must recognize that the stage of illness has reached where the therapeutic window is narrowing. The goal of therapeutic interventions for LID needs to be discussed between patients and physicians since it depends on a patient's personal circumstances. The treatment options for Peak-Dose Dyskinesia are based on the following principles. First, adjusting intervals and doses of the available and suitable oral or transdermal dopaminergic treatments. Second, adding antidyskinetic drugs. Third, neurosurgical intervention such as deep brain stimulation. Forth, administering antiparkinsonian drugs continuously via pumps. Similar principles can be applied for the management of Biphasic Dyskinesia. Increasing the size and frequency of levodopa dose or a dopamine agonist may be helpful for Biphasic Dyskinesia at the risk of increasing Peak-Dose Dyskinesia. All strategies to improve wearing-off can be applied for OFF-Period Dystonia.

O24

To learn how to recognize and manage impulse control disorders and dopa-dysregulation syndrome

*Annette Hand**
Northumbria University, Newcastle, United Kingdom

It is estimated that as many as one in four people with Parkinson's will develop an impulse control disorder due to taking medication for Parkinson's. Impulse control disorders can include binge eating, excessive spending, an increase in sex drive, gambling and increased creativity. It is reported that younger males, with previous impulsive behaviours taking a dopamine agonist are at greatest risk of developing this condition. In reality anyone with Parkinson's, of any age and on any of the Parkinson's medications, is at risk of developing an impulse control disorder. The impact of an impulse control disorder can be devastating, not only for the person with Parkinson's but also for their family and loved ones. Healthcare professionals should discuss impulse control disorders when starting someone on a medication for Parkinson's, and at each review appointment. Having an open and honest conversation about this potential drug side effect with people with Parkinson's, and their loved ones, can help with early identification and management of this problem if it does occur.

O25

Coping day to day – Managing the emotional roller coaster

*Allison Allen**
Durham Parkinson's Disease Support Group, Duke Health, Durham, NC, USA

At this round table discussion the participants are the real experts! We will use your experiences to normalize the roller coaster of emotions for the person with Parkinson's (PWP) and care partners (CP). Biodots will measure your mood state during the discussion. Emotional responses to the challenges of PD are real; figuring out strategies to best manage them is not a luxury. Research clearly documents the emotional impact of PD for both PWP and CP. How can you pace yourself when living with chronic illness? Experience teaches you that mood and coping vary day to day and sometimes hour by hour! Questions are often raised about what is "normal anger" or "normal depression" versus feelings that need professional attention. The leader will introduce the concept of chronic sorrow: does it translate to hitsuu in Japanese? We will consider antidotes for demoralization. While it may seem basic, sometimes asking for needed help can be difficult. We will exchange ideas about how you can be most successful in developing this needed skill. The practice of self care will be a theme throughout the WPC. We will identify roadblocks to self care and what resources to promote it. Importantly, this round table will highlight the critical factor of resilience. We will explore how participants use sources of strength and spirituality to help with coping. Participants will have some practical "takeaways" and will benefit from an opportunity for small group discussion that connects them in meaningful ways to others. At we end, we will see if biodots indicate that your mood is more relaxed!

O26

Tips on getting your research published
*Elena Becker-Barroso**
The Lancet Neurology, London, United Kingdom

Parkinson's disease in The Lancet and The Lancet Neurology: two decades of advances
The Lancet journals are committed to increasing the social impact of medical science. The Lancet was founded in London (UK) in 1823, whereas The Lancet Neurology was launched almost two centuries later, in 2002. Both journals set high standards for clinical research and share the end goal of improving clinical practice. In my presentation, I will describe the editorial procedures that we use to select and report the best original research in this field, and explain our focus to serve the neurological research community. The landmark Articles published in the journals over the past two decades reflect the remarkable progress in Parkinson's disease research that has taken place in the 21st century. But research findings are only relevant if they impact on human lives. The editors at The Lancet journals strive to contextualise scientific evidence and to disseminate it broadly. Our aim is to inform scientific and public-health debates, and to advocate for the Parkinson's disease community.

O27

Insights into the function of LRRK2 from a genetic point of view
*Matt Farrer**
University of British Columbia, Vancouver, British Columbia, Canada

The round table will be a review and interactive discussion focused on leucine-rich repeat kinase 2 (LRRK2), from its original discovery to the mechanistic insights that have subsequently been made about its biological functions, to the potential for LRRK2 competitive kinase inhibitors, that are now in clinical trials, to modify disease.

O28

LRRK2 and PD
*Jie Shen**
Harvard Medical School, Boston, MA, USA

LRRK2 mutations are the most common genetic cause of Parkinson's disease (PD). The LRRK2 gene encodes a multi-domain protein containing a leucine-rich repeat, and kinase and GTPase domains. Among the LRRK2 mutations, the G2019S mutation in the kinase domain, is most common, representing approximately 1–2% of all PD cases and ~20% of the Ashkenazi Jewish PD population. Our genetic studies of LRRK2 in mice revealed unexpectedly that LRRK2 is a key regulator of the protein degradation pathways and α-synuclein homeostasis. Our further generation and characterization of double knockout (DKO) mice lacking both LRRK2 and its functional homologue LRRK1 showed that LRRK DKO mice develop selective, age-dependent dopaminergic neurodegeneration, whereas the cerebral cortex and cerebellum are unaffected. The neurodegeneration is accompanied with increases in apoptotic cell death, increased levels of α-synuclein, and impaired autophagy-lysosomal pathway. Furthermore, motor deficits and autophagic impairment in the substantia nigra pars compacta of LRRK DKO mice occur before the onset of dopaminergic neurodegeneration and increases of apoptosis. Thus, LRRK plays an essential role in the regulation of the autophagy-lysosomal pathway and the maintenance of the dopaminergic function and survival in the aging brain. We will discuss the normal physiological role LRRK2 and the pathogenic mechanism underlying LRRK2 mutations at the Round Table, and will also debate how these studies may influence LRRK2-based drug development.

O29

Combined pharmacotherapy and neuromodulation approaches to PD
*John Rothwell**
UCL Queen Square Institute of Neurology, London, United Kingdom

This round table will introduce the various methods of non-invasive neuromodulation that are currently available to supplement treatment of Parkinson's disease. It will discuss the merits and limitations of each approach and give indications of how best to integrate these methods with conventional pharmacotherapy.

O30

What is α-synuclein – The biology
*Ronald Melki**
Institut François Jacob (MIRCen), CEA and Laboratory of Neurodegenerative Diseases, CNRS, Fontenay-aux-Roses, France

The aggregation of proteins within the central nervous system is deleterious and associated to neurodegenerative disorders. The aggregation of the protein α-synuclein is associated to synucleinopathies, in particular Parkinson's disease. How α-synuclein aggregates, how those aggregates traffic between cells, amplify by recruiting endogenous monomeric α-synuclein and cause distinct synucleinopathies is unclear.
I will explain the molecular events that lead to α-synuclein aggregation. I will show that α-synuclein aggregates bind to neurons cell membranes and explain the cellular consequences of binding. I will explain how the aggregates penetrate the cells and get transported. Finally, I will describe how α-synuclein fibrillar polymorphs cause distinct diseases. Strategies targeting the propagation of aggregated α-synuclein will be presented and discussed.

O31

Pathological features of α-synucleinopathies
*Peter Riederer**
University of Würzberg Medical School, Würzberg, Germany

There is sample evidence that αSYN pathology is relevant in genetic mutations of the SNCA gene leading to parkinsonism. In sporadic forms, αSYN is a pathological component of PD, PDD, MSA and other neurodegenerative disorders, but it is a component of the normal aging process too, without evidence for neurodegeneration. In addition, there is a synergism of αSYN pathology with other major pathological proteins, like beta amyloid, tau or TDP-43, suggesting common and overlapping pathogenic mechanisms leading to spectrum disorders like PD, PDD, PDAD, AD and others.
In PD, αSYN can be detected in brain tissue, CSF, blood, skin, peripheral nerves, in the olfactory system, the gastrointestinal tract etc. According to Braak, the origin of pathology is in the peripheral organs like th egut with an upsteram pathology via the vagus nerve to finally attack CNS brain areas including the dopaminergic substantia nigra (SN). However, there might also be a brain-gut pathology as described in the 6-OHDA model.

The clinical-pathological features of αSYN pathologies are less understood. Braak himself did not describe clinical-pathological correlations in his seminal publications on PD staging using αSYN immunohistochemistry. Follow-up studies in part confirmed Braaks pathological staging, but there are several other publications which critically discuss this by presenting retrospective clinical-pathological correlation. Accordingly, roughly 50% of PD does not follow the Braak staging, indicating more complex pathological mechanisms, multi-genetic and multifactorial interactions in another 50% of patients.
Further post mortem studies and correlations to clinical symptoms in the course of the disease are urgently needed to elucidate the pathological mechanisms behind αSYN and other „protein disorders". This, however, is only possible, if patients are willing to donate their brain for science after they have died, to build up brain banks to study human disease processes in more detail. This also will contribute to deliver valid targets for drug development and will help to enlarge the armamentarium to fight „protein diseases" like PD, PDD, MSA, AD and others.

O32

The importance of participating in clinical trials
*Soania Mathur**
Designing A Cure, Ajax, ON, Canada

Clinical trials in Parkinson's add to our understanding of this disease and how effective or safe certain treatments, interventions or diagnostic tests are. One of the greatest barriers that research studies face is difficulties in recruitment of participants. In order for medical research to develop new treatments and ultimately a cure, it is imperative for studies to recruit enough participants. There are a number of roles that patients can play to improve research participation, recognizing first and foremost that without patient involvement, research cannot progress.
There are a multitude of reasons for the shortage in medical research participation, some logistical such as accessibility, or not meeting the study criteria. But more significantly is that there is often a lack of knowledge and a number of myths about clinical trials that may influence a potential participant's decision to enrol. Education and dispelling myths and misconceptions about clinical trials is key to increasing informed and continued research participation. These barriers and potential solutions will be explored in greater detail as well as the benefits to the patient and in turn the greater global Parkinson's community, will be discussed.

O33

Approaches to voice training in PD
*Darla Freeman**
Florida E.N.T. and Allergy, Tampa, Florida, USA

Communication difficulty is considered one of the first signs of Parkinson's disease with an estimated 75–89% incidence while only 10% seek services. The ability to communicate involves an intricate three-part system. Together the lungs, ribs, diaphragm muscle, chest muscles, and the abdominal and back muscles provide the respiratory support needed to produce voice. The sound source of the system is the larynx which contains the vocal cords. There are about 30 muscles within and around the larynx that function together to move and adjust the vocal cords. When the vocal cords close during speaking or singing, air from the lungs passes between them, causing them to vibrate and produce a sound. The final stage of the system is the resonator including the throat, mouth and nasal cavities. Resonance refers to the shaping of sound waves within a chamber to produce a particular sound output. The sound that is produced by the vocal cords is likened to a buzz. The remainder of the vocal tract refines the sound through resonance.
People with Parkinson's oftentimes present with a decline in one or more of these subsystems as they progress through the stages of the disease. Respiratory dysfunction is common and contributes to reduced ability to secure the necessary breath support needed during the process of phonation. Weakened vocal cords make it difficult to control the airflow and reduced oral/motor agility and strength makes articulation a struggle.
An interactive conversation regarding scientifically based treatment approaches, potential barriers to treatment and ways to select providers are among several topics to be discussed.

O34

How PD affects sexuality and intimacy in PwPD and their care-partners
*Sheila Silver**
Private Practice, Portland, OR, USA

Sexuality is a topic that many patients and health care professionals are reluctant to talk about. There is often not time during appointments to discuss this very intimate topic. This roundtable will be an opportunity to sit down with an intimacy and sexuality expert, and ask the questions you have been wanting to ask. You will learn more about how doctors can help their patients and what patients and partners need to know.

O35

Planet Patient vs planet Research: How do we align instead of collide?
Simon Stott[1], A.C. Woolnough*[2]*
[1] The Cure Parkinson's Trust, London, United Kingdom
[2] Ambassador for the World Parkinson Congress 2019, Sandpoint, Idaho, USA

Based on the goal of how both the patient and research communities can better collaborate to achieve the ultimate goal of curative therapies for Parkinson's, this roundtable will review the research process, how patients can participate in that process, bioethics, and improving communication between researchers and patients. The majority of the time will be spent on Q/A, discussion and participant input.

O36

New insights into the function of LRRK2 from a genetic point of view
*Matt Farrer**
University of British Columbia, Vancouver, British Columbia, Canada

Pathogenic mutations in LRRK2 were first described in many families with multi-incident, dominantly inherited parkinsonism. Subsequently, LRRK2 substitutions were observed to profoundly influence Parkinson's disease risk in African, Asian and American/European populations. While aging and environmental factors are important, the role of genetics became indisputable. Although many patients with LRRK2 parkinsonism develop Lewy body disease those aggregated protein inclusions appear to be a secondary consequence. Leucine-rich repeat kinase proteins, similar to LRRK2, were first characterized in the slime mold (D. discoideum) and regulate chemotaxis and cell polarity. In nematode worms (C.elegans), in neurons, LRK1 (LRRK2's homologue) is

required for the sorting of synaptic vesicle proteins and their polarized localization in axons. LRRK2 'decorates' endosomes and plays an important regulatory role in vesicular trafficking, largely mediated through Rabs, regulating autophagosome formation, inhibiting chaperone mediated autophagy and synaptic homeostasis. Current biology will be reviewed but much remains to be elucidated. Nevertheless, in humans, dopaminergic neurons maintain a striatal arbor of 1–2.5 million synapses and are evidently sensitive to LRRK2 mutant dysfunction. Hence, LRRK2 kinase activity and competitive inhibition remain one of the most exciting avenues for neuroprotection through precision medicine.

O37

LRRK2 in dopaminergic neuronal survival and Parkinson's disease

*Jie Shen**
Harvard Medical School, Boston, MA, USA

LRRK2 mutations are the most common genetic cause of Parkinson's disease. Our analysis of LRRK2-deficient mice revealed a novel role of LRRK2 in the regulation of protein degradation pathways and homeostasis of α-synuclein. Specifically, inactivation of LRRK2 results in age-dependent impairment of the autophagy-lysosomal pathway, α-synuclein accumulation and aggregation, and increases in apoptosis in the kidney. Interestingly, there is no detectable phenotype in LRRK2-/- brains, suggesting that LRRK2 homologue LRRK1 may be sufficient to carry out LRRK function in LRRK2-/- brains. Our further development of LRRK1/2 double knockout (LRRK DKO) mice indeed showed that LRRK DKO mice, but not LRRK1 or LRRK2 single KO mice, develop age-dependent dopaminergic (DA) neurodegeneration. The cerebral cortex and cerebellum, however, are unaffected, though noradrenergic neurons in the locus coeruleus and medium spiny neurons of the striatum are also reduced in LRRK DKO mice. The selective, age-dependent neurodegeneration is accompanied with increases in apoptotic cell death, increased levels of α-synuclein, and impaired autophagy-lysosomal pathway. Quantitative electron microscopy analysis further revealed dramatic increases of autophagic vacuoles in the substantia nigra pars compacta of LRRK DKO mice at 10 months, before the onset of DA neuron loss and increases of apoptosis. LRRK DKO mice also exhibit age-dependent motor impairment, reduction of evoked dopamine release, and loss of dopaminergic terminals in the striatum. These results demonstrate that LRRK plays an essential role in the regulation of the autophagy-lysosomal pathway and the maintenance of the dopaminergic function and survival in the aging brain.

O38

LRRK2 as a therapeutic target

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

Mutations and variation in the gene LRRK2 (leucine rich repeat kinase 2) are a common cause of genetically linked Parkinson's disease with varying prevalence across ethnic populations. As mutations lead to enhanced kinase activity of the LRRK2 protein, development of small molecule kinase inhibitors represents a leading therapeutic strategy with at least one company (Denali Therapeutics) in early human testing. Moreover, with the identification of bone fide LRRK2 substrate proteins in the family of Rab GTPases and increased understanding of LRRK2 biology, there may be opportunities for not only expanding treatments targeting the LRRK2 cellular pathway, but also in assessing the benefit of LRRK2-based therapies in more common idiopathic Parkinson's disease.

O39

The vermiform appendix contributes to the development of Parkinson's disease

*Viviane Labrie**
Van Andel Research Institute, Grand Rapids, MI, USA

Parkinson's disease (PD) pathogenesis involves the accumulation of aggregated α-synuclein, which has been suggested to begin in the gastrointestinal tract. We determined the capacity of the vermiform appendix to modify PD risk and influence pathogenesis. In two independent epidemiological datasets, involving more than 1.6 million individuals and over 91 million person-years, we observed that removal of the appendix decades before PD onset was associated with a lower risk for PD, particularly for individuals living in rural areas, and delayed the age of PD onset. We also found that the healthy human appendix contains intraneuronal α-synuclein aggregates and an abundance of PD pathology-associated α-synuclein truncation products, which are known to accumulate in Lewy bodies. Remarkably, these aggregates were present at all age groups, including young individuals (<20 years of age). Furthermore, the appendix contained soluble oligomeric α-synuclein as well as truncated forms of α-synuclein that were prone to rapid aggregation. Truncated α-synuclein was present in the healthy appendix, but was more abundant in the appendix of PD patients. Taken together, we propose that the normal human appendix contains pathogenic forms of α-synuclein that impact the risk of developing PD.

O40

What is evidence for, and the relevance of, GIT pathology in PD?

*Pascal Derkinderen**
Inserm U1235, Nantes, France

It is now well established that Parkinson's disease (PD) is not only a movement disorder of the CNS but also a gastrointestinal disorder affecting the enteric nervous system (ENS). The gut-brain axis is a bidirectional communication between the brain and the gastrointestinal tract, which comprises besides the CNS and the ENS, the intestinal epithelial barrier, the intestinal microbiota and the enteroendocrine systems. In this talk, we present the clinical and pathological evidence suggesting that the gut-brain axis is dysfunctional in PD by discussing the possible role of ENS lesions, gut microbiota, inflammation and permeability in the development of the disease.

O41

Is there any evidence that nutrients modify PD

*Laurie Mischley**
Bastyr University Research Institute, Seattle, WA, USA

Following diagnosis, does it matter what you eat? We'll discuss why people with PD are at increased risk of nutritional deficiencies, and the reasons malnourished indiviudals are more likely to develop depression, anxiety, constipation, and cognitive impairment. Nutrition-based strategies will be reviewed for improving intestinal health, preventing weight loss, and for making levodopa more effective. The evidence that some foods are associated with faster and slower rates of Parkinson progression will be reviewed and the

potential risks and benefits of nutritional supplements will be addressed.

O42

Understanding apathy: What it is, what it is not and its impact on disease

*Kathy Dujardin**
Lille University medical center, Lille, France

Apathy corresponds to a lack of motivation. Objectively, it is characterized by a significant reduction of goal-directed activity either in the behavioral, cognitive, emotional or social domain in comparison to the patient's previous level of functioning. It is a persistent state and symptoms are observed in several of these domains.
Among the non-motor manifestations of Parkinson's disease (PD), apathy is one of the most disabling behavioral disorders. It may occur as a syndrome per se or as part of other disorders (namely depression and cognitive decline). It has a strong impact on the level of functioning and quality of life of PD patients and their caregivers.
Apathy is usually not related to the severity of the motor symptoms, but frequently associated with the severity of cognitive impairment. Apathy may also be an adverse effect of some symptomatic treatment of PD, namely stimulation of the subthalamic nucleus. Screening and assessment of apathy require the use of specific tools, some of which are validated in PD. From a pathophysiological point of view, several studies have suggested that apathy results from dysfunction of the limbic circuit connecting the ventral striatum to orbito-frontal and anterior cingulate cortex. The dopaminergic denervation in these regions seems to play a key role, but other mechanisms are probably involved.

O43

Anxiety in Parkinson's disease – symptoms, frequency, and neurobiology

Roseanne Dobkin[*,1], Nadeeka Dissanayaka*[2]
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Anxiety is a prominent non-motor symptom in Parkinson's disease (PD) with a global average prevalence of 31%. The occurrence of anxiety in people with PD (PWP) is significantly higher than that observed in the general population. Anxiety detrimentally impacts activities of daily living in PWP, even more so than motor symptoms. In comparison to PWP without anxiety disorders, those with anxiety experience 50% poorer quality of life, 5 times more complications from PD therapy, and 10 times greater disability. Generalized anxiety disorder, panic disorder, agoraphobia and social phobia are common anxiety disorders experienced in PD. A high proportion of PWP also experience anxiety that cannot be classified into clear diagnostic categories, as unique characteristics of anxiety are present due to fluctuations in motor symptoms, medication timing, and dyskinesias. Common symptoms of anxiety in PD include excessive non-specific or health-related worries, panic like feelings, fears of certain objects or situations, and physical tension, and restlessness. Anxiety may be triggered by a variety of internal (bodily sensations, negative thoughts or predictions, physical, cognitive, and emotional effects of "wearing off") and external cues (a crowded shopping mall, eating in a restaurant, speaking in public) and often results in social withdrawal and avoidance behavior. Anxiety may be persistent, episodic, or both, and may present with or without co-occurring depression. The Parkinson's Anxiety Scale (PAS) was recently developed and validated to evaluate the unique characteristics of PD anxiety and is suggested superior to other widely used anxiety scales for PWP. While anxiety may present for the first time at any point in the Parkinson's journey, anxiety preceding a diagnosis of PD is also common. The causes of anxiety in PD are both diverse and complex, involving biological, cognitive, behavioral, and social risk factors. Neurobiological mechanisms include changes in neurotransmitter systems, as well as abnormalities in specific brain regions, and pathways. Recent advances in the understanding of the clinical presentation, measurement, and impact of anxiety in PD will be highlighted throughout this presentation.

O44

Understanding depression in Parkinson's disease – Symptoms, frequency, and neurobiology

Murat Emre, Zeynep Tüfekçioğlu*
Istanbul Faculty of Medicine, Istanbul, Turkey

Disorder of affect ranging from major depression to dysthymia is one of the most frequent non-motor symptoms in Parkinson's disease (PD). The prevalence varies depending on the definition and the population studied, on average one third to half of patients suffer from major depression or depressive symptoms during their disease course. Depression may antedate motor symptoms and may be one of the pre-monitory symptoms. The profile of depression is typically different than that seen in major depression, feeling of guilt is rare, suicidality is uncommon. Etiology is multifactorial and includes reaction to a chronic disabling disease as well as neurotransmitter changes including dysfunction in dopaminergic, serotoninergic and noradrenergic modulatory systems. Assessment of depression can be achieved using a semi-structured interview or clinical scales, as yet there are no reliable biomarkers. Depression remains undetected in half of patients. It is one of the main non-motor symptoms impairing quality of life, it should be actively searched for and treated as indicated.

O45

Deciphering transcranial magnetic stimulation mechanisms in early and late experimental parkinsonism

*Veronica Ghiglieri**
University of Perugia, Perugia, Italy

In Parkinson's disease (PD) therapy, current treatments are not able to arrest the progression of neurodegenerative events and the risk to develop L-Dopa-induced side effects is still not predictable. Novel therapeutic approaches that combine early pharmacological and non-pharmacological interventions may foster intrinsic brain repair potential and improve patients' response to therapy with limited side effects.
Animal models of PD have helped to demonstrate that, in patients, basal ganglia alterations are associated with loss of synaptic plasticity and that identifying the mechanisms underlying the response to treatments, can optimize therapeutic outcomes.
In this talk recent data collected by our recent group will be presented on the possible mechanisms underlying transcranial magnetic stimulation (TMS)-induced beneficial effects in a rat model of PD, with distinct degrees of dopamine denervation. Electrophysiological, behavioral, morphological and molecular evidence of the changes in striatal functions, in response to different patterns of stimulation, will be discussed. An overview of the current studies aimed at deciphering molecular mechanisms underlying effects of this noninvasive brain stimulation in animal models of disease will be also provided.

O46

Combined pharmacotherapy and neuromodulation approaches to PD

*John Rothwell**
UCL Queen Square Insitute of Neurology, London, United Kingdom

Neuromodulatory approaches to treatment of Parkinson's disease can be employed in a variety of ways depending on the area of brain stimulated and the type of stimulation applied. In general neuromodulation is not intended to replace conventional pharmacotherapy since it has less effect on motor symptoms than L-Dopa. However, since the mechanism of action differs from that of dopaminergic drugs, it can be used successfully to add to pharmacological benefits and enhance overall patient response. In this type of approach, neuromodulatory interventions target motor areas of cortex in order to increase their responsiveness and excitability. In a second approach, neuromodulation has been employed to try to reduce the side-effects of medication, in particular to reduce dyskinesias. In this case, stimulation has been directed at cerebellum. A third, and perhaps largest category of neuromodulatory applications is to tackle symptoms that are less responsive to conventional pharmacology. Examples of this are to treat symptoms of depression (with the primary target being frontal cortical areas), speech articulation (auditory areas of cortex), swallowing (frontal motor areas) and freezing of gait (frontal cortex). I will describe the scientific rationale and evidence base for these approaches and discuss ways foward for future treatments.

O47

How do journals decide what to publish and promote?

*Elena Becker-Barroso**
The Lancet Neurology, London, United Kingdom

Parkinson's disease in The Lancet and The Lancet Neurology: two decades of advances
The Lancet journals are committed to increasing the social impact of medical science. The Lancet was founded in London (UK) in 1823, whereas The Lancet Neurology was launched almost two centuries later, in 2002. Both journals set high standards for clinical research and share the end goal of improving clinical practice. In my presentation, I will describe the editorial procedures that we use to select and report the best original research in this field, and explain our focus to serve the neurological research community. The landmark Articles published in the journals over the past two decades reflect the remarkable progress in Parkinson's disease research that has taken place in the 21st century. But research findings are only relevant if they impact on human lives. The editors at The Lancet journals strive to contextualise scientific evidence and to disseminate it broadly. Our aim is to inform scientific and public-health debates, and to advocate for the Parkinson's disease community.

O48

How does the media choose stories and sell them?

*Jon Palfreman**
University of Oregon, Lexington, OR, USA

Journalists are storytellers. Rather than using their expertise to write dry essays on (say) health policy, they much prefer personal narratives with characters, scenes, conflict and resolution. Science journalists are naturally drawn to medical topics, where they can report on researchers and clinicians struggling to defeat terrible diseases that wreak suffering and death on their human victims. In this quest, they are supported by researchers (who seek attention for their work) and patients (who desperately seek new therapies and cures for their malady). What emerges is a "conspiracy of hope" between patients, researchers and journalists that at best exaggerates medical progress and at worst hypes totally fake new "cures." Parkinson's disease is especially prone to hype. Being a movement disorder it is highly visual and video showing a patient before and after an intervention can create a strong belief in efficacy. Yet the history of Parkinson's research is replete with therapies that appeared effective (e.g. Madrazo's use of adrenal grafts in the 1980s) only to be abandoned as mere placebos.
While it's crucial to keep hope alive, it can be argued that medical journalism has been insufficiently skeptical of the glacial rate of progress in biomedical research, using phrases like "scientists hope that one day this will lead to a cure" to imply research is further along than it actually is.
This talk will use examples from medical journalism to illustrate the kinds of stories journalists and editors prefer.

O49

How do you assess all the information that is out there?

*Benjamin Stecher**
Toronto, Ontario, Canada

Parkinson's disease is an incredibly complex field. Those diagnosed have a particularly tough time navigating and making sense of all the information that is out there as they are thrust into it in the middle or late in life. Yet, understanding it is crucial to coming to terms with one's diagnosis and empowering each person to make informed decisions about their health. This talk is intended to help people understand the state of research by giving a broad overview of what the world is working on, what some of the major hurdles are in our quest for better therapies and what needs to be done to overcome those hurdles. Some of the other themes that will be covered include: cure vs. care, what a cure will look like, individuals vs. populations, precision medicine, measuring PD, therapies on the horizon and what to look forward to.

O50

How PD affects sexuality and intimacy of PwP and their care-partners

*Sheila Silver**
Private Practice, Portland, OR, USA

Living with Parkinson's disease sometimes creates physical or emotional distance in a relationship. Patients and their partners often need to talk about sexuality and intimacy, in ways they may have never needed to before. This presentation will offer practical tools to help with these conversations. It will help all those affected by PD to broaden the way they think about sex, and will offer tools to increase both physical closeness and emotional intimacy.

O51

Medical and non-medical management of sexual problems in PD

*Jim Bender**
Basalt Rehabilitation Centra, The Hague, The Netherlands

This presentation will be focussing on 6 challenges around sexuality that people with PD are often confronted with and how to manage them practically and medically.
The six challenges are:
1. My "users manuel" concerning my sexual functioning has changed since I have PD.

2. My experience of sexuality has changed since I have PD and I'm not so happy about it.
3. Sex for my partner has changed since I have PD and I'm not sure if she/he is happy about it.
4. Doing sex isn't easy since I have PD. Practical sexual issues need practical answers.
5. Since I have PD, sex has changed so much I don't desire it any more. I'm stuck and don't know how to proceed.
6. I don't know with whom or how I can talk about my concerns regarding my changed sexual life.
These challenges will be illustrated with stories that people with PD have shared with me when adressing them in their physical rehabilitation treatment.

O52

How to communicate on sexual issues with my inter-professional team
*Gila Bronner**
Sheba Medical Center, Ramat-Gan, Israel

Introduction: Motor and non-motor changes in Parkinson's disease (PD), as well as treatment may have a dramatic effect on sexual life of people with PD (PwPD) and their partners. Sexual dysfunction can cause ongoing emotional distress by reinforcing negative body image, reducing self-esteem and disrupting relationships. On the other hand, maintaining sexual function can act as an anchor during the disease experience, allowing patients to feel "normal." Sexual dysfunction may develop at any point during the disease course, including at diagnosis.
Most of the PwPD are at risk of impairment of their sexual life and general satisfaction. The prevalence of sexual problems (approx.40%–80%) demands that health providers proactively address sexual issues within the routine treatment of PwPD. Due to time limitation and need to address other PD symptoms, sexual issues may be neglected. Therefore, PwPD and their partners may have to raise questions concerning their sexual problems their health care providers. Discussing sexual problems with a doctor or health professional can be embarrassing. However, it is important not to suffer in silence.
Methods and Results: This talk will present tips how to overcome obstacles in initiating a "sex talk" with PD experts and in getting help for sexual problems.
Conclusions and recommendations: PwPD and their partners should be encouraged to raise their sexual problems. They need to describe the problem and understand that doctors will not be judging their sex life, but need to have information to be able to come to a diagnosis and recommend a treatment. There are a few steps that make it easier to talk about sexual issues. Before presenting a problem to the health provider, some preparations are essential: (1) defining the problem, when and how it started, and how it affects the relationship, (2) describing the sexual problems of both partners is important to evaluate and choose an appropriate intervention, (3) defining what the patient needs: information and explanation or personal counseling; specific treatment or medications; referral to experts in sexual medicine and sex therapy. Ideally, these issues will be discussed and agreed by both partners before initiating a discussion with the health provider.

O53

Sleep & PD: Tips and tricks
*Aleksandar Videnovic**
Massachusetts General Hospital/Harvard Medical School, Boston, MA, USA

Sleep dysfunction is one of the most common non-motor manifestations of Parkinson's disease (PD) that has gained significant interest over the past two decades due to its impact on the daily lives of PD patients, poorly understood mechanisms, and limited treatment options. The etiology of impaired sleep-wake cycles in PD is multifactorial. Sleep dysfunction in PD encompasses insomnia, REM sleep behavior disorder, sleep-disordered breathing, restless legs syndrome, and circadian dysregulation. Evidence supporting the efficacy of pharmacological and non-pharmacological treatment strategies in PD is limited. There is thus a great need but also opportunity for development of well-designed clinical trials for impaired sleep and alertness in PD. Providing education about sleep hygiene and strategies for its implementation represent the initial step in management. Prompt diagnosis and treatment of co-existent primary sleep and psychiatric disorders are critical, as this may significantly improve sleep and alertness. While the optimal treatment for insomnia in PD has not been established, available strategies include cognitive-behavioral therapy, medications with soporific properties, and light therapy. Safety measures, clonazepam, and melatonin are the mainstay of treatment for RBD. Continuous positive airway pressure is an effective treatment for SDB in PD. The treatment algorithm for RLS associated with PD mirrors that used for idiopathic RLS. Circadian disruption has emerged as an important etiology of impaired sleep-wake cycles in PD, and circadian-based interventions hold promise for novel treatment approaches. We are at the opportune time to advance our understanding of sleep dysfunction in PD, which will hopefully lead to mechanisms-driven interventions for better sleep and allow us to approach sleep as a modifiable therapeutic target for other non-motor and motor manifestations in PD.

O54

Therapeutic programs for cognitive health in PD
*Atsushi Takeda**
National Hospital Organization, Sendai-Nishitaga Hospital, Sendai, Japan

Cognitive declines in Parkinson disease (PD) are shown to be mainly mediated by fronto-striatal dopaminergic dysfunction, frontal noradrenergic dysfunction and frontal cholinergic dysfunction. Among them, activation of cholinergic pathway is established to be able to alleviate cognitive impairments in PD. However, their efficacy is not so high in later stages of dementia and it is often too late to start therapeutic interventions after the apparent manifestation of dementia, thus limiting the efficacy of cholinesterase inhibitors. In addition, there are not a few PDD cases in which dopamine replacement therapy must be restricted and motor function sacrificed due to accompanying psychiatric symptoms such as hallucinations and delusions, which can further worsen prognoses of PDD cases. Although the appropriate timing for therapeutic intervention has not been established yet, early intervention with cholinesterase inhibitors for PD has been recently proposed. For examples, activation of the cholinergic system has been suggested to improve motor function in PD, based on a recent report of reduced risk of falling and improvement of walking-speed following the use of cholinesterase inhibitors in PD patients without dementia. From these backgrounds, we think that it may be possible to improve PD prognosis by intervening with cholinesterase inhibitors prior to the onset of PDD. In the previous study, we showed that severe hyposmia could predict later PDD development within several years. Therefore, we planned and finished a therapeutic intervention study using cholinesterase inhibitor in the non-demented PD group that showed severe hyposmia, one of the strongest predictors of cognitive decline in PD. Although the data of this study are under analyses at present, the result will be presented in this session. In addition to such medication-based therapies, the

efficacy of cognitive training has been recently suggested to improve cognitive decline in PD. This topic will also be introduced.

O55

Cognitive deficits in Parkinson's disease: Clinical features, diagnosis, and evolution

*Caroline Williams-Gray**
University of Cambridge, Cambridge, United Kingdom

People with PD are around 2.5 times more likely to develop dementia than other people of a similar age, and nearly half will have developed dementia by 10 years into their illness. This has a major impact on quality of life, care requirements, and survival. Milder cognitive problems occur earlier in the disease, with one quarter to one third having 'mild cognitive impairment'. Subtle cognitive deficits have even been reported to occur in some 'prodromal' PD cases, before movement problems emerge.
Several different domains of cognitive function can be affected, including executive function (which includes planning and organisational abilities), memory, and visuospatial function. In more advanced PD, cognitive problems can be associated with behavioural changes and visual hallucinations. Diagnostic criteria for PD-Dementia have been established by the Movement Disorder Society, which are based on neuropsychological test scores, evidence of progressive decline, and impairment of day-to-day functioning due to cognitive deficits. Diagnostic criteria have also been developed for PD-associated Mild Cognitive Impairment (PD-MCI). However, there has been some debate about whether this is a useful diagnosis, as early cognitive impairment in PD is highly variable and not all patients with 'PD-MCI' will go on to develop a dementia.
Through studying a population-representative cohort of Parkinson's patients from diagnosis over time (the CamPaIGN study), we have demonstrated that there are distinct cognitive syndromes in PD which evolve differently. In particular, early problems with semantic memory and visuospatial function are predictive of developing a dementia, whereas problems with executive function are not necessarily predictive of dementia, and can even improve over time. We have used genetic and brain imaging studies to demonstrate that these syndromes have distinct underlying biological bases: semantic/visuospatial problems reflect a posterior cortically-based process which is influenced by ageing and genetic variants promoting formation of protein aggregates in the brain; in contrast, executive problems reflect dysfunction in frontostriatal dopamine networks and are influenced by genetic variants affecting dopamine breakdown, and by dopaminergic medication. Through better defining and understanding these separate cognitive syndromes, we can give more accurate prognostic information to patients, and target these different syndromes with more tailored therapies.

O56

The challenges of making authentic midbrain dopamine neurons from stem cells

*Agnete Kirkeby**
NNF Center for Stem Cell Biology (DanStem), University of Copenhagen, Copenhagen, Denmark

We will discuss the use of human pluripotent stem cells to produce subtype-specific neurons, including directed differentiation into midbrain dopaminergic neurons. Also how the safety and efficacy of such stem cell-derived neurons is tested in animal models of PD including the importance of functional integration, synaptic connectivity, widespread innervation and proper maturation into neurons with authentic midbrain dopaminergic phenotype. We will also discuss how a stem cell-derived product is taken through GMP adaptation and how quality control should be performed on a stem cell derived product to ensure its safety and efficacy in clinical trial.

O57

Clinical application of stem cell transplantation therapy

*Asuka Morizane**
CiRA, Kyoto University, Kyoto, Japan

The innovation of induced pluripotent stem cells (iPSCs) and previous embryonic stem cell (ESC) technologies are drawing attention to their application for regenerative medicine. Parkinson's disease is one of the most promising target diseases based on the history of fetal nigral transplantation in clinics. Although pharmacological treatments for PD, such as L-dopa, show good response in the early phase, patient outcomes over the long term are unsatisfactory. As an additional treatment, cell therapy with aborted fetal tissues has been performed since 1980's. The limited supply of donor source and the unstable quality of the cells prevent this therapy with fetal tissue from becoming standard. The technology of iPSCs offers a limitless and more advantageous donor source. One of the advantages is possibility of preparing immunologically compatible donor cells from self-derived or allogeneic iPSCs. Our group has successfully established a protocol for donor induction with clinically compatible grade. The preclinical studies transplanted these donor neurons into PD models of mice, rats, and cynomolgus monkeys, showing graft survival with functional recovery. Based on these preclinical results, Kyoto University has started a clinical trial for Parkinson's disease that transplants dopaminergic progenitors generated from iPSCs; Kyoto Trial to Evaluate the Safety and Efficacy of iPSC-derived dopaminergic progenitors in the treatment of Parkinson's disease (Phase I/II). The original donor source is iPSCs prepared at the iPS Cell Stock for Regenerative Medicine at CiRA, derived from third-party donor blood cells, meaning the transplantations are allogeneic. The subjects will be observed for two years post transplantation. In this session we can discuss on the translational research, in vitro differentiation of iPSC-dopamine neurons, research on animal models, setting up clinical trials, and future perspective.

O58

The role of cellular thresholds in selective neuronal vulnerability in PD

*David Sulzer**
Columbia University, New York City, NY, USA

While adult human neurons are not typically antigen presenting cells, many substantia nigra dopamine neurons express MHC-I. The death of these neurons causes the motor disorders of Parkinson's, and in mouse substantia nigra neurons, the appropriate combination of neuronally presented antigen and T cell causes cell death. In blood of ~40% of Parkinson's patients and few age matched controls, CD4+ and CD8+ T cells are present that respond to two regions in α-synuclein, a protein misprocessed in the disorder. As degradation of α-synuclein and other proteins by lysosomes changes with disease, changes in cytosolic dopamine, and age, it is possible that autoimmune response to neoepitopes play roles in neurodegenerative and other aging related disorders.

O59

The history of levodopa and dopamine agonists, benefits and myths

*Stanley Fahn**
Columbia University Medical Center, New York, NY, USA

Levodopa and dopamine agonists (DAg's) are effective agents in treating most motor symptoms of PD, such as slowness, stiffness, tremor, gait, mobility and dexterity. Both provide this benefit because they activate the dopamine receptors in the striatum, which had become inactive in PD due to loss of dopamine. Levodopa was adopted first as a treatment. In 1957 Arvid Carlsson (Sweden) found that the chemical reserpine depletes dopamine in brain causing drug-induced parkinsonism in animals, and that levodopa restores brain dopamine and eliminates the parkinsonism. In humans, early use of levodopa resulted in nausea and vomiting (N&V), preventing adequate, effective doses. But in 1967, George Cotzias (New York) found a way to avoid N&V, achieving high doses that could dramatically improve PwP. Subsequently, drugs (carbidopa, benserazide) were developed that could block N&V and allow more levodopa to enter the brain.
DAg's are drugs that directly act on the dopamine receptors. They are the second most powerful drugs to improve the motor symptoms of PD. The first recognized DAg, apomorphine, was synthesized from morphine in the 19th century. In 1951, injections into PwP resulted in transient improvement. In 1970 its beneficial effects were rediscovered. Because it needed to be injected, and its action was short-lived, it was not widely accepted. Derivatives of ergot were soon found to have dopaminergic properties. Bromocriptine was the first ergot tested in PwP. Lisuride and pergolide soon followed. Because of ergot's side effects, non-ergot agents (pramipexole, ropinirole, rotigotine) were tested and developed and became widely used in PD. Apomorphine became utilized as a continuous subcutaneous infusion to treat motor complications of levodopa, and then became available as a single injection to rescue a PwP from a deep OFF state. Sublingual apomorphine is undergoing clinical trials.
If levodopa is superior in efficacy, why even consider DAg's? The answer lies in the side effect profiles of the two. Levodopa can cause dyskinesias and the wearing-off effect; DAg's don't. However, DAg's have their own side effects; the worst are hallucinations, falling asleep without warning (sleep attacks) and impulse control disorders (ICDs), rendering DAg's less suitable and less utilized today.

O60

Living well with Parkinson's: What's the secret?

Kathie Hill, Nancy Peate*
Parkinson's Resources of Oregon, Portland, Oregon, USA

Overall goal: To discuss behaviors and attitudes that contribute to living well with Parkinson's disease.
This round table is focused on discussing traits that contribute to living well with Parkinson's disease, including socializing, group exercise, seeking gratitude and cultivating mindfulness. The co-facilitators share personal stories about their diagnosis of Parkinson's disease in mid-life and their journeys to find resilience, and they look forward to your contribution to the discussion. Come to this round table to hear more about the process of finding community and founding a wellness-focused support group in Portland, Oregon.

O61

α-synuclein and the immune response in PD

*Ashley Harms**
University of Alabama, Birmingham, Alabama, USA

There is mounting evidence for a central role of the immune system in the pathophysiology of Parkinson's disease (PD), via activation of both the innate and adaptive immune systems. In both human patients and rodent models, α-synuclein pathology is accompanied by microglial activation, T cell infiltration, hyper-reactive monocytes, and increased cytokine and chemokine release. However, the triggers responsible for initiating this immune response and the mechanisms behind peripheral cell recruitment remain poorly understood. In the CNS, antigen presenting cells such as microglia express major histocompatibility complex II (MHCII) proteins that are crucial for the presentation of foreign proteins to CD4+ T lymphocytes, a process that links the innate and adaptive immune response. Genome wide association studies have found that genetic polymorphisms found in the HLA-DR locus, a component of MHCII, are associated with late onset PD, implicating a role for MHCII proteins in disease pathogenesis. In further support, HLA-DR is highly expressed on reactive microglia in PD post-mortem brain, and recent studies have shown that α-synuclein peptides can activate T cells. In our lab, we have used both an in vivo mouse model induced by viral over-expression of α-synuclein as well as in vitro systems to study the role of the MHCII in α-synuclein-induced inflammation and neurodegeneration. We have found that interaction of microglia and CD4 T cells are critical for the neuroinflammatory response in response to α-synuclein, and strategies targeting expression of MHCII are protective, by attenuating neuroinflammation, peripheral immune cell infiltration, and neurodegeneration. The results from these studies indicate that α-synuclein is pro-inflammatory by activating both the innate and adaptive immune system, and that disruption or modulating antigen processing and presentation via targeting MHCII is a neuroprotective and promising therapeutic target for future investigation.

O62

Mechanisms underlying impulsive behaviors and addictions in Parkinson's disease

*Christelle Baunez**
Institut de Neurosciences de la Timone, UMR7289 CNRS & Aix-Marseille Université, Marseille, France

We will review the data from the litterature published in both Parkinsonian patients, but also animal models regarding Impulse Control Disorders (ICD) that include addiction. We will thus try to explain how these severe side-effects could possiby be anticipated and how they could be treated, especially with an emphasis on the impact of STN deep brain stimulation.

O63

Diagnosed with PD – Now what?

*Andy McDowell**
PwP, Westmere, New Zealand

Family and friends and work are common enough issues PwP have to deal with but when faced with an early (young) onset diagnosis these issues become magnified.
The implications of no longer be being able to have 'normal' career and working life alone are enormous.
The impact on families with children (or considering), significant.

The pressure Parkinson's puts on relationships, marriages and friendships, huge
Not withstanding the aforementioned reality, or ignoring the emotional rollercoaster that comes with a diagnosis the roundtable will moot the philosophical proposition of "Keeping calm, and carrying on" and yet redefining oneself.

O64

Managing dyskinesias
*Masahiko Tomiyama**
Department of Neurology, Aomori Prefectural Central Hospital, Aomori, Japan

Once L-dopa induced dyakinesia (LID) has developed management becomes very complex. Therefore, efforts are made to minimize or prevent the appearance of LID. While mild dyskinesia often unnoticed by patients may not necessarily require changes in medication, physicians must recognize that the stage of Parkinson's disease has reached where the therapeutic window is narrowing. The goal of therapeutic intervention for LID needs to be discussed between the patient and physician at any stage since the goal actually depends on a patient's personal and professional circumstances. The current treatment options for Peak-Dose Dyskinesia, the most common subtype of LID, are based on the following principles. The first, adjusting intervals and doses of the available and suitable oral or transdermal dopaminergic treatments. Practically, reducing individual levodopa dose at the risk of increasing OFF time. The latter can be compensated for by increasing the number of daily doses of L-dopa, or by increasing a dopamine agonist, or both. Discontinuation or reduction of MAO-B inhibitors, COMT inhibitors, or istradefylline (available only in Japan) at the risk of worsening of wearing-off. The second, adding oral drugs with direct antidyskinetic effects such as amantadine and clozapine (if available). The third, neurosurgical intervention such as deep brain stimulation to the subthalamic nucleus or internal globus pallidus. The forth, administering antiparkinsonian drugs continuously via pumps such as apomorphine continuous subcutaneous infusion and intrajujenal L-dopa infusion. Similar principles can be applied for management of Biphasic Dyskinesia. Increasing the size and frequency of levodopa dose or a dopamine agonist at the risk of increasing Peak-Dose Dyskinesia. All strategies to improve wearing-off including long-acting and transdermal dopamine agonists and rasagiline can be applied for OFF-Period Dystonia. Additional L-dopa or dopamine agonist upon awakening during night may be helpful.

O65

Heterogeneity of Parkinson's disease
*Connie Marras**
University of Toronto, Toronto, Ontario, Canada

It is clear that no two patients with Parkinson's disease are the same from a clinical point of view. The clinical heterogeneity is apparent in the waiting room and even more apparent when examining the presenting symptoms, response to treatment, rate of progression and survival. The heterogeneity of PD has also been demonstrated at the etiological level; patients vary in their combination of genetic and environmental risk or causative factors. Pathological heterogeneity is also seen, which has even led to the demonstration that clinically classical Parkinson's disease can occur in the absence of the supposedly disease-defining Lewy body pathology. This presentation will describe the heterogeneity from the clinical, genetic, environmental exposure and pathological perspectives. The approaches that have been used to find subtypes of Parkinson's disease will then be reviewed, considering empirical, data-driven and biomarker-based approaches. Finally the implications of the heterogeneity for both clinical care (personalized medicine) and for research will be discussed, considering past failures and future opportunities.

O66

New trial approaches to treating Parkinson's disease
*Olivier Rascol**
University UPS of Toulouse III, Toulouse, France

Parkinson's disease (PD) is heterogeneous, with different mechanisms and different phenotypes, each patient presenting with different age at onset, various combination of motor and non-motor symptoms, evolution over time, response to therapies… Trying to make one drug work for all PD patients is therefore an unachievable challenge.
Classical randomized clinical trials (RCTs) try to assess the effects of therapies based on a global approach, comparing means of groups to capture statistics of central tendencies. This provides useful data from a public health perspective, but gives little information to predict individuals' responses, while patients respond differently in terms of efficacy and safety according to age, symptoms, co-medications, co-morbidities, but also genetic and physiological background, adherence to treatment… Moreover, patients enrolled in RCTs cannot represent the entire PD spectrum, as many patients are excluded (oldest, most severe, demented cases…).
There is therefore a need for more personalized approaches in future trials. Genetics suggesting that the mechanisms triggering neuronal death in PD differ according to genes and mutations, "neuroprotective" RCTs will then focus on corresponding genetically pre-specified sub-groups of patients (ex: kinase inhibitors in patients carrying LRRK2 mutations). Novel biomarkers being developed, they will guide adaptive designs adjusting and personalizing the dose on an individual basis (ex: achieving proper level of LRRK2 inhibition or using per-surgical MRI-gadolinium-guided gene therapy delivery). Progresses in pharmacogenetics and pharmacogenomics based on large-scale rigorously planned genome-wide studies should allow identifying and stratifying patients for better efficacy responses (ex: COMT polymorphism and COMT inhibitors) or poorer tolerability (ex: dyskinesia or impulse control disorders). Finally, accurate computer models of treatments and patients characteristics, based on proper clinical database, should allow developing in the future "in silico" trials, where "virtual" patients given a "virtual'" treatment, will enable simulated observations of how drug candidates produce the intended effect without inducing adverse effects.

O67

What's it like to live with a gene for Parkinson's disease?
*Benjamin Stecher**
tmrwedition.com, Toronto, Ontario, Canada

We are at the dawn of the age of precision medicine for Parkinson's disease. That movement is being led by a series of new therapies designed for people that carry specific genetic variants associated with PD. As a carrier of one of the variants, specifically the N370s GBA mutation, this is promising news. While it does make me eligible for a series of new trials, it can raise more questions than it answers. Why do so few people with this mutation get Parkinson's? What other factors might be able to account for the incomplete penetrance of this mutation? Why do I have a family history of the mutation but no family history of PD? How much of my disease can I

attribute to this genetic variant? These and more seem to be questions that no one can quite answer and leave me scratching my head thinking will therapies designed to treat this mutation be enough to modify the progression of this disease?

O68

Living well with Parkinson's disease
*Omotola Thomas**
ParkinStand, Surrey, United Kingdom

Background: After experiencing symptoms for over five years, I got diagnosed with Parkinson's disease in 2016 at the age of 35. I don't remember feeling sad or troubled about the diagnosis, at least not immediately. What I do remember, however, was a clear resolve not to let the illness get the best of me. Over time, that resolve would propel me to venture into doing things I would have never attempted to do before my diagnosis. Consequently, I would start to live my most fulfilling life, albeit a challenging one, post-diagnosis.
Overview of Talk:
a. Introduction: My definition of "Living Well"
b. Overview of how I "Live Well"

O69

Living well with Parkinson's disease: What's your secret?
*Yoshiko Okada**
Japan Parkinson's disease Association, Hakusan, Ishikawa, Japan

My thinking about PD is as follows:
I have been living with PD (this guy) more than 40 years. He is the partner whom I would like to leave off, if possible.But after 10 to 20 years going with him reluctantly, it became to take for granted to stay always with me. He is not the person I could be friendly. As soon as I relaxed my guard and would be careless a little bit, he begins to have everything his own way. However, recently I feel like being able to go with him pretty well.
He is the partner according to word "Good match for an opponent".
I investigate him thoroughly, and look for the capture method desperately, even after that he is very tough to go with.
He gives me difficult problems in sequence, even if I managed one of them. Anyway, he is a partner who is not boring.
I was able to get to know various people through him. I really thank for this.
This guy disturbs me in various scenes, but I hope to enjoy my life in the face of many difficulties.
One of the tips living well with PD is to make a compromise with symptom of PD to a certain extent. After 40 years with PD, I noticed that it is important to make a good relationship with PD. If we want to get rid of all the symptom, we do have to be on many kinds of medication for long time. Because PD is systemic and progressive disease, various kinds of symptom come out and we need to take many kinds of medicine. I chose to think the priority of ranking for getting rid of symptom. In early stage, I concentrated to control the efficacy of the medicine, its' duration and how to decrease dyskinesis.
Now, the biggest problem is walking difficulty. Especially it is related to freezing of gait (FOG) in "on"phase, and impaired balance,

O70

Living well with Parkinson's disease: What's your secret?
*Emma Lawton**
Parkinson's UK, London, United Kingdom

In my presentation I will discuss the role of technology in the self-management and wellbeing of people living with Parkinson's. Using specific examples I will suggest that technology should be part of the arsenal of methods used to help monitor and control symptoms, alongside diet, exercise, medication, complementary therapies, speech therapy, physiotherapy and sleep.
With over 40 symptoms of Parkinson's there is no one size fits all treatment for individuals. I will suggest that technology can help people to create their own toolkit, whether they need help sleeping, swallowing or rejigging their memory.
I will cover:
- Apps and devices
- Social media platforms
- Digital advocacy including blogging and vlogging
- Telecare
- AI
- Smart homes

O71

Living well with Parkinson's disease: What's your secret?
*Elizabeth Ildal**
Cure4Parkinson, Copenhagen, Denmark

Parkinson's is not just a disease that affects older people. No, Parkinson hits of all ages, and more than 5% are very young people. It's about much more than to shake. It's about everything from difficulty swallowing, difficulty speaking, lacked scents to frostbite, cramps, bladder challenges, stiffness, pain, depression, of changes, side effects of the medicine. Quality of Life need to be equally important as finding a cure.
"What can PwP do for them self to changes the mindset at a European level?
People with Parkinson's can:
1. Strengthen Their network
2. Learn something new
3. Take life activity
4. Be present in the Present
5. Give of themselves

Parkinson's community have to come together and focus on activism. The current and future burden of this debilitating disease depends on the whole Parkinson community work together and takes action. It also includes the Leaders of the world, governments and of course members of European Parliament. Please understand its now, we have to change the mindset of Parkinson's, because the cost to treatment will increase to a very high level.

O72

Living well with Parkinson's disease: What's your secret?
*Benjamin Stecher**
tmrwedition.com, Toronto, Ontario, Canada

Parkinson's is a product of the universe. The reason why you have Parkinson's disease has nothing to do with you per se, it is a by-product of billions of years of atoms bumping into each other. Eventually those atoms came together in such a way that life emerged on earth. The genius of life is in its ability to make slightly imperfect copies of itself. It is the greatest story the universe has ever told. But it is an imperfect process, some of those imperfections we call disease, but it is still just life doing what life does.
The day-to-day struggle sucks, and it will continue to suck for some time. No one in their right mind would choose this fate, but it is what it is, embrace the grind and count yourself lucky that of all the

generations of people to get this disease, you have a chance of being part of the one that ends it.

O73

Abnormal neural activities in the cortico-basal ganglia networks in animal models of PD

*Atsushi Nambu**
National Institute for Physiological Sciences, Okazaki, Aichi, Japan

It is very important to understand neural activity changes in the cortico-basal ganglia (BG) networks in PD, because it can explain pathophysiological mechanisms for PD symptoms in human patients. Besides, normalizing or modulating abnormal neural activity can ameliorate PD symptoms. So far, there are three models to explain pathophysiology of PD symptoms. One is the "firing rate model". Spontaneous firing rate changes along the cortico-BG networks were originally reported in MPTP (dopaminergic neurotoxin)-induced PD monkeys. The most characteristic finding was an abnormal increase in firing rates in the output nucleus of the BG. However, recent electrophysiological studies have failed to detect expected neural activity changes in the BG. Instead, the "firing pattern model" was proposed. Abnormal firing patterns, such as oscillatory and synchronized activity, were observed in the BG of PD models and patients, which may disturb normal information processing through the cortico-BG networks. The third one is the "dynamic activity model". Stimulation in the cortex normally induces triphasic responses, i.e., early excitation, inhibition and late excitation, in the output nucleus of the BG, and the inhibition is important for the initiation of voluntary movements. Our group have found that cortically induced inhibition in the output nucleus is abnormally reduced in PD models, and this may cause a failure in releasing appropriate movements at an appropriate timing. We believe that such dynamic activity changes in the BG are fundamental features of PD, and that firing rate and pattern changes may merely be epiphenomena. Indeed, PD symptoms can be ameliorated by making a small lesion or applying high-frequency electrical stimulation (deep brain stimulation, DBS) in the BG. Both lesions and DBS can block abnormal information flow from the BG to the cortex, and may be useful in suppressing the expression of PD symptoms. Their effectiveness is compatible with the "dynamic activity model".

O74

Optogenetic modulation of basal ganglia activity in Parkinsonian models

*Stella Papa**
Emory University, Atlanta, GA, USA

Models of the basal ganglia circuitry in health and disease states have been developed on the basis of solid anatomical, biochemical and physiological data. Over the past three decades, these models have gone through a series of revisions incorporating newer experimental data and key information obtained from patients undergoing deep brain stimulation. However, a tour de force refinement came from new technologies such as optogenetics that can provide cell resolution in a variety of functional studies. Its application has shed light into the role of key basal ganglia circuits and the mechanisms regulating their function. Among recent examples is the combination of optogenetic and chemogenetic approaches, which has revealed the interacting influences between the striatal indirect pathway and the cortical hyperdirect pathway on the function of the subthalamic nucleus in Parkinson's disease (PD). Another important progress comes from the analysis of active cells in association with dyskinesias showing that there are subsets of striatal neurons that are specifically involved with the expression of involuntary movements. This field has progressed significantly since the initial application in transgenic animals, and currently, sophisticated optogenetic tools can be used in non-transgenic animals including primates. Because of the refined phenotype in the primate model of PD, optical stimulation in this model may allow us to examine the particular motor correlates of manipulating specific cell populations, and thus expand our understanding of the disease pathophysiology. Furthermore, the high resolution of optical stimulation is now beginning to interrogate the therapeutic targeting of specific basal ganglia loops, providing grounds to develop new PD therapies.

O75

Adaptive brain stimulation for the treatment of PD: Where are we with this?

*Alberto Priori**
University of Milan, Milan, Italy

Parkinson's disease (PD) is typically a fluctuating condition, especially in its advanced stage. Despite the efficacy of conventional Deep Brain Stimulation (cDBS), it does not abolish completely motor fluctuations. Most PD patients undergoing cDBS of the subthalamic nucleus still complain motor fluctuations variably interfering with the quality of life. Under these premises, our group in the last fifteen years conducted research to develop an innovative methodology of DBS "adapting" (then called adaptive DBS or aDBS) moment-by-moment to the clinical motor state of the patient. Basically, aDBS changes its strength accordingly to a control signal reflecting the clinical state ("closed-loop approach"). Researches in the last 20 years demonstrated that the oscillatory electrical activity captured by the stimulating DBS electrode in the subthalamic nucleus is a reliable instantaneous marker of the clinical motor condition of the patient. Although different frequencies in the oscillatory activity correlate with different motor disturbances of PD, the beta activity (i.e. in the range of 13–30. Hz) appears to reflect the negative motor symptoms (bradykinesia and rigidity). Clinical trials using beta-controlled aDBS in PD have shown that the adaptive approach is technically feasible, safe, well tolerated by patients, and delivers significantly less energy to the brain than cDBS. More importantly, reported data show that aDBS induces a better control of motor fluctuations than cDBS in PD.
In conclusion, despite the available clinical research trials with aDBS are still few, conducted on small sample of patients and for short period of observation, adaptive DBS strategy promises to be an important advancement in the DBS technology, further improving its efficacy and tolerability. Notably, despite researches conducted so far essentially tested beta activity as control signal for changing DBS voltage, future trials will also test different oscillation frequencies as control signals and the effects of controlling different DBS variables (site of stimulation, frequency, etc). Other fluctuating neuropsychiatric conditions treated with DBS could also hypothetically benefit of adaptive approaches in the near future.

O76

α-synuclein: A story of accumulation and spread

*Maria Grazia Spillantini**
University of Cambridge, Cambridge, United Kingdom

The neuropathological features that characterize Parkinson's disease, are intracellular proteinaceous inclusions that were described for the first time by Friedrich Lewy in 1912. The nature of these inclusions remained unknown for long time due to the difficulty

in identifying the main component of their filaments. In 1994 in collaboration with Michel Goedert and Ross Jakes
we identify two small proteins in human brain that we named α-synuclein and beta-synuclein and localized their genes (SNCA) to chromosome 4 and (SNCB) 5 respectively. Following the identification of the first genetic mutation causing familial forms of Parkinson's in the α-synuclein gene, in 1997 with our collaborators we showed that α-synuclein was present in Lewy bodies and Lewy neuritis in brains of sporadic cases of the disease. In 1998 we demonstrated that α-synuclein is the main component of the filaments present in the Lewy bodies and Lewy neuritis as well as of the filamentous inclusions present in multiple system atrophy leading to the definition of these diseases as α-synucleinopathies.
We also showed that α-synuclein staining identifies more inclusions than ubiquitin, the marker normally used until then for detection of Lewy pathology. α-synuclein staining helped others to determine how the protein aggregates spread in the nervous system and to identify new symptoms associated with progression of α-synuclein aggregation and spreading. Recently we have produced a transgenic mouse model expressing aggregation prone α-synuclein and have been able to show that in these mice dopaminergic dysfunction starts at the synapse in the striatum and precedes both terminal loss and dopaminergic neuronal death in the substantia nigra, features that, we show can be prevented by a compound affecting α-synuclein aggregation. This transgenic mouse represents a useful model where to test compounds for the treatment of α-synucleinopathies.

O77

Preclinical and prodromal PD: Predictive and risk factors
*Walter Maetzler**
Christian-Albrechts-Universität zu Kiel, Kiel, Germany

There is rapidly increasing recognition that neurodegeneration begins years or even decades before clinical diagnosis of Parkinson disease (PD) is currently possible. This recognition has turned recent attention to markers of, and methods for, diagnosis of PD in this preclinical or prodromal phase, and to risk factors for future PD. A diagnosis in the prodromal phase could help affected persons by receiving improved clinical counselling. It could also help the research and industry fields to develop disease-modifying and compensatory therapies. This talk will present the currently available risk factors as well as motor, non-motor, biofluid and imaging markers of preclinical PD. A special emphasis will be given to the respective potential of these markers (i) for accurate population screening for the disease ("enriched risk cohorts"), (ii) to serve as preclinical state markers, and (iii) to serve as preclinical progression markers. Due to the relatively low sensitivity and specificity of all these markers, it is well imaginable that any population-based approach to diagnose PD earlier must consider a panel of preclinical markers and include PD risk factors to improve predictive values.

O78

iPS and PD
*Jun Takahashi**
Center for iPS Cell Research and Application, Kyoto University, Kyoto, Japan

Human induced pluripotent stem cells (iPSCs) can provide a promising source of midbrain dopaminergic (DA) neurons for cell replacement therapy for Parkinson's disease (PD). Towards clinical application of iPSCs, we have developed a method for 1) scalable DA neuron induction on human laminin fragment and 2) sorting DA progenitor cells using a floor plate marker, CORIN. The grafted CORIN+ cells survived well and functioned as midbrain DA neurons in the 6-OHDA-lesioned rats, and showed minimal risk of tumor formation. In addition, we performed a preclinical study using primate PD models. Regarding efficacy, human iPSC-derived DA progenitor cells survived and functioned as midbrain DA neurons in MPTP-treated monkeys. Regarding safety, cells sorted by CORIN did not form any tumors in the brains for at least two years. Finally, MRI and PET imaging was useful to monitor the survival, expansion and function of the grafted cells as well as immune response by the host brain.
Based on these results, we have started a clinical trial to treat PD patients at Kyoto University Hospital in Kyoto, Japan in 2018. This is to evaluate the safety and efficacy of transplanting human iPS cell-derived dopaminergic progenitors into the putamen of PD patients. We will implant approximately 5 million cells to each of 7 patients and observe for 2 years.

O79

State of the art of palliative care in Parkinson's disease: A global perspective
*Victor McConvey**
Parkinson's Victoria, Melbourne, Victoria, Australia

Palliative care has been considered a taboo subject in Parkinson's for many years- while the condition is not currently able to be cured or slowed down, it does not have any life ending symptoms. This combined with the reality that most Palliative care services are geared toward people with a cancer diagnosis, discussing palliative care which was often unavailable became an un necessary conversation.
This paper will explore the rise in demand for palliative care which accommodates the needs of people living with Parkinson's, and how services and the health care professionals with in them are changing respond to this need. We will acknowledge the vast difference in availability of Palliative care from highly sophisticated trans-disciplinary services to a complete absence, and the factors influencing this. This paper will also challenge us to consider that a developing a palliative response to support people with Parkinson's will need resources and thoughtful consideration by both health care professionals and by people living with Parkinson's and their families.

O80

Palliative care in your hands: Advance care planning in parkinsonian disorders
*Roongroj Bhidayasiri**
Chulalongkorn Centre of Excellence for Parkinson's disease & Related Disorders, Bangkok, Thailand

Caring for patients with Parkinson's disease (PD) and other atypical syndromes at the end of their lives is an important role for many health and social care professionals. One of the aspects of this role is to discuss with individuals their preferences regarding the type of care they would wish to receive and where they wish to be cared for in case they lose capacity or are unable to express a preference in the future. These discussions need to be handled with skill and sensitivity. The outcomes of such discussions may then need to be documented, regularly reviewed and communicated to other relevant people, subject to individual's agreement. This is the process of Advance Care Planning (ACP).
As parkinsonian disorders are not conceptualised as a 'terminal illness' by those who involve in the care of such a patient, it remains a challenge for both health and social care professionals to incorporate ACP into daily patient care. Although the European

Association for Palliative Care recommends the adaptation of ACP based on the readiness of the individual and targeting ACP content as the individual's condition worsens, preferences regarding end-of-life discussions amongst parkinsonian patients can vary. Patients in the early stage may consider the discussion about ACP too depressing, hoping that a cure would come in time for them. Very few literature studied the attitudes of PD patients towards ACP. Whilst a recent survey indicated that most PD patients preferred early information on prognosis and treatment, only half of those patients would like to discuss about ACP early and even fewer patients (approx. 20%) prefer early discussions about end-of-life care planning.
ACP is one of the fundamental tenets of palliative care and should be viewed as a process that focuses on patient preferences with physician guidance at that point of time and is likely to evolve as the disease progresses. The approach should be individualised, reflecting positive factors or obstacles that may vary amongst patients and their families. More studies are needed to raise awareness and identify a proper framework to address challenges of incorporating ACP into the care of patients with parkinsonian disorders.

O81

Case studies in palliative care for parkinsonian disorders
*Barry Snow**
Auckland City Hospital, Auckland, New Zealand

The neurodegenerative parkinsonism disorders are progressive, and currently there is no cure. As the neuronal loss progresses, pre-existing symptoms intensify and new symptoms develop. Some of these symptoms respond to levodopa, but many do not and must be managed on their own merits. As the disease progresses, and as the symptoms intensify, quality of life decreases. End of life care has evolved away from the previous cancer model to any disease that is life limiting and requires symptom management. Because the aim is not curative, the goals of care need to be redefined and as much as possible determined by the PWP. Amongst the many potential symptoms, and therefore management possibilities, it is important to move from "What's the matter?" to "What matters to you?" Advance Care planning is a structured approach to helping a person to describe themselves, their goals, their wishes and their needs about end of life care. When an ACP has been developed it can be used as the base for working with the PWP and their family to design best care. This care should be multidisciplinary and pay specific attention to the physical, psychosocial and spiritual domains. Many of the needs of a person with advanced parkinsonism are most expertly managed by palliative care teams. It is important that anxiety about discussing end of life issues do not restrict the PWP's option to access this expert care.

O82

Can we predict falls?
*Colleen Canning**
The University of Sydney, Sydney, Australia

People with Parkinson's disease (PD) fall frequently, with 60% falling annually and two-thirds of these falling recurrently. Given the high prevalence of falls, we need to be able to predict the level of risk, which enables targeted delivery of fall minimization and management strategies. Over 30 risk factors for falls have been identified, but risk factors are not necessarily good predictors in clinical practice. For predictors to be useful in clinical practice they need to be accurate and able to be quickly and efficiently assessed. This presentation will provide an overview of the current evidence for accuracy of falls prediction and identify how this information can be used to minimize falls. The following questions with respect to people with Parkinson's disease will be addressed?
1. What is the accuracy of models predicting one or more falls in the next 6 to 12 months,
   – when individuals who have fallen (fallers) and who have not fallen (non-fallers) in the past year are included?
   – when only individuals who have not fallen (non-fallers) in the past year are included?
2. What is the accuracy of models predicting recurrent or frequent falls in the next 6 to 12 months,
   – when individuals who have fallen (fallers) and who have not fallen (non-fallers) in the past year, are included?
   – when only individuals who have not fallen (non-fallers) in the past year are included?
3. Can model-free machine learning techniques be used to improve accuracy of fall prediction?
4. What is the feasibility of implementing fall prediction models in the clinic?
5. Can technology be used to predict imminent falls in the free-living environment?
Examples will be provided to demonstrate how fall prediction tools can be used to stratify individuals according to level of risk, facilitating strategic assessment and implementation of personalized interventions, targeting remediable risk factors.

O83

Factors that contribute to falls
*Anat Mirelman**
Tel Aviv Medical Center, Tel Aviv, Israel

Falls are a large-scale health and social problem. It is estimated that between 60–80% patients with Parkinson's disease fall at least once a year. For many years, muscle weakness and disturbances in equilibrium were considered the main causes of falls. In recent years, studies have shown that other factors such as cognitive aspects are essential for safe walking. Walking in daily-living environments requires planning, proper organization in the environment, good ability to respond to obstacles, and the ability to perform multiple actions simultaneously. These processes require cognitive resources operating in conjunction with balance and motor function. Motor and cognitive co-dependencies are essential for ambulation and when one or both systems are impacted, this may result in gait impairments and increased fall risk such as in the case of freezing of gait. This talk will review different factors associated with increased fall risk, possible mechanisms underlying increased fall-risk in PD and potential ways to address these.

O84

Solutions to minimize falls
*Lynn Rochester**
Newcastle University, Newcastle upon Tyne, United Kingdom

Historically, falls were seen as a late manifestation of the disease caused by a progression of axial motor problems combined with the effects of aging. Although this is true, falls are not exclusive to older and advanced PD patients. Falls aetiology in people with Parkinson's disease (PD) is complex and multidimensional. Falls are associated with primary features (age, disease severity, gait and balance deficit, cognitive impairment), and secondary features that occur in response to falling (anxiety, reduced self-efficacy, weakness and loss of mobility). Ideally, management of falls risk should begin early and aim to prevent or at least delay the onset of falls. Recognising falls risk as early as possible and understanding

how this may change with increasing disease severity is fundamental, allowing a comprehensive approach to falls risk management. Individual falls risk factors have been identified through extensive studies and reviews and targeted in interventions individually and in combination with varying levels of success. Falls occur when an individual is moving around in the real-world highlighting the dynamic nature of risk and expand opportunities to understand and minimize it. This presentation will solutions to mitigate falls risk from two perspectives: evidence from clinical trials and associated research and practical approaches in the clinic and will be informed by stages of disease severity.

O85

α-synuclein and the immune response in PD
Ashley Harms, Gregory P. Williams*
University of Alabama, Birmingham, Alabama, USA

There is mounting evidence for a central role of the immune system in the pathophysiology of Parkinson's disease (PD), via activation of both the innate and adaptive immune systems. In both human patients and rodent models, α-synuclein pathology is accompanied by microglial activation, T cell infiltration, hyper-reactive monocytes, and increased cytokine and chemokine release. However, the triggers responsible for initiating this immune response and the mechanisms behind peripheral cell recruitment remain poorly understood. In the CNS, antigen presenting cells such as microglia express major histocompatibility complex II (MHCII) proteins that are crucial for the presentation of foreign proteins to CD4+ T lymphocytes, a process that links the innate and adaptive immune response. Genome wide association studies have found that genetic polymorphisms found in the HLA-DR locus, a component of MHCII, are associated with late onset PD, implicating a role for MHCII proteins in disease pathogenesis. In further support, HLA-DR is highly expressed on reactive microglia in PD post-mortem brain, and recent studies have shown that α-synuclein peptides can activate T cells. In our lab, we have used both an in vivo mouse model induced by viral over-expression of α-synuclein as well as in vitro systems to study the role of the MHCII in α-synuclein-induced inflammation and neurodegeneration. We have found that interaction of microglia and CD4 T cells are critical for the neuroinflammatory response in response to α-synuclein, and strategies targeting expression of MHCII are protective, by attenuating neuroinflammation, peripheral immune cell infiltration, and neurodegeneration. The results from these studies indicate that α-synuclein is pro-inflammatory by activating both the innate and adaptive immune system, and that disruption or modulating antigen processing and presentation via targeting MHCII is a neuroprotective and promising therapeutic target for future investigation.

O86

Enhancing clearance of α-syn by immune related cells for neuroprotection
*Nadia Stefanova**
Medical University of Innsbruck, Innsbruck, Austria

Neuroinflammation is a leading feature of the neuropathology in α-synucleinopathies. The innate immune responses in the brain are mostly mediated through microglia. Microglial activation has been evidenced in the brains of patients with Parkinson's disease, dementia with Lewy bodies and multiple system atrophy. Furthermore, microglial activation linked to α-synucleinopathy has been replicated in different experimental models. Experiments show that cytotoxic neuroinflammatory responses may mediate the neurodegeneration in these disorders. However, the possible role of subsets of activated microglia to clear α-synuclein has been proposed. One suggested mechanism of this beneficial action of microglia is mediated through toll-like receptor 4 (TLR4). Furthermore, modulation of microglial responses through the adaptive immune system may provide beneficial control in the handling of pathologic α-synuclein species. Recent advances on targeting α-synuclein clearance through immune mechanisms in α-synucleinopathies will be discussed.

O87

LRRK2 in the immune system
*Nicolas Dzamko**
University of Sydney, Sydney, Australia

Mutations in the leucine-rich repeat kinase (LRRK2) protein were first linked to autosomal dominantly inherited Parkinson's disease (PD) in 2004, and today, LRRK2 is considered the most common genetic contributor to inherited PD. LRRK2 polymorphisms can also increase the risk of developing non-inherited PD, and indeed, LRRK2 has emerged as a potential therapeutic target for the treatment of PD. As well as PD however, LRRK2 polymorphisms have also been linked to an increased risk of developing inflammatory bowel disease, and an increased susceptibility to infection. Thus, there is considerable interest in if/how LRRK2 regulates inflammatory pathways and the extent to which this may contribute to the onset of PD. Work from our group and others have demonstrated a high expression of LRRK2 protein in peripheral immune cells, in particular inflammation-regulating monocytes and neutrophils. We have further demonstrated in these cell types that LRRK2 is linked to the bodies main pathogen response inflammatory pathway, namely the toll-like receptor (TLR) pathway. We have measured circulating inflammatory proteins in serum from patients with and without LRRK2 mutations, and with and without PD, and find higher levels of inflammation in a distinct population of LRRK2 mutation carriers. These results suggest that LRRK2 mutations may potentiate inflammatory responses, and we have recently been able to demonstrate this using induced pluripotent stem cells derived from patients with LRRK2 mutations. Our ongoing work aims to better understand how LRRK2, and in particular emerging LRRK2 therapeutics, modulate inflammation and what this means for PD.

O88

Pain syndromes occurring in Parkinson's disease: Presentations and assessment
*Santiago Perez-Lloret**
Cardiology Research Institute, National Research Council, Buenos Aires, Argentina

Pain affects up 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 type 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. This scale explores the frequency and severity of frequent pain domains: musculoskeletal, chronic, fluctuation-related, nocturnal, oro-facial, discolouration/swelling, and radicular. After assessment of pain characteristics by rating scales, specific diagnostic studies, such as neuroimaging, quantitative sensory testing, evoked potentials, or laboratory tests, may also be necessary in some patients. Clinical characteristics of pain and results from specific diagnostic studies, if available, should then be used to identify the most likely etiology of the pain syndrome, which in turn will guide the choice of the most effective therapeutic strategy.

O89

Treatment approaches and clinical trials for pain in PD
*Beomseok Jeon**
Seoul National University Hospital, Seoul, South Korea

Even though James Parkinson is mainly remembered as describing motor features of Parkinson's disease, most of the non-motor symptoms including pain are clearly included in his "An essay on Shaking Palsy". He recognized that pain can precede motor symptoms, and can be very severe, and shares territory with motor. There have been subsequent descriptions of pain such as by Charcot. However, pain has been largely overlooked by motor symptoms. The first systemic study on pain in PD is ascribed to Snider et al in 1976, where the prevalence was 43%. Epidemiological studies have shown prevalence of pain ranging from 40–83% depending on the population studied and methods employed. There are many classifications of pain. But it is important to recognize that there are several types of pain with different pathomechanisms. Thus management differs according to the pathomechanism. In this presentation, the importance of pain as a main determinant of quality of life will be emphasized, and mechanism-based treatment will be discussed.

O90

Diagnosed with YOPD – Next steps
*Andy McDowell**
PwP, Westmere, New Zealand

Family and friends and work are common enough issues PwP have to deal with but when faced with an early (young) onset diagnosis these issues become magnified.
The implications of no longer be being able to have 'normal' career and working life alone are enormous.
The impact on families with children (or considering), significant.
The pressure Parkinson's puts on relationships, marriages and friendships, huge
Not withstanding the aforementioned reality, or ignoring the emotional rollercoaster that comes with a diagnosis the talk will moot the philosophical proposition of "Keeping calm, and carrying on", but offering the audience some options to consider.

O91

Tips and tricks for maintaining work/life balance
*Rebecca Miller**
New Haven, CT, USA

Becca Miller was diagnosed with YOPD at age 39 when her daughter was 9 months old. As a single mother working full time as a psychologist, she certainly has drawn on some magic or just plain old trickery to try and keep a work-life balance without completely falling flat on her face. She discusses drawing from the concepts of Acceptance and Commitment therapy (Hayes and Wilson, 2003), focusing on values-based living, acceptance of thoughts and circumstances, and drawing upon mindfulness exercises. She also tries to maximize her 'on' times, and share her PD with others to have allies at work who understand. She has improved on asking for help and taking breaks as needed. Letting go of expectations for some things (being the mom who sews doll clothes), delegating other things (housecleaning), and holding tight to certain things (attending the school field trip instead of the meeting), has allowed for some balance.

O92

PD is in the house – Impact on children/teens/young adults
*Elaine Book**
Pacific Parkinson's Research Centre, Vancouver, British Columbia, Canada

This talk will address both the positive and potential negative impact of PD on the family, discussing the common emotions experienced by children/teens/young adults and strategies to maintain family wellness. Ideas and resources to support children as well as the PWP in parenting while living life with a chronic condition.

O93

Living well with young-onset Parkinson's
*Tim Hague**
U-Turn Parkinson's, Winnipeg, Manitoba, Canada

Abstract: 'My goal would be to have all my patients become athletes' Dr. Borys a movement disorders neurologist.
The goal of this session is to provide people living with Parkinson's the tools to understand the mindset of a seasoned athlete in the area of Wellness. We will look at wellness from a holistic viewpoint considering all of its spheres. Exploring the mindset of the traditional athlete we will discover what sets that individual apart and how we can incorporate their thinking into our personal plan of action to live well with Parkinson's disease. Key take always will be learning how to craft your plan of action in living well with Parkinson's; gaining POIS2E as you learn a holistic approach to caring for the whole you, and discovering again the 'secret' hiding in plain sight – wellness – what the research has said all along.
Bio: Tim is a retired nurse of 20+ years who now devotes his time to professional speaking, writing and as founder of the Parkinson's wellness centre, U-Turn Parkinson's. He is the author of the bestselling book Perseverance: The Seven Skills You Need To Survive, Thrive And Accomplish More Than You Ever Imagined. He has spoken for Tedx and is sought after across North America for his motivational and inspiring topics, Live Your Best and The Power of Perseverance. After having been diagnosed with Young Onset Parkinson's disease at the age of 46 Tim and his son went on to win the first season of the reality television series The Amazing Race Canada. He is an outspoken and effective advocate on behalf of people living with Parkinson's around the

world. To learn more about Tim's work visit www.TimSr.ca and www.UTurnParkinsons.org

O94

Inflammation, microbiome and PD: What is all the fuss about?
*Viviane Labrie**
Van Andel Research Institute, Grand Rapids, MI, USA

We now recognize that inflammation is intimately involved in the progressive neurodegeneration occurring in Parkinson's disease. Elevated expression of α-synuclein, a key component of Lewy bodies, has been shown to activate the immune system in the brain and gastrointestinal tract. Furthermore, it has been proposed that Parkinson's disease may initiate in the gastrointestinal tract and illnesses characterized by gut inflammation have been linked to an increased risk for Parkinson's disease. The gut also harbors trillions of bacterial micro-organisms, referred to as the microbiome, which affect brain health and are disrupted in Parkinson's disease. Alterations in the microbiome composition could be a route to excessive immune activation in Parkinson's disease, and conversely, may provide previously unexplored therapeutic avenues. Recent evidence also suggests that Parkinson's disease may also have an autoimmune component involving the erroneous destruction of neurons by trespassing blood immune cells in the brain. The role of inflammation in the periphery and brain in Parkinson's disease suggests that medications that suppress the immune system may be have therapeutic effects. Indeed, recent studies on immunosuppressant medications, as well as immunotherapy targeting α-synuclein, offers hope as a new class of drugs for early disease intervention.

O95

Is there any evidence that nutrients modify PD?
*Laurie Mischley**
Bastyr University, Seattle, WA, USA

We'll review the available laboratory tests to assess nutritional status and discuss why neurologists don't routinely order these tests. The role of diet and PD progression will be discussed and recommendations will be provided for inexpensive, easy-to-prepare, nutrient-dense, plant-based foods that taste delicious. We'll also touch on the potential risks and benefits of of nutritional supplements, as well as the ways they interact with pharmaceutical medicines. Symptom-specific nutrition-based treatment strategies will be discussed for dyskinesia, muscle pain, fatigue, weight loss, cognitive decline, depression, and anxiety.

O96

I have Parkinson's and I care about my genetics: You should too
*Martin Taylor**
Parkinson's Research Advocacy Group, Edinburgh, United Kingdom

There are several known genetic forms of Parkinson's disease, each with their own characteristics in terms of symptomatic presentation and rate of progression. Younger onset people are far more likely to have a genetic form of the condition with Parkin/Pink 1 genetic mutation being very common in those diagnosed under 30. This session will explore the genetics of Parkinson's and the influence it is having on current research and future treatment directions. It will also discuss the personal considerations for someone who wants to participate in genetic testing and the impact it could have both on their personal prognosis and future treatment options.

O97

Gut microbiota: Putting the puzzle together
*Filip Scheperjans**
Helsinki University Hospital, Dept. of Neurology, Helsinki, Finland

Gastrointestinal dysfunction affects up to 80% of PD-patients and may precede the onset of motor symptoms by years. Correspondingly, neurodegenerative changes in the enteric nervous system can be found in earliest stages of PD. The colonic mucosa of PD patients shows an impaired barrier function, inflammation, oxidative stress, and bacterial invasion. An environmental factor likely plays a key role in PD pathogenesis probably against a background of genetic vulnerability. The early involvement of the gastrointestinal tract in PD suggests that this environmental factor exerts its influences primarily via the gut. An initiation of PD pathology in the gut with subsequent spreading to the brain via the vagal nerve is supported by a decreased risk of PD after truncal vagotomy. There is accumulating evidence for an intense bidirectional interaction between gut microbiota and the brain influencing neuronal activity, behavior, as well as levels of neurotransmitter receptors, neurotrophic factors, and neuroinflammation. Pathways involving gut inflammation, amyloid cross-seeding, and short chain fatty acids may directly link gut microbiota and neurodegeneration.
Alterations of gut microbiome composition in PD have been shown in multiple studies suggesting that gut microbiota are related to PD. Best reproduced are decreased abundance of Prevotella and increased abundance of Akkermansia and Lactobacillus in PD. Importantly, decreased Prevotella abundance was also found in a small cohort of subjects with idiopathic REM sleep behavior disorder (iRBD), a prodromal syndrome with high risk of progression to PD. While human studies have only documented an association between the gut microbiome composition and PD, animal studies have recently provided evidence for a causal connection between gut microbiota, α-synuclein pathology, neuroinflammation, and motor impairment.
At this round table we will discuss recent findings regarding the gut-microbiota-brain axis in PD and how this may reshape our understanding of disease etiology and pathogenesis and could lead to new diagnostic and therapeutic approaches. We furthermore shall define the most important open questions and lacks of understanding in this context and identify the next steps that are needed to fill these gaps.

O98

Experimental pharmacological treatments for Parkinson's disease
*Jeff Conn**
Vanderbilt Center for Neuroscience Drug Discovery, Vanderbilt University, Nashville, TN, USA

In this round-table discussion, we will discuss new experimental approaches for treatment of Parkinson;s disease. The focus will be on experimental orally-bioavailable medicines that do not act by replacing loss of dopamine and may provide fundamental advances in care of Parkinson's patients. These include novel approaches to treatment of motor symptoms, treatment of non-motor symptoms, and potential disease-modifying therapies.

O99

The challenge of disease classification – What does it look like and what does it mean

*Rejko Krüger**
Luxembourg Centre for Systems Biomedicine (LCSB), University of Luxembourg and Centre Hospitalier de Luxembourg (CHL), Luxembourg

To date, no causative treatments are available for common neurodegenerative diseases like Parkinson's disease (PD). Previously failed trials did not account for the clinical and pathophysiological heterogeneity of PD, so that novel ways for classification of subgroups of PD patients are needed.
Genetics of PD provided first insight into the complexity of this most common neurodegenerative movement disorder and delineated relevant subgroups of patients, who share an underlying molecular pathology. Here novel patient-based models from genetic forms of PD allowed to dissect mechanisms of neurodegeneration and define a first entry point to screen for disease-modifying compounds for more targeted therapies.
Moreover, during the last years, there has been a rapid evolution in novel technologies, e.g. next generation sequencing technologies or device-assisted registrations of PD symptoms. These are linked with a dramatic increase in high quality data characterizing PD at different levels and enables novel strategies for patient classification and identification of markers for therapeutic outcomes, that can be translated into precision medicine approaches and clinical decision support. Here, first genetic predictors for different therapeutic outcomes emerge for either pharmacological or neuromodulation treatment in PD.
Together the implementation of novel technologies allows not only for novel ways to classify PD, but also for a more direct participation of patients in ongoing research thereby strengthening patient's autonomy and responsibility for future research.

O100

What is α-synuclein and what goes wrong with it in PD

*Jeffrey Kordower**
Rush University Medical Center, Chicago, IL, USA

α synuclein (α-syn) is a protein expressed normally as a monomer in both the peripheral and central nervous system and is involved in a variety of aspects of vesicular trafficking. In PD, as well as other synucleinopathies, α-syn becomes misfolded and renders certain brain regions dysfunctional and when present at high levels can cause neurodegeneration.. Within the nigrostriatal system, we have posited that α-syn pathology initially causes alterations in axonal transport defects. These axonal transport defects cause accumulation of α-syn within the cell soma that initially is cleared via autophagy but then becomes so excessive that lysosomal function is impaired causing further accumulation of misfolded alphas synuclein. We further propose that these changes in PD are an exacerbation of cellular events that occur via normal aging. Lastly, we propose that one of the initiating events following accumulation of misfolded proteins is phenotypic downregulation of dopaminergic markers and not frank cellular degeneration. Lastly the extrusion of α synuclein into the extracellular space either through cellular degeneration of exocytosis is responsible for the prion like transmission of α-syn which may be responsible for disease progression.

O101

LRRK2 as a therapeutic target

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

Mutations and variation in the gene LRRK2 (leucine rich repeat kinase 2) are a common cause of genetically linked Parkinson's disease with varying prevalence across ethnic populations. As mutations lead to enhanced kinase activity of the LRRK2 protein, development of small molecule kinase inhibitors represents a leading therapeutic strategy with at least one company (Denali Therapeutics) in early human testing. Moreover, with the identification of bone fide LRRK2 substrate proteins in the family of Rab GTPases and increased understanding of LRRK2 biology, there may be opportunities for not only expanding treatments targeting the LRRK2 cellular pathway, but also in assessing the benefit of LRRK2-based therapies in more common idiopathic Parkinson's disease.

O102

LRRK2 and Parkinson's

*Mark R. Cookson**
NIH, Laboratory of Neurogenetics, Bethesda, MD, USA

Mutations in the Leucine-rich repeat kinase 2 (LRRK2) gene are a relatively common cause of familial Parkinson's disease (PD). Due to age-dependent but incomplete penetrance, such amino-acid changing mutations also occur in apparently sporadic PD. Furthermore, non-coding variation at the LRRK2 locus influences risk of sporadic PD and several interaction partners of LRRK2 also impart genetic risk for PD. Therefore, LRRK2 plays a critical role in both inherited and sporadic PD and is therefore a likely therapeutic target to inhibit disease progression. However, the biological function(s) of LRRK2 remain unclear. It has been established that several mechanisms can activate LRRK2 kinase activity and that downstream targets include small GTPases of the Rab family. Therefore, LRRK2 plays a critical role in control of membrane associated intracellular trafficking. Potential links to neurodegeneration includes regulation of neuroinflammation and altered neuronal function in several neuronal circuits. The roundtable will discuss each of these aspects of LRRK2 biology with the aim of clearly outlining those aspects of LRRK2 biology that will need to be clarified in the future.

O103

How do you find a good "druggable" candidate in the lab?

*Erwan Bezard**
Institute of Neurodegenerative Diseases, University of Bordeaux, Bordeaux, France

The search for therapies of Parkinson's disease actually covers a number of fundamentally different objectives: either alleviating a given symptom, decreasing the severity of therapy-induced side-effects, or slowing down disease's progression. Although serendipity or drug repositioning have shown great value in proposing treatments, a clear development plan should be envisioned for the systematic educated search of such new therapies. Researchers have first to clearly define what type of solution they aim at developing. The target (i.e. the biological actor on which the researcher wants to act) selection then heavily depends upon the conceptual framework, the current knowledge of the considered pathophysiology, the delicate selection of the most relevant in vitro

and in vivo models, etc... The target validation comes next with a particular emphasis put upon the model selection. A “druggable candidate” should fulfill other criteria such as brain penetrability, target engagement, lack of toxicity, etc... and needs to pass additional screens for paving the way to a successful translation to the clinic.

O104

Stem cell tourism – Why is it dangerous?
*Jonathan Kimmelman**
Biomedical Ethics Unit/McGill University, Montreal, Quebec, Canada

Many clinics around the world market unproven stem cell-based interventions (SCBIs) to patients outside the context of clinical trials or other forms of rigorous evaluation – in many cases with the legal sanction of regulatory authorities. In this round table discussion, I will describe several ethical and policy problems associated with such practices. First, provision of unproven SCBIs to patients outside of clinical trials shifts the costs and burdens of treatment development from drug companies to patients and healthcare systems. Second, such clinics shift the burden associated with medical uncertainty from patients who have undergone a rigorous informed consent process to patients who have not. Third, such clinics often appropriate the simulacrum of scientific authority without its substance- potentially undermining public confidence in serious research activities. Fourth, such clinics erode the ability of methodical research groups to recruit patients to well designed clinical trials- thereby prolonging the clinical development process. Last, such clinics very likely expose patients to more harm than clinical benefit, and often exploit the vulnerability of desperate patients.

O105

Synuclein and its role at the synapse
Robert Edwards, Jacob Bendor*
UCSF School of Medicine, San Francisco, CA, USA

Like many other proteins implicated in neurodegenerative disease, the normal function of α-synuclein has remained poorly understood. Its presynaptic location has suggested a role in neurotransmitter release and over-expression inhibits synaptic vesicle exocytosis. In vitro, synuclein promotes membrane curvature and bending. However, synuclein knockout mice have shown little if any physiological phenotype. During exocytosis, the fusion of secretory vesicles with the plasma membrane establishes a pore that initiates the release of transmitter. Using mice that lack all three synuclein genes, we now find that synuclein normally serves to promote dilation of the fusion pore made by peptidergic large dense core vesicles and synaptic vesicles. In its absence, the vesicles collapse much more slowly than normal. We will discuss the implications for Parkinson’s disease.

O106

Mechanistic insights into GBA1-associated Parkinson’s disease: therapeutic implications
*Dimitri Krainc**
Northwestern University, Chicago, IL, USA

There is an urgent need to identify effective neuroprotective therapies for synucleinopathies such as Parkinson’s disease (PD) and Diffuse Lewy Body Dementia (DLB). Recent emergence of genetic forms of PD has facilitated identification of potential targets for therapeutic development. One of the most promising and extensively studied targets has been lysosomal glucocerebrosidase (GCase) in patients with GBA1-linked PD and DLB. These patients exhibit loss of GCase activity in lysosomes which in turn results in downstream neuronal dysfunction. Therefore, chaperoning and/or direct activation of GCase in lysosomes has been postulated as viable therapeutic strategy. Several ongoing therapeutic efforts have focused on chemical chaperones to promote translocation of mutant GCase to the lysosome. We found that wild-type GCase activity is also reduced in sporadic and genetic forms of PD, suggesting that wild-type GCase could serve as promising therapeutic target in synucleinopathies. Therefore, we explored whether activation of wild-type GCase could enhance lysosomal function and rescue downstream pathological phenotypes in dopaminergic neurons from patients with sporadic and familial forms of PD. We identified GCase activator S-181, which was able to increase the activity of wild-type GCase, and partially ameliorated lipid substrate accumulation, lysosomal dysfunction and dopamine oxidation, in both GBA1-linked and non-GBA1-linked PD patient-derived dopaminergic neurons. Our work thus suggests that rescuing GCase activity is sufficient to improve lysosomal function and to reduce accumulation of toxic oxidized dopamine in midbrain neurons. In turn, decreased accumulation of oxidized dopamine resulted in diminished downstream pathogenic effects, including oxidation-mediated modifications of GCase which disrupt its enzymatic activity. We found that this vicious feedback cycle could be interrupted by targeting wild-type GCase with small molecule activators in human DA neurons. Moreover, our in vivo analysis in mice revealed that S-181 could penetrate CNS and enhance wild-type GCase enzyme activity in brain tissue. In sum, these findings point to the relevance of therapeutically targeting GCase across multiple genetic and sporadic synucleinopathies.

O107

PINK1, Parkin and the ubiquitin system
*Noriyuki Matsuda**
Tokyo Metropolitan Institute of Medical Science, Tokyo, Japan

Parkinson’s disease (PD) is a common movement disorder characterized by dopaminergic neuronal loss. The majority of PD cases are sporadic, however, the discovery of the genes linked to hereditary forms of PD (i.e., hereditary Parkinsonism) has provided important insights into the molecular mechanisms. For example, functional analysis of the recessive familial PD-related genes has revealed that the disease is relevant to mitochondrial quality control. This is consistent with the prior idea that several cases of sporadic and chemical-induced PDs have been associated with mitochondrial dysfunction.
We have focused on PINK1 and PARKIN, responsible genes for hereditary recessive PD. PINK1 and PARKIN encode Ser/Thr kinase and ubiquitin ligase (E3), respectively. We revealed that when the mitochondrial membrane potential decreased, PINK1 phosphorylates ubiquitin at Ser65, and the phosphorylated ubiquitin functions as an activator for E3 function of Parkin (Koyano et al., Nature 2014). Moreover, phosphorylated poly-ubiquitin chain catalyzed by PINK1 recruits Parkin to damaged mitochondria by functioning as a Parkin receptor (Okatsu et al., JCB 2015). Consequently, trio of PINK1, Parkin, and phospho-ubiquitin rapidly tag outer membrane proteins on depolarized mitochondria with ubiquitin. This ubiquitin chain is recognized by RABGEF1, and it directs the downstream Rab proteins, RAB5 and RAB7A, to damaged mitochondria for degradation by lysosome (Yamano et al, eLife 2018). Impairment of this process predisposes to familial PD. Summary of the latest knowledge for relationship between

mitochondrial quality control, ubiquitin, autophagy, and Parkinson's disease will be discussed.

O108

Where are we with clinical trials right now in PD?
*Tom Foltynie**
UCL Institute of Neurology, London, United Kingdom

In this talk, I will discuss an overview of the most important clinical trials in set-up, in progress and recently completed in PD. I will focus predominantly on trials searching for interventions that may modify the course of PD. This will include some discussion of licensed drugs being repurposed for PD, as well as targeted approaches aimed at the PD risk genes and at α synuclein pathology and transmission.

O109

What do the guinea pigs really think?
*Richard Windle**
Porters House, Southampton, United Kingdom

In 2011 I responded to a call for volunteers to take part in a new clinical trial involving a transplant of fetal material into the brain. This was TRANSEURO a project built on earlier work in this field to identify rules for the harvesting and processing of fetal cells. Given the sensitive nature of the work it was of great interest to ethics committees and delays meant that I did not actually receive the implant until September/October, 2015. This was a major operation lasting several hours.
It is important to define the criteria for success. These are usually based on changes in the Unified Parkinson's disease Rating Scale (UPDRS). I was required to attend a meeting at Cambridge lasting 2–3 hours once every three months. This collected all the measures necessary to calculate the UPDRS score (both on and off meds). I was also required to have three PET scans during my involvement with the project.
There are several ways of mounting a clinical trial but the 'gold standard' methodology is known as a double-blind trial where participants are randomly allocated to either a test or a control group. Participants in a clinical trial are given copies of the 'Informed Consent' form, which describe in detail everything that they are committing to. The involvement of patients in research management is considered to be essential. They bring to the table direct experience of the condition.
There are three main factors patients consider when deciding whether to take part in a trial: concerns about taking unproven medicines, possible impact on their current medication and being given a placebo.
At the end of the trial there should be a procedure for participants to feedback observations, good and bad, as to what might have been done differently. This information should be widely disseminated and made available to future studies.
TRANSEURO was always intended to be a long-term study and data are not expected until later in 2019. I feel as if I have bee involved in TRANSEURO as long as I have had Parkinson's. In fact, I have!

O110

Using real-world data as an alternative to clinical trials
*Bas Bloem**
Department of Neurology, Radboud MC, Nijmegen, The Netherlands

The outcome in clinical trials and other research studies typically depends on either patient-completed questionnaires or rating scales of physical signs completed by an observer. These traditional approaches are increasingly criticized, in part because they are time consuming, but in part also because questionnaires are subjective and subject to recall bias, while observer-based rating scales are subject to high degrees of intra- and inter-rater variability. Moreover, both approaches can be time consuming. Finally, both questionnaires and rating scales may offer an incomplete understanding of the patient's actual functioning in their own home situation, particularly over longer periods of time. Therefore, there is an increasing interest to use real-world data, both to improve care in daily clinical practive and also as surrogate outcomes in clinical studies, and perhaps with time, even as novel primary outcomes. Examples include existing large datasets, such as medical claims databases that can be provided by healthcare insurance companies. Other examples include unobtrusive measurements of for example mobility, using either body-worn sensors, smartphones or sensors built into the patients' houses. In my presentation, I will illustrate how the use of such "big data" obtained from real world environment can provide very useful information about the patients actual functioning over time, and how as such these can provide a more accurate perspective on the patients' performance in their own living environment as compared to the more traditional outcomes.

O111

Evaluating and managing sexual dysfunction in PD
*Sharon Hassin-Baer**
Department of Neurology and Sagol Neuroscience Center, Tel-Hashomer, Israel

Patients with Parkinson's disease (PD), both males and females, exhibit an array of nonmotor symptoms of which sexual dysfunction is one that is commonly under-reported and usually left untouched in the patient-neurologist interaction. These sexual dysfunctions include mainly loss of desire, erectile dysfunction, ejaculatory and orgasmic disorders. There are many aspects contributing to sexual dysfunction in PD that encompass physical, psychological, neurobiological and pharmacological areas, and they usually interact and merge and thus become barely distinguishable. Some patients may present with hypersexual behaviors which may cause additional problems in relationship and may lead to adverse consequences.
It is not uncommon that neurologists are not knowledgeable enough and feel uncomfortable to deal with the various sexual complaints; however patient and spousal education and specific interventions may improve patient's sexual life and couple relationship.

O112

Urological dysfunction in PD – What is it and what can be done about it?
*Ryuji Sakakibara**
Neurology, Internal Medicine, Sakura Medical Center, Toho University, Sakura, Japan

Bladder dysfunction is a significant burden in Parkinson's disease (PD), and overactive bladder (urinary urgency/frequency) is the most common. PD patients rarely have large post-void residuals; this is in clear contrast with that in multiple system atrophy patients, who often need clean, intermittent catheterization. Studies have shown that the bladder dysfunction has great significance in relation to quality-of-life measures, early institutionalization, and health economics. Bladder dysfunction in PD usually starts with or just after the onset of motor disorder; this is in clear contrast to

gastrointestinal (GI) dysfunction that precedes motor disorder for decades. Urodynamic measurement common shows bladder overactivity, which may reflect the central nervous system (CNS) pathology; this is in clear contrast to GI dysfunction that mostly reflects the peripheral myenteric pathology. The CNS pathology for bladder dysfunction in PD are thought to be: disturbed prefrontal-D1 dopaminergic direct pathway that normally suppress the spino-bulbo-spinal micturition reflex. This is documented by functional neuroimaging as well as experimental studies. Dopaminergic drugs have presumable biphasic effects on PD bladder, i.e., initial worsening (hours) but late improving (weeks/months). Deep brain stimulation in the subthalamic nucleus improves PD bladder. If these are not working, addition of anticholinergic agents and possibly beta-3 adrenergic receptor agonists are the choice to that do not easily penetrate the blood-brain barrier, in order to avoid cognitive adverse events. The International Continence Society (ICS) Guideline is a good reference for all doctors and nurses to manage such patients. These treatments are beneficial in maximizing patients' non-motor quality of life.

O113

Can we predict falls in PD?

*Lynn Rochester**
Newcastle University, Newcastle upon Tyne, United Kingdom

Falls are ubiquitous in Parkinson's. Managing falls risk presents us with multiple challenges. To date, the strongest predictor of a future fall is a prior fall, and clinical fall assessment is typically triggered when falls are established and not prior to their occurrence. Although pragmatic, this approach is limited and important to recognise because effective falls management becomes more challenging when secondary features are established. Recognising falls risk as early as possible and understanding how this may change with increasing disease severity is fundamental, allowing a comprehensive approach to falls risk management. Individual falls risk factors have been identified through extensive studies and reviews and targeted in interventions individually and in combination with varying levels of success. Falls risk also changes dynamically depending upon contextual, personal and environmental factors. Understanding the static and dynamic nature of falls risk is therefore important. Exposure to risk – in terms of the amount of time an individual is active and mobile remains a poorly understood area. Finally, classification schemes that group fallers into a single or recurrent faller provide limited information that misses important contextual and dynamic characteristics. This presentation aims to provide an overview of current knowledge of falls risk, drawing from a novel longitudinal falls data set in an incident cohort study (ICICLE) and other studies. It will highlight the natural history of falls evolution, consider falls risk factors within a dynamic model of falls risk and a contemporary approach to categorise falls and fallers, and, finally the evidence to mitigate risk will be considered.

O114

Facial masking and drooling: The impact on communication, social interaction, and swallowing

*Hanneke Kalf**
Radboud University Medical Center, Nijmegen, The Netherlands

Hypomimia or facial masking is a manifestation of hypokinesia, one of the main motor consequences of Parkinson's disease. Although is a known phenomenon, only recently the consequences for people's wellbeing have become the focus of scientific research. Facial masking can be easily confused with negative effect or with change in cognitive status. Also when the masking is not recognized as being part of the disease, it may hamper interpersonal relationships. There is growing evidence that hypomimia indeed can have a negative impact on socialization and social wellbeing, suggesting a strong need for education.
Another consequence in severe hypomimia may be that people have their mouth open for longer periods of time, which is a risk for drooling of saliva, in particular when attention is distracted.
This presentation will provide an overview of results from recent studies on hypomimia and its consequences including options for support for people with Parkinson's and caregivers.

O115

Early management of swallowing disorders: Can we prevent aspiration pneumonia?

*Corinne Jones**
University of Texas, Austin, Texas, USA

Aspiration pneumonia is considered a leading cause of death in Parkinson's disease and is closely linked with the high prevalence of swallowing disorders (or dysphagia) in this population. Additionally, disordered cough has been found to co-exist with dysphagia in patients with PD. Therefore, management of swallowing and cough dysfunction in patients with parkinsonism is of utmost clinical importance. Speech-language pathologists play a critical role in the early identification, assessment and management of these disorders. The goal of this talk is to discuss the methods for assessment and management of swallowing and cough disorders in patients with PD for the prevention of aspiration pneumonia.

O116

Experimental pharmacological treatments for Parkinson's disease

*Jeff Conn**
Vanderbilt Center for Neuroscience Drug Discovery, Vanderbilt University, Nashville, TN, USA

Dopamine replacement therapies, including the dopamine precursor levodopa (L-DOPA) and dopamine receptor agonists are the primary pharmacological agents used for symptomatic treatment of Parkinson's disease (PD). While these treatments provide relief of motor symptoms for several years in most patients, motor complications and psychiatric side effects develop in a subset of individuals, and end-of-dose "wearing off" of the drug effects limits their long-term efficacy. Furthermore, dopamine replacement therapies do not reduce all motor symptoms and are without efficacy in reducing non-motor symptoms in PD patients. Finally, currently available medicines do not reduce progression of PD. In recent years, multiple novel pharmacological approaches for treatment of PD have emerged that have potential for filling these gaps in treatment of this disorder. For instance, we have identified a specific subtype of metabotropic glutamate (mGlu) receptor, termed mGlu4, as an exciting new target for treatment of Parkinson's disease. Activation of mGlu4 reduces excessive transmission at a specific synapse in the "indirect pathway" of the basal ganglia motor circuit, where activity is pathologically increased in Parkinson's patients. Novel positive allosteric modulators (PAMs) of mGlu4 improve motor function in rodent and non-human primate models of parkinsonian motor disability. In addition, mGlu4 PAMs can reduce death of dopamine neurons in toxin-based models of dopamine neuron death. We and others have now optimized highly selective mGlu4 PAMs that are advancing in preclinical and clinical development for future evaluation in clinical studies in patients suffering from PD. In addition, we and others have developed other novel approaches that may be useful in reducing tremor, reducing L-

DOPA-induced dyskinesia, and in some cases, may slow disease progression. These new efforts have the potential to provide new medicines that could lead to fundamental improvements in the standard of care of PD patients.

O117

New insights into L-Dopa induced dyskinesias

*Barbara Picconi**
IRCCS San Raffaele Pisana, and University San Raffaele, Rome, Italy

Levodopa-induced dyskinesias (LIDs) represent the major motor disability associated with chronic therapy in Parkinson's disease (PD) patients. Unfortunately, to date, the first events driving the dopaminergic neurodegeneration is unknown and the only therapeutic tool in the hands of the clinicians is the chronic treatment with levodopa and dopaminergic agonists. The long-term treatment with this dopamine precursor does not arrest the progressive neuronal degeneration of mesencephalic area. The abnormal activation of striato-pallidal direct pathway, and the concomitant downregulation of the indirect pathway's activity, lead to a complex pattern of basal ganglia/cortical alterations that give rise to the characteristic uncontrollable dystonic and dyskinetic manifestations of LIDs. Although the incidence of these motor complications in chronically treated patients is impressive, this drug is still considered the gold-standard symptomatic therapy. The main goal of both preclinical and clinical research studies is to find the neuronal and molecular mechanisms causing LIDs and to delineate a therapeutic approach allowing anti-parkinsonian effects with a lower incidence of dyskinetic features. For this reason, experimental animal models provide useful tools in exploring the potential of different pharmacological approaches.
The present talk will present the latest pathophysiologic approaches aimed at providing the rationale for currently available as well as for emerging treatments of this disabling effect associated to dopamine-replacement therapy adverse. The presentation will go deeper through some recent molecular and synaptic studies, performed in experimental models of LIDs, to end with the therapeutic outcomes emerged from these pre-clinical studies.

O118

Mechanisms underlying impulsive behaviors and addictions in Parkinson's disease

*Christelle Baunez**
Institut de Neurosciences de la Timone, UMR7289 CNRS & Aix-Marseille Université, Marseille, France

Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is now widely used as a treament for Parkinson's disease. Understanding the effects of manipulations of the STN or its abnormal oscillatory activities is therefore important to better understand and possibly anticipate side-effects of this surgical treatment. We have thus studied the activity of STN and the impact of STN lesions or DBS on various forms of impulsivity in rats, but also in Parkinsonian patients. We have shown that the STN is part of a brain circuit involved in the control of inhibition, a process that is dysfunctional in impulsive disorders. Since addiction can be seen as a form of impulsive behavior, we have also assessed the effects of STN manipulations in the context of addiction. Our rats studies suggest that STN inactivation could serve as a possible therapeutical tool to treat addiction. We have confirmed this in the monkey. In Parkinsonian patients suffering from addiction to their levodopa treatment (dopamine dysregulation syndrom), STN DBS has proven to be beneficial to reduce this form of impulse control, but also other impulse control disorders.

O119

The role of genetics in increasing our understanding of the pathophysiology of PD

*John Hardy**
UCL Institute of Neurology, London, United Kingdom

As we analyse the genetics of the late onset neurodegenerative diseases, we are finding that many of the genes involved are either directly or indirectly involved in damage repair. I will give examples from other diseases. In late onset Parkinson's disease we are finding genes involved in the control of lysosome function and in inflammatory pathways. Heterozygosity for lysosome storage diseases, most famously GBA, but also other LSD genes is one factor and LRRK2's seems to function as a controller of lysosome metabolism. Work from several groups shows that synuclein is metabolised through the lysosome leaving open the idea that it's deposition is a result of a lysosome insufficiency. I will discuss these issues and make the suggestion that two ways of treating PD could be either via reducing the substrate through, antibody or antisense approaches or through potentiating lysosome function. In early onset Parkinson's disease, the dominant pathways are those involved in mitophagy, the removal of damaged mitochondria. I will argue that these may specifically affect the migrant because of the oxidative damage inherent in dopamine metabolism and discuss what this may mean for therapeutic interventions in this form of the disease.

O120

Genetic testing in PD – What is possible and why is it important?

*Vincenzo Bonifati**
Erasmus MC, University Medical Center Rotterdam, Dept. Clinical Genetics, Rotterdam, The Netherlands

Several laboratory methods are available for the detection of DNA variants. Small sequence variants (single nucleotide substitutions, or small insertions/deletions) are detectable by DNA sequencing methods (such as classical Sanger methods, or next-generation sequencing). These methods might be employed to study single small DNA fragments in candidate genes, or entire coding regions of one gene or sets of genes (gene panels), or the entire coding region of the human genome (exome sequencing), or even for whole-genome sequencing.
Other types of variants, such as large genomic deletions or multiplications are more easily detected by different methods (copy-number assays, such as qPCR or SNP-arrays). Each of these techniques has advantages and disadvantages, and the strategy of choice will depend on different factors, among which, the available resources, the number of candidate genes, and number and types of variants to expect.
With the exception of some populations, only a small minority of cases of PD are caused by known mutations in single genes. Moreover, no specific treatment is currently available for PD, based on a specific genetic etiology. While this situation might change in the future, still, at the moment genetic testing remains useful in order to provide accurate etiological diagnosis, and to offer patients and family members proper counseling about the risk to unaffected relatives, and disease course. The recommendations for the diagnosis of PD, issued by a task force of the EFNS/MDS-ES, also discussed genetic testing (Eur J Neurol 2013; 20:16–34).

The attitudes of PD patients towards clinical genetic testing remains poorly explored. The final decision of whether to perform genetic testing for PD for diagnostic or predictive purposes should be taken by the subject involved, after proper information about the advantages and disadvantages of such testing. The results of diagnostic genetic testing performed in a patient might have consequences for the entire family. Due to the potential implications in the psychological, social, and professional domains for both patients and relatives, the genetic testing for diagnostic, and especially for predictive purposes, should be performed by a professional team, including neurologists, genetic counselors, and psychologists. The procedure should always include pre-test and post-test counseling.

O121

Ethical and legal aspects of genetic testing in PD

*Yann Joly**
Centre of Genomics and Policy – McGill University, Montréal, Quebec, Canada

Parkinson's disease (PD) involves both genetic and environmental factors. Thus, it appears to be a multifactorial disease in the majority of patients. Having a positive family history for PD is one of the strongest risk factors for the disease, highlighting the importance of genetic factors. While our knowledge of the genetics of PD is rapidly expending, there remains significant uncertainty as to when clinical genetic testing for some of the more known mutations is appropriate. Beyond the scientific validity and clinical utility of such tests, concerns about the social and ethical implications of the results add to ambiguity. To provide some clarification on this last point, this presentation will critically review the major social, ethical and legal concerns associated with genetic testing for mutations associated with PD. These concerns include unnecessary psychological distress, potential stigmatization/discrimination, interpretation of tests of asymptomatic individuals obtained in the context of DTC-GT, etc. The complex, probabilistic nature of PD genetic results suggests that testing should be strongly discouraged when there are no preventive measures or effective neuroprotective treatments. However, in rare instances where the test is warranted (or if taken in a context of DTC-GT), awareness of and proactive action against the social and ethical issues we discuss will be very beneficial for patients, at risk individuals, and clinicians.

O122

Dance as exercise for Parkinson's disease

*Meg Morris**
La Trobe University, Bundoora, Victoria, Australia

Movement disorders are a debilitating feature of Parkinson's disease, for which there is no current cure. There is growing evidence that intensive exercise and physical activity has the potential to slow the rate of disease progression in some individuals. Knowing which sort of exercise to do, and for how long, is a key question faced by the PD community. There are now many randomized controlled trials of exercise, physical activity and physiotherapy for people with PD (eg. Canning et al., 2015; Maidan et al 2018; Morris et al., 2015, 2017; Prodoehl et al., 2015; Shanahan et al., 2017; Schenkman et al 2018). These show the importance of regular, high intensity physical activity and falls prevention education. It can be argued that people with mild-moderate PD should exercise at moderate to high intensity for a minimum of 30 minutes per day. Given that PD can span up to 25 years, there is a need to find a diverse range of evidence-based physical activities that are engaging and enjoyable so that exercise is sustained over the long term. Dancing is one such form of exercise (Shanahan et al., 2017). This presentation critical evaluates recent research on the evidence for dance as exercise for people living with Parkinson's disease.

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O123

The effects of music on the brain

*Jeanette Tamplin**
The University of Melbourne, Melbourne, Victoria, Australia

Music participation can literally change brain structure and function. Research with healthy participants has shown improved neural connectivity and increased cerebral blood flow following just listening to music. Active music engagement (eg. singing or playing music) promotes neural plasticity and can induce grey and white matter changes in multiple brain regions. In music therapy and other therapeutic approaches using music, we utilise this enriching effect of music on the brain in therapeutic interventions for people with neurological conditions.

For people with Parkinson's rhythmic music can help compensate for impaired internal timing mechanisms. External musical rhythms can be used to stimulate and entrain movement by activating the neural circuits involved in motor actions. This external cueing provided by music explains the positive effects of rhythmic auditory stimulation and dancing interventions for people with Parkinson's. The repetitive and coordinated movement patterns stimulated by active music interventions (combined with auditory feedback and extensive cognitive processing) can stimulate structural and functional neuroplastic changes in the brain.

Singing is an engaging and enjoyable way to exercise and strengthen the respiratory and speech systems. When we sing, we use more air than when we speak. This is because singing requires greater lung volumes excursions, and higher expiratory and subglottic air pressures. Singing also makes us feel better and group singing can increase feelings of social connectedness.

Music activates the reward, arousal and emotion networks in the brain. Specifically, music stimulates the release of dopamine, oxytocin, melatonin, and endorphins, and lowers cortisol levels. These neurochemical and hormonal changes positively affect memory, attention, executive functions, mood, motivation, and stress. These positive changes may also enhance recovery of cognitive functions.

In this presentation Dr Tamplin will provide an overview of current research in the areas of music neuroscience, music psychology and music therapy in neurorehabilitation. She will present video footage to demonstrate a number of unique techniques used by music therapists in rehabilitation more broadly, but also specifically in

Parkinson's treatment. A summary of the positive results from a recent Australian pilot study on singing-based therapy (ParkinSong) for communication and wellbeing in Parkinson's will also be presented.

O124

Why partnered dance might optimize motor and cognitive rehabilitation in Parkinson's

*Madeleine Hackney**
Emory University, Atlanta, GA, USA

To address PD-related dementias, researchers and clinicians constantly seek to improve cognitive rehabilitation. As a result, many studies are beginning to examine the combination of physical and cognitive training delivered simultaneously or in close serial fashion (e.g., stationary bicycling while also completing computerized cognitive training on a screen). In keeping with animal literature, rehabilitation offering a combination of physical and cognitive challenges may be most effective in inducing beneficial, lasting effects on the brain's structure and function. Evidence suggests that cognitive elements of dance are a cogent vehicle for delivering cognitive rehabilitation. Dance has been shown to improve spatial cognition in people with PD, likely because dance requires participants to learn, memorize, recall, use, and be cognizant of spatial postures, relationships, patterns, and paths. Dance, through imagery and creative movement, engages other cognitive processes, which may act as cognitive rehabilitation. These cognitive domains include attention/working memory, executive function, memory, and language, as well as musical beat detection and interpretation. Dance requires: attention to partner (the next step), storage and of new steps from memory, detection and interpretation of musical beats, coordination of body and movement with external musical source and partner; use of working memory via learning and practicing steps, and language via a new vocabulary for a dance context and the abstract concept of combining steps into phrases, i.e. holding 'conversations' with partners via non-verbal communication. Spatial function may improve from dance given its central role and considering that cardiovascular fitness modulates brain activation associated with spatial learning. Partnered dance, such as Argentine Tango, or the adapted form designed for people with PD, represents a physical training framework that integrates fundamental physical and cognitive function. Involving human-human interaction that uniquely stimulates the tactile sensory system, partnered dance can serve as a model for investigating the interplay between haptic feedback (the tactile sensory system), cognition, and motor control. With respect to the partnered dance model, human-human interactions are uniquely and non-verbally expressed via pressure and contact at the arms or torso between a leader (determining timing, amplitude and direction of choreography) and a follower (detecting and responding to the messages conveyed by leader.

O125

Palliative care is in your hands

*Roongroj Bhidayasiri**
Chulalongkorn Centre of Excellence for Parkinson's disease & Related Disorders, Bangkok, Thailand

The area of advance care planning (ACP) plays an increasingly important role in the management of parkinsonian patients, particularly in the advanced stage. However, many health and social care professionals may be unfamiliar with this area despite their involvement in the management of these patients. ACP should be viewed as a process, requiring a multidisciplinary approach to focus on patient preferences and, as such, it should be handled with skill and sensitivity. During this roundtable, we will discuss on the principles of ACP, the key issues and challenges of incorporating ACP into the care of patients with Parkinson's disease and atypical disorders. Case examples with scenarios that we commonly encounter in clinical practices will be presented and shared to stimulate the discussions during this session.

O126

iPS cells and PD – What does this mean in 2019?

*Jun Takahashi**
Center for iPS Cell Research and Application, Kyoto, Japan

Human induced pluripotent stem cells (iPSCs) can provide a promising source of midbrain dopaminergic (DA) neurons for cell replacement therapy for Parkinson's disease (PD). Towards clinical application of iPSCs, we have developed a method for 1) scalable DA neuron induction on human laminin fragment and 2) sorting DA progenitor cells using a floor plate marker, CORIN. The grafted CORIN+ cells survived well and functioned as midbrain DA neurons in the 6-OHDA-lesioned rats, and showed minimal risk of tumor formation. In addition, we performed a preclinical study using primate PD models. Regarding efficacy, human iPSC-derived DA progenitor cells survived and functioned as midbrain DA neurons in MPTP-treated monkeys. Regarding safety, cells sorted by CORIN did not form any tumors in the brains for at least two years. Finally, MRI and PET imaging was useful to monitor the survival, expansion and function of the grafted cells as well as immune response by the host brain.
Based on these results, we have started a clinical trial to treat PD patients at Kyoto University Hospital in Kyoto, Japan in 2018. This is to evaluate the safety and efficacy of transplanting human iPS cell-derived dopaminergic progenitors into the putamen of PD patients. We will implant approximately 5 million cells to each of 7 patients and observe for 2 years.

O127

Predicting who will get Parkinson's disease

*Isabelle Arnulf**
Sorbonne University, Paris, France

Numerous premotor markers of PD have been identified, the most specific being REM sleep behavior disorder (RBD), whereas sleepiness and constipation are less specific. The rate of conversion from RBD to PD and dementia with Lewy bodies is greater than 80%, with a median conversion rate of 6–7 years across countries. Several genetic and environmental factors have been associated with idiopathic RBD, and the lesion responsible for RBD in the pons has been identified using 3T melanin-sensitive MRI. Familial RBD cases, which are around 4 times more frequent than in controls, have led to research on genetic predisposition to RBD, with a specific role of GBA mutation and several polymorphisms associated with RBD. In addition, very mild motor, cognitive, autonomic (constipation, orthostatic hypotension), sensory (olfaction, color vision) and psychiatric symptoms, as well as the DAT scan abnormalities are observed in patients with idiopathic RBD. Each of them predict a different speed of conversion from RBD diagnosis to onset of motor disorders. Eventually, the strong association of RBD with PD (and the rarity of diagnosed idiopathic RBD cases) highlights the importance of detecting RBD, referring patients to reference center for counseling them, implementing research and inclusion in neuroprotective trials.

O128

Shining a light on Parkinson's: Optogenetic modulation of basal ganglia activity
*Stella Papa**
Emory Universtiy, Atlanta, GA, USA

Optogenetics has been used to study the function of basal ganglia circuits in animal models of Parkinson's disease (PD). This technology provides a means to express opsins in specific cell populations to make them responsive to illumination and thereby study their specific function or dysfunction. In primate models of PD, there is close resemblance of motor symptoms to the human disease, and this allows us to study the specific relationship between dysfunctional circuits and particular motor abnormalities. Optogenetic modulation of striatal projection neurons in parkinsonian monkeys is generating novel data to understand the abnormalities that are specific to indirect and direct striatal output pathways, particularly in states of advanced parkinsonism. In addition, optogenetically identified striatal neurons display a particular response to dopamine modulation that can undergo a significant adjustment during the evolution of PD. These mechanisms are responsible for abnormal responses to dopamine and loss of dopamine efficacy to restore normal motor function in the late-stage disease. Ongoing studies are also focused on testing the optogenetic manipulation of specific circuits downstream the striatum to influence the basal ganglia output for the treatment of parkinsonian motor deficits. This research is making significant progress towards a better understanding of pathophysiologic mechanisms and potentially to developing new therapeutic strategies. Current work on shining a light in the parkinsonian brain may reveal a new therapeutic avenue to improve mobility in patients with PD.

O129

Treatment approaches and clinical trials for pain in PD
*Beomseok Jeon**
National University Hospital, Seoul, South Korea

1. Discuss types of pain in Parkinson disease and pathomechanism
2. Review of epidemiology of pain in PD
3. Discuss impact of pain on quality of life
4. Review therapies for pain in PD
5. Review clinical trials

O130

The heterogeneity of Parkinson's disease – What does it mean and why is it important
*Connie Marras**
University of Toronto, Toronto, Ontario, Canada

Clinical heterogeneity in Parkinson's disease is well known and obvious to even casual observers. No two patients are exactly alike. This heterogeneity may reflect differences at various levels upstream; etiologic differences between patients, including environmental and genetic differences or different pathogenetic processes. The relationship between the clinical heterogeneity and the underlying etiologic and pathologic processes is not well understood. Understanding these relationships is important, however, because the heterogeneity may present opportunities to tailor our clinical treatment at the individual level or to refine our research designs to study more homogeneous subsets of patients. This round table will explore these issues, discussing what the heterogeneity of Parkinson's disease can tell us and what can be done with what we learn from it.

O131

Maintaining balance and optimism when working and raising children with young onset PD
*Rebecca Miller**
New Haven, CT, USA

Is balance really ever a thing as a parent, even without PD? As a person with YOPD, I sometimes have to try harder to keep my balance! I am a single mom to a 6 year old, and happy to share my experiences, ups, downs and in-betweens of navigating parenting, work, and life with YOPD, sometimes with a hitch in my step but always trying to keep moving. Letting others know about my condition and keeping things as regular as I can for my daughter are two things I focus upon. Accepting help and keeping a broad circle of friends is important. I am lucky to have supportive family and friends who jump in when they can to give me some time on my own. And maximizing what I do for work is important; not taking on too much, and focusing best I can on those things most important to keeping up at my job. And having PD friends who are up at 3am like me and can chat about parenting and life. I look forward to connecting with others about how to strategize, raise healthy kids, and keep ourselves from falling over too often!

O132

Parkinson's and the gut microbiome
*Haydeh Payami**
University of Alabama, Birmingham, AL, USA

The gut microbiome refers to the collective genomes of the tens of trillions of microorganisms that live in the human gut. A well-balanced microbiome is essential to human health. The microorganisms in the gut shape and maintain the immune system, mediate the biochemical signaling between the gastrointestinal tract and the central nervous system, help digest food and produce vitamins, and metabolize drugs and degrade toxins. Dysbiosis of the gut microbiome has been noted in many disorders, including PD. Dysbiosis of gut microbiome in PD is particularly relevant considering several well-established links between the gut and PD: Gastrointestinal symptoms (e.g., constipation) often precede the motor signs of PD. There is inflammation in the gut. The lining of the gut shows increased permeability. Vagotomy decreases the incidence of PD. Lewy bodies and α-synuclein appear in the gut before they appear in the brain. These new lines of evidence support Braak's hypothesis that non-inherited forms of PD are caused by an as yet unidentified pathogen that can pass through the mucosal barrier of the gastrointestinal track and spread to the brain through the enteric nervous system. If true, the gut microbiome may reveal the pathogens of the Braak hypothesis. Another important aspect of gut microbiome is its impact on the treatment of PD. It has already been shown that microorganism in the gut can have a profound effect on response to L-dopa. There is great anticipation that the microbiome research will fill many of the gaps in our current knowledge about how PD starts and progresses, that it will give us new biomarkers, and may even yield new treatments. But will it? Microbiome research in PD is just getting started: early findings are promising but nowhere near conclusive yet.

O133

Measuring gut function in PD
*Kathleen Shannon**
University of Wisconsin School of Medicine and Public Health, Madison, WI, USA

Complaints related to abnormal gut function are nearly universal in PD. Most relate to decreased motility, related to changes in the neurons in the intestinal wall. These include drooling, swallowing disorders, dyspepsia, nausea, bloating, constipation and difficulty with stool elimination. Some of these complaints may predate the diagnosis of PD. This altered motility also predisposes to changes in the intestinal bacterial populations, and to immune activation in the gut. However, there is not a good correlation between individual symptoms and specific intestinal changes. A number of diagnostic tools may help elucidate the intestinal abnormalities that underlie intestinal complaints. These include swallowed wireless capsules that collect data on the intestinal environment and transit time, devices that can record changes in pressure associated with defecation, chemical breath tests that show changes related to bacterial overgrowth, and imaging studies that assess the integrity of the intestinal nervous system. Better understanding the causes of these symptoms may help target specific therapeutic strategies including dietary changes, drugs that increase motility, laxatives, and antibiotics.

O134

Is inflammation important in PD?
*David Standaert**
University of Alabama, Birmingham, Alabama, USA

Inflammation and activation of the immune system are increasing recognized as important factors in Parkinson disease. This roundtable will discuss how inflammation may participate in the cause and/or progression of Parkinson disease, and how research in this area may lead to novel approaches to treatment.

O135

New causative genes for PD
*Alexis Brice**
ICM – Institut du Cerveau et de la moelle épinière/Brain and Spine Institute, Paris, France

Many genes have already been identified and validated in monogenic forms of PD. However, for several of them, particularly the most recent ones, suggestive but not definite genetic evidence is provided. So far, most genes involved in PD have been identified using exome sequencing in multiplex families in which the causal variant segregates with the disease. Usually additional families are tested for replication. There are, however, limitations to this approach : i) co-segregation is not always observed because of phenocopies, ii) it is difficult to predict the pathogenicity of variants, particularly missense mutations, despite criteria based on frequency and the use of predictive algorithms, iii) new genes are often rare or limited to a given population and replication in other families is not always obtained. These factors may explain why certain candidate genes are not replicated in follow-up studies casting doubt about their pathogenicity. Often functional data, obtained mostly in cell systems or small organisms, demonstrate that one or several mutations identified modify the function of the gene product in this context. Again, it remains difficult to extrapolate to the human condition based only on such data which provides only indirect evidence. Although it is not difficult to find coding variants in familial PD, it remains much more difficult to provide strong evidence of their causal relationship with PD.

O136

Is there a Parkinson's diet?
*Karin Overbeek**
ParkinsonNet The Netherlands, Nijmegen, Gelderland, The Netherlands

What we eat and drink has a big influence on how we feel physically and mentally. This is also valid for patients with Parkinson's disease. Patients want to know how they can do more self-management. Professionals want to get to know the diet related problems for patients with Parkinson's disease and want to get tools for good treatment.
In this presentation, we will focus on (1) the most important recommendations for patients in relation to their diets, (2) how can patients improve their self-management regarding diets and (3) what are criteria for referral to dieticians with expertise in Parkinson's.

O137

Your radical new life: Creative ways to overcome our challenges
*Heather Kennedy**
Kathleenkiddo.com, Oakland, CA, USA

Forget everything you knew about health and living well prior to diagnosis. Our bodies are slowly becoming cages, and there is no time to waste. The grief accompanying the constant loss of a progressive and degenerative disease strips us of coping mechanisms, masks of comfort and shelter and the physical strength required to function. Despite our best efforts, absolutely everything is in a constant state of dissolving and demolition. To survive and thrive, we must develop and expand a radical form of compassion, and learn to develop a completely new ways of living. I'll be exploring the outrageous unpredictability and ruthlessness of our condition, with ideas on how to find joy and pleasure, even when we feel defeated and exhausted. We've got to find a way to be comfortable with uncertainty, and loss- beginning with loss of smell and changes in gut mitochondria

O138

Overview of peripheral (non-brain/CNS) abnormalities in PD
*Jeffrey Kordower**
Rush University Medical Center, Chicago, IL, USA

In recent years it has become quite clear that Parkinson's disease affects the periphery as well as the central nervous system and in fact the changes in the periphery may precede those in the brain and serve as a nidus of disease transmission. Furthermore, certain symptoms such as constipation clearly affect the quality of life of PD suffers and clearly originates in the GI tract. This lecture will examine many of the peripheral aspects of disease pathogenesis in PD. Inclusive of this topic is 1) the dual hit hypothesis of Braak and Braak; 2) the pattern of α synuclein pathology in different structures of peripheral organs; 3) the controversy of colonic and α synuclein as a biomarker for PD and an assessment of other peripheral organs that might serve as the same. Furthermore, the concept that aggregated α synuclein in the periphery may serve as site of initial pathology that then spreads to the brain in a prion like fashion will be discussed. Finally, the role of inflammation and subsequent

alterations in the microbiome and its role in PD pathogenesis will. be discussed.

O139

Does PD start outside the brain?

*Per Borghammer**
Department of Nuclear Medicine & PET Centre, Aarhus University Hospital, Aarhus, Denmark

Parkinson's disease (PD) is a multi-system disorder with involvement of the central & peripheral nervous systems. Misfolding and aggregation of the protein α-synuclein (Lewy pathology) is central to the pathogenesis of PD. It has been postulated that PD in some cases may originate in olfactory and gastrointestinal nerve terminals and spread to the CNS via the autonomic nervous system. A prion-like behavior of α-synuclein has been convincingly demonstrated in vitro and in animal models of PD.
Lewy-type pathology have been detected in the gut many years prior to PD diagnosis. Two independent epidemiological studies have suggested that truncal vagotomy may be protective against the disorder. In vivo imaging studies of patients with REM sleep behavior disorder have shown that these prodromal patients display severe damage to the autonomic nervous system (equal to diagnosed PD patients), while their dopamine system is still relatively intact. In addition, recent studies have implicated the gut microbiome in PD pathogenesis, and α-synuclein may serve a role as an immune system defence mechanism preventing neuroinvasive viruses from accessing the brain.
This talk will summarize the current evidence for and against the hypothesis that PD may start in the gut.

O140

Managing the peripheral problems in PD

*Shen Yang Lim**
Division of Neurology, University of Malaya, Kuala Lumpur, Malaysia

Many symptoms experienced by patients with Parkinson's disease (PD) have their origin outside of the brain, as discussed by previous speakers in this session.
Medication control of PD motor symptoms can be significantly impacted by the occurrence of gastroparesis, which results in impaired absorption of levodopa, with reduced efficacy of treatment, and delayed or no-ON in patients with motor fluctuations. A variety of methods can be used to counter this problem, including modification of the levodopa preparation; and use of gastrokinetic agents (e.g., domperidone), non-oral routes (e.g., transdermal rotigotine), and device-aided therapies.
Important motor features such as imbalance may be contributed by peripheral neuropathy, which has been documented in a substantial proportion of patients. It has been postulated that this may be due to levodopa therapy causing a functional deficiency of vitamin B12 and high levels of homocysteine and methylmalonic acid. Research suggests that these factors (low B12 and elevated homocysteine) may be associated with greater motor and cognitive worsening. However, whether nutritional modification is helpful remains to be determined.
Many PD non-motor symptoms have their basis, at least partially, in dysfunction of peripheral organs, for example, autonomic features (orthostatic hypotension [OH], constipation, overactive bladder [OAB], drooling), sleep-related disorders (e.g., restless legs syndrome), and pain. The management of each of these will be discussed in turn, including whenever possible evidence from level 1 studies (randomized clinical trials) – although on the whole these remain limited currently. Agents discussed include fludrocortisone, midodrine, droxidopa, and domperidone for OH; solifenacin for OAB; botulinum toxin for drooling; opioid for pain; etc. Non-pharmacological management will also be addressed.
Comorbidities are increasingly recognized to contribute to PD burden, including diabetes and osteoporosis which are highly prevalent in Asia. Management of these problems will be briefly covered. (Cerebrovascular disease is also prevalent, but being a "brain" problem will not be discussed further in my talk).
As highlighted throughout the lecture, many things can be done to help relieve the symptoms and problems posed by "peripheral" problems in PD; accordingly, clinicians and patients/caregivers should have a broad understanding of this important topic.

O141

Current status of iPS cells and efforts for medical application

*Shinya Yamanaka**
Center for iPS Cell Research and Application (CiRA), Kyoto University, Kyoto, Japan

Induced pluripotent stem cells (iPSCs) can proliferate almost indefinitely and differentiate into multiple lineages, giving them wide medical application. As a result, they are being used for new cell-based therapies, disease models and drug development around the world.
In 2014, the world's first clinical study using iPSC-derived RPE (retinal pigment epithelium) sheets began for the treatment of age-related macular degeneration (AMD). iPSCs can be used for regenerative medicine to restore organ function. To push these efforts, we are proceeding with an iPSC stock project in which clinical-grade iPSC clones are being established from "super" donors with homologous HLA haplotypes. Homologous HLA haplotypes are associated with decreased immune response and therefore less risk of transplant rejection. In 2015, we started distributing an iPSC stock clone to organizations in Japan. The aim of the stock is to hold iPS cells of guaranteed quality which can be supplied quickly to medical care institutions and research institutions in Japan and overseas when required. In 2017, clinical study using the iPSC stock began for AMD patients, and the transplantation of 5 cases have completed. Additionally, clinical trial for Parkinson's disease has started using the iPSC stock-originated neurons in this August, and the surgery to transplant dopaminergic progenitors into the patient's brain has been just conducted at Kyoto University Hospital.
Other applications of iPSCs include drug screening, toxicity studies and the elucidation of disease mechanisms using disease-specific iPSCs from patients with intractable diseases. In addition, iPSCs may be resourceful for preventative measures, as they make it possible to predict the patient condition and provide a preemptive therapeutic approach to protect against the onset of the disease or to establish personalized medicine. We reported a new drug screening system using iPSCs derived from fibrodysplasia ossificans progressiva (FOP) patients, revealing one drug candidate, Rapamycin. Based on these findings, we have achieved to initiate a clinical trial to treat FOP patients in 2017.
Over the past decade iPSCs research made a great progress. However, there are still various hurdles to be overcome, iPSC-based science is certainly moving forward for delivering innovative therapeutic options to the patients with intractable diseases.

O142

Gut microbiota, 10^{13} new pieces in the Parkinson's disease puzzle

*Filip Scheperjans**
Helsinki University Hospital, Dept. of Neurology, Helsinki, Finland

Gastrointestinal dysfunction affects up to 80% of PD-patients and may precede the onset of motor symptoms by years. Correspondingly, neurodegenerative changes in the enteric nervous system can be found in earliest stages of PD. The colonic mucosa of PD patients shows an impaired barrier function, inflammation, oxidative stress, and bacterial invasion. An environmental factor likely plays a key role in PD pathogenesis probably against a background of genetic vulnerability. The early involvement of the gastrointestinal tract in PD suggests that this environmental factor exerts its influences primarily via the gut. An initiation of PD pathology in the gut with subsequent spreading to the brain via the vagal nerve is supported by a decreased risk of PD after truncal vagotomy. There is accumulating evidence for an intense bidirectional interaction between gut microbiota and the brain influencing neuronal activity, behavior, as well as levels of neurotransmitter receptors, neurotrophic factors, and neuroinflammation. Pathways involving gut inflammation, amyloid cross-seeding, and short chain fatty acids may directly link gut microbiota and neurodegeneration.
Alterations of gut microbiome composition in PD have been shown in multiple studies suggesting that gut microbiota are related to PD. Best reproduced are decreased abundance of Prevotella and increased abundance of Akkermansia and Lactobacillus in PD. Importantly, decreased Prevotella abundance was also found in a small cohort of subjects with idiopathic REM sleep behavior disorder (iRBD), a prodromal syndrome with high risk of progression to PD. While human studies have only documented an association between the gut microbiome composition and PD, animal studies have recently provided evidence for a causal connection between gut microbiota, α-synuclein pathology, neuroinflammation, and motor impairment.
This talk will give an overview of recent findings regarding the gut-microbiota-brain axis in PD and how this may reshape our understanding of disease etiology and pathogenesis and could lead to new diagnostic and therapeutic approaches.

O143

Parkinson's disease and Parkinson's disease medications have distinct signatures with respect to the gut microbiome

*Haydeh Payami**
University of Alabama, Birmingham, AL, USA

PD is complicated; it is probably not a single disease, and currently, we have no way of telling the disease entities apart. We once believed that if we find all the PD genes and environmental factors, we can put the pieces together, see the full picture and be able to separate disease subtypes. After exhaustive searches that uncovered over 40 genetic loci and several environmental risk factors, we still do not have the full picture. None of the known risk factors are sufficient to cause disease, not individually, not in combination, and not in interaction. What are we missing? We questioned if the gut microbiome holds the missing pieces. The first set of experiments, which are published (PMID:28195358: Parkinson's disease and Parkinson's disease medications have distinct signatures of the gut microbiome), revealed altered gut microbiome in Persons with PD; established that the alterations in PD gut could not all be explained by factors that correlate with PD (medication, constipation, diet, gender, etc.), and detected other alterations that correlated with specific PD medications. These findings were the impetus to launch a large multi-center study, with a projected 1,000 persons with PD, 600 neurologically healthy controls, and 100 persons with REM sleep behavior disorder. We intend to identify microorganisms in the gut that contribute to the pathogenesis of PD, determine if specific microorganisms are responsible for triggering disease in genetically susceptible individuals, investigate the role of microbiome in mediating the toxicity of environmental risk factors and beneficial effects of protectants, and explore the possibility of developing microbial biomarkers for disease subtyping, early identification of prodromal PD, predicting disease progression, and response to treatment. I will present an update at the meetings.

O144

Measuring GI function in Parkinson's disease

Per Borghammer, Karoline Knudsen, Tatyana Fedorova*
Department of Nuclear Medicine & PET Centre, Aarhus University Hospital, Aarhus, Denmark

Gastrointestinal (GI) symptoms and dysfunction is prevalent in Parkinson's disease (PD) and significantly impacts the quality of life. It has also been suggested that PD may in some cases originate in the autonomic nerve terminals of the gut. Our current knowledge about GI dysfunction in PD is based mostly on questionnaire-based assessments of patient symptoms, which is not adequate to measure subclinical dysfunction. Also, several different GI-related questionnaires are in use, which do not always show concurrent results and display only limited correlation to objective markers of GI dysfunction.
This talk will summarize the current knowledge about measurement techniques to assess GI dysfunction in PD, including

- Esophageal motility & gastric emptying measures
- Radio-opaque markers (transit times)
- Endo-capsule methods (transit times & motility)
- CT-based intestinal volumes

O145

Immune therapies for PD

*Seung Jae Lee**
Seoul National University, Seoul, South Korea

Immunization therapy targeting α-synuclein has emerged as a promising approach for Parkinson's disease and perhaps for other synucleinopathies. Several antibodies have shown therapeutic effects in mouse models of synucleinopathies and have alleviated the pathological and behavioral phenotypes of these mice. The mechanisms through which the immunization therapy works were initially puzzling, especially given that α-synuclein is a typical cytosolic protein. Recent studies, however, suggested that extracellular α-synuclein is an important pathogenic entity, and hence, a target for immunotherapy. In this talk, I will review the literature describing immunization therapy for synucleinopathies in mouse models and provide current thoughts on the potential mechanisms underlying the therapeutic effects of α-synuclein immunotherapy. In addition, I will review the current state of clinical trials for immune therapy and provides potential targets for immunotherapy other than α-synuclein.

O146

New surgery for PD
*Binit Shah**
University of Virginia, Charlottesville, Virginia, USA

There are have been substantial advances in the use of surgical therapies in Parkinson disease over the last two decades. The role of deep brain stimulation in PD is larger and is being applied earlier in the disease. New ways of stimulating the brain with DBS are being explored and may have an impact on reducing adverse effects and maximize battery life. Additionally, new lesioning therapies like high intensity focused ultrasound and gamma knife are providing options for non-incisional lesioning therapies in PD. We will review advances in DBS, focused ultrasound, and gamma knife in PD as well as review the evidence of more traditional radiofrequency lesioning.

O147

Repurposing drugs that target risk factors for PD
*Michael Schwarzschild**
Massachusetts General Hospital, Boston, MA, USA

Parkinson's disease (PD), to the extent that it can be considered a single disease, is caused by a complex interplay of genetic and environmental factors. Recent identification and investigation of gene mutations that can cause PD (e.g., SNCA, LRRK2, GBA) are leading to promising therapeutic candidates targeting the mutations' pathogenic effects. Enthusiasm for targeting these mutations is warranted by our confidence in their causal role, but is tempered by the relatively small proportion of PD caused by these mutations and uncertainty of their relevance to the vast majority of PD that does not result from the targeted mutation. On the other hand, traditional epidemiologic studies have identified a number of exposures or behaviors as 'reduced risk' factors that reflect protective influences likely of relevance to all forms PD. However, their association with resistance to the disease does not necessarily mean they are preventing it, as association does not prove causality. Nevertheless, some of these 'reduced risk' factors have been found to confer neuroprotection in laboratory models of PD, demonstrating the biological plausibility of a causal basis for the reduced risk. This convergence of epidemiological and biological findings has prompted clinical testing of a number of these environmental, dietary, pharmacological or behavioral factors as candidate disease-modifying therapy. Their translation back to the clinic has been accelerated by the repurposing of existing drugs or activities that constitute or target these 'reduced risk' factors, which takes advantage of their established safety and features that can take years to demonstrate in the early stages of drug development. Repurposed therapies targeting 'reduced risk' factors – which recently have been, currently are, or soon may be in clinical trials for PD – include smoking or tobacco components, caffeine, calcium channel blockade, urate-elevating inosine, exercise, ibuprofen, deferiprone, exenatide-like drugs, statins, albuterol and ambroxol. The results, status and plans for these trials will be briefly presented for discussion.

O148

Aerobic exercise for PD
*Terry Ellis**
Boston University, Boston, MA, USA

In this presentation, the evidence supporting the role of aerobic exercise in the treatment of Parkinson disease will be discussed. The data suggesting disease-modifying effects of aerobic exercise will be presented with potential underlying mechanisms explored. This session will also emphasize the effects of aerobic exercise across a variety of outcomes including motor and non-motor signs, functional outcomes and quality of life. The benefits of various modes of aerobic exercise will be discussed. The effects of aerobic exercise across the disease continuum will also be highlighted. Furthermore, this session will address issues related to dosing frequency and intensity. Recommendations for implementation of aerobic exercise and future research directions will be suggested.

O149

Strengthening exercise for PD
*Lee Dibble**
University of Utah, Salt Lake City, UT, USA

The slow and small movements associated with Parkinson disease are caused in part by reduced skeletal muscle force production. This reduced force production primarily results from alterations in the output of central nervous system centers and is not a direct product of muscle problems. For this reason, skeletal muscle will respond to resistance training by increasing muscle size and the nervous system drive to the muscle. Regardless of the mechanism of response, muscle force production is improved and these improvements appear to translate to improvements in variety of functions. Although the majority of studies examining this topic focus their attention on limb muscle function and mobility, there are intriguing findings that suggest benefits for mid-line body functions such as coughing and respiratory function as well as urinary continence. This presentation will review the rationale and evidence for the safety and efficacy of strengthening exercise and the use strengthening exercise as a means of improving strength, movement speed, and overall function.

O150

Complex balance training for PD
*Margaret Mak**
The Hong Kong Polytechnic University, Hong Kong

Falls is one of the most disabling symptoms in Parkinson's disease (PD) with incidence rate up to 70% and 25% of them have repeated falls. Falls would lead to major injuries such as fracture, loss of independence, reduced quality of life and early institutionalization. Falls in PD is multifactorial and may be contributed by physical, psychological, cognitive, and environment factors. Bradykinesia and rigidity are responsive to dopaminergic treatment, however postural impairment persists and it comprises biomechanical constraint, reduced stability limit, impaired anticipatory postural adjustment, delayed and reduced response to perturbation. Gait disturbance especially freezing of gait has been found to associate with falls. Fear of falling, an adverse psychological outcome, could lead to self-induced restriction and increase future risk of falling. In fact, fear of falling is a strong predictor of recurrent falls in people with PD. Executive dysfunction such as impaired initiation, delay in task switching, or difficulties in prioritizing postural or cognitive tasks during dual-task walking may increase the risk of falling. Finally, falls could result from environmental hazards.
Fall reduction or prevention have been actively researched in people with PD. Encouragingly, most studies reported positive effects on balance performance, gait ability, balance confidence and alleviation of motor symptoms, with carry-over effects up to 12 months after treatment ended. A few studies reported a reduction in fall rate and injurious fall risk. Despite the positive effects, the training protocols were diverse and mainly addressed some

impaired postural domains, gait or mobility. Some programs included shifting of postural tasks, motor response inhibition, or cognitive loading during balance training. One study blended the training in both indoor and outdoor environment. Falls is complex and involves intrinsic and extrinsic fall risk factors. Ideal fall prevention program has to be multi-dimensional, task- and context-specific, and practiced at different level of complexity. The talk will review the available balance training programs, appraise the evidence on the efficacy of multi-dimensional balance programs, and formulate strategies for designing comprehensive fall management interventions for people with PD.

O151

Aging of the immune system and relevance to brain health and disease

*V. Wee Yong**
University of Calgary, Calgary, AB, Canada

The impact of aging on the immune system is complex. While the ability to mount an efficient innate and adaptive immune response to newly encountered pathogens is impaired, the immune system in general undergoes a shift toward a proinflammatory status with aging, also referred to as “inflammaging”. For microglia, the sentinel immune cell of the CNS, its production of pro-inflammatory cytokines and potentially damaging factors including oxygen radicals is elevated with aging; yet, its capacity to phagocytose and remove debris and harmful protein aggregates appear diminished with senescence, as is its production of trophic molecules. The density and activated morphology of microglia have also been noted to increase with age in several CNS compartments. These attributes of the aging immune system heighten the potential detrimental roles of immune cells with senescence, particular with regards to the neurodegenerative potential of aging microglia within the CNS. We will discuss the characteristics of immune senescence, the mechanisms that underlie aging-associated immune dysregulation, and consider medications that normalize microglia activity to reduce the neurodegenerative potential of aging microglia, and to enhance their phagocytic and repair potential.

O152

Proteostasis, molecular chaperones and aging – Implications for PD

*Heath Ecroyd**
Illawarra Health and Medical Research Institute, and The University of Wollongong, Wollongong, New South Wales, Australia

Parkinson’s disease (PD) is the second most prevalent age-related neurodegenerative disorder. The pathogenesis of PD, and other neurodegenerative diseases, has been inextricably linked with the amyloid fibrillar aggregation and deposition of α-synuclein. The cell has a range of defense mechanisms in place to prevent aggregation and maintain protein homeostasis (proteostasis). An important element of this proteostasis network are the molecular chaperone proteins. However, the persistence of diseases associated with α-synuclein aggregation indicates that their protective capacity can be ‘overwhelmed’ in the context of PD. Moreover, there is evidence that the levels of molecular chaperones proteins decrease in the brain with age. Our work seeks to investigate the role of the heat shock molecular chaperone proteins (Hsps) in protecting against α-synuclein aggregation as part of the proteostasis network. Specifically, we examine interactions between α-synuclein and Hsps at various stages along α-synuclein’s aggregation pathway using a range of bulk and single molecule techniques. Our results demonstrate that Hsps interact transiently with aggregation-prone monomeric α-synuclein to inhibit its aggregation in vitro. However, the efficiency by which Hsps inhibit α-synuclein aggregation is highly dependent on the rate at which it aggregates. Decreases in the levels of chaperones during aging likely facilitate the onset and progression of α-synuclein aggregation associated with PD. We have also recently characterized the ability of the Hsps to interact with mature fibrillar aggregates formed by α-synuclein and established a physiologically relevant role for this interaction in preventing the cytotoxicity of the aggregates. By pursuing the mechanistic details of the manner by which Hsps interact with α-synuclein, we aim to uncover potential mechanism(s) by which Hsp chaperone activity may be targeted to attenuate diseases associated with α-synuclein aggregation.

O153

Aging of mitochondrial function and bioenergetics – What does this mean for PD pathogenesis?

*Carolyn Sue**
Kolling Institute, University of Sydney, Sydney, Australia

Mitochondria are key organelles that provide the main source of cellular energy. Cellular energy (ATP) is produced by the mitochondrial respiratory chain via a process called oxidative phosphorylation. During oxidative phosphorylation, oxygen free radicals are generated and these may result in mitochondrial damage, triggering “mitophagy”, a process by which damaged mitochondria are selectively removed to maintain mitochondrial quality and cellular health. During aging, damaged mitochondria may accumulate resulting in reduced bioenergetic function, increased ROS production and eventually cell death.
Mitochondrial toxins and loss of mitophagic proteins that are linked to Parkinson’s disease related genes both can cause Parkinson’s disease, underpinning the importance of mitochondrial function to the pathogenesis of this disorder. Methods to improve the maintenance of healthy mitochondria and preserve mitochondrial quality and function represent a promising and new therapeutic approach to treating Parkinson’s disease.

O154

The use of neuroimaging as a biomarker in PD

*Stephane Lehericy**
ICM – Institut Cerveau Moelle (Brain and Spine Institute), Paris, France

Parkinson’s disease is characterized by degeneration of neurons at several levels of central nervous system. Recent imaging approaches have provided a number of qualitative and quantitative brain biomarkers that have been able to detect with increasing accuracy the alterations in brain structure and function in patients with Parkinson’s disease. These biomarkers are used for diagnosis, prognosis, early detection, monitoring of treatment response and understanding of the pathophysiology of the disease. The three main imaging methods are magnetic resonance imaging (MRI), radiotracer studies using positron emission tomography (PET) or single photon emission computed tomography (SPECT), and transcranial sonography (TCS), which provide complementary qualitative or quantitative information. TCS and MRI using neuromelanin-sensitive imaging and susceptibility-weighted imaging detect qualitative changes in the substantia nigra. MRI quantitative markers can be derived from diffusion weighted and iron-sensitive imaging, or volumetry. Radiotracer imaging shows changes in the dopaminergic and non-dopaminergic systems in relation with motor and behavioral symptoms and their treatment as well as inflammation and abnormal protein deposition. Functional brain

alterations at rest or during task performance have been captured with functional MRI and PET. This presentation will review recent advances in imaging biomarker research in Parkinson's disease and present perspectives in this domain.

O155

The current status of "wet" biomarkers (blood, CSF etc) in PD

*Lucilla Parnetti**
University of Perugia, Dept. of Medicine, Section of Neurology, Perugia, Italy

In the management of Parkinson's disease (PD), reliable diagnostic and prognostic biomarkers are highly needed. The diagnosis of PD mostly relies on clinical symptoms and this hampers the detection of the earliest phases of the disease, when treatment with forthcoming disease-modifying drugs may have the highest therapeutic impact. Reliable prognostic markers could help in foreseeing the response to treatments. Several putative diagnostic and prognostic cerebrospinal fluid (CSF) and blood biomarkers have been proposed in PD.
CSF total α-syn is lower in PD compared to healthy controls and to other neurological conditions different from synucleinopathies. Its diagnostic accuracy is low and does not allow considering this biomarker useful in the diagnosis of PD. CSF oligomeric α-syn and phosphorylated α-syn are higher in PD compared to healthy and neurological controls as well as other neurodegenetaive diseases not belonging to synucleinopathies; further studies are required to confirm their potential diagnostic value and to overcome analytical issues. CSF pro-aggregating forms of α-syn have shown preliminary promising results as diagnostic markers in PD, although larger studies and analytical issues (i.e. reproducibility and assays' time) have to be addressed. Plasma and serum α-syn species measurement is at high risk for erythrocyte contamination. Intra-erythrocyte α-syn species might represent a valid alternative, but their diagnostic and prognostic value have to be confirmed on larger studies.
Classical AD biomarkers alone are not helpful in the diagnostic process, but can improve prognostic assessment, with CSF Aβ42 being a valid marker of risk for cognitive decline, and CSF t-tau being a potential marker of motor progression.
Lysosomal enzymes activities, namely glucocerebrosidase, are reduced in CSF of PD patients. Together with other biomarkers, their activity measurement can improve diagnostic accuracy.
CSF and blood neurofilament light (NfL) measurement represents a valid biomarker for discriminating PD from other parkinsonisms (PSP, MSA and CBS).
A combination of multiple CSF (and probably blood) biomarkers reflecting different pathogenic mechanisms taking place in PD might enable earlier diagnosis and more accurate prognostic assessment, also in view of having available disease modifying drugs.

O156

Could biopsies from outside the brain help in the diagnosis and tracking of PD?

*Kathleen Shannon**
University of Wisconsin School of Medicine and Public Health, Madison, WI, USA

The development of putative disease-modifying therapies in Parkinson's disease (PD) is hampered by: (1) the appearance of diagnostic signs relatively late in disease course; (2) low diagnostic accuracy in early disease; and (3) outcome measures that are influenced by symptomatic treatments. The central role of α-synuclein (AS) in disease pathogenesis and its detection in multiple post-mortem tissues outside the central nervous system suggest it may be the optimal biomarker candidate in PD. Immunohistochemical studies tissues from living subjects suggest AS accumulation can be demonstrated in skin, salivary gland and intestinal tissues. However, most studies are small and there is wide methodological variability (primary antibody, epitope exposure and signal development). It is critical that additional study be done to elucidate the potential role of tissue AS as a biomarker of the PD prodrome, diagnosis and progression

O157

Overview of voice and breathing in Parkinson's disease

*Corinne Jones**
University of Texas, Austin, Texas, USA

Voice and speech deficits occur in approximately 90% of individuals with Parkinson's disease (PD) at some point during the course of the disease. Voice and speech impairments secondary to PD can be due to changes in any of the subsystems of speech: respiratory, laryngeal, articulatory, and/or resonatory. Specific areas of voice and speech impairment that have been reported include: vocal fold atrophy; reduced amplitude of vibration, mucosal wave, and closure of the vocal folds during phonation; laryngeal tremor; reduced loudness; dysphonic voice quality; hypokinetic articulatory movements; distorted articulation; neurogenic stuttering; and reduced prosodic variability. People with PD are also seen to present with reduced respiratory muscle weakness; rigidity of the respiratory muscles, less efficient respiratory kinematics, and variable lung volume initiation during speech. This presentation will highlight the physiologic deficits of the respiratory and laryngeal systems resulting from PD and how these deficits then impact speech and voice production.

O158

Approaches to voice training in PD

*Darla Freeman**
Florida E.N.T. and Allergy, Tampa, Florida, USA

Communication difficulty is one of the first symptoms of Parkinson's disease with an estimated 75–89% incidence. The ability to communicate involves an intricate three-part system. Together the lungs, ribs, diaphragm muscle, chest muscles, and the abdominal and back muscles provide the respiratory support needed to produce voice. The sound source of the system is the larynx which contains the vocal cords. There are nearly 30 muscles within and around the larynx that function together to move and adjust the vocal cords. When the vocal cords close during speaking or singing, air from the lungs passes between them, causing them to vibrate and produce a sound. The final stage of the system is the resonator including the throat, mouth and nasal cavities. Resonance refers to the shaping of sound waves within a chamber to produce a particular sound output. The sound that is produced by the vocal cords is likened to a buzz. The remainder of the vocal tract refines the sound through resonance.
People with Parkinson's oftentimes present with a decline in one or more of these subsystems as they progress through the stages of the disease. Respiratory dysfunction is common and contributes to reduced ability to secure the necessary breath support needed during the process of phonation. Weakened vocal cords make it difficult to control the airflow and reduced oral/motor agility and strength makes articulation a struggle.
This presentation will feature a discussion on scientifically based treatment approaches aimed at addressing communication disorders across the progression of the disease.

O159

Maintenance of intelligibility after speech therapy in PD
*Jennifer Cody**
Parkinson Voice Project, Dallas, Texas, USA

Speech therapy has been shown to be highly effective for improving the speech of people with Parkinson's. However, completion of a speech therapy program is actually just the beginning of a journey in maintaining one's speech, not the end! Continued practice and maintenance activities are essential for achieving optimal outcomes for people with Parkinson's disease.
First, it's important to recognize that even the best speech therapy cannot cure the underlying cause of speech disorders in Parkinson's, nor does it stop the progression of the disease. Speech therapy provides a means of compensating for how Parkinson's affects speech. Second, discontinuing any exercise, including speech exercise, leads to "detraining," or a gradual loss of strength over time. This loss may occur more rapidly in those with a progressive disorder like Parkinson's. Third, people with Parkinson's may experience deficits in sensorimotor processing and motivation, leading to reduced awareness of changes in speech and difficulty initiating home practice sessions on their own.
This presentation will discuss various options and strategies for maintaining gains made during speech therapy. Daily practice can seem daunting and even worse, boring, but ideas for keeping a life-long speech maintenance program fun, fresh, and effective will be presented, including group speech exercises, tips for home practice, singing programs, and the benefit of regular, proactive visits to speech professionals.

O160

What is left to be discovered in PD?
*Tim Anderson**
University of Otago, Christchurch, New Zealand

We will explore and debate major discoveries that need to be made and what are, or will be, the foundations of these discoveries. Some of the topics we will discuss are:
1. Disease triggers:It seems that some environmental factor or factors trigger PD in person's with a particular susceptibility. There are some clues but is there one major trigger yet to be identified?
2. Genetics: Several causative and susceptibility genes, and "protective" genes, have been identified but there are more to be discovered. Such discoveries may lead to new therapies.
3. αsynuclein conformation: There is still much to discover about αsynuclein subspecies and which one or combination does the most damage to neurons and perhaps other brain cells.
4. αsynuclein spread. We know much about αsynuclein in the brain but we still don't really know how it accumulates and "spreads". Future discoveries will surely lead to treatments that limit this damage.
5. αsynuclein imaging. The ability to image αsynuclein in the brain is still not possible. The discovery of a reliable tracer that binds to the toxic αsynuclein species inside brain cells, providing a robust and useful biomarker for use in disease modifying therapeutic trials, is critical.
6. Precison drug delivery: A methodology for delivering continous (tonic) and on demand (phasic) dopamine, and potentially other neurotransmitters and brain nutrients, to relevant brain regions, thereby mimicking non-PD brain function, is yet to be discovered.
7. Treating "treatment-resistant" symptoms: We sorely need effective new therapies for freezing and postural instability, as well as non-motor symptoms such as apathy, anxiety, depression and cognitive impairment.
8. Precision medicine: Will we be able to discover a cocktail of disease modifying agents and lifestyle measures tailored to individual patient's genetic and phenotypic profile?
9. Neurorestoration: The ability to generate new brain cells to replace lost cells in the right places and quantities, and with normal physiological function, is vital but still represents a major challenge.
10. Prevention through screening. A sensitive population screening blood biomarker, or combination, that identifies those at high risk is a key future discovery to ultimately stop PD before it starts.

O161

PINK1, parkin and the ubiquitin system – How do they link to what goes wrong in PD
*Noriyuki Matsuda**
Tokyo Metropolitan Institute of Medical Science, Tokyo, Japan

Parkinson's disease (PD) is a common movement disorder characterized by dopaminergic neuronal loss. The majority of PD cases are sporadic, however, the discovery of the genes linked to hereditary forms of PD (i.e., hereditary Parkinsonism) has provided important insights into the molecular mechanisms. For example, functional analysis of the recessive familial PD-related genes has revealed that the disease is relevant to mitochondrial quality control. This is consistent with the prior idea that several cases of sporadic and chemical-induced PDs have been associated with mitochondrial dysfunction.
We have focused on PINK1 and PARKIN, responsible genes for hereditary recessive PD. PINK1 and PARKIN encode Ser/Thr kinase and ubiquitin ligase (E3), respectively. We revealed that when the mitochondrial membrane potential decreased, PINK1 phosphorylates ubiquitin at Ser65, and the phosphorylated ubiquitin functions as an activator for E3 function of Parkin (Koyano et al., Nature 2014). Moreover, phosphorylated poly-ubiquitin chain catalyzed by PINK1 recruits Parkin to damaged mitochondria by functioning as a Parkin receptor (Okatsu et al., JCB 2015). Consequently, trio of PINK1, Parkin, and phospho-ubiquitin rapidly tag outer membrane proteins on depolarized mitochondria with ubiquitin. This ubiquitin chain is recognized by RABGEF1, and it directs the downstream Rab proteins, RAB5 and RAB7A, to damaged mitochondria for degradation by lysosome (Yamano et al, eLife 2018). Impairment of this process predisposes to familial PD. Summary of the latest knowledge for relationship between mitochondrial quality control, ubiquitin, autophagy, and Parkinson's disease will be discussed.

O162

Medical and non-medical management of sexual problems in PD
*Jim Bender**
Basalt Rehabilitation Centra, The Hague, The Netherlands

This presentation will be focussing on 6 challenges around sexuality that people with PD are often confronted with and how to manage them practically and medically.
The six challenges are:
1. My "users manuel" concerning my sexual functioning has changed since I have PD.
2. My experience of sexuality and intimacy has changed since I have PD and I'm not so happy about it.
3. Sex and intimacy for my partner has changed since I have PD and I'm not sure if she/he is happy about it.
4. Doing sex isn't easy since I have PD. Practical sexual issues need practical answers.

5. Since I have PD, sex has changed so much I don't desire it any more. I'm stuck and don't know how to proceed.
6. I don't know with whom or how I can talk about my concerns regarding my changed sexual life.
These challenges will be illustrated with stories that people with PD have shared with me when adressing them in their physical rehabilitation treatment.
Participants will be encouraged to ask questions about the impact of PD on sexuality and intimacy in their own lives or the lives of their patients.

O164

Where are we with clinical trials in PD in 2019?
*Tom Foltynie**
UCL Institute of Neurology, London, United Kingdom

In this round table, we will discuss the most important clinical trials in set-up, in progress and recently completed in PD, focussing predominantly on trials searching for interventions that may modify the course of PD. This will include some discussion of licensed drugs being repurposed for PD, as well as targeted approaches aimed at the PD risk genes and at α synuclein pathology and transmission.

O165

How and why you should be a guinea pig in a trial
*Richard Windle**
Porters House, Southampton, United Kingdom

Not everyone has the opportunity to take part in a clinical trial but, if you do, I would urge you to do so. If better treatments and a cure for Parkinson's are to be discovered this will be a joint effort between patients and doctors. It is acknowledged that some people cannot take the risk, however small, especially those with young dependents.
My experience of a clinical trial is based on the TRANSEURO project – a cell replacement therapy that involves the implantation of fetal material into the brain (not deep brain stimulation). Participants are assessed on the Uniform Parkinson' s Disease Rating Scale (UPDRS) at quarterly intervals for up to three years after the implant. It is important that the patient is aware of what is required and that they should ask any questions in advance. Changes in the UPDRS will be used to determine the effectiveness of the treatment. The UPDRS is sometimes referred to as the 'best worst' measurement that we have.
Participants in a clinical trial are given a copy of the 'Informed Consent', which describes everything they are committing to. The involvement of patients in the research is considered to be essential. They bring to the table direct experience of the condition.
There are several ways of mounting a clinical trial but the 'gold standard' methodology is known as a double-blind trial where participants are randomly allocated to either a test or a control group. Factors that patients worry about when considering taking part in a trial include the risks of taking unproven medicines, disrupting their current medication regime and the possibility that they may be given a placebo.
At the end of the trial there should be a procedure for participants to feedback observations, good and bad, as to what might have been done differently. This information should be widely disseminated and made available to future studies.
There are three main factors patients consider when deciding whether to take part in a trial: concerns about taking unproven medicines, possible impact on their current medication and being given a placebo.
TRANSEURO was always intended to be a long-term study.

O166

Using real world data as an alternative to clinical trials
*Bas Bloem**
Department of Neurology, Radboud MC, Nijmegen, The Netherlands

The outcome in clinical trials and other research studies typically depends on either patient-completed questionnaires or rating scales of physical signs completed by an observer. These traditional approaches are increasingly criticized, in part because they are time consuming, but in part also because questionnaires are subjective and subject to recall bias, while observer-based rating scales are subject to high degrees of intra- and inter-rater variability. Moreover, both approaches can be time consuming. Finally, both questionnaires and rating scales may offer an incomplete understanding of the patient's actual functioning in their own home situation, particularly over longer periods of time. Therefore, there is an increasing interest to use real-world data, both to improve care in daily clinical practive and also as surrogate outcomes in clinical studies, and perhaps with time, even as novel primary outcomes. Examples include existing large datasets, such as medical claims databases that can be provided by healthcare insurance companies. Other examples include unobtrusive measurements of for example mobility, using either body-worn sensors, smartphones or sensors built into the patients' houses. In my presentation, I will illustrate how the use of such "big data" obtained from real world environment can provide very useful information about the patients actual functioning over time, and how as such these can provide a more accurate perspective on the patients' performance in their own living environment as compared to the more traditional outcomes.

O167

Molecular advances in stem cell and reprogramming strategies to treat PD
*Ernest Arenas**
Karolinska Institute, Stockholm, Sweden

Current cell replacement therapies for Parkinson's disease (PD) focus on the transplantation of stem cell-derived or reprogrammed cells, or the direct reprogramming of somatic cells in situ, in the host brain. In both cases it is essential to understand the molecular mechanisms controlling cell identity and function during development and adulthood, to enable the generation of new midbrain dopaminergic neurons as identical as possible to their healthy endogenous counterparts. In addition, the development of in vivo cell reprogramming strategies requires a greater understanding of the cellular and molecular composition of the brain of PD patients at a single cell level, to define the cell types and the molecular trajectories that cells should follow during reprogramming.
Recent advances in single cell biology have allowed the characterization of all the cell types in the midbrain tissue and the identification of their gene expression profiles with exquisite detail. Application of methods such as single cell RNA sequencing, single molecule FISH, in situ sequencing and novel bioinformatics tools are enabling researchers to analyze development, stem cell differentiation, reprogramming and neurodegeneration with an unprecedented breadth, depth and precision.
In this round table we will discuss how these methodologies have contributed and will continue contributing in the near future both to understand the natural history of midbrain dopaminergic neurons from development to neurodegeneration; and to develop novel therapeutic opportunities for PD.

O168

Pain and PD: Patient reality and what we know
*Karen Raphael**
New York University, New York, NY, USA

As a Professor and Clinical Research Scientist who has devoted most of her career to conducting research on chronic pain disorders, Karen Raphael brings a unique perspective to pain in PD: She has lived with PD and related pain for approximately nine years, not including various manifestations of pain prior to onset of motor symptoms. She will attempt to bridge knowledge about mechanisms of and treatment for different types of chronic and episodic pain syndromes, to provide insights into current understanding and management of various types of pain experienced by people living with PD.

O169

The role of genetics in better understanding the pathophysiology of PD
*John Hardy**
UCL Institute of Neurology, London, United Kingdom

Through the genetic analysis of inherited and sporadic Parkinson's disease, we have now identified about 20 genes which cause Parkinson's disease and about 40 which influence the risk of disease. These findings implicate the failure of the process by which damages mitochondria are removed from cells: this pathway seems to be particularly important in early onset disease, and the process involving the general removal of damaged cellular components (autophagy) especially in late onset disease. Of particular relevance has been the identification of, first glucosecerebrosidase mutations in the disease and then the realisation that the genes involved in other lysosomal storage diseases also showed association with disease. Interestingly, synuclein, the major component of Lewy bodies, appears to be largely metabolised through the lysosome and lysosome insufficiency may explain why this protein is deposited in the disease and why, over production of this protein increases the risk of disease. I will also suggest that while research has focussed on neuronal metabolism, recent data suggest that microglia play an important role in the relevant damage response pathways.
I will discuss how these findings are consistent with the view that the disease, in general, can be seen as a failure of damage response pathways and that this has parallels with the other late onset neurodegenerative diseases, Alzheimer's disease, Frontotemporal dementia and motor neuron disease. These findings have implications for therapy… we can either try ad potentiate the damage response pathways, or we can try and reduce the substrates which use those pathways: in the case of Parkinson's disease, that would be synuclein reduction.

O170

Insulin resistance, diabetes and Parkinson's disease
*Dilan Athauda**
The National Hospital for Neurology and Neurosurgery & UCL Institute of Neurology, London, United Kingdom

The incidence of both Type 2 diabetes and Parkinson's disease is increasing. Accumulating research studies suggest that both diseases share some pathophysiological features such as mitochondrial dysfunction, abnormal inflammatory responses and protein accumulation. Furthermore, epidemiological evidence suggests that Type 2 Diabetes is a risk factor for the development of Parkinson's disease and can influence its disease course. In addition, emerging evidence suggests that insulin resistance, which is a core feature of Type 2 diabetes may play an important role in neurodegeneration. The aim of this talk will be to review the experimental data exploring the links between insulin resistance, Type 2 diabetes and Parkinson's disease, and the role Insulin signaling plays within the brain. The concept of "brain insulin resistance" will be introduced and the evidence that patients with Parkinson's disease demonstrate dysfunctional brain insulin signaling will be discussed. Although it is currently unclear whether insulin resistance is a cause or consequence of neurodegeneration, there is growing interest that existing treatments used to treat Type 2 diabetes that act on insulin signaling could be used as novel therapeutics in Parkinson's disease. This talk will conclude by highlighting some of the most recent clinical trial data exploring the use of these treatments in Parkinson's disease and possible future directions.

O171

The links between mitochondrial failure and lysosomal dysfunction and α-synuclein aggregation
*Dimitri Krainc**
Northwestern University, Chicago, IL, USA

There is an urgent need to identify effective neuroprotective therapies for synucleinopathies such as Parkinson's disease (PD) and Diffuse Lewy Body Dementia (DLB). Recent emergence of genetic forms of PD has facilitated identification of potential targets for therapeutic development. One of the most promising and extensively studied targets has been lysosomal glucocerebrosidase (GCase) in patients with GBA1-linked PD and DLB. These patients exhibit loss of GCase activity in lysosomes which in turn results in downstream neuronal dysfunction. Therefore, chaperoning and/or direct activation of GCase in lysosomes has been postulated as viable therapeutic strategy. Several ongoing therapeutic efforts have focused on chemical chaperones to promote translocation of mutant GCase to the lysosome. We found that wild-type GCase activity is also reduced in sporadic and genetic forms of PD, suggesting that wild-type GCase could serve as promising therapeutic target in synucleinopathies. Therefore, we explored whether activation of wild-type GCase could enhance lysosomal function and rescue downstream pathological phenotypes in dopaminergic neurons from patients with sporadic and familial forms of PD. We identified GCase activator S-181, which was able to increase the activity of wild-type GCase, and partially ameliorated lipid substrate accumulation, lysosomal dysfunction and dopamine oxidation, in both GBA1-linked and non-GBA1-linked PD patient-derived dopaminergic neurons. Our work thus suggests that rescuing GCase activity is sufficient to improve lysosomal function and to reduce accumulation of toxic oxidized dopamine in midbrain neurons. In turn, decreased accumulation of oxidized dopamine resulted in diminished downstream pathogenic effects, including oxidation-mediated modifications of GCase which disrupt its enzymatic activity. We found that this vicious feedback cycle could be interrupted by targeting wild-type GCase with small molecule activators in human DA neurons. Moreover, our in vivo analysis in mice revealed that S-181 could penetrate CNS and enhance wild-type GCase enzyme activity in brain tissue. In sum, these findings point to the relevance of therapeutically targeting GCase across multiple genetic and sporadic synucleinopathies.

O172

PARIS: The Rosetta Stone to understanding Parkinson's disease

*Ted Dawson**
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Parkinson's disease (PD) is due, in part, to the progressive loss of dopamine neurons in the substantia nigra pars compacta, which leads to bradykinesia, rigidity, rest tremor and postural instability. Degeneration of other neuronal populations and/or neuronal dysfunction due to the accumulation and aggregation of α-synuclein, the major protein constituent of Lewy Bodies and Lewy Neurites leads other clinical features including autonomic dysfunction, anxiety, depression, abnormalities of sleep, cognitive impairment, among others. Fresh insights into the pathogenesis of PD have come from understanding the genetic underpinnings of PD. Mutations in the cytosolic ubiquitin E3 ligase, parkin and the protein kinase PINK1 cause autosomal recessive PD. Defects in mitochondrial quality control contribute substantially to the demise of DA neurons due to parkin and PINK1 inactivation. PARIS (ZNF746) is a cytosolic protein that shuttles between the cytosol and nucleus, where it acts a co-repressor to control the levels of PGC-1alpha, a master co-regulator of mitochondrial biogenesis and mitochondrial anti-oxidant defenses. Knockout of PARIS dramatically prevents the loss of DA neurons due parkin and PINK1 inactivation as well as accumulation and aggregation of α-synuclein through preventing the down regulation of PGC-1alpha thereby maintaining mitochondrial biogenesis and mitochondrial anti-oxidant defenses. Strategies aimed at inhibiting or reducing PARIS levels in PD hold exciting promise as disease modifying therapies for the major causes of autosomal recessive PD and sporadic PD.

O173

Insulin resistance, diabetes and Parkinson's disease – How do they link together?

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The incidence of both Type 2 diabetes and Parkinson's disease is increasing. Accumulating research studies suggest that both diseases share some pathophysiological features such as mitochondrial dysfunction, abnormal inflammatory responses and protein accumulation. Furthermore, epidemiological evidence suggests that Type 2 Diabetes is a risk factor for the development of Parkinson's disease and can influence its disease course. In addition, emerging evidence suggests that insulin resistance, which is a core feature of Type 2 diabetes may play an important role in neurodegeneration. The aim of this talk will be to review the experimental data exploring the links between insulin resistance, Type 2 diabetes and Parkinson's disease, and the role Insulin signaling plays within the brain. The concept of "brain insulin resistance" will be introduced and the evidence that patients with Parkinson's disease demonstrate dysfunctional brain insulin signaling will be discussed. Although it is currently unclear whether insulin resistance is a cause or consequence of neurodegeneration, there is growing interest that existing treatments used to treat Type 2 diabetes that act on insulin signaling could be used as novel therapeutics in Parkinson's disease. This talk will conclude by highlighting some of the most recent clinical trial data exploring the use of these treatments in Parkinson's disease and possible future directions.

O174

Glial and immune basis of chronic stress-induced neurodegeneration in Parkinson's disease

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Despite considerable research and funding efforts, efficient curative treatment for Parkinson's disease (PD) are still lacking. Among the reasons evoked is a gap in knowledge concerning gene-environment interaction in the etiopathogenesis of this complex disease. In line with this, stress, a phenomenon encountered in daily living, has emerged as an important environmental factor potentially involved not only in the emergence but also the progression of PD. Chronic stress is most known for its role in neuropsychiatric conditions such as depression. It is noteworthy that depression is a common co-existing condition in neurodegenerative diseases such as PD and it has been suggested that depression itself, particularly in late life, may be an indication of latent neurodegeneration. Environmental stress induces complex interactions between neuroendocrine, neuronal and immune systems, resulting in outcomes that are beneficial and adaptive. Glucocorticoids (GCs) released by HPA axis stimulation activating glucocorticoid receptors (GRs) play a central biological role upon stress by modifying immune and neuronal functions. However, "chronic" (i.e. sustained) stress over protracted period can result in deregulation of HPA axis, which compromises GR functions. Our central hypothesis is that chronic stress may favor harmful and/or overactivated immune responses contributing to neurodegeneration in PD. Our data indicate that (i) chronic unpredictable mild stress (CUMS), a model of daily living stress resulting in anxiety- and depressive-like behavior in mice, leads to increased loss of DA neurons in both genetic (synuclein)- and toxic (MPTP)-based mouse models of PD; (ii) increases innate (microglia) and adaptive (T cell infiltration) immune responses in PD mice; and (iii) alters GR (decrease) and IL-1beta (increase) mRNA levels. Using cell-specific deletion strategies, we further show that microglial and astrocytic GR are essential in controlling neuroinflammation and dopamine neurodegeneration. Overall, our data provide mechanistic insights into stress-related changes in immune and glial cells affecting PD pathology.

O175

How do you find a good candidate in the lab?

*Erwan Bezard**
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The search for therapies of Parkinson's disease actually covers a number of fundamentally different objectives: either alleviating a given symptom, decreasing the severity of therapy-induced side-effects, or slowing down disease's progression. Although serendipity or drug repositioning have shown great value in proposing treatments, a clear development plan should be envisioned for the systematic educated search of such new therapies. Researchers have first to clearly define what type of solution they aim at developing. The target (i.e. the biological actor on which the researcher wants to act) selection then heavily depends upon the conceptual framework, the current knowledge of the considered pathophysiology, the delicate selection of the most relevant in vitro and in vivo models, etc... The target validation comes next with a particular emphasis put upon the model selection. A "good candidate" in the lab would pass the different screens but may need further refinement for paving the way to a successful translation to the clinic.

O176

How do you take a therapy from the lab, to the clinic, to the market?

*Kalpana Merchant**
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Development of a therapy aimed at slowing the progression of Parkinson's disease or providing symptomatic benefit is a multi-stage process. At a high level, these stages are classified as: (i) discovery, (ii) lead optimization, (iii) preclinical development and (iv) clinical development. In the discovery stage, a therapeutic target is selected on the basis of scientific evidence of its role in the biology of the disease. Next, robust and reproducible assays are employed to screen thousands of molecules to identify ones that have the desired activity on the therapeutic target. These molecules are rarely ideal as drugs and need to be modified through the process of lead optimization to incorporate drug-like properties such as potency, selectivity, pharmacokinetic characteristics, etc. In the next stage of preclinical development, a small number of optimized compounds are tested further to establish activity or efficacy in animal models, ensure safety through toxicology studies and formulated for human clinical trials. Once a regulatory authority reviews the preclinical data package and grants approval to initiate human studies, the drug candidate is tested in a series of trials termed Phase I, II and III. In aggregate the clinical trials have to establish that the therapeutic molecule is safe, well tolerated and produces meaningful efficacy prior to getting approval for marketing. This talk will discuss ways to de-risk drug development at each stage with a specific emphasis on developing the so-called "tailored therapies" for individual patients – from target discovery to use of biomarkers to inform clinical doses, enrich trials with patients most likely to respond and monitor disease modification.

O177

How to get food & liquid in despite swallowing problems?

*Sonoko Nozaki**
Kansai Rosai Hospital, Amagasaki, Hyogo, Japan

Swallowing problems are common in Parkinson disease (PD). Dysphagia in PD is a prognostic determinant and significantly reduces quality of dietary habits. Dysphagia is present in the majority of PD patients; it sometimes manifests in the early stages of the disease, but is not necessarily limited to any specific Hoehn-Yahr stage. PD patients consequently have poor awareness of dysphagia and silent aspiration is common. Long-term consumption of L-DOPA can cause an off phenomenon that leads to worsening dysphagia during the "off" phase. Consequently, the medication becomes more difficult to administer and residual drugs in the oro-pharynx lead to reduced effectiveness.
In PD, a variety of disorders affect the voluntary movements, reflex actions, and autonomous movements that occur during swallowing. Abnormal posture, hesitation of tongue movement, decreased swallowing action, nasopharyngeal reflux and attenuation of esophageal peristalsis further complicate dysphagia.
Neuroleptic malignant syndrome can also result in severe dysphagia. The drooling occurs as a result of decreased salivary deglutition. The efficacy of deep brain stimulation as treatment for this form of dysphagia remains unclear. Complications can result due to decreased cough volume acceleration which increases the risk of aspiration, and postprandial hypotension which sometimes induces suffocation during or after meal consumption.
Basic management of dysphagia symptoms consists of adjusting the timing of medication administration and mealtimes during the "on" phase; dietary modification to include thickeners to aid liquid consumption; adjusting food textures in accordance with evaluations of swallowing; and adjusting patients' seating positions.
As posture support for patients with Pisa syndrome, the patient is sat up straight and encouraged to swallow with their chin facing downwards so that aspiration can be avoided.
Evidence of intervention to improve the swallowing function of PD patients was reported to comprise positioning the chin face-down, food texture modification, expiratory muscle strength treatment, rhythm treatment using a metronome, and Lee Silverman Voice Treatment.
Treatment aims to ensure that swallowing is safe and requires less effort while maintaining optimal nutritional intake. With appropriate management, quality of dietary habits can be maintained at better levels for patients in all stages of PD.

O178

Is there a Parkinson's diet?

*Karin Overbeek**
ParkinsonNet The Netherlands, Nijmegen, Gelderland, The Netherlands

What we eat and drink has a big influence on how we feel physically and mentally. This is also valid for patients with Parkinson's disease. Patients want to know how they can do more self-management. Professionals want to get to know the diet related problems for patients with Parkinson's disease and want to get tools for good treatment.
The ParkinsonNet published a Dietetic Guidlines for Parkinson's disease. It gives an overview of the key questions and recommendations for each diet related problem.
In this presentation, we will focus on (1) the most important recommendations for patients in relation to their diets, (2) how can patients improve their self-management regarding diets and (3) what are criteria for referral to dietitians with expertise in Parkinson's.

O179

Food for thought: The gut-immune-brain axis in Parkinson's disease

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Division of Pharmacology, Utrecht Institute for Pharmaceutical Sciences, Faculty of Science, Utrecht University, Utrecht, The Netherlands

Many CNS disorders are associated with gastrointestinal deficits characterized by motility problems, low-grade inflammation, pain, alteration of microbiome composition and activity and leaky gut. The recently reported leaky gut, intestinal inflammation and changes in the composition of the microbiome in patients point to the relevance of gut-microbiome-immune-brain axis in neurodegenerative disorders such as Parkinson's disease. Based on (pre)clinical data the talk will shed some light on the possible mechanism of the crosstalk between gut and brain in Parkinson's disease with a focus on immunological mechanisms. Clinical data from patients show a leaky gut, changed microbiome composition, enhanced markers of microbial translocation (endotoxemia) and higher levels of relevant inflammatory profiles associated with an increased expression of toll like receptor 4 (TLR4) in the colon. To further specify the role of TLR4 in Parkinson's disease, results from a parkinsonism model in wild type and TLR4KO mice will be presented. Both human and animal studies suggest that TLR4-mediated gut-induced neuroinflammation could play an important role in intestinal as well as central neurodegenerative processes in Parkinson's disease.

There is a great need for additional therapies for Parkinson's disease that reduce/modulate both motor and non-motor symptoms. We recently have shown that a diet containing nutritional precursors and cofactors required for membrane phospholipid synthesis, as well as prebiotic fibres, had therapeutic effects in a mouse model for PD. The effects of combined administration of the dietary intervention together with levodopa treatment are also studied in this murine PD model.
A poor gut function leads to a poor brain function and vice versa; therefor targeting the microbiome/gut with nutritional interventions or pharmaceutical compounds targeting immune processes could be a new approach for the therapy of neurodegenerative disorders for the treatment of both motor and non-motor dysfunction.

O180

New causative genes for PD
*Alexis Brice**
ICM – Institut du Cerveau et de la moelle épinière – Brain and Spine Institute, Paris, France

It is now well established that monogenic forms of PD represent a subset of cases with variable frequencies according to the age at onset, family history and geographical origin. The definitely validated genes include SCNA, LRRK2, VPS35, SCA2, CGH1 for autosomal dominant (AD), PKRN, PINK1, DJ1, ATP13A2, PLA2G6, FBXO7, DNAJC6, SPG11, SYNJ1, VPS13C for autosomal recessive (AR) and RAB39B for X-linked forms. In contrast to other disorders, the explosion of exome or whole genome sequencing in PD cases has not led to a great increase in new genes. Furthermore, most of the newly identified genes seem very rare and are not always replicated in follow-up studies, questioning their implication in PD. Since 2016, familial studies identified CHCHD2 and LRP10 as candidate genes for AD and PODXL, ADORA1, PTRHD1 and VPS13C for AR PD. Interestingly, all AR cases were associated with early or juvenile onset and, most of them, with other signs in addition to Parkinsonism. So far, only VPS13C has been fully replicated as a PD gene. Of note, VPS13C is also a risk factor for idiopathic PD. This demonstrates that that genetic factors may play a dual role in monogenic and idiopathic PD, as already described for LRRK2 and SNCA. The rarity of cases caused by new genes, the presence of phenocopies in families and the lack of definite criteria for functional studies makes the validation of new candidate genes very difficult. Large scale studies and international collaborations are needed to validate or exclude newly identified candidate genes.

O181

Next generation sequencing strategies and its role in identifying genetic risk factors for Parkinson's disease
*Tatsushi Toda**
Department of Neurology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

Parkinson's disease (PD), one of the most common neurodegenerative diseases, is caused by multiple genetic and environmental factors. ~16 disease causing genes have been identified for familial form of Parkinson's disease (PD), studies of which indicate a cell death pathway in dopaminergic neurons induced by defective protein degradation as a key molecular mechanism underlying the pathogenesis of PD. Yet the majority of PD cases are sporadic, which is a multifactorial genetic disorder. We performed genome-wide association study (GWAS) and two replication studies in a total of 2,011 PD cases and 18,381 controls from Japan. We identified a novel PD-susceptibility locus on 1q32 and designated this as PARK16. BST1 also showed a novel and strong association with PD. We detected a strong disease association at SNCA and LRRK2 on 12q12, both causative genes for autosomal dominant parkinsonism. Now, large-scale meta-analysis of GWAS identifies total of ~30 genes. Rare variants, less common yet associated with high risks for the disease onset, are also important, and Gaucher disease mutations are proven to be a definite rare variant risk factor for PD.
To identify further common variant PD-risks, we performed Japanese 2nd SNP-GWAS that expanded our previous one. In 2nd GWAS using 1,948 cases and 28,990 controls, we identified a novel susceptibility locus with $P < 5 \times 10\text{-}8$. Expression level of a gene within the locus was reduced when the risk SNP exists. In a fly model, knockout of the gene worsened motor function.
Moreover, to search for further PD-risks in exonic areas, we performed exome sequencing of ~1800 PD patients using Sureselect and HiSeq2500. At first, using exome sequencing data of 625 PD cases and 259 controls, we tested association between PD and exonic SNVs within the 4 PD-loci reported by SNP-GWAS. Genetic variants with strong PD-risk did not exist within these 4 PD-loci, indicating that these 4 PD-loci will contribute to this disease as common SNP variants. We will subsequently test association between whole exonic SNVs and PD to identify novel PD-genes harboring rare-variant risks.

O182

The challenge of disease classification in PD – What does it look like and what does it mean
*Rejko Krüger**
Luxembourg Centre for Systems Biomedicine (LCSB), University of Luxembourg, Luxembourg

To date, no causative treatments are available for common neurodegenerative diseases like Parkinson's disease (PD). Previously failed trials did not account for the clinical and pathophysiological heterogeneity of PD, so that novel ways for classification of subgroups of PD patients are needed.
Genetics of PD provided first insight into the complexity of this most common neurodegenerative movement disorder and delineated relevant subgroups of patients, who share an underlying molecular pathology. Here novel patient-based models from genetic forms of PD allowed to dissect mechanisms of neurodegeneration and define a first entry point to screen for disease-modifying compounds for more targeted therapies.
Moreover, during the last years, there has been a rapid evolution in novel technologies, e.g. next generation sequencing technologies or device-assisted registrations of PD symptoms. These are linked with a dramatic increase in high quality data characterizing PD at different levels and enables novel strategies for patient classification and identification of markers for therapeutic outcomes, that can be translated into precision medicine approaches and clinical decision support. Here, first genetic predictors for different therapeutic outcomes emerge for either pharmacological or neuromodulation treatment in PD.
Together the implementation of novel technologies allows not only for novel ways to classify PD, but also for a more direct participation of patients in ongoing research thereby strengthening patient's autonomy and responsibility for future research.

O183

Stem cell and reprogramming strategies to treat PD
*Ernest Arenas**
Karolinska Institute, Stockholm, Sweden

Parkinson's disease (PD) is an incurable neurodegenerative disorder characterized by the loss of midbrain dopaminergic (mDA) neurons. Current efforts in cell replacement therapy focus on the generation of human mDANs by differentiation of pluripotent stem cells or reprogramming of somatic cells. However, our knowledge of the molecular mechanisms controlling the generation of mDA neurons is still limited.
To address this issue we recently performed single-cell RNA-sequencing (scRNA-seq) of the developing human midbrain. This method allowed the identification of new cell types and uniquely expressed genes with unprecedented detail (RNA molecules per cell). We are currently performing scRNA-seq and ATAC-seq of human pluripotent stem cell-derived midbrain cell preparations to be used for transplantation in PD. These data are being compared to our human midbrain developmental standards in order to determine the quality of cells to be used for cell replacement therapy in PD and devise ways to further improve their properties.
We are also working to develop direct in vivo reprogramming as a therapeutic alternative to cell transplantation for PD. We previously found that lentiviral delivery of reprogramming factors to human astrocytes in vitro induced functional dopamine neurons. Moreover, reprogramming of adult mouse striatal astrocytes in situ into induced dopamine neurons partially improved motor function in a mouse model of PD. ScRNA-seq and bioinformatics analysis are currently being used to identify novel factors capable of improving direct in vivo reprogramming of astrocytes into induced dopaminergic neurons, as a source of cells for cell replacement therapy for PD. We found that different combinations of transcription factors are capable of reprogramming human astrocytes into induced dopaminergic neurons in vitro. Our results open the door for the development of cell replacement therapies for PD that may not require cell transplantation.

O184

Using stem cells to treat PD
*Jun Takahashi**
Center for iPS Cell research and Application, Kyoto University, Kyoto, Japan

Human induced pluripotent stem cells (iPSCs) can provide a promising source of midbrain dopaminergic (DA) neurons for cell replacement therapy for Parkinson's disease (PD). Towards clinical application of iPSCs, we have developed a method for 1) scalable DA neuron induction on human laminin fragment and 2) sorting DA progenitor cells using a floor plate marker, CORIN. The grafted CORIN+ cells survived well and functioned as midbrain DA neurons in the 6-OHDA-lesioned rats, and showed minimal risk of tumor formation. In addition, we performed a preclinical study using primate PD models. Regarding efficacy, human iPSC-derived DA progenitor cells survived and functioned as midbrain DA neurons in MPTP-treated monkeys. Regarding safety, cells sorted by CORIN did not form any tumors in the brains for at least two years. Finally, MRI and PET imaging was useful to monitor the survival, expansion and function of the grafted cells as well as immune response by the host brain.
Based on these results, we have started a clinical trial to treat PD patients at Kyoto University Hospital in Kyoto, Japan in 2018. This is to evaluate the safety and efficacy of transplanting human iPS cell-derived dopaminergic progenitors into the putamen of PD patients. We will implant approximately 5 million cells to each of 7 patients and observe for 2 years.

O185

Stem cell tourism – What is it all about?
*Jonathan Kimmelman**
Biomedical Ethics Unit/McGill University, Montreal, Quebec, Canada

Numerous clinics in both high-income countries as well as low and middle-income countries market unproven stem cell-based interventions (SCBIs) for the treatment of Parkinson's disease (PD) and other neurological diseases. In this presentation, I will describe the prevalence of such clinics around the world, reasons why they have flourished, and the ethical and policy concerns associated with the marketing of unproven SCBIs, or otherwise offering unproven SCBIs to patients outside clinical trials. I will also address the ethical and policy dimensions of "pay to participate" clinical trials, where patients underwrite the costs of trials where they receive cells. I will close by describing various policy initiatives that might curtail or reshape the marketing of unproven SCBIs to patients (either within or outside trials), including changes in regulation, professional society policy, and policies in medical licensing authorities.

O186

Apathy: Is there a treatment?
*Kathy Dujardin**
Lille University medical center, Lille, France

Apathy corresponds to a lack of motivation. It is characterized by a significant reduction of goal-directed activity in domains like behavior, cognition, emotion or social interaction. Apathy is a frequent non-motor manifestation of Parkinson's disease (PD). It has a strong impact on the level of functioning and quality of life of PD patients and their caregivers.
From a pathophysiological point of view, several studies have suggested that apathy results from dysfunction of the limbic circuit connecting the ventral striatum to the frontal cortex. The dopaminergic denervation in these regions seems to play a role in the origin of apathy. However, the mechanisms underlying this syndrome remain largely unknown. As a consequence, available therapies are very limited. In some cases, an adjustment of the dopaminergic medication may produce a benefit. Medications targeting the cholinergic and serotoninergic systems have also shown some efficacy. Non-pharmacological approaches are also to be considered even though we lack controlled trials proving their effectiveness.
Caregivers play an essential role but the risk of burn-out is very high. Education programs specifically dedicated to the caregivers and family members are absolutely needed.

O187

Anxiety: How best to manage it
Roseanne Dobkin[1], Nadeeka Dissanayaka[2], Alejandro Interian[3]*
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While common and disabling, anxiety is a modifiable factor that can positively influence all aspects of Parkinson's disease (PD) care, when effectively managed. Behavioral interventions are of great interest to the PD community and excellent complements (or

alternatives) to pharmacological treatment. The applications of two specific non-medication approaches, Cognitive Behavioral Therapy (CBT) and Mindfulness Based Stress Reduction (MBSR), to the treatment of anxiety in PD, will be highlighted throughout this presentation. For example, CBT is a change-based approach that aims to modify specific negative thoughts (e.g., "I have no control; It will be horrible if people see me shake; DBS failed because I still have PD symptoms") and behaviors (avoidance, withdrawal, social isolation) associated with anxiety in PD. It is a structured and active approach that focuses on concrete coping skills, incorporates multiple techniques, commonly involves family members, and is tailored to meet the needs of each unique PWP. Examples of specific CBT treatment strategies for anxiety include relaxation training, scheduling and postponing worry time, exercise, problem-solving around physical limitations, modifying negative thinking patterns, gradual exposure to feared situations, addressing lifestyle factors such as sleep hygiene, and increasing involvement in meaningful, pleasurable, and social activities. In contrast, MBSR is considered an acceptance-based approach, that teaches people how to observe thoughts and feelings in a purposeful way, without judgment, and with a present-moment focus, with the goal of responding to difficulty in ways that are less reactive (e.g., without preoccupation, rumination, and negative judgments). MBSR pursues this goal by teaching a diverse array of meditation techniques including mindfulness of breath and body, body scan, mindfulness of eating, mindfulness of thoughts, and kindness meditation. All elements are designed to address the 5 facets of mindfulness- observing, describing, acting with awareness, non-judging of inner experience, and non-reactivity to inner experience. In addition to comparing and contrasting CBT and MBSR treatment approaches for PD anxiety, this talk will also highlight self-assessment tools to help determine if anxiety treatment is indicated, strategies for locating treatment providers in the local community, and the use of telemedicine to leverage access to informed mental health care.

O188

Depression in Parkinson's disease: How best to treat it

Murat Emre, Zeynep Tüfekçioglu*
Istanbul Faculty of Medicine, Istanbul, Turkey

Depression in Parkinson's disease (PD) is multi-factorial, it involves response to a chronic disabling disease as well as dysfunction in modulatory neurotransmitter systems such as dopaminergic, serotoninergic and noradrenergic pathways. Management requires recognition, assessment of necessity to treat and choice of the modality for treatment. Treatment involves both pharmacological and non-pharmacological approaches. Large randomized control trials in PD patients with depression are scarce. There are several small placebo controlled trials with tricyclic anti-depressants desipramine, amitripyline, nortriptyline; selective serotonin reuptake inhibitors citalopram, paroxetine, sertraline and serotonin/noradrenalin reuptake inhibitor venlafaxine suggesting efficacy. The dopaminergic agonist pramipexole has been tested in a large scale randomized controlled trial and found to be effective. Non-pharmacological approaches include education about coping mechanisms, the most evidence for structured psychotherapy exists for cognitive behavioral therapy. Trans-cranial magnetic stimulation is experimental, in resistant cases electro-convulsive therapy may be considered. The choice of treatment should be based on the age as well as accompanying motor and non-motor symptoms.

O189

Abnormal neural activities in the cortico-basal ganglia networks in animal models of PD

*Atsushi Nambu**
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It is very important to understand neural activity changes in the cortico-basal ganglia (BG) networks in PD, because it can explain pathophysiological mechanisms for PD symptoms in human patients. Besides, normalizing or modulating abnormal neural activity can ameliorate PD symptoms. So far, there are three models to explain pathophysiology of PD symptoms. One is the "firing rate model". Spontaneous firing rate changes along the cortico-BG networks were originally reported in MPTP (dopaminergic neurotoxin)-induced PD monkeys. The most characteristic finding was an abnormal increase in firing rates in the output nucleus of the BG. However, recent electrophysiological studies have failed to detect expected neural activity changes in the BG. Instead, the "firing pattern model" was proposed. Abnormal firing patterns, such as oscillatory and synchronized activity, were observed in the BG of PD models and patients, which may disturb normal information processing through the cortico-BG networks. The third one is the "dynamic activity model". Stimulation in the cortex normally induces triphasic responses, i.e., early excitation, inhibition and late excitation, in the output nucleus of the BG, and the inhibition is important for the initiation of voluntary movements. Our group have found that cortically induced inhibition in the output nucleus is abnormally reduced in PD models, and this may cause a failure in releasing appropriate movements at an appropriate timing. We believe that such dynamic activity changes in the BG are fundamental features of PD, and that firing rate and pattern changes may merely be epiphenomena. Indeed, PD symptoms can be ameliorated by making a small lesion or applying high-frequency electrical stimulation (deep brain stimulation, DBS) in the BG. Both lesions and DBS can block abnormal information flow from the BG to the cortex, and may be useful in suppressing the expression of PD symptoms. Their effectiveness is compatible with the "dynamic activity model".

O190

Immune therapies for PD

*Seung Jae Lee**
Seoul National University, Seoul, South Korea

Immunization therapy targeting α-synuclein has emerged as a promising approach for Parkinson's disease and perhaps for other synucleinopathies. Several antibodies have shown therapeutic effects in mouse models of synucleinopathies and have alleviated the pathological and behavioral phenotypes of these mice. The mechanisms through which the immunization therapy works were initially puzzling, especially given that α-synuclein is a typical cytosolic protein. Recent studies, however, suggested that extracellular α-synuclein is an important pathogenic entity, and hence, a target for immunotherapy. In this roundtable discussion, I will review the literature describing immunization therapy for synucleinopathies in mouse models and provide current thoughts on the potential mechanisms underlying the therapeutic effects of α-synuclein immunotherapy. In addition, I will review the current state of clinical trials for immune therapy and provides potential targets for immunotherapy other than α-synuclein. I will also discuss the potential obstacles we face in immune therapies.

O191

Repurposing drugs that target risk factors for PD
*Michael Schwarzschild**
Massachusetts General Hospital, Boston, MA, USA

Parkinson's disease (PD), to the extent that it can be considered a single disease, is caused by a complex interplay of genetic and environmental factors. Recent identification and investigation of gene mutations that can cause PD (e.g., SNCA, LRRK2, GBA) are leading to promising therapeutic candidates targeting the mutations' pathogenic effects. Enthusiasm for targeting these mutations is warranted by our confidence in their causal role, but is tempered by the relatively small proportion of PD caused by these mutations and uncertainty of their relevance to the vast majority of PD that does not result from the targeted mutation. On the other hand, traditional epidemiologic studies have identified a number of exposures or behaviors as 'reduced risk' factors that reflect protective influences likely of relevance to all forms PD. However, their association with resistance to the disease does not necessarily mean they are preventing it, as association does not prove causality. Nevertheless, some of these 'reduced risk' factors have been found to confer neuroprotection in laboratory models of PD, demonstrating the biological plausibility of a causal basis for the reduced risk. This convergence of epidemiological and biological findings has prompted clinical testing of a number of these environmental, dietary, pharmacological or behavioral factors as candidate disease-modifying therapy. Their translation back to the clinic has been accelerated by the repurposing of existing drugs or activities that constitute or target these 'reduced risk' factors, which takes advantage of their established safety and features that can take years to demonstrate in the early stages of drug development. Repurposed therapies targeting 'reduced risk' factors – which recently have been, currently are, or soon may be in clinical trials for PD – include smoking or tobacco components, caffeine, calcium channel blockade, urate-elevating inosine, exercise, ibuprofen, deferiprone, exenatide-like drugs, statins, albuterol and ambroxol. The results, status and plans for these trials will be briefly discussed.

O192

Why partnered dance is a valuable therapy for people with Parkinson's
*Madeleine Hackney**
Emory University, Atlanta, GA, USA

Rehabilitative programs for balance problems are most effective if they incorporate moving and then catching your balance repeatedly while continually adjusting to new environmental challenges, which dance provides. While un-conventional, dance appears to be appropriate and pleasurable as a therapeutic activity, because of its benefits to physical, mental and emotional states. Group social dance can enhance motivation in participants to be active and pursue healthy, exercise-related behaviors in older individuals. Older adults who participated in dance also demonstrated improved balance and functional mobility. When balance is practiced in the guise of dance it may be just as effective as, and more enjoyable than, traditional balance training. In the last 10 years, it has been demonstrated that individuals with idiopathic PD who participated in adapted Argentine tango (adapted tango) dance lessons improved their mobility, balance, gait, and quality of life. Adherence is crucial to any exercise program, but 60–85% adherence to physical activity in impaired older adults is considered high. With an 85% compliance rate, adapted tango's feasibility and benefits on mobility and quality of life for persons with PD was demonstrated. Maintenance of these gains was also demonstrated and participants reported favorable impressions and interest in continuing. It is likely that this adapted tango program creates a social, supportive nature and a sense of community involvement, which enhances exercise adherence. Even a program of adapted tango offered 5 times per week for 3 weeks, has been feasible and with low attrition for individuals with mild-moderate PD. Further studies in adapted tango have demonstrated benefits to cognitive and psychosocial function in addition to motor symptom relief. Adapted tango and other partnered dances might provide a cogent option for maintaining multiple aspects of fitness in PD.

O193

Aerobic exercise for Parkinson's disease – Useful or not?
*Terry Ellis**
Boston University, Boston, MA, USA

In this round table session, we will discuss the role of aerobic exercise in the treatment of Parkinson disease. The following questions will guide our discussion: What makes an exercise "aerobic?" What is the difference between physical activity and exercise? What types of exercise meet the guidelines for aerobic exercise? Is there a "best" type of aerobic exercise? What is the recommended dose of aerobic exercise for persons with Parkinson disease? How intense does the exercise need to be to realize a benefit? How do you know if you are working hard enough when engaging in aerobic exercise? Is there a best time, during the course of the PD, to engage in aerobic exercise? What is so special about aerobic exercise – is it better than other types of exercise? Why is aerobic exercise beneficial – how does it affect the brain? How do you fit exercise into to your busy schedule? We will discuss strategies to help you make exercise part of your usual routine.

O194

New insights into L-dopa induced dyskinesias
*Barbara Picconi**
IRCCS San Raffaele Pisana, and University San Raffaele, Rome, Italy

The round table will opened by an introduction from experts in the field of Parkinson's disease and then extended to patients that would like to learn more on the neuronal mechanisms underlying LIDs.

O195

Aging of the immune system and its relevance to brain health and PD
*V. Wee Yong**
University of Calgary, Calgary, AB, Canada

The impact of aging on the immune system is complex. While the ability to mount an efficient innate and adaptive immune response to newly encountered pathogens is impaired, the immune system in general undergoes a shift toward a proinflammatory status with aging, also referred to as "inflammaging". For microglia, the sentinel immune cell of the CNS, its production of pro-inflammatory cytokines and potentially damaging factors including oxygen radicals is elevated with aging; yet, its capacity to phagocytose and remove debris and harmful protein aggregates appear diminished with senescence, as is its production of trophic molecules. The density and activated morphology of microglia have also been noted to increase with age in several CNS compartments. These attributes of the aging immune system heighten the potential detrimental roles

of immune cells with senescence, particular with regards to the neurodegenerative potential of aging microglia within the CNS. We will discuss the characteristics of immune senescence, the mechanisms that underlie aging-associated immune dysregulation, and consider medications that normalize microglia activity to reduce the neurodegenerative potential of aging microglia, and to enhance their phagocytic and repair potential.

O196

Medical and surgical advances in Parkinson's

*Genko Oyama**
Department of Neurology, Juntendo University Faculty of Medicine, Tokyo, Japan

Since the first description of the disease by Dr. James Parkinson, many discoveries and advances have occurred regarding symptomatic treatments. Before the introduction of stereotactic surgery in the 1950s, there were only a few medications such as anticholinergics and its effectiveness was limited. Surgical treatments such as thalamotomy and pallidotomy resulted in excellent outcomes but it also brought serious adverse events such as gait problem. Since then, two big milestones in the treatment for Parkinson's disease have been achieved.
The first milestone was a discovery of levodopa. It provided a bright future for people with Parkinson (PwP), but levodopa-induced motor complications were recognized several years after the introduction of levodopa. Wearing off and dyskinesia limited the benefit of levodopa. Subsequently, development of dopamine agonists and MAO-B inhibitors started with the hope of preventing motor fluctuation and disease progression, followed by the development of several formulations of dopamine agonist including long-acting and sustained-release type. The recent challenge to overcome motor fluctuation includes continuous delivery of medications using a pump, such as continuous subcutaneous apomorphine pump, and levodopa/carbidopa intestinal gel (LCIG).
The second milestone was the development of deep brain stimulation (DBS). This technique could modulate brain circuit and result in a tremendous symptomatic benefit for PwP. With the accumulation of large-scale studies, DBS of the subthalamic nucleus and globus pallidus interna have been established the firm position as a treatment for the advanced Parkinson's disease. Recent advancement of magnetic resonance-guided focused ultrasound therapy has shed a light on the old-fashioned lesioning surgery again.
In this session, the history of the development of these medical and surgical evolvements and current status of potential future treatment will be discussed.

O197

A family affair: Well-being for everyone when a diagnosis of PD knocks on the door

*Jasmine Sturr**
Whittier, CA, USA

While most people might think of Parkinson's as being a 'grandparent's diagnosis,' it is evident by the vibrant young onset population that anyone could be the next PD patient lined up at the movement disorder specialist's office. The few of us running around with juvenile onset PD prove that the next person with Parkinson's could even be your child.
When PD hits anyone, your grandfather, partner, parent, or teenage daughter, it's a family affair. Keeping your beloved PWP alive and well is not an easy task, it requires a lot of adapting and learning to really thrive with a neurodegenerative illness. In this round table I will share my family's journey- one that began ten years ago, with my PD onset at age 14. The next decade was trying as a family, my sister was only 8, I was in my first year of high school. We went from the typical american 'two kids and a dog' family to navigating the waters of the health care system. As my disease became more complex we had to navigate the world of disability and culture as we had to figure out how to explain to my korean immigrant relatives what was going on. As I grew up I had to navigate college and eventually living on my own with my partner, who became a new part of the village it takes to maintain a good life with dying dopaminergic neurons. This round table session will examine how a family copes with both the shock of the diagnosis and the resulting physical changes that occur, the importance of the Parkinson's community, navigating the health care system, and walking multi-cultural lines with this disease. It will also touch upon accommodations and adaptations in the home and work environment that are necessary for one to thrive with PD. While many think of Parkinson's as an end, for us it was only a new beginning and a different journey that we did not expect to take. Perhaps it was a harder one, but one that nonetheless became not only my story but the story of my family.

O198

Music & dance for Parkinson's disease

*Meg Morris**
La Trobe Universtiy, Bundoora, Victoria, Australia

This round table will bring together clinicians, research experts and consumers on the benefits of music, singing and dancing for people living with Parkinson's disease (PD). It will explore which music and dance genres improve movement, balance, well-being, social participation and quality of life in people with PD and the significant others in their lives. Research on the outcomes of community singing programs and choirs for people with PD will also be discussed. Recommendations for how to use music and dance to increase exercise, physical activity and social engagement will also be explored.

O199

Sexual intimacy and Parkinson's

*Gila Bronner**
Sheba Medical Center, Ramat-Gan, Israel

Introduction: Intimacy is a special way to be close with another person, to feel warmth and experience authentic interaction. It plays a major role in people's life, because humans need emotional and physical closeness. Intimacy contributes to well-being, health promotion, self-esteem and confidence. It is essential for all of us like oxygen. Sexual intimacy may include erotic activities (feeling desire, arousal, orgasm) and non-erotic activities (hugging, caressing, kissing in a pleasant and comforting manner for both partners). Having sex will usually be more satisfying when intimacy exists between the parties involved. It is recommended that couples will be able to lead intimate life and sexual life in an independent existence. This means, that couples will be able to touch, kiss and hug without being obliged to move to sexual-erotic activity (erection, lubrication, sexual arousal and orgasm). Couples who have both options: to enjoy a relaxing and loving touch on one occasion, and to enjoy sexual activity on another time, may have a better emotional and intimate relationships. People with Parkinson's disease (PD) and their partners are coping with multi-faceted challenges and their sexual intimacy may be impaired.
Methods and Results: Participants will be able to practice verbal and non-verbal communication, to present questions regarding

intimacy, and to discuss options to increase intimacy. A “Time Allocation Model”, an effective and practical model designed to increase couple intimacy will be presented and discussed. This interactive dialog may enable couples living with PD to communicate effectively, increase sensations of intimacy and empower their motivation 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 coping together and feel good with one another.

O200

Where are we with DBS?
*Elena Moro**
Centre Hospitalier Universitaire de Grenoble, Grenoble, France

Deep brain stimulation (DBS) is a standard treatment for advanced Parkinson’s disease (PD). Since the first surgery in a PD patient in Grenoble (France) in 1987, more than 160,000 patients have benefitted from this therapy over the world. Beside improving motor symptoms responding to levodopa, DBS has been shown to ameliorate also several non-motor symptoms. We have also learned about the long-term effects of DBS, both positive and negative.
Over the years, this technique has allowed clinicians and scientists to better understand the pathophysiology of Parkinson’s disease. Moreover, the success of DBS in movement disorders has been applied to several other neurological and psychiatric diseases. Advances in technology have allowed the introduction of more flexible and smaller devices to better adapt stimulation to the patient’s needs. For example, leads allowing to steer current and shape the stimulation area, and closed-loop stimulation allowing to deliver current on-demand, are likely only the beginning of a new technological era for neuromodulation. Furthermore, other brain targets beside the thalamus, the subthalamic nucleus and the globus pallidum, are under investigation.
However, after more than 30 years, there are still several areas that need to be improved. DBS is not a cure but a symptomatic treatment of the relative advanced phases of PD. DBS candidates represent less than 10% of the overall PD population since surgical indications remain quite strict despite some recent changes within the last few years. One example concerns former absolute contraindications, like the presence of impulsive control disorders at time of surgery, that are not valid nowadays. There is a trend to operate earlier within the course of the disease, before PD has greatly impacted patient’s quality of life. Nevertheless, the DBS journey requires a specialized multidisciplinary team to achieve satisfactory results.
Although several new drugs are under study and development for early and advanced PD, DBS allows to have a more independent life compared to the other invasive treatments. Compared to the modern lesions, DBS has a safer and more solid effective profile as bilateral intervention. DBS technology continues to advance, and new devices will permit better patient’s management.

Poster Presentations

BASIC SCIENCE: Etiology, genetics, epidemiology and toxicants

P01.01

Effect of MHCII-transactivator on aggregation, propagation, and toxicity induced by α-synuclein fibrils
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Chronic inflammation involving activation of microglia and infiltrating lymphocytes is a characteristic of neurodegenerative disorders, including Parkinson´s Disease (PD). Microglia are macrophage-like cells of the CNS that secrete pro- and anti-inflammatory molecules and present antigens on MHCII molecules to T-lymphocytes. HLA alleles that modulate the sequence and expression levels of MHCII are genetically associated to PD risk. We have previously shown that common variations of the MHCII transactivator (Mhc2ta) gene induce differential MHCII expression levels and are associated with susceptibility to human α-synuclein (α-syn)-induced neurodegeneration in rats.
Objectives: To study the effect of Mhc2ta on microglial activation profile as well as aggregation and propagation of α-syn.
Methods: The α-syn seeding model, with a low-dose injection of rAAV-α-syn into the SNpc followed by intra-striatal administration of α-syn pre-formed fibrils (PFFs), was used in DA and VRA4-congenic rats with lower levels of Mhc2ta (DA.VRA4).
Results: Allelic variants of Mhc2ta, regulated the microglial activation profile, behavioral motor impairments, lymphocyte- and cytokine profile as well as aggregation and propagation of α-syn, dopaminergic fiber pathology and density in the striatum and dopaminergic cell survival in SNpc.
Conclusions: Mhc2ta regulates the inflammatory response and toxicity of α-syn in rats. Common genetic variations of the Mhc2ta are also present in the human MHC2TA gene and regulate the susceptibility to inflammatory disease, e.g. multiple sclerosis. Thus, Mhc2ta is a promising potential upstream target to regulate MHCII and the inflammatory response in human α-syn pathology including PD.

P01.02

The risk of Parkinson's disease in chronic hepatitis C virus-infected patients with and without antiviral therapy

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Objective: Hepatitis C virus (HCV) infection has been regarded as a risk factor for Parkinson's disease (PD) based on the recent epidemiologic studies. The antiviral therapy for HCV infection was not considered in those studies, and it remains unclear whether interferon and antiviral agents affects the incidence of PD. Our research was designed to compare the risk of PD in the HCV-infected patients with and without antiviral therapy.
Methods: We enrolled 188,152 HCV-infected patients, on the basis of Taiwan National Health Insurance Research Database, for the analysis. Several comorbidities and medications were identified that they probably affect the incidence of PD. All the subjects were categorized into treated and untreated groups using propensity score matching, to minimize the effect of confounding factors. The covariates were balanced across the groups after matching, and 39,936 subjects in each group were analyzed subsequently.
Results: The incidence density of PD is 1.00 and 1.39 per 1000 person-years in the treated and untreated group, respectively. The hazard ratio for PD in the patients receiving antiviral therapy was 0.71 (P=0.001).
Conclusions: Our study provides the evidence that interferon-based antiviral therapy may reduce the incidence of PD in the chronic HCV-infected patients. It also supports the hypothesis that HCV is a risk factor for PD.

P01.03

The risk of colorectal cancer and stomach cancer in Parkinson's disease: A systematic review and meta-analysis

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Monash University, Bandar Sunway, Selangor, Malaysia

Introduction: Recent studies have reported altered gut microbiota and a high prevalence of Helicobacter pylori infection among Parkinson's disease (PD) patients. Inflammatory bowel disease is also reported to be associated with increased risk of PD. These findings suggest a change in the gastrointestinal physiology in PD patients. Stomach cancer and colorectal cancer (CRC) are the two of the most common cancers of the gastrointestinal system. Earlier epidemiological studies have looked into the risk of these two cancers in PD patients but the results were contradictory. This study aims to determine the risks of colorectal cancer and stomach cancer among PD patients.
Methods: A comprehensive literature search was performed in 3 electronic databases including Medline, Embase and Cochrane Library using the following keywords: COLON, COLORECTAL, CANCER, CARCINOMA, NEOPLASM and PARKINSON'S DISEASE for CRC; and STOMACH, GASTRIC, CANCER, CARCINOMA, NEOPLASM and PARKINSON'S DISEASE for stomach cancer from inception to November 2018. Studies describing the risk of colorectal cancer and stomach cancer among PD patients were included. Pooled risk (RR) for colorectal cancer or stomach cancer among PD patients were calculated with 95% confidence intervals (CI).
Results: For colorectal cancer, a total of 546 studies were retrieved from the databases. 20 studies were identified in this study, of which 9 were cohort studies and 11 were case-control studies. Pooled analysis of the 9 cohort studies comprising of 484,716 PD patients showed a lower risk of developing colorectal cancer (RR: 0.83; 95% CI=0.62–1.13) among PD patients. As for stomach cancer, 210 studies were retrieved from the databases. Twelve studies were included in the systematic review. These studies had described a total of 1,213,782 patients with PD and 9,393,607 controls from America, Asia and Europe. Pooling of the 5 cohort studies showed that there was an increased risk of developing stomach cancer among PD patients (RR: 2.95; 95% CI=0.63–13.87).
Conclusion: There is limited evidence to suggest a lower colorectal cancer risk in PD patients. As for stomach cancer, PD patients may be at a higher risk of developing stomach cancer but larger studies are needed to clarify this link.

P01.04

The clinical profile of GBA-associated Parkinson's disease: A seven year study of motor disease burden

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Objectives: To study the effect of GBA variants on the development of motor symptoms and motor complications in three Northern European population-based studies of patients with incident Parkinson's disease (PD).
Methods: A total of 440 patients were followed from the time of PD diagnosis and a comprehensive battery of motor scales measured annually for up to seven years. GBA variant carriers were analysed as one group, and subcategorised into "polymorphism" or "deleterious mutation" carriers. Mixed linear regression analysis and Cox survival analysis were used to assess the associations between GBA carrier status and longitudinal measure of motor progression or the development of motor problems, respectively.
Results: A total of 12% of patients with PD carried a GBA variant (10% carried a GBA polymorphism and 2% carried a GBA deleterious mutation). The profile and severity of motor symptoms in GBA-PD patients were indistinguishable from non-carriers at the time of diagnosis. However, carriers of GBA variants had a hastened decline in UPDRS motor score compared to non-carriers (0.9; 95% CI, 0.3 to 1.5; P=0.003). The association remained significant for subgroup analysis of GBA polymorphism carriers (0.8; 95% CI, 0.2 to 1.5; P=0.013). No differences were observed in the development of motor complications.
Conclusions: These data add to the clinical profile of GBA-associated PD and show that in addition to earlier and more rapid cognitive decline, these patients also experience more rapid progression of motor symptoms. These results help to build a framework for innovative, genetics-inspired personalised trials in GBA-associated PD. This is especially important as the first clinical trials targeting GBA are underway in PD and PD with dementia.

P01.05

Sequencing known Parkinson's disease genes in Latino PD patients with positive family history from the LARGE-PD consortium

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Objective: Our primary aim was to sequence all known Parkinson's disease (PD) genes in Latino PD patients with family history from South America in order to assess the number and type of mutations present in Latin America.
Background: PD is the second most common neurodegenerative disease after Alzheimer's disease. Almost 30 causative genes have been identified so far in familial PD and related parkinsonisms. However, most of these genes have been identified in families of European origin. Little is known about the role of these genes in Latin America.
Methods: We selected 97 PD patients that reported family history of PD (defined as having a first or second degree family member also affected) from the Latin American Research Consortium on the Genetics of PD (LARGE-PD). We capture-sequenced all coding regions using a neurodegenerative panel including 25 PD related genes: ATP13A2, ATP1A3, DNAJC13, DNAJC6, EIF4G1, FBXO7, GBA, HTRA2, LRRK2, PARK2, PARK7, PINK1, PLA2G6, RAB39B, SNCA, TARDBP, TH, TMEM230, VPS13C, VPS35, GCH1, SLC6A3, SNCB, SYNJ1 and TAF1. Sequencing was performed using 1 µg of DNA in an Illumina sequencer (HiSeq 2000) using standard 150 bp paired-end sequencing technology. RESULTS. We identified pathogenic mutations in 25 patients (26%) including mutations in DNAJC13, DNAJC6, FBXO7, GBA, LRRK2, PARK2 and VPS13.
Conclusions: This is the first screening of a large cohort of PD patients from Latin America for all known PD genes. There were substantial differences in the mutation spectrum of known PD genes in our LARGE-PD cohort in comparison to previously published PD families of European origin. Out of all the variants identified, 9 are novel and could be specific of Latinos. CNV analysis is required to find the second mutation in some of our families. Further analyses, such as exome sequencing, in the reminder families may allow the identification of novel PD genes, which will contribute to a better understanding of PD pathophysiology.

P01.06

Impact of offering genetic testing and counseling to people with Parkinson's disease in a clinical setting

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Objectives: The Parkinson's Foundation genetic research initiative is a five-year, multi-center study in the United States (U.S.) that aims to offer Clinical Laboratory Improvement Amendments (CLIA)-certified genetic testing of LRRK2 and GBA1 genes and genetic counseling to people with Parkinson's disease (PD) via the Parkinson's Foundation Center of Excellence (COE) and the Parkinson Study Group (PSG) network. Study objectives include: 1) accelerate referral to precision medicine clinical trials; 2) improve PD care and research through knowledge of genetic status and clinical phenotype; 3) empower patients by providing genetic status within a clinical setting; 4) evaluate the impact and feasibility of returning genetic results through clinician vs. genetic counselor.
Methods: The study will target enrollment of up to 15,000 PD participants (early to advanced disease severity) across 50 sites distinguished as a COE or a PSG site in the U.S. All participants will be offered pre- and post-test genetic counseling services through virtual or local site counseling. After consent, DNA will be sequenced at the coding regions of LRRK2 and GBA1 genes through a CLIA-certified genetic testing laboratory and banked for future research use. Participants will also undergo clinical assessments to characterize disease status and severity. A subset of sites will be randomized to return genetic testing results through a Movement Disorders clinician or a genetic counselor. Follow-up will occur at 3 and 12 months after baseline visit, where participants and clinicians will complete validated questionnaires to evaluate empowerment, satisfaction and determine changes in clinical care and/or enrollment in a clinical trial.
Results: The primary endpoint is to determine the number of participants that receive genetic testing and subsequently enroll in a precision medicine clinical trial.
Conclusions: The study will provide a large-scale patient registry that links clinical phenotype with genetic status for up to 15,000 people with PD in the U.S.

P01.07

Deletion of GBA2 in neuronopathic Gaucher's disease medaka could not rescue the phenotype

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Objectives: Recent genetic studies have identified that heterozygous mutations in the GBA1 gene is a strong risk factor for sporadic Parkinson's disease (PD). The GBA1 mutations are responsible for Gaucher's disease (GD), the common autosomal recessive lysosomal storage disease. We have reported that the GBA1 knock-out (KO) medaka can survive long enough for pathological analysis of disease progression in contrast to the

perinatal death of GBA1 KO mice. The non-lysosomal β-Glucosidase (GBA2), which is localized at the endoplasmic reticulum and Golgi apparatus, also cleaves glucosylceramide to glucose and ceramide. A recent study has reported that the deletion of GBA2 rescues the visceral manifestations in type1 GD mice model through reduction of sphingosine. To date, it remains unclear whether the deletion of GBA2 can modify the central nervous(CNS) manifestations of GD. This study was performed to determine the pathological role of GBA2 in the CNS in GD and GBA1-related PD.
Methods: We generated GBA2 KO medaka by clustered regularly interspaced short palindromic repeat (CRISPR)/CRISPR-associated nuclease (Cas9) system. Then, we crossed GBA2 KO medaka with GBA1 KO medaka to examine the genetic interaction between GBA1 and GBA2 in GD and GBA1-related PD.
Results: GBA2 KO medaka lack both GBA2 enzymatic activity and protein expression. The deletion of GBA2 in GBA1 KO medaka strongly shorten the life span. Moreover, the deletion of GBA2 in GBA1 KO medaka did not reduce the amount of sphingosine, which is thought to be the culprit of the pathophysiology of GD, and increased the amount of α-synuclein. However, there were no differences in the loss of dopaminergic cells between GBA1-/-; GBA2+/+ and GBA1-/-; GBA2-/-.
Conclusions: The deletion of GBA2 in GBA1 KO medaka did not reduce the amount of sphingosine or rescue the pathology of CNS. Moreover, the aggregation of α-synuclein was enhanced by the deletion of GBA2 in the reduced GBA1 enzyme activity.

P01.08

Lifestyle-gene interaction in Parkinson's disease
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Background: Caffeine consumption was demonstrated in several studies to reduce risk of Parkinson's disease (PD). LRRK2 (leucine-rich repeat kinase 2) variant (rs7133914: G>A: p.R1398H) was suggested in previous studies to confer protection against PD. However, the potential interaction of caffeine and this gene is still unclear.
Objectives: We investigated the gene-environment interaction between caffeine and genetic susceptibility to PD at LRRK2 R1398H variant.
Method: A prospective case-control study of 4488 subjects (1790 PD cases and 2698 matched healthy controls) was conducted. Genotyping for LRRK2 R1398H was performed. All study subjects were evaluated for their caffeine intake using a validated tool. Statistical analysis was conducted with logistic regression models. Gene-caffeine interactions were evaluated using an additive statistical model. Interactions were quantified using attributable proportion (AP) due to interaction (AP>0 shows positive interaction).
Results: R1398H protective variant non-carriers who were non-caffeine drinkers had a 2.6 times higher PD risk than carriers who were caffeine drinkers (OR=2.63, 95% CI=1.93–3.59, p<0.001; AP=0.63).
Conclusion: We showed that LRRK2 R1398H variant interacts with caffeine intake, thereby influencing the risk of PD. This interaction can be used as one of the parameters for developing individualised treatment for PD patients with specific genetic background.
The authors declare that this abstract had been presented at the 59th Annual Meeting of the Japanese Society of Neurology, 23 May 2018, Hokkaido, Japan.

P01.09

Survival of patients with Parkinson's disease is influenced by the mutations in the LRRK2 but not GBA gene
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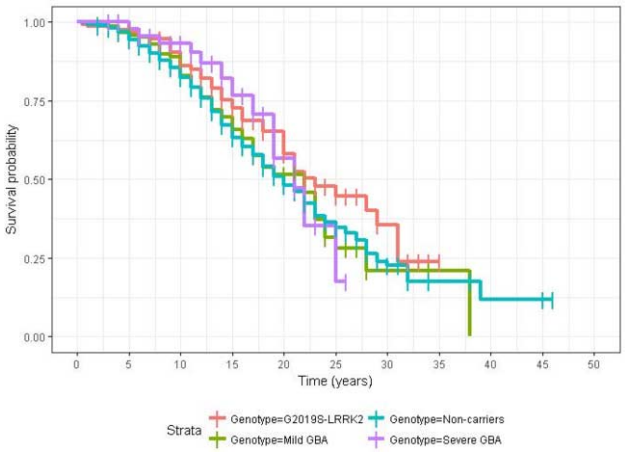
Introduction: The prognosis of Parkinson's disease (PD) is heterogeneous with many factors influencing disease severity and mortality. The G2019S mutation in the LRRK2 gene generates a mild PD phenotype while mutations in the GBA gene are considered to result in a worse PD phenotype, genetic based survival studies are lacking.
Methods: Patients with PD were screened for the G2019S mutation in the LRRK2 gene and the seven most common Ashkenazi Jewish GBA mutations which were classified as mild (N370S or R496H) or severe (L444P, c.84insG, IVS2+1G->A, V394L or 370Rec) (mGBA, sGBA respectively) and underwent comprehensive medical and neurological assessments. Disease onset and date of death were ascertained, with mortality rates calculated for each group of patients.
Survival curves were calculated, stratified by genotype, comparing each group of genetic PD patients to idiopathic PD patients (iPD) with a Benjamini-Hochberg (BH) multiplicity correction for FDR control at a 0.1 significance level.
Results: 1086 idiopathic PD patients (380 died), 159 LRRK2-PD (49 died), 148 mGBA-PD (56 died) and 49 sGBA-PD (13 died) participated in this study.
The average life expectancy for Israeli males and females in 2016 was 80.7 yrs and 84.2 respectively. Both female and male PD patients had significantly lower mean life expectancy (Female mean: 79.23, adjusted p-value <0.001; Male mean: 77.85; adjusted p-value <0.001). However, LRRK2-PD men (79.73 yrs) and sGBA-PD men (78.22 yrs) did not have significantly lower life expectancy compared to the Israeli registry.
Comparing the iPD survival curve with those of LRRK2-PD, mGBA-PD and sGBA-PD using the Yung & Prentis adjusted log-rank test (adjusted p-values: 0.079, 0.662 & 0.248 respectively) indicating better survival rates for LRRK2-PD.
Multivariate analysis results: In the Multivariate analysis significant prediction value for age at onset (with higher age of onset increasing hazard probability) and female gender (having longer life expectancy compared with males) were detected (HR: 1.17, adjusted p-value <0.001, HR: 0.4, adjusted p-value: 0.027, respectively).
Discussion: LRRK2-PD patients have longer survival periods compared with iPD and GBA-PD as assessed by mortality ratios. This reinforces the notion that LRRK2-PD has a milder phenotype compared with both iPD and GBA-PD.



P01.10

Ratio of neutrophil to white blood cell, ratio of neutrophil to lymphocyte and weight loss in de novo Parkinson's disease

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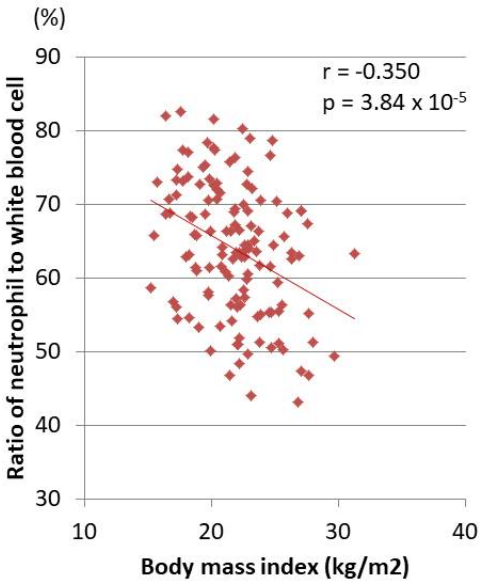
Objective: It is considered chronic inflammation is one of major causes developing Parkinson's disease (PD). Weight of PD patients goes down before the onset of motor symptom, and fluctuates during the course of PD. It is unaware whether subclinical chronic inflammation is associated with weight loss. The aim of this study is to investigate the association of subclinical inflammation reflected in differential count of leukocytes with weight loss in patients with PD.
Methods: We enrolled 132 patients with de novo PD and no sign of active inflammation such as fever and elevated C-reactive protein. Baseline characteristics, ratio of neutrophil to white blood cell and ratio of neutrophil to lymphocyte were used for evaluating the correlation with body mass index (BMI).
Results: BMI was inversely related to ratio of neutrophil to white blood cell (r=-0.350, p<0.001) and the ratio of neutrophil to lymphocyte (r=-0.273, p=0.002). Negative correlation was also found between BMI and age, motor severity, presence of constipation or presence of orthostatic hypotension. After adjustment for these covariables, inverse association between BMI and ratio of neutrophil to white blood cell or the ratio of neutrophil to lymphocyte remained statistical significance (both, p<0.01).
Conclusions: Subclinical inflammation should play a pivotal role in weight loss of PD patients.



P01.11

Association of α-synuclein and DAT-SPECT imaging in Parkinson's disease patients of Coimbatore population, India

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α-synuclein (SNCA) is a neurodegenerative biomarker in Parkinson's disease (PD). Studies have shown that protein α-synuclein regulates the neurotransmitter release and pliability of dopaminergic neurons. The study aims to correlate SNCA mutation and dopamine transporter in 8 PD patients of Coimbatore population. PD subjects were interviewed using Unified Parkinson's disease Rating Scale (UPDRS) questionnaire and informed consent has been obtained from the patients. Molecular genetic study is done by PCR and sequencing along with clinical diagnosis by dopamine transporter – single-photon emission computed tomography (DAT-SPECT) in affected individuals and in equal control subjects. The significance rate has been measured through statistical mean. Intestinally we obtained some point mutation in SNCA gene of PD patients and the SPECT imaging found with severe striatal binding defect. This shows the relevance between the mutation and dopaminergic binding rate in PD. The findings show a profound correlation between α-synuclein and dopamine in our PD population. Hence, the study suggests that the dopaminergic defect is early with SNCA mutation in PD.
Keywords: Parkinson's disease; SNCA; DAT-SPECT; dopamine; mutation

P01.12

Large multi-center study reveals robust and replicable evidence for dysbiosis of gut microbiome in PD

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Introduction: The human gut harbors billions of microbial cells whose collective genomes make up the human gut microbiome. Changes in the gut microbiome have been detected in many disease states including Parkinson disease (PD). Multiple studies have confirmed changes in the gut microbiomes of PD patients but produced varied lists for what specific microorganisms are altered in PD. Inconsistent findings might be due to differences in study populations and methodological differences. Even when analyzing the same dataset using multiple analytical methods, different results can be produced.

Purpose: We aimed to detect gut microorganism-PD associations that are robust to different analytical methods and replicable across datasets.

Methods: Persons with PD and neurologically healthy control subjects were enrolled from NeuroGenetics Research Consortium (NGRC) affiliated movement disorder clinics in Seattle, WA, Albany, NY, and Atlanta, GA (dataset 1 discovery: 201 PD, 132 controls) and Birmingham, AL (dataset 2 replication: 323 PD, 184 controls). We extracted DNA from stool and sequenced for 16S rRNA gene V4 amplicons. Amplicon sequences were processed using DADA2 bioinformatics pipeline. We tested relative abundances of 166 genera for association with PD using 13 different analytical methods. An association was considered significant in the discovery dataset if at least two non-parametric methods (KW and ANCOM) and one parametric method (log t-test) yielded multiple testing corrected significant P-value, and they were considered replicated if they achieved multiple testing corrected significance in the second dataset.

Results: The findings that were significant in discovery and were replicated included reduced levels of butyrate producing genera from Lachnospiraceae and Ruminococcaceae families, elevated abundance of opportunistic pathogens, and elevated levels of Lactobacillus and Bifidobacterium in PD.

Conclusion: We detected gut microorganism–PD associations that were robust to different analytical methods and consistent across datasets. The reduction in butyrate producing genera was consistent with the literature and may not be specific to PD. The higher abundance of opportunistic pathogens in PD is consistent with Braak's hypothesis. Results caution against the use of probiotics to self-medicate because the main commercial probiotics, Bifidobacterium and Lactobacillus, may already be abnormally high in PD.

ZW was supported by T32NS095775 Training Grant.

BASIC SCIENCE: Cell death, disease modification, and trophic factors

P02.01

Intracerebral delivery of VEGF-B improves motor function in PINK1-knockout rats: A follow-up study investigating the effects on dopaminergic neurons

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Current treatments for Parkinson's disease (PD) focus on dopamine replacement therapy. Disease-modifying therapies that delay disease progression are a critically unmet need in PD. While a number of neurotrophic factors (NTFs), including the glial-cell line derived neurotrophic factor (GDNF) family, have shown potential in animal models of PD, they have failed to meet clinical endpoints. However, optimization of delivery systems for clinical studies are ongoing, and success might require combination of multiple NTFs with non-overlapping mechanisms.

We have previously identified a novel growth factor, vascular endothelial growth factor B (VEGF-B), and published on its neuroprotective effects in vitro (Falk et al., Molecular Neurodegeneration, 2009) and in vivo (Yue et al., Neuroscience, 2014) in the 6-hydroxydopamine toxin model. Here, we investigate VEGF-B's neuroprotective effects in the PTEN-induced putative kinase 1 (PINK1) knockout (KO) rat, a genetic model of early, mild PD with a progressive phenotype.

In our initial pilot, we injected adeno-associated virus expressing human VEGF-B (AAV2/1-hVEGF-B) unilaterally into substantia nigra (SN) and striatum of a PINK1 KO rats at 5 months of age (n=3–5 per group). Rats treated with VEGF-B showed a reduction in cumulative foot slip errors bilaterally during monthly tapered balance beam tests as compared to untreated PINK1 KO rats. Rats were euthanized at 12 months of age and showed, via HPLC-EC, an ~30% increase in striatal dopamine (DA) content in the VEGF-B-injected hemisphere compared to the untreated PINK1 KO rats. In a second pilot, the same experiment was repeated (n=8–9 per group), but the rats were transcardially perfused (n=6 per group) to perform ongoing unbiased stereology of dopaminergic neurons in the SN after immunostaining for tyrosine hydroxylase and the neuronal marker, NeuN. Combined these results will determine if VEGF-B is neuroprotective and capable of slowing disease progression or if the motor improvement results from a functional improvement in the surviving dopaminergic neurons. Additionally, we are investigating the potential mechanisms behind VEGF-B's therapeutic effects. We hypothesize that these include an improvement in mitochondrial function via the upregulation of PGC1-alpha and fatty acid transporters and the inhibition of apoptosis, by upregulation of pigment epithelium-derived factor, mediated through mTOR signaling.

P02.02

Honokiol, a natural compound to alleviate α-synucleinopathies?

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Honokiol, a natural phytochemical derived from the bark of magnolia plant, is widely used in traditional Chinese medicine and has shown promise in preclinical cancer and neurodegenerative disease research. A wide range of biological properties have been attributed to the presence of polyphenol groups on honokiol, including antioxidant, anti-inflammatory, and anti-amyloidogenic characteristics. Interestingly, honokiol can penetrate the blood brain barrier, has high systemic bioavailability, and seems to act on multiple signaling pathways, making it an attractive molecule and offering new therapeutic promise for Parkinson's disease (PD) patients. Here we investigated whether honokiol has any beneficial effect and clinical relevance in models of α-synucleinopathies such as PD. There is compelling evidence linking the accumulation of the synaptic protein, α-synuclein (αsyn), and the pathogenesis of PD. Genetic multiplications of the SNCA gene that result in increased protein burden are associated with increased risk of PD. Additionally, Lewy bodies, one of the primary pathological hallmarks of PD are mainly composed of aggregated αsyn. Given these associations, reducing brain αsyn levels and dysfunctions associated with increased αsyn levels, represents a promising therapeutic approach for PD patients
Using human neuroglioma cells stably overexpressing αsyn, mouse primary neurons, and human skin-derived fibroblasts from PD patients harboring a SNCA triplication, we demonstrate that 10 uM honokiol can induce a significant decrease in αsyn at both the protein and mRNA level compared to vehicle control (DMSO). Additionally, our data support a mechanism whereby honokiol acts by transcriptional modulation of SNCA production rather than enhancing αsyn protein degradation. After 72 hours of honokiol treatment αsyn protein is reduced by 76.2% and SNCA mRNA by 52.3% in our cellular model. Pulse-chase experiments support no increase in protein or mRNA degradation in the presence of honokiol. Ongoing studies are investigating potential pathways by which honokiol may modulate SNCA transcription, including sirtuin 3, PGC-1α, and PPARγ pathways and in vivo studies to assess the potential neuroprotective effect of honokiol in preclinical animal models of PD are in progress.
Overall, these data highlight a viable strategy to reduce αsyn levels which represents a promising target to modify disease progression in synucleinopathies.

P02.03

Protective effect of anodal transcranial direct current stimulation on methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced neurotoxicity in mice via modulating mitochondrial dynamics

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Introduction: Parkinson disease (PD) is a neurodegenerative disorder characterized by accumulation of protein inclusions and loss of dopaminergic neurons. Abnormal mitochondrial homeostasis is thought to be important for the pathogenesis of PD, and recent studies have demonstrated dysregulation of mitochondrial quality control such as mitophagy and fission/fusion in the brain PD patients and animal PD models. Transcranial direct current stimulation (tDCS), a non-invasive brain stimulation technique, constitutes a promising approach for promoting recovery of various neurological conditions. However, little is known about its mechanism of action. The present study elucidated the neuroprotective effects of tDCS on mitochondrial quality control pathway in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) induced PD mouse model.
Methods: As an in vivo model of PD, we adapted the MPTP induced neurotoxicity model. Mice were stimulated for consecutive 5 days with MPTP treatment. After observation of behavioral alteration using Rota-rod test, mice were sacrificed for the measurement of the PD and mitochondrial quality control related protein levels in substantia nigra.
Results: tDCS improved the behavioral alteration and tyrosine hydroxylase level in MPTP-treated mice. Furthermore, tDCS attenuated the mitochondrial damage, as indicated by diminished mitochondrial swelling and mitochondrial glutamate dehydrogenase activity in MPTP-induced PD mice model. MPTP significantly increased the level of mitophagy-related proteins, such as PTEN-induced putative kinase 1, Parkin, microtubule-associated protein 1 light chain 3 and decreased the level of p62. These changes were attenuated by tDCS. MPTP also increased mitochondrial biogenesis-related proteins, including peroxisome proliferator activated receptor -γ coactivator 1α, nuclear respiratory factor 1 and mitochondrial transcription factor A and tDCS decreased this increases. MPTP significantly increased fission-related protein dynamin-related protein 1 with no effect on fusion-related protein mitofusin-2 and tDCS attenuated these changes.
Discussion: Our findings demonstrated the neuroprotective effect of anodal tDCS against MPTP-induced neurotoxic mouse model through suppressing excessive mitophagy and balancing mitochondrial dynamics. The neuroprotective effect of anodal tDCS with mitochondrial dynamics modulation provides a new therapeutic strategy for the treatment of PD.

P02.04

Constitutive activation of pro-survival pathway ameliorates aggregation of α-synuclein in dopaminergic neurons

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Parkinson's disease (PD) is an incurable neurodegenerative disorder, primarily characterized by progressive death of dopaminergic (DA) neurons and widespread accumulation of α-synuclein (α-syn) aggregates called Lewy bodies (LB). Some data suggest that α-syn aggregation is playing important role in disease onset and progression; however, formation of LB is still poorly understood. Here, we investigate the role of activation of pro-survival signaling pathway X in accumulation of α-syn and additionally its role in promoting survival of DA neurons.
In our study we utilize primary embryonic midbrain and hippocampal cultures treated with lentiviral vector to overexpress constitutively active element of pro-survival pathway X. To investigate its ability to inhibit accumulation of α-syn, we use our previously established model of α-syn aggregation by seeding preformed fibrils (PFFs) in midbrain and hippocampal cultures with subsequent quantification of phospho-αsyn aggregates in TH- and NeuN-positive cells, respectively. Additionally, we study neuroprotective properties of active element X against ER stress by treating cells with thapsigargin for 48 hours and then quantifying number of TH-positive cells.
Here we demonstrate that activation of pro-survival signaling pathway X is capable of interfering with formation of LB-like structures in primary DA and hippocampal neurons and additionally ameliorate ER stress-induced DA neuronal loss, modulated by thapsigargin treatment. Furthermore, we investigate mechanism of its action and confirm this data in vivo.

P02.05

How dopamine neuron survival promoting neurotrophic factors CDNF and MANF regulate the unfolded protein response

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Unconventional neurotrophic factors cerebral dopamine neurotrophic factor (CDNF) and mesencephalic astrocyte-derived neurotrophic factor (MANF) have been shown to promote the survival and regeneration of dopamine neurons, degenerating in Parkinson's disease (PD). Normally these neurotrophic factors are endoplasmic reticulum (ER)-located, but in conditions of ER-stress they can be secreted. It has been proposed that they exert cytoprotection through the alleviation of unfolded protein response (UPR). However, how exactly CDNF-MANF function inside the ER regulating UPR and what is their mode of action after secretion is not very clear to date. Considering that CDNF is now in phase I-II clinical trials for the treatment of PD the investigation of the modes of action both CDNF and MANF is becoming even more urgent.
Firstly, we have shown that addition of MANF to the medium of cultured dopamine neurons promoted their survival in thapsigargin (TG)-induced ER stress. Secondly, we have analysed the expression levels of ER stress marker transcripts and revealed MANF's survival promoting effect might be realized through the downregulation of IRE-1 and ATF6 pathways.
Thirdly, using microscale thermophoresis (MST) and purified recombinant proteins, we have been able to show that both CDNF and MANF interact with a major player of UPR ER chaperone GRP78 (known also as BiP) in a cofactor-manner
Since in CDNF and MANF knockout mice UPR-pathways are chronically activated, we went to test whether CDNF/MANF are able to bind to the luminal domains (LDs) of UPR sensors (PERK, IRE1 and ATF6). We have observed that CDNF/MANF interact directly with UPR sensors and they compete for the binding with BiP.
Our results on CDNF/MANF interactors in the ER can be of interest in context of development of new strategies to treat PD, by regulating the UPR.

P02.06

Effect of CDNF in novel α-synuclein fibril models of Parkinson's disease

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The existing therapies for Parkinson's disease (PD) mainly aim at mitigating the symptoms of the disease and do not stop or even slow down the degeneration of nigrostriatal dopamine (DA) neurons. One obstacle for PD drug research is the lack of a PD model that would recapitulate both formation of Lewy body (LB)-like inclusions and robust enough DA neuron death within an optimal timescale for testing candidate drugs. Cerebral dopamine neurotrophic factor (CDNF) has, in previous studies, shown evidence for neuroprotection and restoration in preclinical animal models and is currently in phase I/II clinical trials for PD. We have discovered a novel variant of CDNF, called the next-generation CDNF (ngCDNF), which has shown promising results in animal model of PD. In this study, our first aim was to develop a model that would exhibit the α-synuclein (αSyn) aggregation pathology and also lead to degeneration of the nigral DA neurons over an optimal time course. To obtain this, we combined overexpression of αSyn in mouse primary midbrain neuronal cultures in vitro with seeding of pre-formed αSyn fibrils to them, or added another stressor to the nigrostriatal DA pathway in vivo, in addition to the pre-formed αSyn fibrils. The second aim was to test the effects of ngCDNF in this novel model of PD for neuroprotection and restoration. The progression of pathology was analyzed by quantifying the intraneuronal LB-like inclusions as well as DA neuron loss at different time-points and correlating them with the deficits in the motor behavior of mice monitored throughout the in vivo experiment.

P02.07

Effect of CDNF in N171-82Q mouse model of Huntington's disease

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Huntington's disease (HD) is an inherited progressive neurodegenerative disorder characterized by motor and non-motor symptoms. The main possible cause of neuropathology of HD is the degeneration of striatal neurons. Moreover, protein folding stress at the endoplasmatic reticulum (ER) may contribute to not only the neurodegeneration in Parkinson's disease (PD), but also HD-related neuropathology. The actual causes of ER stress in HD are poorly understood. Currently, no effective treatments for HD is yet available.
Cerebral dopamine neurotrophic factor (CDNF), discovered in our laboratory, is an evolutionarily conserved protein located and secreted in the ER. CDNF demonstrates the neuroprotective and neurorestorative effects in mammalian, rodent and non-human primate models of PD. CDNF has a unique structure, which differs from other neurotrophic factors (NTFs), consisting of two structural domains, a saposin-like N-terminal domain, and a carboxy-terminal SAP-like domain with ER retention signal. CDNF decreases the level of ER-stress markers and regulates unfolded protein response (UPR) intracellularly. Furthermore, CDNF diffuses in brain tissue better than any other NTFs. Importantly, CDNF is currently in clinical phase I/II trials on PD patients. Additionally, our unpublished data shows that CDNF has a positive effect in Quinolinic acid-toxin model of HD. All these evidence and some commonalities in the pathogenesis of PD and HD, such involving of ER-stress, shows the importance to test CDNF also in genetic mouse model of HD.
This report represents the first positive neuroprotective effects of chronic CDNF infusion in the transgenic N171-82Q model of HD. Mice received a continuous unilateral intrastriatal CDNF infusion or vehicle. Chronic CDNF- treatment improved clasping behaviour and motor coordination. This report is the first evidence of positive effect of CDNF in transgenic mouse model of HD.

P02.08

α-synuclein interacts with BAF complex in nucleus

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Background: As known, much of α-synuclein (αS) could be seen in presynaptic terminal, while it is also be evident that αS reside in nucleus. This study aims to uncover the pathophysiological functions of αS in nucleus.
Method: Fine nuclear lysates were extracted from 293 cells stably expressing HA-tagged αS using modified standard method. To avoid non-specific binding of nucleic acids to the sepharose beads,

RNAse, DNAse, and Benzonaze were supplemented with the buffers. 800 ug of nuclear lysates were incubated with anti-HA antibody-conjugated-beads overnight. After intensive washes, HA-αS interacting proteins were competitively collected by HA peptides. Digested samples were thoroughly analyzed by nanoLC-MS/MS. Protein, which had at least 5 spectral counts (SpC) in the HA-αS sample, which was not detected in the 293 sample, and which was detected with a 4-fold or more increase based on dividing SpC values, were given as meaningful binding.
Result: Based on the criteria described above, 216 nuclear proteins were qualified. Functionally, several of them were member of BAF (BRG1-Associated Factor) complex by which some of the components are replaced to another during neuronal differentiation. In mature neuronal cells as well as HEK cells, αS was interacted with SMARCC1 and SMARCC2, key players of that complex. Furthermore, switching of developmental components was robustly disturbed in the presence of αS.
Discussion: We found putative αS-interacting proteins belong to BAF complex. αS may alter the physiological function of that complex.

P02.09

Identification of novel DJ-1 protein targeting small molecule for the potential treatment of Parkinson's disease
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Familial mutations in the DJ-1 gene have been linked to the early-onset of Parkinson's disease (PD), and studies of neurotoxicant- and α synuclein-based in vivo PD models suggest a role for DJ-1 in sporadic 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 fragment and lead-like compounds that bound to DJ-1 protein. We report herein on one selected compound developed from one of the hits, that alleviated neuroblastoma cell toxicity mediated by paraquat, MPP+, 6-OHDA and MG132 treatment. In addition, this compound significantly protected from dopamine loss and totally alleviated dopaminergic neuronal death in a MPTP mice model of PD when administered orally. This compound binds to native and oxidized DJ-1 potently and stabilizes the active 3D structure of the protein in vitro. In conclusion, our studies show that the DJ-1 protein can be targeted by a variety of drug-like small molecules, and that the presented selected compound is a novel promising drug candidate for the treatment of PD. (A version of this study was presented at EFMC-ISMC 2018, September 4, 2018.)

BASIC SCIENCE: Protein misfolding, handling, and transmission

P03.01

Patient-derived α-synuclein assemblies/strains display distinct functional characteristics in cells and in vivo
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Synucleinopathies such as Parkinson's disease (PD), Multiple System Atrophy (MSA) and dementia with Lewy bodies (DLB) are determined by the deposition of αSYN aggregates but segregate in distinct pathological phenotypes and diagnostic criteria. αSYN was shown to assemble into different polymorphs or 'strains' (Bousset et al., 2013, Nature Comm). This has led to the hypothesis that strains might account for the distinct clinico-pathological traits within synucleinopathies (Peelaerts et al., 2015, Nature). The purpose of this study was to compare different αSYN assemblies derived from the brain of patients with PD, MSA and DLB and assess their capacities to amplify, propagate and induce neurodegeneration in vivo. Fresh human brain material, extensively characterized from a clinico-pathological point of view, was homogenized and used to amplify patient-derived human αSYN strains via a protein misfolding cyclic amplification assay (PMCA) where brain homogenates were used to seed the aggregation of monomeric αSYN. Brain homogenates and the products of PMCA reactions were injected in the substantia nigra of wild-type rats and viral vector-based αSYN overexpressing rats. Animals were followed up for 5 months by behavioral analysis and then the brains were processed for histopathological analysis. The results showed some striking differences between the different patient-derived strains, with MSA assemblies inducing the most pronounced phenotype. In addition, patient-derived assemblies displayed enhanced activity compared to controls in a cellular αSYN seeding assay. The existence of αSYN strains may provide a basis for the heterogeneity observed in synucleinopathies and open new therapeutic opportunities such as targeting the degradation or spreading of specific αSYN assemblies.

P03.02

Neuroprotective role of Andrographolide in in vitro model of Parkinson's disease: Possible role in α synuclein aggregation
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Parkinson's disease (PD) is a devastating neurodegenerative disorder histologically characterized by dopaminergic neuronal loss and the presence of the Lewy bodies, a proteinaceous aggregate mainly constituted by phosphorylated α-synuclein (α-syn). Accordingly, it has been suggested that modulation of the α-syn pathology should constitute a main goal of the future PD therapeutics. In this regard, andrographolide (ANDRO), the main component of the extract obtained from the Andrographis paniculata, has demonstrated interesting effects in Alzheimer's

disease research, including reduced protein aggregation, improved mitochondrial function and neuroinflammatory regulation. Thus, we hypothesize that ANDRO can protect the neurons from the damage observed in an in vitro PD-like model, also modulating the α-syn dynamics. SH-SY5Y cells were treated with ANDRO (10 uM) for 3h, followed by a 24h treatment with 200 nM of Rotenone. At the end of the treatment, immunofluorescence, PCR and Western Blot analysis were carried out to evaluate the effects of ANDRO on the α-syn dynamics. While Rotenone induced the increase of α-syn levels and aggregation, seriously affecting the cell morphology, ANDRO pre-treatment was able to prevent this effect. Relevantly, ANDRO treatment also induced an increase in the levels of α-syn levels; however, this increase was not related with the aggregation dynamic of the α-syn. Discussion: It is well known that α-syn aggregation depends on the specific phosphorylation at the ser129. In this regard, and although preliminary, our results suggest that ANDRO it might represent an interesting molecule to evaluate in the context of PD because its seems able to modulate the expression and aggregation of α-syn.

P03.03

Bidirectional gut-to-brain and brain-to-gut propagation of α-synuclein pathology in non-human primates

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Objective: The aim of this study was to test the hypothesis that synucleinopathy can develop upward but also downward, i.e. from the gut to the brain but also from the brain to the gut.
Background: The prototypic synucleinopathy Parkinson's disease (PD) is hypothesized to spread out from the enteric nervous system (i.e. the gut) via the vagal nerve up to the central nervous system (Lionnet et al., 2017). Such popular hypothesis is supported by indirect clinical evidences and by experimental data showing gut-to-brain transfer of synucleinopathy using either viral vector delivery of synuclein or recombinant synuclein preformed fibrils.
Methods: To this end, we used our primate model of synucleinopathy obtained with administration of α-synuclein species contained in PD-derived Lewy bodies (LB) (Recasens et al., 2014). We examined in non-human primates, (i) if LB administration in the ventral wall of the stomach (n=5) leads to central nervous α-synuclein aggregation and possibly nigrostriatal degeneration and (ii) if LB administration in the striatum (n=6) might lead to synucleinopathy into the enteric nervous system.
Results: Two years after injection, extensive analysis was performed to assess qualitatively, quantitatively and spatially in the whole brain and in the enteric nervous system the extent and pattern of lesion as well as the occurrence of synucleinopathy using both biochemical and histochemical procedures. Enteric injection of LB in non-human primates results in enteric nervous system pathology and nigrostriatal lesion in keeping with the well-accepted hypothesis. However, striatum LB-injected animals, in addition to the expected nigrostriatal degeneration, showed also enteric nervous system pathology at the stomach level.
Conclusion: This study establishes that α-synuclein species might move up and down the neural axis in non-human primates questioning (i) the hypothesis of a peripheral origin of synucleinopathies (ii) and the specificity of enteric nervous system as biomarker of early/presymptomatic PD.

P03.04

Machine learning reveals different pathological signatures induced by distinct patient-derived – synuclein pathogenic structures in monkeys

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Background: Emerging evidence strongly suggests that α-synuclein, a major protein component of LB, may be responsible for the spreading of the pathological process within affected individuals. Recently, through an innovative strategy based on the purification of Lewy bodies (LB) containing aggregated α-synuclein from the substantia nigra pars compacta of PD patients, we assessed the prion-like properties of endogenous α-synuclein assemblies in wild-type mice and non-human primates (Recasens et al., Ann. Neurol. 2014).
The pilot nature of the demonstration however called for a properly powered demonstration in non-human primates, which was the aim of this study, achieving in a large group of baboons (n=49).
Methods: After in vitro and in vivo (in wild-type mice) LB-induced toxicity validation, α-synuclein-containing extracts were injected bilaterally into the striatum (either a mixture of LB fractions or no-LB fractions derived from the same 3 PD patients, which contains soluble or finely granular α-synuclein but lacks large LB-linked α-synuclein aggregates.
Results: After a live phase of 2 years, extensive analysis was performed using biochemical and histochemical techniques in the whole brain. This study collected over 180 variables in each monkey. To overcome the roadblock associated to the "p>n" problem that occurs when the number of variables measured is greater than the sample size, we developed a multiple layer perceptron (MLP), i.e. an artificial neural network commonly used in machine learning. The performance of a given combination of variables was measured to predict the level of degeneration and extract meaningful variables. Variables were then sorted according to their occurrence in the top 1% of the best combinations.
Conclusion: This MLP allowed to identify two types of variables: the ones that reflect the actual neurodegeneration - the variables that describe the phenomenon to be explained - and the ones that might contribute to the pathogenic mechanism - the variables that could be useful to explain the phenomenon. Overall, this study using this unbiased methodology, confirmed highly-expected variables but, more importantly, also identified unexpected variables that appear to be excellent predictors for dopaminergic neurodegeneration.

P03.05

The autophagic secretion of α-synuclein is dependent on galectin 3

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The misfolding and subsequent accumulation of α-synuclein (α-syn) is central to the pathogenesis of Parkinson's disease (PD). While a vast body of both genetic and experimental evidence indicates that α-syn is critical to PD development, how α-syn induces progressive neuronal dysfunction and cell death remains unclear.
Several lines of evidence suggest pathological α-syn spread cell-to-cell via a "prion-like" mechanism. Furthermore, this pathological α-syn is capable of "seeding" further misfolding of non-pathological α-syn, converting them to the pathological form. These newly afflicted cells can then perpetuate this cycle by further releasing the newly formed pathological α-syn. While individual steps in this "pathological cycle" have been elucidated, the exact mechanisms surrounding how α-syn is released and accesses the cytosol while invading other cells are not understood.
Our work attempts to unify these two mechanisms through the autophagic-lysosomal pathway (ALP) which is dysfunctional during disease pathogenesis. Our previous work has demonstrated that pathological α-syn can enter cells and damage endosomal and lysosomal vesicles, leading to the recruitment of galectin proteins and autophagic proteins to these damaged vesicles. Here, we examined how this ALP dysfunction promotes the release of α-syn from cells. We found that release of α-syn was altered by pharmacological agents that disrupt ALP function or by CRISPR or siRNA knockdown of autophagic effectors in neuronal cell lines and IPSC derived dopaminergic (DA) neurons. Using an imaging based approach to interrogate populations of extracellular vesicles, we also observe that release of α-syn occurs in the context of extracellular vesicles (EVs) which are positive for galectin proteins and other proteins of the ALP, suggesting that these are not canonical exosomes. Finally, we observe that knocking down Gal3 in our derived IPSCs reduced α-syn secretion. These studies provide insight into the mechanism of α-syn release and functionally connect the ALP dysfunction induced by pathological α-syn to the prion-like transfer of α-syn to neighboring cells.

P03.06

Inhibition of α-synuclein aggregation and prion-like propagation as intervention strategies to slow the progression of Parkinson's disease

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A practical therapeutic goal for Parkinson's disease (PD) should be slow the progression of the pathology by (i) preventing the formation of new aggregates in existing live dopaminergic neuronal cells; and (ii) inhibiting propagation of the disease by interfering with cell-to-cell spreading of aggregated α-synuclein (αSyn), which is thought to be the major toxic species. αSyn has been shown to bind to anionic phospholipid vesicles, and recent studies by our lab and other groups suggest that αSyn-membrane interactions can catalyze the protein's aggregation at the membrane surface, a process that leads to vesicle permeabilization. We have identified four heptapeptides that interact with membrane-bound αSyn and inhibit membrane-induced aggregation and vesicle permeabilization. These peptides have been shown to exhibit neuroprotection in a primary midbrain neuronal culture model of PD. Interestingly, NMR studies and other biophysical experiments indicate that the interaction does not involve direct perturbation of αSyn-lipid binding. Current efforts are focused on understanding the detailed mechanism of interaction and testing these peptides and their derivatives for neuroprotective effects in other cellular and in vivo models of PD.
In parallel, to understand molecular mechanisms behind the prion-like progression of αSyn aggregates, we have developed a cellular model that enables us to examine the internalization of αSyn PFFs and the fate of the fibrillar seed in the recipient cell. With the use of a pH-dependent fluorophore-conjugated αSyn which fluoresce only in the acidic environment, we have been able to monitor the dynamics of sonicated fibril uptake and gain an understanding of the lifetime of aggregates in the endo-lysosomal compartment of recipient neurons. Current studies are focused on elucidating the mechanism of endosomal escape in primary neurons and glial cells via correlative light and electron microscopy (CLEM) and super-resolution microscopy.
Together, these studies will yield insights into the molecular underpinnings of αSyn neuropathology in PD and other synucleinopathy disorders and set the stage for developing therapeutic strategies to slow disease progression.

P03.07

Identification of a factor reducing PFF-induced Lewy body pathology in dopaminergic neurons

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Degeneration of dopaminergic neurons in the substantia nigra (SN) is the reason behind the motor symptoms of the world's second most common neurodegenerative disorder, Parkinson's disease (PD). Histopathology of Lewy Bodies (LBs) accompanies the progression of PD. Identifying the exact role of LBs and their main component, α-synuclein, is still one of the biggest quests in the field. Seeding α-synuclein aggregation with preformed fibrils (PFFs) of the protein provides a powerful model which mimics prion-like behaviour and slow progress of its aggregation into LBs. By using PFFs, we have established in vitro phosphoSer129-α-synuclein positive, LB-like aggregates in primary embryonic dopaminergic neurons. Administration of exogenous factor X, pre- or post- PFF treatment are both protective against the formation of LB-like inclusions in dopaminergic neurons. Involvement of specific signalling pathway was supported by knocking down factor X receptor with our in-house established, neuron specific CRISPR-Cas9 system and protective effect of lentiviral over-expression of constitutively active receptor. Pharmacological benefit of factor X was validated in vivo via AAV-mediated over-expression of it in SN followed by PFF injection into striatum. Development of novel, pathology-oriented therapies for dopaminergic neurons has a great potential to prevent the progression of PD. Further dissection of the downstream pathways will be beneficial for identification of new targets for prevention of LBs.

P03.08

Involvement of the CD163 receptor in the α-synuclein induced neurodegeneration in Parkinson's disease

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The occurrence of inflammatory changes in the brain and periphery in Parkinson's disease (PD) patients has been documented, but how the brain and the peripheral immune system interact and the consequence of this interaction is yet undetermined. Our fundamental hypothesis is that immune system is actively involved in the neurodegenerative process associated to α-synuclein in PD, therefore, its modulation may have a therapeutic potential. CD163 is a scavenger receptor expressed in macrophages but not in brain microglia. CD163 expression is increased in certain inflammatory conditions, but its role in the immune system is still unknown. We have observed infiltration of CD163+ cells into the area of neurodegeneration in a PD toxic rat model. In addition, we have data showing changes of CD163 (at cellular and soluble level) in PD patients. This strongly suggest a role for the CD163 macrophages in the disease that we believe might be a key population involved in the crosstalk between brain and periphery. Here, we aim to determine whether the CD163 receptor is directly involved in the immune events occurring in PD and how it might relate to α-synuclein pathology and associated degeneration. To do so, we have injected aggregated fibrillar α-synuclein into the Striatum of CD163 knock-out (KO) animals and wild-type (WT) littermates. Mice were analysed to evaluate motor and cognitive behaviour, α-synuclein pathology, immune response and dopaminergic degeneration at short (1 month) and long term (6 month) post-injection. Our preliminary data at the early time-point suggest that the injection of α-synuclein fibrils leads to significant α-synuclein pathology and neuronal degeneration associated to motor defects and cognitive impairment. This was linked to a significant increase of MHCII immune activity that appeared different in the KO mice. Our data strongly suggest that CD163 has a relevant role in the α-synuclein induced pathology and immune response.

P03.09

Extracellular α-synuclein enters dopaminergic neurons by modulating flotillin-1-assisted dopamine transporter endocytosis

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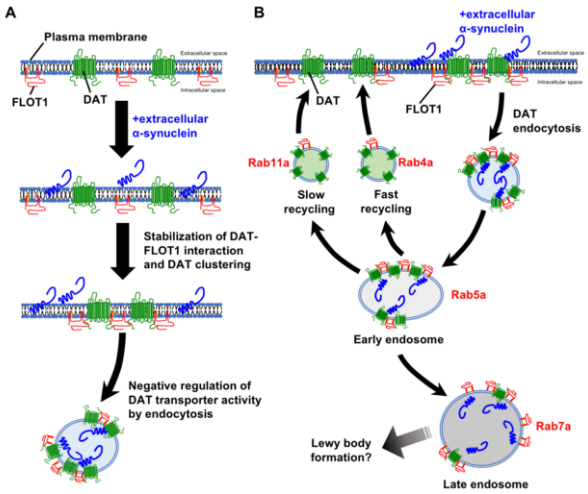
The neuropathological hallmarks of Parkinson's disease (PD) include the appearance of α-synuclein (αSYN)-positive Lewy body (LB) and the loss of catecholaminergic neurons. Thus, a potential mechanism promoting the uptake of extracellular αSYN in susceptible neurons may exist. Of the various differentially expressed proteins, we are highly interested in flotillin-1 (FLOT1) since this protein is highly expressed in the brainstem catecholaminergic neurons and is strikingly upregulated in PD brains. In this study, we found that extracellular αSYN potentiates FLOT1-dopamine transporter (DAT) binding and pre-endocytic clustering of DAT on the cell surface, thereby facilitating DAT endocytosis and downregulating its transporter activity. Moreover, we demonstrated that αSYN itself exploited DAT endocytic process to enter neurons and both FLOT1 and DAT were found to be the components of LB. Altogether, these findings unveil a novel role of extracellular αSYN on cellular trafficking of DAT and may provide a rationale for the cell-type specific, functional and pathological alterations in PD.



P03.10

Effects of the intracellular milleu on α synuclein fibril formation: A study by Kyoto University, Japan

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Background: Multiple system atrophy (MSA) and Parkinson's disease (PD) are adult-onset progress neurodegenerative diseases which are pathologically hallmarked by α synuclein cytoplasmic inclusions and thus called α-synucleinopathies. In MSA there are big mysteries of how α synuclein accumulates in oligodendrocyte where α synuclein expression level is very low and what makes the faster disease progression than in PD.
Recent studies showed that aggregated α synuclein in brains of patients with MSA and PD were different in terms of the resistance against proteinase K treatment, morphological conformation

observed in electron microscopy and the seeding ability in vivo. The salt concentration is a well-known factor which has an influence on the formation of α synuclein fibril. Other factors such as intracellular concentration of metals and the component of lipid membrane, which are different between neuron and oligodendrocyte, also possibly contribute to the diversity of α synuclein fibrils.
Objective: The aim of this study is to examine whether the oligodendrocyte specific factors can contribute to the formation of α synuclein fibrils with high seeding activities in MSA.
Methods: We performed in vitro fibrillation assay by using synthetic α synuclein made from E. coli. Extract of PD brain, MSA brain and various membrane proteins/lipids were used as seeds, and the effect of various buffer conditions with salt or divalent metal ions were also examined. The synthesis of asyn fibrils were monitored by thioflavin activities, and fibrils were transfected to cells expressing α synuclein-GFP fusion protein to examine their seeding activity by counting GFP-positive dots.
Results: The synthesized fibrils had various thioflavin activities which reflected variations in their secondary structures or contents ofβ-sheet conformation. The thioflavin activities of the fibrils were inversely correlated with the in vitro seeding activity.
Conclusions: The seeding activities of fibrils depended on various condition such as concentration of salt and divalent metals. The high concentration of metal ions or myelin specific membrane components in oligodendrocytes may contribute to the formation of characteristic α synuclein fibrils which can account for the high seeding activity of brain lysate and acute progression of the disease in MSA.

P03.11

The effect of reduced retromer function on the clearance and transfer of intra- and extra- cellular α-synuclein and beta-amyloid in neurons
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Objectives: The vacuolar sorting protein 35 (VPS35) is a central component of the retromer system, which is responsible for intracellular cargo sorting and recycling. A reduction in this protein was detected in the hippocampus of late-onset Alzheimer's patients. Mutations in the VPS35 protein have also been linked to Parkinson's disease. The objective of this study was to determine the effect of reduced retromer function on the accumulation, transfer and clearance of oligomeric beta-amyloid and α–synuclein in neuronal cells.
Methods: We established a stable cell line with reduced retromer function by selectively inhibiting VPS35 gene expression using siRNA in differentiated neuronal SH-SY5Y cells. We then investigated the effect of VPS35 reduction on the accumulation, transfer and clearance of oligomeric beta-amyloid in a co-culture system that allows the quantification of cell-to-cell protein transfer between donor and recipient cells.
Results: We show that reduced retromer function increases oligomeric beta-amyloid accumulation in neuronal cells regardless if the oligomeric beta-amyloid originates from extracellular milieu or direct neuronal cell-to-cell transfer. The oligomeric beta-amyloid also colocalises with VPS35 and early endosome markers suggesting the involvement of the endosomal pathway in the uptake of oligomeric beta-amyloid.
Conclusions: These findings provide evidence that reduced retromer function decreases the ability of neurons to transport and clear neurotoxic oligomeric beta-amyloid resulting in its accumulation. We predict that reduced retromer function will also result in the accumulation of α–synuclein and cause a failure in its clearance through a similar mechanism. Therapeutic intervention to enhance retromer function may potentially slow down disease progression.

P03.12

Misfolded α-synuclein hampers oligodendroglial maturation in multiple system atrophy
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Objective: The present study aims to clarify the impact of misfolded α-synuclein (α-syn) on oligodendrocyte (OLG) maturation and subsequent neurodegeneration in multiple system atrophy (MSA).
Background: MSA is one of parkinsonian disorders, which causes relentless worsening of autonomic failure, cerebellar ataxia, and parkinsonism. Pathologically, these symptoms and neuronal death are assumed to be resulted from OLG dysfunction. Oligodendroglial pathology primarily observed in MSA includes not only cytoplasmic accumulation of fibrillar α-syn in OLGs, known as glial cytoplasmic inclusions (GCIs), but altered expressions of myelin-associated proteins such as myelin basic protein (MBP) and tublin polymerization-promoting protein (TPPP). Although a few postmortem studies reported dysfunction in myelin formation and loss of mature OLGs in MSA cases, the detail and pathomechanism of insufficient maturation in MSA has not been fully evaluated. Previously we have reported that primary oligodendrocyte precursor cells (OPCs) incorporate fibrillar α-syn, leading to insufficient MBP expression after maturation induction. The present study describes post-mortem analysis of altered oligodendroglial cell population due to α-syn accumulation and in vitro investigation of α-syn-induced inhibition of OLG maturation.
Method: For histopathological analysis, formalin-fixed, paraffin-embedded sections from MSA patients were deparaffinized and immunostained with primary antibodies for phosphorylated α-syn and oligodendroglial markers. For in vitro analysis, primary OPCs were prepared from neonatal rats. Bacterially obtained human α-syn pre-formed fibrils (PFFs) were applied to oligodendroglial cells. The protein expressions of these markers as well as neuro-supportive functions were chronologically assessed.
Results: The presence of misfolded α-syn may interfere the early phase of OLG maturation in both conditions; MSA brains and primary oligodendroglial cell culture.
Conclusions: The present study confirms the close association between α-syn accumulation and compromised maturation of OLGs. These results suggest that modification of OLG maturation and concomitant acquisition of neuro-supportive function may regulate the progressive neurodegeneration in MSA.

P03.13

Comprehensive screening of the cell surface receptor for α-synuclein fibrils using a MPL/BLOTCHP®-MS technology
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Background: Cell-to-cell transmission of α-synuclein (αS) is supposed to play a key role in the pathological progression of Parkinson's disease (PD). There is strong evidence that αS preformed fibrils (PFFs) can enter cells via endocytosis. Furthermore, this process could be facilitated by the binding of αS PFFs to the cell membrane through specific receptors.

Objectives: The purposes of this study were to (1) perform high-throuput screening for the putative receptors of αS PFF using whole brain tissue in combination with mass-spectroscopy (MS), and (2) to isolate bona fide hits by secondary screening using cell culture system.
Methods: To identify novel membrane receptors for αS PFF, we conducted a unbiased, comprehensive screening of membrane proteins extracted from mouse brain while retaining the ligand-binding capability using a Membrane Protein Library (MPL)/BLOTCHIP®-MS technology (Protosera Inc. Osaka). Candidates from a primary screening was narrowed based on the predetermined affinity ratio of fibrillar versus monomeric αS. Next, secondary screening was performed to facilitate the discovery of reliable hits using cell culture model, i.e., SH-SY5Y cells transfected either with a candidate cDNA or a candidate-specific siRNA were exposed to αS PFF. The uptake of αS PFF was quantitatively measured by immunoblotting and immunohistochemistry. Specific binding between candidate molecules and αS PFF was also assessed by co-IP.
Results: Primary screening gave 106 candidates for αS PFF receptors. From secondary screening, X membrane proteins out of 106 candidates were found to significantly increase the internalization of αS PFF, and Y membrane proteins out of X candidates demonstrated specific binding with αS PFF by co-IP.
Conclusions: These novel strategies enable us to find the novel cell surface receptors for αS PFF, and may provide useful information for identifying disease-modifying candidates in PD.

P03.14

Deciphering the role of posttranslational modifications on α-synuclein aggregation and toxicity
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The aggregation of α-synuclein (ASYN) in Lewy bodies and Lewy neurites is the typical pathological hallmark of Parkinson's disease (PD) and other synucleinopathies. Furthermore, mutations in the gene encoding for ASYN are associated with familial and sporadic forms of PD, suggesting this protein plays a central role in the disease. However, the precise contribution of ASYN to neuronal dysfunction and death is still unclear. There is intense debate on the nature of the toxic species of ASYN, and little is still known about the molecular determinants of oligomerization and aggregation of ASYN in the cell. By taking advantage of studies in model organisms, we are investigating the effect of various posttranslational modifications on the toxicity and aggregation of ASYN. We found that glycation and acetylation are emerging as important modifications affecting ASYN aggregation. In addition, we are also defining the molecular mechanisms triggered by extracellular forms of ASYN, a process associated with the spreading of pathology.
In total, our data shed light into the molecular underpinnings of synucleinopathies, opening novel perspectives for future therapeutic interventions.

P03.15

The role of RNA in synapse physiology and neurodegeneration in PD
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Synaptic dysfunction is observed in conditions such as neurodegenerative and neuropsychiatric disorders [1]. Parkinson's disease (PD), the second most common neurodegenerative disorder, is characterized by gradual loss of dopaminergic neurons in the substantia nigra, and for a series of typical motor and non-motor symptoms that include cognitive dysfunctions [2]. One of the hallmarks of PD is the accumulation of the presynaptic protein α-synuclein (αsyn). αsyn is involved in synaptic vesicle trafficking, and SNARE complex formation at the nerve terminals. In pathological conditions, it is associated with alterations of synaptic functions [3]. αsyn is also identified in the nucleus where it seems to exert toxicity, and induce epigenetic changes such as chromatin remodeling, DNA modifications and RNA editing. RNA-based processes are known to contribute to synaptic remodelling by RNA translocation to the synaptic compartment. This is particularly true for mRNA [4, 5] and non-coding RNAs (ncRNAs) such as microRNAs that can regulate mRNA expression by complementary binding [6].
In order to identify microRNAs leading synaptic processes contributing to synapse degeneration, we used a transgenic mouse model of PD expressing A30P mutant αsyn, which is linked with familial forms of the disease. Using RNA- and small RNA-Seq, we identified differentially expressed genes and microRNAs in midbrain of 6 month-old αsyn transgenic mice when compared with wild-type littermates. Gene ontology (GO) functional annotation and pathway enrichment analysis of the identified deregulated genes and target genes of deregulated microRNAs revealed biological processes linked with the synaptic compartment suggesting a strong synaptic phenotype. Further analysis indicated the most prominent microRNA leading to alterations in synapse structure and activity upon αsyn expression. We are now employing primary cultured neurons to indentify the exact synaptic phenotype produced upon manipulation of the leading microRNA in vitro.
Our preliminary data support the emerging role of microRNAs as key regulators of gene expression involved in αsyn-mediated pathology. Identification of RNA based processes leading synaptic compromise may serve as novel diagnostic and therapeutic approaches in the context of synucleinopathies and other neurodegenerative disorders.

P03.16

On the mechanism of inhibition of α-synuclein aggregation by the DJ-1 protein
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Familial mutations in the DJ-1 gene have been linked to the early-onset of Parkinson's disease (PD). DJ-1 is a redox activated multifunctional protein, which has been shown to be able to reduce the aggregation of α-synuclein (αSyn). Herein, the mechanism of inhibition of αSyn aggregation by the DJ-1 protein is elucidated by focusing on the biophysical and structural nature of the interaction between native dimeric DJ-1 and monomeric αSyn. Strong binding (Kd=80 nM) was observed between DJ-1, in oxidized Cys106-SO2) and over-oxidized (Cys106-SO3) states, with monomeric αSyn, while reduced native DJ-1 bound significantly weaker to αSyn based on microscale termophoresis studies. The thermal stabilities of DJ-1 in oxidized and over-oxidized states were significantly increased by the presence of αSyn, while the thermal stability of DJ-1 in reduced state was less affected. NMR HSQC experiments of 15N labelled

monomeric αSyn and DJ-1 showed that DJ-1, in oxidized state, binds to the N-terminal first 20 amino acids of αSyn, while no interaction was observed between αSyn and DJ-1 in reduced state. Dynamic light scattering studies showed that only oxidized DJ-1 can inhibit significantly αSyn oligomerization and aggregation. In summary, our studies suggest that the oxidation of DJ-1 during disease conditions can trigger the formation of DJ-1 – monomeric αSyn complexes, which may prevent the aggregation of αSyn and therefore may protect neurons from αSyn aggregation caused deficits. These results propose a unique chaperone mechanism by DJ-1 toward αSyn, in which DJ-1 sequesters monomeric αSyn and thereby reduces αSyn oligomerization and aggregation.

P03.17

Suppression of amyloid fibril formation of α-synuclein by the human molecular chaperone Hsp60

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Background: One of the characteristics of Parkinson's disease is the presence of intraneuronal accumulation known as Lewy bodies. Their main component is amyloid fibrils of α-synuclein. We have been studying the inhibition of amyloid fibrillation of intrinsically disordered proteins such as α-synuclein using E. coli molecular chaperone Hsp60 (GroEL). Since GroEL G192W mutant showed a strong suppression of the amyloid fibril formation of α-synuclein, it became clear that G192 was an important site for GroEL function. We are currently focusing on the effect of the human-derived molecular chaperone Hsp60 on α-synuclein aggregation for future clinical applications.

Objective: The purpose of this research was to analyze the effect of Hsp60 on the fibril formation of α-synuclein to understand the mechanism.
Methods: Fibril formation of α-synuclein was measured using thioflavin-T which is a sensitive fluorescent marker of amyloid fibrils. The secondary structures of proteins were evaluated by the circular dichroism spectroscopy. The transmission electron microscopy was used to probe the fibril morphology. The binding interactions between Hsp60 and α-synuclein were monitored by quartz crystal microbalance. The surface hydrophobicity of Hsp60 (WT and G190W) was assessed using 8-anilinonaphthalene-1-sulfonic acid (ANS).
Results: Both of Hsp60 WT (WT) and Hsp60 G190W (GW) suppressed amyloid fibril formation of α-synuclein. WT and GW inhibited fibril formation of α-synuclein dose-dependently. In particular, GW was shown to be a more powerful inhibition effect than WT. ANS fluorescence of GW was higher than that of WT, suggesting that GW had a higher surface hydrophobicity. Estimated dissociation constant of GW toward immobilized α-synuclein was smaller than that of WT, indicating a strong binding affinity of GW for α-synuclein. WT and GW inhibited amyloid fibrils formation of α-synuclein, whereas they could not disassemble mature amyloid fibrils into soluble monomers. Furthermore, we found that the isolated apical domain of Hsp60 also suppressed the fibrillation of α-synuclein.

BASIC SCIENCE: Mitochondria, oxidative stress, and pathogenesis

P04.01

Cytosolic PINK1 promotes ubiquitin phosphorylation and Parkin-mediated mitophagy independently of mitochondrial-localized PINK1

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The function of PINK1 has been a subject of intense investigations due to its role as a genetic contributor of Parkinson's disease (PD). Recent studies have revealed that full length PINK1 collaborates with another PD-linked gene product known as Parkin to mediate mitophagy. Comparatively, the function of the cytosolic form of PINK1 (PINK1Δ104) is often overlooked due to its rapid degradation by the proteasome upon its production. We have previously demonstrated that PINK1Δ104 may be stabilized whereupon it similarly promotes mitophagy, although we could not rule out then the participation of endogenous full length PINK1. Here, we demonstrated in PINK1-deficient HeLa cells that the expression of cytosolic PINK1Δ104 alone is sufficient to promote ubiquitin phosphorylation and Parkin's translocation to the mitochondria to trigger mitophagy. We further showed that PINK1Δ104-mediated Parkin translocation to the mitochondria is dependent on the H302 (but not the S65) residue on Parkin. Not surprisingly, we found that the kinase activity of PINK1Δ104 is important for the phenomenon and that disease-associated PINK1Δ104 mutants fail to promote Parkin-mediated mitophagy. Finally, we showed in the Drosophila model system that PINK1Δ104 expression alone can rescue the phenotypes of PINK1 loss-of-function flies, but not disease-associated PINK1Δ104 mutant. Thus, suggesting the possibility that the two forms of PINK1 functionally converge to maintain mitochondrial quality control. Taken together, our results revealed the physiological and patho-physiological relevance of PINK1Δ104, and emphasize the need to understand this oft-overlooked PINK1 species better.
Abstract has been presented at meeting 1 and 2 and will be presented at meeting 3 listed below:
1. EMBO Workshop: Mitochondrial quality control, 02–05 July 2017 (Xi'an, China)
2. Society for Neuroscience: Neuroscience 2017, 11–15 November 2017 (Washington D.C., USA)
3. Keystone Symposia: Mitochondria in Aging and Age-Related Disease, 13–17 January 2019 (Keystone, Colorado, USA)

P04.02

Unravelling mitochondrial dysfunction in Parkinson's disease
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Parkinson's disease (PD) is characterized by the preferential loss of dopaminergic (DA) neurons in the Substantia Nigra pars compacta leading to dopamine depletion in the striatum that ultimately manifests as motor symptoms. To date, there is no cure for PD. Over the past decades, tremendous efforts have been made to understand the pathophysiology of both genetic and sporadic forms of the disorder. Several lines of evidence indicate that mitochondrial dysfunction plays an essential role in DA cell death, although the underlying molecular mechanisms are still unclear. In this project, we investigated how impaired mitochondrial functions can interfere with processes responsible for the survival and maintenance of the identity of DA neurons. To this end, we have generated and characterized a series of conditional knockout animal models with various degree of mitochondrial dysfunction in DA neurons and we have performed transcriptomic or proteomic analyses of isolated DA neurons from these models. Our study provides a large-scale set of data that accurately describes the molecular changes occurring in DA neurons when mitochondrial processes are impaired, improving our current understanding of how mitochondrial dysfunction affects the survival and maintenance of the identity of DA neurons.

P04.03

α-synuclein and LRRK2's cooperation in mitochondrial dysfunctions in Parkinson's disease
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Parkinson's disease (PD) is the most frequent neurodegenerative disease after Alzheimer's Disease. It is characterized by the selective loss of dopaminergic (DA) neurons in the substantia nigra pars compacta (SNpc) and the formation of Lewy bodies, composed primarily of aggregates of α-synuclein (α-syn). Familial forms of PD are due to the duplication/triplication of the gene encoding α-syn, or to certain point mutations, such as the A53T mutation which can accelerate α-syn aggregation. Another gene, encoding the Leucine-Rich Repeat Kinase 2 (LRRK2), also shows autosomal dominant mutations linked to PD. Among these, the G2019S mutation is the most frequent leading to familial forms of PD and these patients cannot be clinically distinguished from idiopathic patients. It has also been suggested that α-syn and LRRK2 act in concert in the pathogenesis of PD, and this hypothesis is supported by the in vivo results of our laboratory. Indeed, we demonstrated that the AAV-mediated overexpression of LRRK2G2019S in the SNpc of rats increases the dopaminergic cell death induced by the AAV-mediated overexpression of α-synA53T.
Now, our goal is to determine how these two proteins, α-syn and LRRK2, can potentiate neuronal cell death. We focus on the cellular mechanisms linked to mitochondria, as this organelle has been shown to be implicated in the pathogenesis of PD. Moreover, α-syn and LRRK2 have both been found to induce mitochondrial defects. For this purpose, we use a model of rat primary cortical neurons infected with lentiviral vectors in order to overexpress the wild type or mutant forms of α-syn and LRRK2. We characterize the effect of co-expressing these two proteins on mitochondrial physiology by different biochemical (ATP and ROS production) and imaging methods (mitochondrial morphology) and on cell viability. Preliminary results support the existence of an interplay between α-syn and LRRK2 in our model.
Our long term objective is to find the main pathways impacted by α-syn and LRRK2 to identify new molecular targets and thereafter develop new therapeutic strategies for the treatment of PD.

P04.04

Identification and validation of new therapeutic targets against Parkinson's disease by CRISPR-CAS9 screening at the genome level
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Parkinson's disease (PD) is one of the most common neurodegenerative disorders affecting around 1% of the population aged 60 and over. It is characterized by the progressive loss of dopaminergic (DA) neurons in the substantia nigra par compacta (SNc) causing the majority of PD symptoms. It is now well accepted that oxidative stress, mitochondrial defects or the toxicity of protein aggregate, α-synuclein, are associated with the DA neuron degeneration. However, the mechanisms underlying this neuronal death remain unclear. There is no cure for PD and current treatments only alleviate symptoms of the disease. It is therefore essential to discover new therapeutic approaches for this devastating disease. The aim of the current study is to identify new therapeutic targets against PD. To address this question, we carried out a genome-wide screening by applying a CRISPR-CAS9 library to identify target genes rescuing degeneration of DA neurons induced by the neurotoxin rotenone. Results from this non-bias screening revealed several candidate target genes that could potentially protect against oxidative stress and mitochondrial dysfunction.
One of these candidates could abolish cell toxicity induced by rotenone in DA neurons in vitro. To validate these data in vivo, we generated mice expressing CAS9 in DA neurons and injected an adenoviral vector encoding specific guides RNAs directed against one of our previously identified target gene. In agreement with our in-vitro data, gene inactivation in vivo could protect dopamine neurons from parkinsonian phenotype induced by the neurotoxin 6-hydroxydopamine (6-OHDA). Our study identified new targets that confer neuroprotection both in vitro and in vivo models of PD. We are currently testing the neuroprotective potential of these targets against α-synuclein toxicity. Following this validation, drug screening will be performed to identify new compounds able to block or reduce the expression of our identified target genes. Results from this study could lead to new therapeutic treatments against neurodegeneration in PD.

P04.05

The AMPK-PGC-1a axis in neuroprotection – implications for energy deficits in Parkinson's disease
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Emerging studies implicate energy dysregulation as an underlying trigger for Parkinson's disease (PD), suggesting that a better understanding of the molecular pathways governing energy homeostasis could help elucidate therapeutic targets for the disease. Using the Drosophila system, we previously showed that activation of AMPK, a master regulator of cellular energy homeostasis, rescues the pathological phenotypes of Drosophila

models of PD (Ng et al., 2012 J. Neurosci.; 2017 Neurobiol. Aging). Notwithstanding the above findings, whether they are relevant to the mammalian context were unclear. Here, we found that phospho-AMPK (pAMPK), i.e. the activated form of AMPK, and PGC-1α are disproportionately distributed in the adult mouse brain, being relatively higher in the ventral midbrain where the substantia nigra (affected in PD brains) resides - reflecting perhaps the unique energy demands of midbrain dopaminergic neurons. Importantly, the physiologically higher levels of midbrain pAMPK and PGC-1α are significantly and selectively reduced in mice deficient in Parkin- or PINK1; the loss of function of which in humans causes recessive Parkinsonism. The deficient midbrain AMPK level in these mutant mice can be restored following metformin (an AMPK activator) treatment. This potentially represents a viable strategy to restore energy dysregulation in PD brains. Finally, to further clarify the role of AMPK in PD, we ablated the AMPK catalytic subunits in Tyrosine hydroxylase (TH)-expressing neurons of mice and performed detailed characterization of these mice. Our preliminary results showed that TH-specific AMPK-KO mice exhibit motoric deficits that resemble the features of PD. Moreover, AMPK-deficient dopaminergic neurons are more susceptible to 6 OHDA-induced degeneration. Accordingly, one could envisage AMPK activity to be critical to the survival of PD-related dopaminergic neurons and that the AMPK-PGC-1α axis may be important for the maintenance of neuronal energy homeostasis. Consequently, therapeutic exploitation of this pathway holds promise to mitigate the pathogenesis of PD.

Supported by NMRC-TCR grant (LKL). Ms. Hang LT is supported by a graduate scholarship from the National University of Singapore Graduate School for Integrative Sciences and Engineering

P04.06

Neuroprotective effect of stomatin-like protein 2 overexpression in A53T- α-synuclein Parkinson's disease mice model

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One of the main histological hallmarks in Parkinson's disease (PD) is the apparition of abnormal protein aggregates, mainly constituted by α-synuclein (α-syn) known as Lewy bodies. These structures are involved in toxic processes leading to mitochondrial dysfunction and increase the vulnerability of dopaminergic neurons to degeneration.

Objective: Stomatin-like protein 2 (SLP-2) is a protein located in the inner mitochondrial membrane and acts as a membrane scaffold regulating mitochondrial functions, integrity and bioenergetics. In this study, we tested the neuroprotective potential of SLP-2 in PD cells and mice models. Our hypothesis is that SLP-2 overexpression will protect dopaminergic neurons against α-syn toxicity and associated locomotion impairment.

Methods: We have assessed mitochondrial morphology and indicators of mitochondrial function and stress in SH-SY5Y cells upon overexpression of α-syn. Immunochemistry and fluorescence quantification were also used to measure SLP-2 and phosphoSer129-α-syn levels present in dopaminergic neurons of control and PD human brains. In mice, we used viral-vector based delivery of adeno-associated viruses containing human mutated A53T-α-syn, and we simultaneously overexpressed SLP-2 in the SNc by stereotaxic injections. Motor activity was assessed using the open field test and cylinder test. Dopaminergic cells survival was quantified by stereological counting.

Results: Fluorescence intensity measurement in control and PD human brains revealed that SLP-2 expression is decreased in PD samples when compared to control. Upon induction of α-syn expression in vitro, we observed fragmented mitochondrial networks, accompanied by decreased mitochondrial membrane potential and ATP synthesis rate as well as elevated levels of superoxide. Notably, enhancement of SLP-2 expression rescued mitochondrial defects in these cells indicating that SLP-2 is able to mitigate α-syn-induced mitochondrial pathology. In vivo, histological analysis revealed that SLP-2 protects against α-syn toxicity.

Conclusion: Our preliminary results indicate that SLP-2 expression is decreased in PD human brains. Our results also indicate that overexpression of SLP-2 can protect dopaminergic neurons against α-syn toxicity both in vitro and in vivo. SLP-2 could thus represent a novel therapeutic target for PD.

P04.07

In silico identification of novel large-scale mtDNA deletion in a patient with Kearns-Sayer syndrome

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Kearns-Sayre syndrome (KSS; OMIM # 530000) is a rare mitochondrial disease characterized by clinical triad of chronic progressive external ophthalmoplegia (CPEO), retinitis pigmentosa (RP) and disease onset before 20 years old. Supportive diagnostic features of KSS include cerebellar ataxia, heart block, deafness and cerebrospinal fluid protein > 100mg/dL. Classically, the clinical diagnosis of KSS was confirmed by the laboratory investigation of mitochondrial DNA (mtDNA) large deletion (1,300 ~ 10,000-bp) in a clinically or morphologically affected tissue, usually in skeletal muscle. We report a Korean 35-year-old female patient with overall clinical (CPEO + RP + onset at 15 years old + heart block) and neuroimaging features (cerebellar atrophy on brain MRI) compatible with KSS. Her peripheral blood mtDNA was addressed by targeted next-generation sequencing (NGS), and sequenced.fasta and.bam data was computationally analyzed by MitoDel version 3.0 in silico. MitoDel successfully detected and verified low-level mtDNA deletion with large scale 5,623-bp deletion (start point: 3,256, end point: 8,879) which involved mitochondrial complex I, complex IV and ATPase6. Our preliminary case report suggests that peripheral blood mtDNA sequencing combined with MitoDel will be helpful for the detection of large mitochondrial deletions in clinical practice.

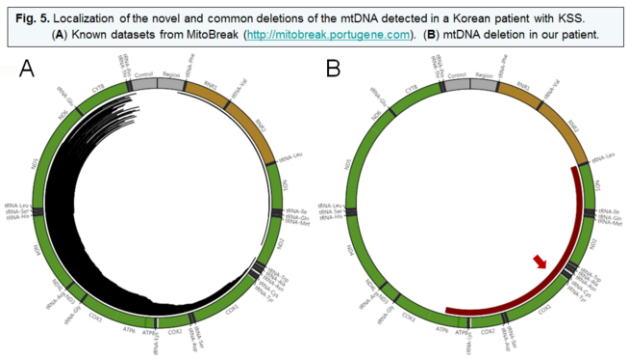

Fig. 5. Localization of the novel and common deletions of the mtDNA detected in a Korean patient with KSS. (**A**) Known datasets from MitoBreak (http://mitobreak.portugene.com). (**B**) mtDNA deletion in our patient.

BASIC SCIENCE: Pathology

P05.01

Validating targets in Parkinson's disease using the Parkinson's UK Brain Bank resource

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The development of new therapies for Parkinson's disease is highly dependent on a detailed understanding of the molecular mechanisms leading to damage within the nervous system. Such an understanding can only truly be gained by studying the human tissues that are affected by the condition. A major aim of the Brain Bank is to acquire tissue samples from the entire continuum of PD pathology and to make those samples and associated data available to neuroscientists worldwide to facilitate research into PD.
Using guidance from several sources, procedures were developed for the collection, processing, storage, retrieval and dissemination of this material. The bank has an extensive collection of brain and spinal cord samples from 1,400 individuals with or without PD. Our collection includes snap-frozen, fixed-frozen/cryoprotected and paraffin-embedded specimens. Sampling and screening procedure allow for precise anatomical and pathological characterisation of each tissue sample. Each tissue donation is annotated with detailed information about the donor, including health and life style questionnaires, medication and clinical history, and a comprehensive neuropathological report. Anonymised data, including images of brains slices and high-resolution images of individual stained sections representing affected areas, are available to registered tissue users in a searchable database accessible through our digital pathology portal. Different preparation methods can be implemented on request making our samples suitable for applications ranging from histopathology to genetic screening and novel 3D tissue visualisation techniques.
The Brain Bank operates an easy and open access policy to tissue and welcomes applications from academic institutions and the biotechnology sector. The Bank represents a valuable source of high quality human tissue samples for successful target validation in projects exploring Parkinson's disease and related neurodegenerative conditions.

P05.02

Cerebral amyloid angiopathy in two autopsy-proven patients with dementia with Lewy bodies

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Backgroud: Dementia with Lewy bodies (DLB) is a pathological disease entity characterized by Lewy bodies in the neocortices. On the other hand, cerebral amyloid angiopathy (CAA) is also a pathological disease entity characterized by deposition of amyloid-beta protein in the walls of cerebral cortices and leptomeninges.
Purpose: To reveal the occurrence of CAA in DLB.
Method: We retrospectively analyzed clinical records and pathological findings in two autopsy-proven patients with DLB.
Results: The age, gender, disease duration, and severity of parkinsonism was 80 years old / 85 years old, male/male, 3 years/12 years and mild/mild, respectively. Lewy bodies were detected in neocortices and brainstem in both of patients. Neurofibrillary tangles (NFT) and senile plaques (SP) were also detected equally in both of the patients (NFT: Braak stage 3, SP: Braak stage C). Whereas distribution and severity of Lewy bodies, NFT and SP were similar, the severity of CAA was quite different, as the patient with long disease duration appeared much severe.
Discussion and conclusion: Previous autopsy studies reported that CAA in DLB patients was more severe than in non-demented PD patients and age-matched controls. However, the process of CAA in DLB is not well understood. The present study showed that deposits of amyloid-beta protein in the walls of cerebral cortices and leptomeninges might be followed by deposits of Lewy bodies and senile plaques in patients with DLB.

BASIC SCIENCE: Animal and cellular models of Parkinson's disease and Parkinsonisms

P06.01

Role of indirect pathway D2 receptors in L-DOPA-induced dyskinesia

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Background: The two most abundant dopamine receptors in the striatum are the D1 and D2 subtypes. D1 receptors are expressed in striatal projection neurons forming the direct pathway, whereas D2 receptors are expressed in neurons forming the indirect pathway (iSPNs) as well as striatal interneurons. While the role of D1 receptors in L-DOPA-induced dyskinesia (LID) has been addressed by previous studies, very little is known about the specific role of dopamine D2 receptors in this complication of dopamine replacement therapy.
Aims: To investigate the role of indirect pathway D2 receptors (D2R) in LID using both pharmacological tools and conditional gene knockout methods in the mouse.
Methods: Mice sustained unilateral injections of 6-OHDA in the medial forebrain bundle, and were then treated with increasing doses of either sumanirole or quinpirole (two D2R agonists) to record dyskinesias and other behaviours. At the end of the chronic treatment, mice received challenge injections of D2- or D3-specific receptor antagonists (L741,626 or PG01037, respectively). Next, we used a virally mediated Cre/loxP system to selectively knockout D2R in iSPNs in adult mice. Thus, intact and 6-OHDA-lesioned Drd2loxP/loxP mice received unilateral striatal injections of an adeno-associated viral vector coding for Cre-recombinase under the control of the preproenkephalin promoter ('D2R-iSPN-KO model'). Four weeks post-surgery, mice were challenged with injections of a D1R agonist (SKF38393), D2R-agonists, and L-DOPA. Abnormal involuntary movements (AIMs) were rated during 3 hours after each drug injection.
Results: In mice with 6-OHDA lesions, both quinpirole and sumanirole induced severe axial AIMs, while limb and orofacial AIMs were very mild or absent. Co-treatment with L741,626 significantly improved D2R-agonist induced axial dyskinesia, while the D3-antagonist PG01037 had no effect. Moreover, quinpirole- and sumanirole-induced axial dyskinesia were completely abolished by the virally mediated D2R knockout in iSPNs. In addition, D2R-

iSPN-KO mice had significantly less dyskinesia than wild-type controls upon treatment with L-DOPA. In contrast, the severity of SKF38393-induced dyskinesia did not differ between D2R-iSPN-KO mice and wild-type animals.
Conclusions: These results show that D2 receptors expressed in iSPNs play a key role in the emergence dyskinesia upon treatment of parkinsonian animals with either D2R agonists or L-DOPA.

P06.02

Converging electrophysiological functions and pathological calcium phenotype over time results in mitochondrial stress: Describing a pathophysiological timeline and neuronal vulnerability in PD
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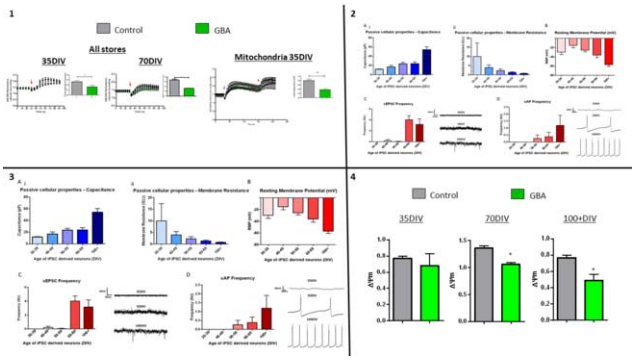
Understanding the pathophysiological timeline of disease is paramount to developing cures and preventative measures for PD. Specifically, identifying when in the disease course the various phenotypes begin and, how they interact with one another, will allow the scientific community to ascertain which mechanisms can be targeted and critically, when. Many useful therapeutics could currently have their validity missed due to administration at the wrong time. Thus generation of a timeline from models mimicking this human disease is of the utmost importance.
With the advent of induced pluripotent stem cell (iPSC) technology, it is now possible to work from a known genetic ontology (using autosomal dominant genetic forms of PD as a model for the mechanisms of late onset PD) and interrogate pathological phenotypes and stress over time in human neurons. Thus using iPSC-derived neurons from carriers of disease-associated mutations in LRRK2 and GBA genes, we have investigated phenotypes at several time points in order to map the pathophysiological disease timeline.
We have found that these mutations cause perturbation in calcium handling within intracellular neuronal stores; specifically in GBA lines, decreased calcium release from mitochondria. This reduced calcium would make generation of ATP harder from an early age (35 DIV). Using transcriptomic and western blot analysis, it was possible to identify changes in the level of key modulators of this calcium-signalling pathway (namely phospholipase D- 1; PLD-1 and calcium independent phospholipase A2; iPLA2) in GBA lines.
Concurrently, we have identified that iPSC neurons develop increased and sustained mature neuronal excitability and neurotransmission function by 70 DIV. The evolution and persistent nature of these functions will provide increased demand for ATP. We hypothesize that this unbalanced supply and demand will result in significant mitochondrial stress.
In line with this, we have found progressive alterations in mitochondrial membrane potential (MMP) over time in GBA lines, which only becomes significantly different at 70DIV and above. This change in MMP indicates perturbation of mitochondrial function. Similar investigations are ongoing in LRRK2 neurons.
These data present that altered mitochondrial calcium handling is a target for disease modulation specifically at early stages of the disease process.



P06.03

Functional analysis and single cell characterization of human fetal ventral midbrain in 2D and 3D cultures
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Parkinson disease (PD) is characterized by a loss of dopaminergic neurons in the substantia nigra pars compacta (SNpc). The selective loss of this cell population makes PD a good candidate for cell-based therapies. Clinical trials using cells derived from human fetal ventral midbrain (hVM) have shown that dopamine release could be restored to normal levels and in some PD patients produced substantial long-term clinical improvement. The ethical issues related to the use of human fetal material as well as the low number of hVM tissue available have limited the spread of this approach and have lead researchers to find new sources of cells such as human embryonic stem cells (hESCs) and pluripotent stem cells (IPCs).
This study was designed to provide a detailed molecular and functional of the fetal VM tissue in order to give a deeper understanding of its composition and characteristics. The characterization is based on the comparison of standard culture conditions (2D) versus organoids of hVM (3D). We used unbiased single cell RNA sequencing to transcriptionally compare fetal VM tissue in 2D and 3D conditions together with a functional analysis performed using whole cell patch clamp technique. Our analysis determined the molecular and functional properties of the tissue that originates dopaminergic neurons and also confirmed important differences between the culture conditions as well as it. The data can be used for quality assessment of new cell sources and provide new molecular targets for improved subtype specificity during stem cell differentiation.

P06.04

C-terminal domain of LRRK2 with the G2019S mutation can enhance α-synuclein toxicity in dopaminergic neurons in vivo
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α-synuclein (α-syn) and LRRK2 play crucial roles in Parkinson's disease (PD). Recent data suggest the existence of interplay

between these two proteins. However, the mechanisms underlying this functional crosstalk between α-syn and LRRK2 are unknown.
We hypothesized that the level of kinase activity of LRRK2 may modulate α-syn toxicity. To address this, we overexpressed in the rat substantia nigra pars compacta (SNc), the mutated (A53T) form α-syn (α-synA53T) with the C-terminal part of LRRK2 (ΔLRRK2) with or without the G2019S pathogenic mutation. This was achieved using adeno-associated virus (AAV). Experiments were also carried out with AAV coding for the dead kinase double mutant form of LRRK2 (G2019S/A1994E). Different time points post-infection (p.i.) were studied (<25 weeks p.i.) at which AAV-ΔLRRK2G2019S alone was not toxic (nor AAV-ΔLRRK2G2019S mixed with AAV-GFP). We also examined the effects of the ΔLRRK2 forms for two different levels of α-synA53T.
Our results were obtained in two different types of experiments. First, AAVs-α-synA53T was injected at relatively low titers (2 1010). This led to a ~35% loss of Tyrosine Hydroxylase positive neurons at 15 weeks p.i.. In this case, injection of a mixture of AAV-ΔLRRK2G2019S and AAV-α-synA53T produced significantly more degeneration than AAV-α-synA53T alone or AAV-α-synA53T mixed with AAV-GFP. In a second set of experiments, AAV-α-synA53T was injected at higher titers (i.e. 5 1010 vg/site) and toxicity was assessed at 8 weeks p.i.. In this case, histological evaluation showed a significant loss of SNc DA neurons and we also found reduced dopaminergic terminals in the striatum as assessed in vivo by PET with the [18F]-LBT9994 (LBT), a radioligand for dopamine transporter (DAT). The neurotoxicity of AAV-α-synA53T was changed by neither AAV-ΔLRRK2WT nor AAV-ΔLRRK2G2019S, whereas AAV-ΔLRRK2G2019S/A1994E tended to be neuroprotective.
These results suggest that, when neurodegeneration of DA neurons results from relatively low levels of α-synA53T, increased levels of the active C-terminal domain of LRRK2G2019S can be sufficient to facilitate α-synA53T toxicity.

P06.05

Parkinson's disease-linked D620N VPS35 knockin mice manifest tau neuropathology and dopaminergic neurodegeneration

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Mutations in the vacuolar protein sorting 35 ortholog (VPS35, PARK17) gene represent a new cause of late-onset, autosomal dominant familial Parkinson's disease (PD). A single missense mutation, D620N, is considered pathogenic based upon its segregation with disease in multiple families with PD. At present, the mechanism(s) by which familial VPS35 mutations precipitate neurodegeneration in PD are poorly understood and whether mutant VPS35 interacts with other PD-linked gene products in rodent models is not known. Here, we employ a new germline D620N VPS35 knockin (KI) mouse model of PD to formally establish the age-related pathogenic effects of the D620N mutation at physiological expression levels. Our data demonstrate that a heterozygous or homozygous D620N mutation is sufficient to reproduce key neuropathological hallmarks of PD as indicated by the progressive degeneration of nigrostriatal pathway dopaminergic neurons and widespread axonal pathology. Unexpectedly, endogenous D620N VPS35 expression induces robust tau-positive somatodendritic pathology throughout the brain as indicated by abnormal hyperphosphorylated and conformation-specific tau, which may represent an important and early feature of mutant VPS35-induced neurodegeneration in PD. In contrast, we find no evidence for α-synuclein-positive neuropathology in aged VPS35 KI mice, a hallmark of Lewy body pathology in PD. D620N VPS35 expression also fails to modify the lethal neurodegenerative phenotype of human A53T-α-synuclein transgenic mice. Finally, by crossing VPS35 KI and knockout mice, our data demonstrate that a single D620N VPS35 allele is sufficient for survival and maintenance of dopaminergic neurons, indicating that the D620N VPS35 protein is fully functional in vivo, suggesting that this dominant PD-linked mutation most likely exerts its pathogenic actions via a gain-of-function mechanism. Our novel findings demonstrate for the first time that a common PD-linked mutation in VPS35 can induce key neuropathological hallmarks of PD in mice with a novel role for the microtubule-associated protein tau, a major genetic risk factor for sporadic PD. Our data firmly establishes an important role for VPS35 and retromer-dependent protein sorting in the pathogenesis of PD and raise the tantalizing possibility of a pathogenic interplay between mutant VPS35 and tau for inducing neurodegeneration in PD.

P06.06

Targeting iron for the development of treatments for multiple system atrophy

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Multiple System Atrophy is an atypical parkinsonian disorder characterized by widespread neuronal loss, predominantly in nigrostriatal, olivopontocerebellar and central autonomic regions. The presence of protein aggregates primarily composed of misfolded α-synuclein in oligodendrocytes is the pathological hallmark of MSA, classifying it as a synucleinopathy. However, the etiology of MSA remains poorly understood and due to lack of identification of potential targets for drug therapy, no treatment is available for MSA patients.
There is a compelling evidence suggesting that iron plays an important role in neurodegenerative synucleinopathies like Parkinson's disease. Our hypothesis is that by removing the iron using chelators (e.g. Deferiprone), this could slow down the disease progression. In human MSA, there is evidence of increased iron in affected brain regions.
In the present work, we used a transgenic mouse model of MSA and found age-dependent increase in iron content in substantia nigra (SN) and striatum which preceded the onset of motor symptoms. Next, we tested whether deferiprone, a clinically approved iron chelator, can alleviate neuronal pathology and motor impairment in MSA mice. Aged MSA mice were treated with deferiprone. Compared to vehicle treated mice, deferiprone treatment rescued the motor performance, prevented loss of SN neurons and reduced the number of α-synuclein aggregates in SN (glial cell inclusions). Overall, the results from this proof of concept pre-clinical trial provide evidence that targeting iron in MSA could be a viable therapeutic option.

P06.07

DNAJC13 in Parkinson's disease; characterization of the p.N855S knock-in mouse model

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Background: Parkinson's disease (PD) is a common neurodegenerative disorder for which genetic studies have discovered multiple causative genetic mutations to highlight convergent cellular pathways. In 2014 DNAJC13 p.N855S was linked to autosomal dominant late-onset PD in Canadian Mennonite

families. In 2016 that assignment was challenged by the publication of TMEM230 p.R141L in the largest pedigree. Here we provide a reanalysis of the human genetic data and illustrate the functional consequences in vivo of DNAJC13 p.N855S in a novel knock-in mouse model.
Material and Methods: Sanger sequencing and segregation analysis of the TMEM230 c.422G>T (p.Arg141Leu) and DNAJC13 c.2564A>G (p.Asn855Ser) mutations in the original Canadian Mennonite family. Generation of the DNAJC13 p.N855S substitution in a knock-in (KI) mouse was achieved using Cre-loxP recombination. Biochemical, physiological and behavioral differences were examined in KI vs wild-type (WT) mice, with emphasis on synaptic vesicle trafficking, and intermembrane transporter activity in the striatum.
Results: Disease segregation shows comparable evidence for TMEM230 and DNAJC13 linkage, depending on the affected phenotypes specified. In contrast to TMEM230, the lifetime penetrance for DNAJC13 p.N855S is greater (73% vs. 53%), the protein is highly conserved (within and across species), and substitutions are rare. In primary cultures, DNAJC13 p.N855S KI neurons show excessive endosomal tubulation, using a GFP-SNX1 reporter, consistent with loss-of-function studies. Heterozygous DNAJC13 p.N855S KI mice have significant behavioral phenotypes (including open field locomotion, grip strength and balance/coordination) at different ages compared to WT littermates. We observed differences in expression of synaptic vesicular proteins and membrane transporters (α-synuclein, VAMP2, VGluT1 and DAT) by immunofluorescence confocal imaging and/or protein biochemistry analysis. Levels of endogenous neurotransmitters and presence of pathology markers ((p-)α-synuclein, (p-)Tau, P62, Iba-1, APP, GFAP) were analyzed by HPLC and immunolabeling, respectively. Preliminary electrophysiological analysis remains unchanged compared to WT littermates.
Conclusions: Overall, the genetic and functional evidence for the pathogenicity of DNAJC13 p.N855S in PD is compelling. DNAJC13 is one of five DNAJC co-chaperones implicated in Parkinsonism, all of which are expressed in the brain, and directly competes with VPS35 in endosomal cargo sorting/recycling. Further study of the complexes formed by these components is needed and appears central to the molecular pathogenesis of PD.

P06.08

Of mice and men, investigating the role of RAB39B in Parkinson's disease

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Loss of function mutations in Ras Analog in Brain 39B (RAB39B) cause X-linked recessive early onset Parkinson's disease (PD), characterised by extensive α-synuclein (αSN) pathology and dopaminergic neuron loss in the substantia nigra. RAB39B encodes a GTPase belonging to the RAB protein family, which regulate intracellular trafficking. Currently, the normal physiological function(s) of RAB39B are largely unknown, as is its role in the pathological mechanism underlying PD.

To investigate the function of RAB39B, we determined the distribution of RAB39B in mouse brain tissue, and assessed the behaviour of mice with knockout of Rab39b generated via CRISPR/Cas9 genome editing. By in-situ hybridisation and immunohistochemistry, we found RAB39B to be localised throughout the mouse cortex and hippocampus, and specifically in the substantia nigra pars compacta. Mice with Rab39b knockout demonstrated significant behavioural phenotypes that recapitulate aspects of human PD. In the tail suspension test, we observed sustained hindlimb clasping suggestive of nigrostriatal disturbance in Rab39b knockout mice compared to wildtype littermates. We observed a range of motor phenotypes, including increased slipping on balance beam, and reduced latency to fall on accelerating rotarod. Further, quantitative gait analysis demonstrated reduced diagonal phase dispersion and increased swing time, indicative of gait instability. To investigate the role of RAB39B in genetic and idiopathic PD, we performed neuropathological studies of an individual with RAB39B-mediated PD, and assessed steady-state RAB39B in the brain of individuals with idiopathic PD. The pathogenic RAB39B T168K loss of function variant was associated with the hallmark pathological features of PD, and additional Lewy pathology in the thalamus and hippocampus. In idiopathic PD cases, we found significant reductions in steady-state RAB39B in the prefrontal cortex and substantia nigra compared to healthy controls.
In conclusion, our findings in mouse and human extended current understanding of the neuropathological mechanisms underlying RAB39B-mediated PD, and suggested a potential role for the protein in idiopathic PD. To further delineate the role of RAB39B in genetic and idiopathic PD, current studies are focused on performing biochemical and proteomic analyses of mouse models, and characterising stem cell models with knockout of RAB39B.

P06.09

Optimization of evans blue quantification as a blood–brain barrier integrity tracer during Parkinson's disease and l-dopa induced dyskinesia

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The loss of dopaminergic neurons in Parkinson's disease (PD) is accompanied by neuroinflammation, whose cause and origin have not yet been elucidated. In this context, a blood-brain barrier (BBB) breakdown could be contributing to perpetuate and amplify the progression of this disease. Evans blue (EB) dye is a commonly used tracer for the quantification of BBB disruption in neurological disorders. Although this method is one of the most used, there are several protocols of analysis in the literature which the most of authors have removed blood by perfusion prior to removing brain samples. However, the possibility of perfusion washing the dye out of brain tissue has not been considered. In this study, we compared the amounts of accumulated stain in brain tissue following intravenous injection in the jugular vein of a 2.5% solution of EB (4 ml/kg of body weight) at 45 min of circulation time in C57/BL6 mice with parkinsonism (unilaterally 6-OHDA-lesioned mice) and levodopa-induced dyskinesia (LID) (L-DOPA, 25 mg/kg i.p.; benserazide hydrazide hydrochloride, 10mg/kg i.p.). Intravenous injection of EB in sham-operated mice was also done. Afterwards, the mice were transcardially perfused with Krebs-Ringer solution or the brain tissue was directly removed without perfusion. Right and left striatum and substantia nigra were put in formamide during 48h for dye extraction at room temperature. EB stain was measured by spectrophotometer (620 nm) and quantified according to a standard curve. All values obtained were corrected by background

subtraction of naïve mice. Dye was not detected in brain structures after perfusion. On the other hand, EB concentration has been detected in all brain areas from not perfused mice, except in sham animals. In the lesioned striatum, mice with LID presented a higher level of dye (5.1±1.9 ng EB/mg of tissue) than parkinsonian animals (2.7±1.9 ng EB/mg of tissue; $p<0.05$). Collectively, these results show that perfusion is not indicated to evaluate BBB integrity associated to EB assay. Moreover, these data provide strong evidence of BBB breakdown in PD and LID, which would enable the entrance of inflammatory substances within the brain, exacerbating neuroinflammation.

Acknowledgements: The São Paulo Research Foundation (FAPESP, grant numbers 2018/00461-1 and 2014/25029-4); CNPq (402370/2016-3 and 301639/2015-9).

P06.10

Auxilin protects against α-synuclein aggregation, cell death and impairment of endocytosis

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Background: A hallmark of Parkinson's disease (PD) is the formation of lewy bodies (LB's) in neurons. LB's are cytoplasmic protein rich aggregates, in which α-synuclein (α-syn) is the most abundant protein. Recently, recessive mutations were discovered in the auxilin (DNAJC6) encoding gene, that were linked to a juvenile form of PD. Auxilin is a DNAJ co-chaperone of the HSP70 chaperones, which are important for protein folding and homeostasis in the cell.
Materials and Methods: To address our questions, we have used HEK293 and N2a cell culture, KO of auxilin by Crispr/CAS9 method, produced recombinant proteins and performed α-syn based thioflavin T assays of α-syn aggregation. Endocytosis has been measured using fluorescently labeled transferrin and cell death using tryphan blue.
Results: We observed that auxilin KO cells, which overexpressed α-syn-Dsred, contained more α-syn aggregates than did the parental control cells. Moreover, we observed an increased cell death in KO cells that overexpressed α-syn-Dsred.The increased cell death in α-syn-Dsred Auxillin KO cells could be prevented by re-introducing Auxilin into these cells. With use of recombinant proteins, we found that auxilin inhibits α-syn aggregation as well in vitro. As both α-syn and auxilin, are important for endocytosis and exocytosis in neurons, we explored how these dynamics were affected in HEK293T cells. We observed that endocytosis was impaired in cells that had KO of auxilin and overexpressed α-syn-Dsred, but not in parental control cells.
Discussion: Our results suggest, that increased aggregation of α-syn-Dsred can impair endocytosis in the absence of auxilin which ultimately affects cell survival.
Conclusions: These results links a cellular role of auxilin in preventing vulnerability to α-syn aggregates, and this provides a possible explanation for how recessive mutations in the auxillin gene could be linked to PD.

P06.11

Therapeutic benefits on motor functions and neuroprotective effect of repetitive transcranial magnetic stimulation on parkinsonian rats

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Non-invasive brain stimulation technique such as repetitive magnetic stimulation (rTMS), has been increasingly developed for the purpose of neuromodulation which is considered having therapeutic potentials in Parkinson's disease (PD). However, the therapeutic value of such approach for PD is still uncertain. The severity of dopamine depletion could be critically involved in the expression of motor plasticity induced by rTMS and might further interfere with the improvement of motor performance. Accordingly, for elucidating the possible therapeutic effects, we conducted to have the early intervention of rTMS before the onset of symptoms and the late rTMS treatment in the chronic stage of PD when the PD phenotype has been fully expressed. A hemiparkinsonian rat model, generated by unilateral injection of neurotoxin 6-hydroxydopamine (6-OHDA) to induce nigrostriatal dopamine depletion, was applied to identify the therapeutic potential of rTMS in neuroprotective effects and motor behaviors. The detailed functional behavior tests including gait, akinesia, rotational behaviors as well as histology were evaluated up to 4–8 weeks after daily administration of rTMS-intermittent theta burst stimulation (iTBS) mode over the motor cortex at the early and late stages of PD rats.
Under rTMS intervention over the course in the early stage of PD rats, we found that the 4 weeks early rTMS intervention significantly alleviates 6-OHDA induced motor deficits in gait, akinesia, and rotational behavior. Immunohistochemically, tyrosine hydroxylase (TH)-positive neurons and fibers were significantly preserved in the early intervention group. Compared with early rTMS intervention, applying 4 weeks rTMS at the late stage of PD rats also improved locomotor function but failed to reduce the rotational behavior, indicating that rTMS would not block striatal dopamine depletion.
Taken together, these results suggest that early rTMS-iTBS protocol exerts neuroprotection and reduces the progression of motor symptoms in early-stage PD rats. Also, our data further highlight the potential therapeutic effects of rTMS and confirm the existence of a long-term effect of consecutive daily applications of rTMS. These findings may have translational relevance for the further potential application of human PD subjects.

P06.12

GBA-associated Parkinson's disease mice model

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Background: Parkinson's disease (PD) is characterized by dopaminergic cell loss and the accumulation of pathological α synuclein (α-syn), but its precise pathomechanism remains unclear. An animal model is essential not only to explore the pathogenesis of PD but to search for the biomarker and validate the candidate drugs for PD. In this study, we generated a novel animal model of GBA-associated PD.

Material and Methods: We previously generated α-syn bacterial artificial chromosome (BAC) transgenic mice with the entire human α-syn gene and its gene expression regulatory regions, expressing 2.7-fold amount of α-syn with similar expression pattern to endogenous α-syn. They manifested decreased anxiety-like behaviors which may reflect non-motor symptoms, but did not show dopaminergic neuronal loss. Recent genetic study showed that PD patients have higher prevalence of heterozygous GBA mutation, and reduced activity of GBA is presumed to accelerate accumulation of α-syn, although underlying precise mechanisms remain unclear. Here, we crossed wild-type α-syn BAC tg mice with GBA heterozygous knockout mice to make double-mutant mice as a model for GBA-associated PD.

Results: These mice showed more pathogenic α-syn species such as phosphorylated α-syn and showed mild dopaminergic neuronal cell loss. Focusing on the in-vivo mechanisms of GBA insufficiency accelerating PD pathology, we performed lipid analysis and found that the level of glucosylsphingosine was significantly increased without any noticeable accumulation of glucosylceramide, which is a direct substrate of GBA, only in double-mutant mice.

Conclusion: We created a novel prodromal mice model to study the disease pathogenesis and develop novel therapeutics for PD, and also revealed the role of heterozygous gba deficiency contributing to PD through an abnormal lipid metabolism under the condition of an altered asyn expression in vivo.

P06.13

Characterization of Rab phosphorylation by LRRK kinases

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Leucine-rich repeat kinase 2 (LRRK2) is one of the responsible genes for familial Parkinson's disease (PD). So far eight missense mutations in the LRRK2 gene (N1437H, R1441C/G/H/S, Y1699C, G2019S, I2020T) were found to be pathogenic. It has been shown that LRRK2 physiologically phosphorylates small GTPase Rab proteins. It has been shown that the pathogenic mutations in LRRK2 increase the Rab phosphorylation in vivo although its involvement in the pathogenesis of PD remains unclear. In this study, we first set out to systematically identify substrate Rab proteins of LRRK2 as well as LRRK1, a mammalian ortholog of LRRK2. For this purpose, we utilized Phos-tag SDS-PAGE by which we can detect protein phosphorylation by a band shift on immunoblots. LRRK1 or2 and one of 62 human Rab proteins with an HA-tag at the amino-terminus were overexpressed in HEK293A cells, and the phosphorylation of the Rab protein was examined by Phos-tag SDS-PAGE followed by immunoblotting with an HA-antibody. Overexpression with LRRK2 caused a band shift of Rab3A/B, Rab8A/B, Rab10, Rab12, Rab29, Rab35 on Phos-tag SDS-PAGE, which were consistent with previous reports. Overexpression with LRRK1 also caused a band shift of several Rab proteins including Rab7A. These results suggested that the LRRK family kinases physiologically phosphorylate distinct sets of Rab proteins. We also investigated the effect of Rab10 phosphorylation by LRRK2 on its subcellular localization. When U2-OS cells were transfected with LRRK2, endogenous Rab10 showed a perinuclear punctate staining in a manner dependent on the LRRK2 kinase activity. CRISPR/Cas9 knockout of Rab10 in U2-OS cells abolished the staining. Taken together, these results suggested that phosphorylation of Rab proteins by the LRRK kinases alter their subcellular localization, presumably by changing the affinity to their interacting partners.

P06.14

1-methylxanthine circling behavior without apomorphine in rats

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A2A adenosine receptors antagonist are potential drugs to help Parkinsonian patients, in many cases, these molecules have a xanthinic core; this structure has a crucial role in their affinity for this receptors.

In previous studies, 1-methylxanthine has shown an affinity for A2A adenosine receptors and antagonism for these receptors, such it could have an antiparkinsonian effect.

Circling behavior, is a worldwide used animal model of Parkinson Disease, based in 6-OHDA unilateral lesión in rats, in this study, we had two groups Control (NaCl 0.9%+NaHCO3 0.08% I.P. n=3) and 1-methylxanthine group (7.5 mg/Kg I.P. n=6), this procedure was realized without apomorphine I.P.

Results have shown a discrete difference between two groups, with a clear tendency to increase in the 1-methylxanthine respect control group; however, it was no significant (p=1.59).

It is possible that the observed tendency, could be significant in other dosages, but more experiments are needed to precise it.

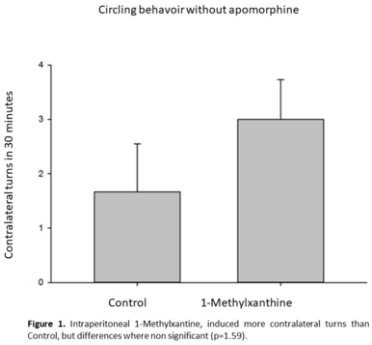

Figure 1. Intraperitoneal 1-Methylxantine, induced more contralateral turns than Control, but differences where non significant (p=1.59).

P06.15

Parkinson's disease-on-a-chip: Reconstructing the nigrostriatal pathway in vitro

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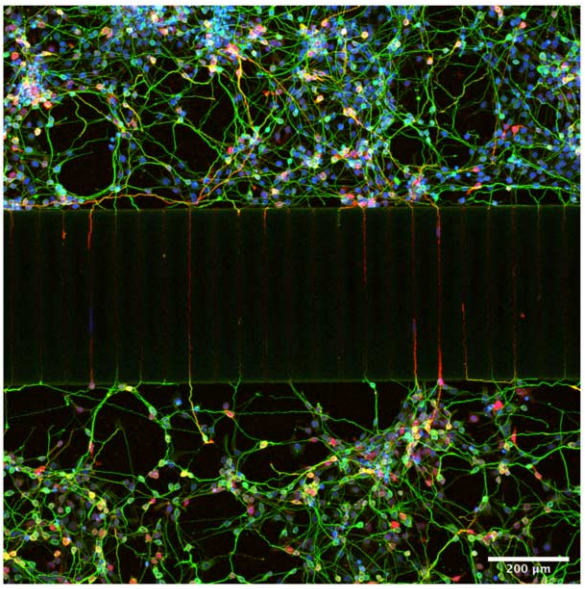
Human population is getting increasingly older. Hence, age-related neurodegenerative diseases like Parkinson's disease (PD) are imposing an escalating threat as a medical, economical, and emotional burden. For decades, PD has been studied in animal models and simple cellular models. While in many aspects these models are irreplaceable, they are inherently limited in others. Low success of clinical trials for new drugs and therapies has recently turned attention to poor translation of animal experiments to human outcomes. On the other hand, simple cell cultures lack in vivo tissue complexity. Therefore, a need for a more advanced human in vitro models has emerged. Here we report a reconstruction of the nigrostriatal pathway on-a-chip to model PD as the hallmark of PD pathology is the loss of nigrostriatal dopaminergic neurons. The model consists of two neuronal populations (one representing substantia nigra and the other striatum) that are spatially separated but connected via microchannels that allow directional axonal growth while preventing cell migration. Dopaminergic neurons generated from human ventral mesencephalic neural stem cells extend axons towards and connect to the opposite population of neurons generated from forebrain neural stem cells representing striatum. Our model introduces anatomical complexity of the in vivo nigrostriatal pathway and provides a tool to study the mechanisms of neurodegeneration and treatments of PD. Further introduction of optogenetic neuronal activation, PD specific mutations in the dopaminergic neurons, and electrodes for the measurement of neuronal activity and dopamine release will further increase the capabilities of our model to investigate the mechanisms underlying PD.



Dopaminergic neurons generated from human neural stem cells extend axons to the opposite neuronal population through axonal guidance microchannels.
ß-tubulin TH DNA

P06.16

Administration of exogenous α-synuclein pre-formed fibrils to primary oligodendrocyte precursor cells

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Multiple system atrophy (MSA) is an adult-onset progressive neurodegenerative disease that is hallmarked at the cellular level by the presence of α-synuclein (α-syn) inclusions. Although α-syn inclusions are prominently observed as glial cytoplasmic inclusions in oligodendrocytes, the origin of α-syn inclusions is still elusive. We try to visualize the uptake of exogenously applied α-syn pre-formed fibrils (PFFs) in primary oligodendrocyte precursor cells (OPCs) in the presence of other glial cells. Recombinant human full length α-syn with a C-terminal Myc-tag (α-syn-Myc) were expressed in BL21(DE3) RIL cells and purified. Fibrillation was conducted by constant agitation at 1,000 rpm for 7 days. Mixed glial cell culture was obtained from cerebral cortices of 1–2 day old Sprague Dawley rats. α-Syn PFFs were added to mixed glial cell culture at 4–5 days. OPCs were collected 8–9 days after the addition of α-syn PFFs. Double immunostaining for Myc and platelet-derived growth factor α receptor, which is a marker of OPCs, did not clearly show the internalization of exogenous α-syn PFFs in OPCs. When applied in the presence of other glial cells, exogenous α-syn PFFs was not clearly detected in primary OPCs by immunostaining. Further investigation, especially concerning the application protocol of α-syn PFFs, may be warranted to reproduce the internalization of α-syn in oligodendroglial cells, the leading pathology of MSA.

P06.17

Production of transplantable CORIN-positive midbrain dopaminergic precursors from human pluripotent stem cells is highly sensitive to small changes in WNT signalling

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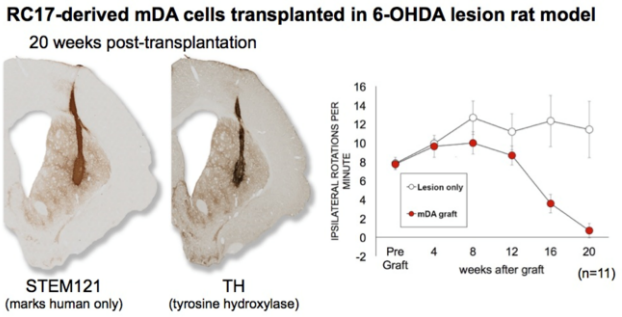
Parkinson's disease (PD) is a progressive neurodegenerative disorder that is characterized by the selective loss of midbrain dopaminergic (mDA) neurons. An emerging regenerative therapy for PD involves the restoration of the dopaminergic network by transplantation of new, immature mDA neurons into the striatum. Human embryonic stem cells (hESCs) and induced pluripotent stem cells (iPSCs) are proven to be the most reliable and effective cell source to produce transplantable mDA cells. However, protocols to differentiate mDA cells from hESCs/iPSCs are complicated and highly sensitive to small changes in conditions. Here we have uncovered and fine-tuned critical parameters in the mDA differentiation protocol for different clinical-grade hESC lines. Amongst the most sensitive variable is the concentration of CHIR99021, the GSK3β inhibitor used to activate the WNT pathway. Changing the concentration of CHIR99021 by less than 10% significantly affects differentiation outcome as measured by flow cytometry for the floor plate marker, CORIN. We demonstrate that endogenous WNT signaling is activate during the differentiation process through the use of the Porcupine inhibitor, IWP-2, and that expression of endogenous WNT ligands are increasing over time. Therefore, we propose that the total WNT signaling in any given cell will be highly dynamic and will be the summation of endogenous and exogenous factors that stabilize β-catenin. We demonstrate that fine-tuning of the WNT signal can produce hESC-derived mDA precursors that are >95% CORIN-positive. Transplantation of these cells into a 6-hydroxydopamine-lesioned rat model of PD resulted in

long-term engraftment and the production of slim, but highly innervating grafts that fully rescue amphetamine-induced rotational dopaminergic phenotypes (figure). This work illustrates that fine-tuning of mDA differentiation protocols especially with respect to WNT signaling, can produce uniform and defined cell populations for transplantation.



P06.18

Novel rat model of Parkinson's: CRISPR-mediated introduction of a G51D mutation into the endogenous rat SNCA gene displaces α-synuclein from the synapse

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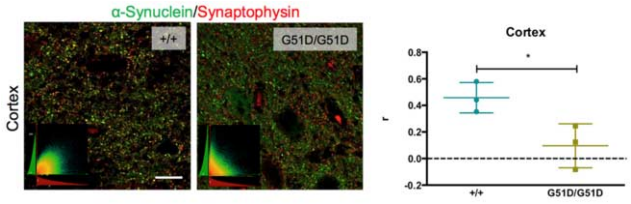
The G51D α-synuclein (αSyn) autosomal dominant mutation is associated with very early onset of Parkinson's (from early 20s) and extremely rapid progression – average of 5–7 years from diagnosis to death. This mutation causes symptoms and pathologies of Parkinson's, dementia with Lewy bodies, and multiple system atrophy combined. We have generated a G51D αSyn rat model using CRISPR/Cas9 technology to mimic this recently described Parkinson's familial mutation. We introduced a 2-bp change in the glycine-51 codon of the endogenous SNCA gene (encoding αSyn) to now encode for aspartic acid-51. This created a new BspHI restriction site making it straight-forward to genotype rats with this mutation. The most striking phenotype was observed when the subcellular localisation of αSyn was investigated in homozygous G51D/G51D rats. In mutant rats, αSyn protein do not co-localise with the synaptic marker, synaptophysin (figure), while co-localisation of synapsin and synaptophysin, two synaptic markers, was normal. This strongly indicated that αSyn was mislocalised away from the synapse in G51D/G51D rats, a potential early molecular change in Parkinson's. Unbiased quantitative mass spectrometry also indicated misregulation of synaptic proteins in G51D/G51D rat striatum. In summary, we have generated a novel rat model with a single amino acid change that mimics some of the early phenotypes of Parkinson's.



P06.19

An iPSC derived model of early onset sporadic Parkinson's disease shows disease relevant phenotypes that are reversed by specific phorbal esters

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Parkinson's disease (PD), one of the most prevalent and debilitating neurodegenerative conditions present in our population, is classically characterized by the progressive loss of dopamine (DA) neurons in the substantia nigra as well as the presence of cytoplasmic inclusions known as Lewy bodies and Lewy neurites within specific brain regions. These inclusions contain large amounts of the protein α-synuclein, which is also associated with a rare form of genetic PD caused by triplication of the SNCA gene. Previous iPSC-based models derived from patients with monogenic mutations in PD genes have shown accumulation of α-synuclein in differentiated DA neurons however, these monogenic mutations account for only a small minority of PD cases. Here, we have utilized multiple iPSC lines derived from sporadic PD patients with very early onset of disease symptoms (early onset sporadic PD: EOSPD). These iPSC lines provide an opportunity to better understand sporadic PD and to investigate the hypothesis that early onset sporadic patients carry unidentified genetic risk factors that cause a more aggressive form of the disease. DA neurons differentiated from these EOSPD iPSCs produce and release dopamine and, critically, exhibit multiple pathologies classically associated with PD including the accumulation of α-synuclein protein (Figure 1a-c). Further proteomic and transcriptomic analysis of these EOSPD DA neurons reveals a full signature PD-in-a-dish model, including dysregulation of pathways associated with mitophagy, synaptic transmission, and lysosomal protein degradation. This is the first iPSC-based model to have demonstrated classical PD phenotypes in a sporadic PD background. The fact that patient iPSC lines acquire these phenotypes demonstrates a clear genetic contribution to EOSPD. Finally, screening with these sporadic PD lines has identified a novel drug that rescues α-synuclein accumulation (Figure 1 d,e), increases TH expression (Figure 1 f,g), and implicates a new signaling pathway in sporadic Parkinson's disease.

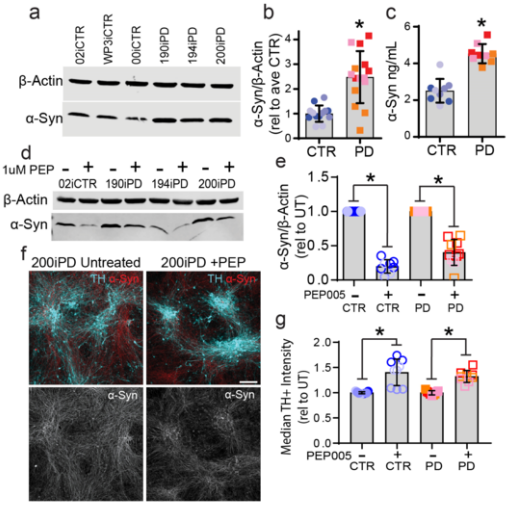

Figure 1: α-synuclein accumulation and drug treatment effects in EOSPD mDA cultures. (a) Western blot of d30 mDA cultures for α-synuclein production and β-actin as a housekeeping control. (b) Relative intensities from multiple western blots, with each point representing a band intensity from a separate differentiation, intensities are relative to average of control lines. (c) α-synuclein ELISA, each point represents an average of 3 wells from a separate differentiation, 3 independent differentiations are represented. Colors on graphs indicate different iPSC lines. *denotes significance from control p<0.0001 via t-test with Welch's correction (b,c). (d) Western blot of d30 mDA cultures treated with small molecule drug (PEP005) from multiple EOSPD and control lines. (e) Quantification of α-synuclein band intensities with and without PEP005 relative to untreated cells of the same line. * indicates significance relative to untreated cells p<.005 paired t-test (e). (f) Immunocytochemistry showing TH and α-synuclein in 200iPD d30 mDA cultures with and without PEP005 treatment. (g) Flow cytometry analysis of d30 mDA cultures treated with PEP005 for 72 hrs, median TH intensity of positive cells relative to untreated mDA cultures of the same line, * indicates significance from untreated (p<0.05) via t-test with Welch's correction. Error bars represent standard deviation (SD).

P06.20

Age – and α-synuclein dependent degeneration of dopamine and noradrenaline neurons in the annual killifish Nothobranchius furzeri

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Parkinson's disease (PD) is a neurodegenerative disease characterized by α-synuclein-positive inclusion bodies and loss of neurons, including dopaminergic neurons. Difficulty in replicating PD phenotypes using animal models partly limits the understanding of PD and the therapy required. Although PD is strongly associated with aging, most experimental animals may not exhibit age-related symptoms. Herein, we demonstrate that Nothobranchius furzeri, a rapidly aging teleost with a short lifespan, exhibits age-dependent degeneration of dopaminergic and noradrenergic neurons and progression of α-synuclein pathologies. These pathological phenotypes are similar to those observed in human patients with PD, especially in those with idiopathic PD. Amelioration of the cell loss by genetic depletion of α-synuclein suggests that α-synuclein is not a bystander but a causative protein of neurodegeneration. α-Synuclein of N. furzeri can exhibit a prion-like property; transection of the neural connections terminated the progression of α-synuclein and occurrence of neurodegeneration. Taken together, N. furzeri can reveal mechanisms underlying PD, especially of the idiopathic form that affects a majority of patients with PD, including α-synuclein-dependent neurodegeneration, age-dependent phenotypes, and progression of α-synuclein pathology.

P06.21

Development of in vitro PARK 9 Parkinson's disease model using carbonate apatite nanoparticles

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Objectives: PARK9 familial Parkinson's disease (PD) is caused by the loss-of-function mutation of ATP13A2 which encodes for the lysosomal P5-type ATPase. Defective ATP13A2 impairs mitochondrial function, alters autophagic-lysosomal degradation pathway and induces intraneuronal accumulation of α-synuclein in PD. A few in vitro models using viral and non-viral vectors have been developed to deliver small interference RNAs (siRNAs) to mimic ATP13A2 loss-of-function. These models suffer from potential drawbacks such as low transfection efficiency, high toxicity, high immunogenicity and high cost. pH-sensitive inorganic carbonate apatite (CA) is an emerging nanoparticle that could bind to negatively charged siRNA molecules and enables low toxic delivery of siRNA with high transfection efficiency. In this study we developed and evaluated a novel in vitro model of PARK9-PD using CA nanoparticle as nanocarrier.
Methods: CA nanoparticle was fabricated as nanocarrier to deliver pre-designed ATP13A2 siRNAs and non-targeting siRNAs control. siRNAs of concentration ranges from 1 pM to 50 nM were used for transfection. Characterization of CA-siRNAs complexes were carried out prior to transfection. Following the transfection of siRNA in SH-SY5Y neuroblastoma cell, western blot was used to check the transfection efficiency based on protein expression of ATP13A2.
Results: We demonstrated that CA-siRNAs complexes formed stable self-assembled colloids throughout 72 hours of incubation at physiological conditions but rapidly destabilized at low pH of cellular endosomal compartment. Fluorescence microscopic images of CA-GFP-siRNA transfected cells showed that nano-scale size distribution of complexes exhibited high uptake efficiency and transfection efficacy without any indication of cytotoxicity. Following 48 hours of transfection of CA-siRNAs complexes, approximately 70% of ATP13A2 gene expression was being knocked down.
Conclusions: Results show that in vitro model of PARK9-PD using CA nanoparticle delivers siRNA with high transfection efficiency, has low cytotoxicity and also efficiently knocking down the protein expression of ATP13A2. Hence this model is ideal for studying the biochemical changes in cell caused by ATP13A2 mutation similar to those happening in PARK9 familial PD.

P06.22

Mutant α-synuclein alters GATA1- dependent transcriptional regulation of the lysosomal ATPase ATP6V0A1 with downstream impact on autophagy

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Mutations and multiplications of the SNCA (αSyn) gene cause familial Parkinson's disease (PD). Here we investigate the functional role of ATP6V0A1 (V-type proton ATPase 116kDa subunit isoform 1) identified as a genetic risk factor in a PD-GWAS with a single-

nucleotide polymorphism (SNP) associated to PD (rs9897702) in its promoter region. An ancestral or PD-associated reporter gene assay (ATP6V0A1 promoter in front of the Gaussia luciferase) was transfected into SK-N-SH cell lines stably overexpressing WT and mutant αSyn and the effect of the SNP on the transcriptional regulation was measured. Interestingly, A53T-αSyn overexpressing cells showed increased activity of the ancestral promoter compared to the PD-associated one. Moreover, both promoter variants showed a higher activity when compared to control cells, respectively. In addition, we observed an enhanced ATP6V0A1 mRNA expression in A53T-αSyn overexpressing cells, compared to SK-N-SH. In silico analysis of the promoter region revealed a binding site for the GATA1 transcription factor on the same promoter sequence containing the PD-associated rs9897702 variant which reduced the predicted binding to GATA1. Consistently, EMSA (electrophoretic mobility shift assay) experiments showed a decreased GATA1 binding to the PD-associated promoter sequence, compared to the ancestral one. Western blot analysis for LC3B showed a decrease in the autophagic flux in cell lines with the overexpression of αSyn (WT and mutant). To dissect the functional consequences of endogenous rs9897702, we obtained human PBMCs (Peripheral blood mononuclear cells) from three carriers of the homozygous wildtype allele (G/G) and three carriers of the homozygous allele, which is associated to PD (A/A). The PBMCs were then immortalized with Eppstein-Barr virus (lymphoblasts). No difference could be observed in the expression levels of ATP6V0A1 mRNA between the genotypes, when measured using digital droplet PCR (ddPCR). mRNA levels are being investigated upon transient overexpression of αSyn in the lymphoblasts.
We have shown that the ATP6V0A1 SNP has a functional role in modulating gene transcription. These results further suggest that ATP6V0A1 transcription is critically modulated by αSyn via a GATA1-dependent mechanism. Importantly, autophagy appears as a cellular process affected by αSyn dysregulation, indicating the importance of this pathway in PD.

P06.23

Rapid dopaminergic neuron loss accompanied by Lewy body-like pathology in fibril-inoculated A53T mutant α-synuclein BAC transgenic mice

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Background: We are in a struggle to overcome Parkinson's disease (PD) because of the lack of good animal models of this disease. We previously generated α-synuclein (α-Syn) bacterial artificial chromosome transgenic (BAC Tg) mice harboring entire wild type or A53T mutant human α-Syn gene. Although these Tg mice expressed 2- to 3-fold α-Syn in the brains compared with wild-type mice, they did not show any pathological change and apparent abnormal motor phenotypes at their early age.
Objectives: To generate a mice model of PD which exhibits dopaminergic neuron loss and motor symptoms accompanied by α-Syn aggregations in a short period enough to be applicable for drug testing.
Methods: We inoculated human or mouse α-Syn pre-formed fibrils (hPFF or mPFF) into the left dorsal striatum of non-Tg mice, wild-type human α-Syn BAC Tg (SNCA BAC Tg) mice and A53T human α-Syn BAC Tg (A53T-SNCA BAC Tg) mice.
Results: MPFF induced more abundant phosphorylated-α-Syn (P-α-Syn) pathology compared with hPFF in the ipsilateral substantia nigra pars compacta (SNc) in each genotype. Among mPFF-inoculated mice groups, A53T-SNCA BAC Tg mice showed the most robust P-α-Syn pathology, despite almost the same expression level of exogenous α-Syn compared with SNCA BAC Tg mice. Consistent with these observations, in vitro aggregation assay revealed A53T mutant human α-Syn aggregated more rapidly than wild-type α-Syn in the presence of mouse α-Syn. A53T-SNCA BAC Tg mice inoculated with mPFF showed 40% reduction of dopaminergic neurons in the ipsilateral SNc and apomorphine-induced rotation behavior two months after inoculation. In these mice, the number of P-α-Syn positive cells in the SNc was reduced in parallel with the dopaminergic neuron loss, indicating that the cells carrying P-α-Syn inclusion died overtime.
Conclusions: The extent of α-Syn pathology induced by PFF inoculation depends on the types of inoculum and exogenously expressed α-Syn in mice. A53T-SNCA BAC Tg mice inoculated with mPFF displayed the most robust α-Syn pathology and most rapid dopaminergic neuron loss among the mice groups we tested. These mice could be useful for testing of disease modifying therapy of PD.

P06.24

Temporal genetic profiling of early synucleinopathy in nigrostriatal dopamine neurons

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The earliest stages of synucleinopathy have been difficult to study due to the fact that most animal models of Parkinson's disease (PD) fail to recapitulate the progression of synucleinopathy to neurodegeneration. The α-synuclein (α-syn) preformed fibril (PFF) synucleinopathy model exhibits a distinct stage of accumulation of α-syn inclusions in tyrosine hydroxylase immunoreactive (THir) neurons in the substantia nigra pars compacta (SNpc) months prior to the ultimate degeneration of the nigrostriatal system. In the present study we leveraged the prolonged pretoxic synucleinopathy stage observed in the rat α-syn PFF model to reveal the genetic signature associated with early synucleinopathy in the SNpc.
Male and female Fischer 344 rats were injected unilaterally into the striatum with 16 total µg of sonicated mouse α-syn PFFs or vehicle. Using these surgical parameters we have routinely observe peak phosphorylated α-syn (pSyn) inclusions in the SNpc between 1 and 2 months following injection. Further, these same model parameters induce a loss of approximately 50% THir SNpc neurons at 6 months. At 1 and 2 months post-injection, animals were saline perfused, with brains removed and flash frozen. Sections through the SNpc were rapidly immunolabeled for either TH or pSyn (phosphorylation at serine 129). Laser capture microdissection (LCM) was used to collect pSyn immunoreactive SNpc neurons in PFF-injected rats and SNpc THir neurons in control-injected rats. RNA was isolated and RNASeq used to identify gene expression changes between SNpc neurons with and without pSyn inclusions.
RNASeq results are pending and will be presented at the meeting. Ultimately, our goal is to identify novel genes and pathways associated with synucleinopathy that may lead to the discovery of targets for genetic or pharmaceutical intervention to prevent or slow neurodegeneration in PD.
Research was supported by United States of America Department of Defense Congressionally Directed Medical Research Programs Early Investigator Award (W81XWH1810233:PD170100)

P06.25

α-synuclein propagation via olfactory pathway in non-human primate model

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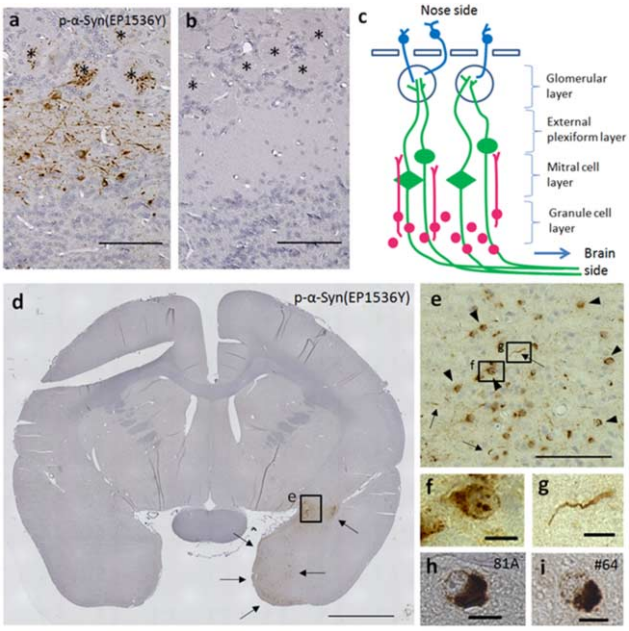
Objective: Parkinson's disease (PD) is a neurodegenerative disease characterized by α-synuclein (α-Syn) aggregates, called Lewy bodies. The α-Syn aggregates are believed to propagate in the brain like prion via two major pathways: the olfactory and vagal pathways. Recently the common marmoset (Callithrix jacchus), a new world monkey, has gathered a lot of attention in the field of neuroscience because of its useful characteristics as a non-human primate model (NHP). In this study, to demonstrate the propagation fashion in NHP and to evaluate consequential brain dysfunction, we analyzed pathological progression of α-Syn fibrils by injection in the olfactory bulb (OB) of common marmosets and measured regional brain activity by [18F]FDG-PET (2-deoxy-2-[18F]fluoro-D-glucose – positron emission tomography).
Methods: Recombinant full-length marmoset α-Syn was purified and incubated with agitation for a week to generate α-Syn fibrils. Two female and two male common marmosets (about two years old) were injected 0.8 ul of α-Syn fibrils solution (4 mg/ml in sterile PBS) stereotaxically using glass capillary at two sites in the unilateral OB under anesthetized condition. Three or six months after the injection, the marmosets were measured regional brain activity by [18F]FDG-PET and then sacrificed. The brains were fixed with 4% PFA in PBS and sliced into 8 μm coronal sections which were immunostained by anti-phosphorylated α-Syn (p-α-Syn), anti-ubiquitin (Ub) and anti-p62 antibodies.
Results: Wide and progressive spreading of p-α-Syn positive aggregates, which were also positive for Ub and p62, were observed in the ipsilateral OB (Fig. a-c), amygdala and entorhinal cortex (Fig d-i) suggesting the propagation of α-Syn pathology along with anatomically connected neurons over 6 months. Importantly, the OB, amygdala and entorhinal cortex are related to PD prodromal symptoms: hyposmia, anxiety and cognitive dysfunction, respectively. In contrast, there was few p-α-Syn positive aggregates in the contralateral side. In addition, [18F]FDG-PET study revealed hemispheric hypoactivity in the injected side.
Conclusions: We created the marmoset showing propagation of α-Syn fibrils via olfactory pathway. This marmoset could potentially be a non-human primate model of prodromal PD.



P06.26

Reprogramming of adult human fibroblasts to dopaminergic neurons

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Parkinson's disease (PD) is a neurodegenerative disease characterised by progressive loss of dopaminergic (DA) neurons in the substantia nigra and accumulation of pathological α-synuclein. Previous work has shown that it is possible to generate DA neurons from fetal tissue and embryonic stem cells and, when transplanted into animal models of PD, these cells can integrate and provide improvement in motor symptoms. However, in order to translate these into clinical therapies there are a number of logistical and ethical concerns with using cells derived from embryonic sources. With new reprogramming technologies, we can now generate DA neurons from somatic cell sources, which also allows for the possibility to use patient specific cells or matched donors. The main purpose of this project is to develop robust protocols for the generation of DA neurons from adult human fibroblasts, from both healthy individuals and PD patients. We will reprogram cells directly into induced neurons (iNs) and also via a pluripotent stem cell (iPSC) intermediate and investigate if there are any differences in gene expression, morphology or phenotype between the DA neurons generated from healthy and PD donors. The results will provide a more robust protocol for the generation of reprogrammed DA neurons from adult donors and will help to pave the way for future research assessing their potential for brain repair and disease modelling.

P06.27

The rat α-synuclein preformed fibril model: Focus on longitudinal PET imaging and behavioral characterization

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The ideal animal model of Parkinson's disease (PD) should exhibit α-synuclein (α-syn) pathology, protracted degeneration of the nigrostriatal system and detectable motor impairments that result in a reproducible time course and magnitude. We have previously optimized and characterized the magnitude of phosphorylated α-syn (pSyn) accumulation and nigrostriatal degeneration following intrastriatal injection of α-syn preformed fibrils (PFFs) into rats. pSyn accumulation in the substantia nigra pars compacta (SNpc) peaks within 2 months, followed by bilateral loss (~50%) of nigral dopamine neurons at 6 months. Further, dopamine transporter (DAT) expression in the striatum exhibited an early bilateral upregulation followed by a downregulation within 4 months. Modest deficits in contralateral forelimb use were appreciable at 6 months. In the present study we sought to examine the longitudinal impact of α-syn PFF injections into rats on DAT activity and dopamine synthesis in the striatum using positron emission tomography (PET). We also examined whether an increased striatal distribution and injection quantity of α-syn PFFs results in neuropathology amplified to a threshold where robust deficits in sensorimotor and cognitive function are observed. Male Fischer 344 rats were injected unilaterally in the striatum with a total of 16µg α-syn PFFs into 2 sites (PFF Double), 24µg into 3 sites (PFF Triple) or an equal volume/site of vehicle as control conditions. PFF Double rats and controls will undergo PET scans for both [18F] fluoro-3,4-dihydroxyphenyl-Lalanine (FDOPA: DA synthesis, storage and turnover) and 11C-methylphenidate (DAT: dopaminergic terminal density) at 2, 4 and 6 months post PFF injection. PFF Triple rats and controls will undergo motor, non-motor and olfactory tests over the 6 months time course. Any motor tests displaying robust deficits will be re-tested using a therapeutic dose of levodopa to determine whether α-syn PFF induced motor deficits are reversible. The magnitude of pSyn accumulation and nigrostriatal degeneration will be evaluated at 2, 4, and 6 months after surgery. Experiments are ongoing with results to be presented at the meeting. The ability to externally validate the progression of α-syn PFF induced nigrostriatal degeneration using PET or levodopa reversibility of α-syn PFF- induced motor deficits would facilitate preclinical assessment of novel disease-modifying therapies.

P06.28

A53T mutant human α-synuclein BAC transgenic mice as a prodromal model for Parkinson's disease

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Objective: Parkinson's disease (PD) is characterized by a variety of motor and non-motor symptoms associated with the loss of dopaminergic neuron in the substantia nigra pars compacta (SNc), and the Lewy pathology that is mainly composed of α-synuclein (α-syn). An appropriate animal model is essential not only to explore the pathogenesis but for the therapeutic intervention in PD. The aim of this study is to create mouse models reproducing the course of PD pathology and symptoms.
Methods: We generated human α-syn bacterial artificial chromosome transgenic mice harboring the entire human α-syn gene and its gene expression regulatory regions with the A53T mutation which is a causative gene mutation for familial PD, a functional repeat polymorphism (REP1) in the α-syn promoter region and single nucleotide polymorphisms (rs3857059 and rs11931074) which increase the risk of sporadic PD. The mice were analyzed behaviorally, histologically and biochemically.
Results: A53T-BAC-Tg mice showed abnormally phosphorylated α-Syn accumulation in the olfactory bulb, the cerebral cortex, the hippocampus, the SNc, the dorsal motor nucleus of vagus nerve and the areas related to rapid eye movement sleep behavior disorder (RBD). The number of dopaminergic neurons in the SNc was significantly decreased in an age-dependent manner, where oligomeric α-syn were detected. In the behavioral analyses, A53T-BAC-Tg mice showed the impaired sense of smell and the RBD-like symptoms, both of which are considered as prodromal symptoms of PD.
Interpretation: A53T-BAC-Tg mice recapitulated the early pathological changes and prodromal symptoms of PD. This novel transgenic mouse model is expected to be a valuable tool to tackle with the PD pathogenesis, especially in the early stage of PD.

P06.29

In vivo generation of SNCA conditional knock-up allele as a new and unique mouse model of Parkinson's disease

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Neuronal loss in the substantia nigra, which causes striatal dopamine deficiency, and intracellular inclusions containing aggregates of α synuclein are the neuropathological hallmarks of Parkinson's disease (PD). PD is currently incurable and it is characterized by progressive rigidity and an inability to initiate voluntary movements. One of the major bottlenecks hindering understanding of PD is the current lack of animal models which reliably phenocopy the PD etiology, greatly hindering progress in developing treatments. In humans, increase in endogenous α synuclein expression via SNCA gene duplication results in PD. So far, many transgenic α synuclein over expressing mouse lines have been generated, but they all display somewhat different phenotypes with unfortunately none fully recapitulating human PD features. However, increase in endogenous α synuclein expression in mice has never been tested. Our laboratory has shown that conditional editing of negative regulatory elements in 3'untranslated region (3'UTR) can be used to upregulate endogenous gene expression strictly in cells that naturally express the gene of interest in vivo. We have called this approach conditional Knock Up (cKU). Because 3'UTR-mediated regulation occurs at the post-transcriptional level, interfering with negative regulation via the 3'UTR does not affect the spatiotemporal regulation of gene transcription and allows the timed onset of endogenous gene overexpression in the desired cell types upon Cre recombinase application. Therefore, our lab is currently generating wild type (wt) and E46K+H50Q+G51D triple mutated knock-in α-synuclein cKU mice. Animals will be tested for motor function, memory and learning, depression, olfaction, social interaction and gut transit time with multiple tests that recapitulate

the main features of PD. Dopamine levels, dopamine cell numbers, Lewy body pathology in the brain and gut will also be studied. Moreover, appropriate CRE lines including the brain-specific Nestin-Cre and the tamoxifen-inducible ERT2-CRE will allow us to analyze the effect of developmental and adult onset of endogenous α-Syn over expression on PD etiology. When successful, SNCA cKU allele will allow us to better understand, study, and find new treatments for PD.

P06.30

Age-dependent intracellular neuromelanin accumulation sets the threshold for Parkinson's disease pathology

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In Parkinson's disease (PD) there is a preferential degeneration of neurons containing neuromelanin pigment, especially substantia nigra dopaminergic neurons. In humans, neuromelanin appears in early childhood and accumulates progressively with age, the latter being the main risk factor for developing PD. The potential contribution of neuromelanin to PD pathogenesis remains unknown because, unlike humans, common laboratory animals such as rodents lack neuromelanin. While the synthesis of neuromelanin is poorly understood, synthesis of peripheral melanins is mediated by tyrosinase, an enzyme that is also present at low levels in the brain, including human substantia nigra. However, whether brain tyrosinase may play a role in neuromelanin synthesis is currently unknown. Here we found that viral vector-mediated overexpression of human tyrosinase in the substantia nigra of rats resulted in an age-dependent production of human-like neuromelanin within nigral dopaminergic neurons, up to levels reached in elderly humans. In these animals, progressive intracellular neuromelanin accumulation above a specific threshold was associated to an age-dependent PD phenotype, including impaired dopamine release, hypokinesia, Lewy body (LB)-like inclusion formation, nigrostriatal neurodegeneration and neuronophagia. Relevant to humans, neuromelanin levels reached this pathogenic threshold in PD patients and pre-symptomatic PD subjects. While α-synuclein was present in LB-like inclusions from neuromelanin-producing rodents, it was actually dispensable for inclusion formation and neurodegeneration in these animals. Instead, the continuous intracellular buildup of neuromelanin within autophagic-related structures ultimately led to a general proteostasis failure, leading to impaired lysosomal proteolysis, reduced ubiquitin-proteasome activity, impaired mitochondrial respiration and increased production of reactive oxygen species, all of which are major cellular alterations occurring in PD patients. Overexpression of transcription factor EB (TFEB), a major regulator of the autophagy-lysosome pathway, reduced intracellular neuromelanin levels by promoting the exocytosis of neuromelanin-filled lysosomes, attenuated PD-type inclusion formation, reduced neurodegeneration and reversed hypokinesia in tyrosinase-overexpressing animals. Our results suggest that intracellular neuromelanin levels may set the threshold for the initiation of PD and that modulation of intracellular neuromelanin levels below this pathogenic threshold may provide unprecedented therapeutic opportunities to prevent, halt or delay neuronal dysfunction and degeneration linked to PD and, in a broader sense, brain aging.

P06.31

A novel target for neuroprotection: The small GTPase Rin inhibits LRRK2 to promote autophagy and reduce α-synuclein pathology

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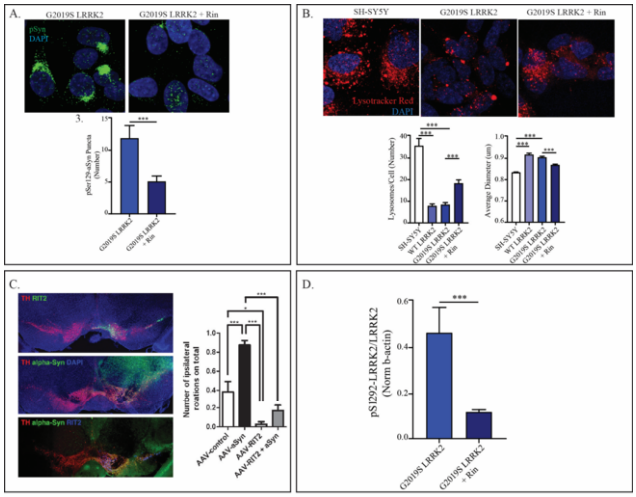
The mechanisms underlying α-synuclein (αSyn) pathology in Parkinson's disease (PD) are still unclear, but hypothesized to involve autophagy and endosome-lysosome pathways. LRRK2 has been reported to play critical roles in these processes.
We observed inclusions of pSer129-αSyn (pSyn) in LRRK2-G2019S neuroblastoma cells, along with accumulations of LC3-positive autophagosomes and abnormalities in lysosome size and abundance. Pharmacological inhibition of LRRK2 kinase activity (PF-06447475) ameliorates autophagy-lysosome pathway (ALP) deficits and reduces pSyn inclusions, indicating these phenotypes depend on LRRK2 hyperactivation. Concomitantly, we observe selective downregulation of the novel PD risk factor RIT2 in LRRK2-G2019S cells. RIT2 codes for the small GTPase Rin (involved in kinase signaling), is enriched in dopamine neurons and reduced in substantia nigra of PD brains. Rin overexpression in LRRK2-G2019S cells rescues the alterations in ALP and diminishes pSyn inclusion burden, displaying a phenocopy of LRRK2 kinase inhibition.
Pharmacological inhibition of LRRK2 has been demonstrated effective against exogenously induced synucleinopathy and viral-mediated αSyn overexpression, which also increases LRRK2 activity. Similarly, we found that Rin overexpression in cultured dopamine neurons transfected with A53T-αSyn reduces pSyn intensity. Importantly, in vivo viral mediated, selective overexpression of Rin in midbrain dopamine neurons prevents motor deficits induced by AAV-αSyn injection in this area. Presently, we are assessing the effects on neurodegeneration and neuropathology in the same mouse model and preliminary results indicate a protection operated by enhanced Rin levels.
We then sought to explore the molecular mechanism underlying Rin therapeutic activity. While Rin gene expression does not appear affected by LRRK2 kinase inhibition, we reasoned LRRK2 kinase activity could be targeted by Rin overexpression. We measured autophosphorylation of LRRK2 in cells as readout of its activity. Consistent with literature evidence, PF-06447475 reduced pS935- and pS1292-LRRK2. Of note, Rin overexpression selectively reduced pS1292-LRRK2 (the actual autophosphorylation site) and did not downregulate pS935- or total LRRK2 levels.
Our data indicate a novel cellular mechanism in PD: Rin inhibits overactive LRRK2 to remove ALP impairment and counteract αSyn aggregation and related deficits. This suggests Rin signaling can constitute a novel experimental strategy to combat neuropathology in familial (i.e. LRRK2) and idiopathic PD, and potentially in related synucleinopathies.



P06.32

The biological compatibility of the circadian system for therapeutic intervention in Parkinson's disease: A study by The Bronowski Institute, Australia

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Over the past decade there has been a growing interest in the role of the circadian system in the aetiology and treatment of Parkinson's disease. This concept emerged from historical accounts, prior to modern pharmacology, whereby the symptoms of this disease can increase or decrease in a rhythmic manner depending on the phase of the circadian cycle. Similarly, it has also been shown that treatments for this disorder may be more effective if they are administered at critical times during the different phases of the circadian cycle. In our examination of the role of the anatomical substrates of the circadian system we have identified the retina and the pineal as two such important locations where chronotherapeutics are most effectively delivered to produce the optimal therapeutic effects while minimising side effects. We will demonstrate how minute injections of anti-Parkinsonian drugs directly adjacent to the retina in models of Parkinson's disease can not only produce therapeutic effects but can also induce side effects that are normally attributed to structures in deep brain while intervention at the level of photoreceptors in the pineal may produce a similar effect. These results highlight the fundamental importance of the circadian system in achieving more effective therapeutic responses by implementing less invasive technology.

P06.33

Does transgenic overexpression of A53T human α-synuclein recapitulate the site-specific iron accumulation of the human Parkinson's disease brain?

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Iron accumulation in the degenerating substantia nigra pars compacta (SNc) is an invariable feature of sporadic Parkinson's disease and forms with known hereditary risk factors, including the alanine-to-threonine mutation at position 53 (A53T) on the α-synuclein gene. Iron is required for a range of processes critical to dopamine metabolism in degenerating neurons, such as the enzyme tyrosine hydroxylase (TH), the rate-limiting step in dopamine synthesis. α-synuclein is involved in vesicular packaging of dopamine and with identified iron responsive elements in mRNA has long been thought to be involved in iron accumulation. Given that Parkinson's disease is likely caused by a combination of genetic and environmental factors, we investigated whether the hallmark iron accumulation specifically observed in the human SNc was also a feature of mice overexpressing the disease-associated A53T mutant variant of α-synuclein. We used imaging mass spectrometry to measure the absolute concentration and spatial distribution of iron in aged A53T and wild-type littermate control mouse brains, focussing on the nigral striatal pathway where iron and dopamine are both highly concentrated and prone to cause oxidative stress when improperly chaperoned. Complementary Perls stain for iron and TH immunolabelling were used as a standardised measure of non-haem iron and corresponding cell loss, respectively. This preliminary baseline data set will initiate further investigation into temporal distribution of metals throughout the lifespan of a both diseased and wild type mice, with the goal to determine whether the emerging concept of 'conservative iron chelation' could be a possible early intervention and disease modifying therapy.

BASIC SCIENCE: Brain physiology, neuroplasticity, and circuitry

P07.01

Quantitative EEG and migraine in patients with Parkinson's disease

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Parkinson's disease (PD) is characterized by the degeneration of dopaminergic systems in the central nervous system. In migraine it is supposed to occur hyperactivation of central dopaminergic pathways. Abnormal electroencephalography (EEG) in migraineurs and Parkinson's disease has been reported in several studies. We aimed to find out which Quantitative EEG (QEEG) parameters could best distinguish patients with Parkinson's disease (PD) with and without migraine.
A total of 81 PD patients with migraine (M+, n=16) and without migraine (M-, n=65) were recruited. Baseline EEGs were analyzed with quantitative spectral analysis. Absolute power, asymmetry and relative power were studied for delta, theta and alpha frequency bands in parieto-occipital, temporal and fronto-central areas.
Compared with M- group, M+ group had increased relative theta power in all cortical regions and increased delta activity in the painful fronto-central region.
These results suggest that QEEG abnormalities are globally increased relative theta activity in migraineurs. A slight interictal brain dysfunction is probably present between attacks.

P07.02

Spatiotemporal patterns of direct and indirect pathway striatal projection neurons in a mouse model of Parkinson's disease and dyskinesia

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L-DOPA is the reference treatment of Parkinson's disease (PD). However, its chronic administration induces abnormal involuntary movements termed L-DOPA-induced dyskinesia (LID). The striatum has a pivotal role in generating PD and LID. PD is related to overactivity of the striatal projection neurons of the "indirect pathway" (iSPN) over the "direct pathway" neurons (dSPN). Conversely, LID is associated to a predominant role of dSPN over iSPN. However, the population dynamics of both SPNs to the generation of these movement disorders is unknown.
Our aim in this study was identify patterns of striatal projection neurons (SPN) activities that code for akinetic and dyskinetic movement disorders in a mouse model of hemiparkinsonism and dyskinesia.
Using in vivo calcium imaging we aimed to identify patterns of striatal SPN activities coding for akinesia and dyskinesia in a mouse model of PD and LID. We used D1-Cre and A2a-Cre transgenic mice to express a calcium indicator GCamp6f in dSPN and iSPN, respectively. Mice were implanted with accelerometer devices to record motor activity while imaging striatal activity in vivo in an open field. We measured motor and neural activity in intact and hemiparkinsonian mice at baseline and after administration of dopamine agonists as D1- and D2-agonits and L-DOPA.
Preliminary data show that calcium activity of both SPNs increases with movement and during movement initiation in intact and hemiparkinsonian mice. We found a significant correlation between body acceleration and calcium signal activity, that was lost after administration of the dopamine agonists. Differences in the number and amplitude of calcium events were observed after D1-agonist between intact and hemiparkinsonian mice in both SPNs.
These preliminary results show that both SPNs are modulated by movement in healthy and parkinsonian conditions, and that administration of dopamine agonists alters the association between striatal neural activity and movement.

P07.03

Early synaptic loss and synaptic instability in a mouse model of prodromal Parkinson's disease

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Recent evidence implicates that the impairment of synapses and neuronal circuitry rewiring as important factors of pathogenesis in neuropsychiatric disorders. The synaptic mechanisms in PD pathogenesis remain to be elucidated, because of the absence of an animal model which replicates neuronal circuitry pathology. We have generated BAC transgenic mice harboring human A53T α-synuclein gene SNCA with PD risk SNPs and its expression regulatory regions. A53T SNCA-BAC mice show progressive neuronal loss of dopaminergic neurons in the substantia nigra and accumulation of phosphorylated α-synuclein in the cerebral cortex. A53T SNCA-BAC mice do not show obvious PD-like motor dysfunctions, however, they exhibit RBD-like behavior at the age of 10 weeks and smell disturbance at 9-month-old. In this study, we focused on presymptomatic synapse pathologies in the primary motor cortex by using A53T SNCA-BAC mice as a model of prodromal PD. By crossing A53T SNCA-BAC mice with Thy1-EGFP mice, layer 5 pyramidal neurons in the cortex of the offspring were labeled. A cranial window was implanted 4 weeks prior to imaging. In vivo two-photon imaging was performed weekly for 4 weeks.
A53T SNCA-BAC mice showed a decreasing density of dendritic spines at the age of 12 weeks, and it reached the plateau at 24-week-old. This was due to the imbalance of enhanced spine formation and elimination at the age of 12 weeks, and the imbalance was equalized in 24-week-old. Although spine formation and elimination rate were balanced when they grow up, both formation and elimination rate of the spine remained to be higher than control mice. A53T SNCA-BAC mice also exhibited lower pre-existed spine stability and newly-formed spine survivability at the age of 24 and 48 weeks. Furthermore, colocalization of presynaptic protein marker and dendritic spine was lower in A53T SNCA-BAC mice. These results suggest that a synaptic loss in the primary motor cortex is occurred even in a prodromal PD model, and this synaptic loss is caused by an excess elimination of dendritic spines. After the abnormal synaptic pruning is finished, the instability of dendritic spines still remains as a neuronal circuitry pathology.

P07.04

Reduced Sonic hedgehog signaling originating from dopamine neurons is necessary and sufficient for levo-dopamine induced dyskinesia formation and expression and causes aberrant learning

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Dopamine (DA) replacement therapy relieves motor signs caused by DA neuron degeneration but has little effect on non-motor symptoms. Worse, long term dosing leads to the appearance of utterly debilitating L-Dopa induced dyskinesia (LID). It is not well understood whether and how LID emergence is linked to the underlying pathology caused by DA neuron degeneration, and a reflection of "pathological" learning caused by a perversion of the "teaching signal" carried by DA neurons. DA neurons act as multi-model signaling centers, communicating with their targets by secreting DA, glutamate, GABA, and several other factors including the morphogen Sonic Hedgehog (Shh), all of which must diminish in Parkinson Disease (PD). We began testing whether the neglect of

augmenting auxiliary modes of DA neuron signaling might play a role in LID.
We found that DA neurons release Shh (ShhDA) during burst firing in the striatum where it activates the Gqi -coupled GPCR Smoothened (Smo) selectively in cholinergic (CIN) and fast spiking interneurons. The pharmacological stimulation of Smo during L-Dopa therapy attenuates LID across murine 6-OHDA – and aphakia -, and macaque MPTP models of PD without curtailing the anti akinetic benefit of L-Dopa. Conversely, genetic and pharmacological experiments reveal that reduced levels of ShhDA relative to dopamine signaling, a situation that must exist in L-Dopa treated PD patients, is sufficient and necessary for the formation of LID-like behavior. Optically-forced, prolonged stimulation of DA neurons reveals that ShhDA stores exhaust more quickly than DA stores, resulting in reduced ShhDA release relative to DA and the display dyskinesia. Reduced ShhDA signaling also causes slowed goal directed reinforcement learning but enhanced habitual responding, a set of non-motor signs often displayed by L-Dopa treated patients. Further, we find that ShhDA signaling blunts DA mediated inhibition of cholinergic neurons selectively in the dorso-lateral striatum where it reduces MAP kinase pathway activity and is critical for the maintenance of cortical glutamatergic synapses. Together, we provide evidence for a novel mechanism by which the degeneration of DA neurons in PD underpins cholinergic neuron mediated LID formation and aberrant learning and suggest that augmenting Shh signaling could ameliorate motor and non-motor complications of dopamine substitution therapies.

P07.05

Simulation based investigation of electrode placement and pulse amplitude for the brain hippocampus

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Introduction: In communicating with neural-systems, there are few in vivo techniques more widely used than microelectrode based stimulation and recording. One of the greatest feats of neural engineering has been the development of implantable medical devices which use multi-electrode arrays (MEAs) to record and stimulate neurons for the therapeutic-treatment of brain-disorders, whether through modulation (i.e. deep-brain-stimulation) or restoration (i.e. proposed hippocampus-memory-prosthesis) [1]. Advancements in medical-implant-technology have a trajectory toward "less and more": tiny electronics and higher-density MEAs [2]-[4]. However, the effectiveness of these engineering advances cannot be maximized.
Goal: The ideal form of a neural-interfacing-device is highly dependent upon the structurey of the region with which it is meant to interface. MEAs provide a system which can be adapted to various neural-geometries. Computational-simulation models of stimulating-systems have proven useful for evaluating electrode-position and stimulation-protocols, but have yet to be adequately adapted to the unique-features of the hippocampus.
Methods: As an approach to understanding potential memory-restorative-devices, an Admittance MethodNEURON model was constructed to predict the direct and synaptic-response of a region of the rat dentate-gyrus to electrical-stimulation of the perforant-path.
Results: A validation of estimated local field potentials against experimental recordings is performed and results of a bi-linear electrode-position and stimulation amplitude-parameter search are presented.
Conclusion: The parametric-analysis presented herein suggests that stimulating-electrodes placed between the lateral and medial-perforant-path, near the crest of the dentate-gyrus, yield a larger-relative population-response to given-stimuli. Significance: Beyond deepening understanding of the hippocampus-tissue-system, establishment of this model-provides a method-to-evaluate candidate-stimulating-devices and protocols.
This study shows that the model-performs the minimum-functions necessary to improve electrical-stimulation-systems. However, future-iterations of the simulation-model and methodology will be improved in many areas. While the list of limitations and proposed improvements is not exhaustive, incorporating these features will provide a robust-framework which can aid the design-of-devices(DoDs) capable-of-improved interfacing with this region-of-the-brain. As the detailed neuronal-componentry of the model is further expanded to include more cell-types and layers-of-tissue it will provide a deeper-understanding of both the network-properties of the hippocampus-circuit and better-strategies of inducing and recording-activity via arrays-of-electrodes.
References:
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P07.06

Genetic barcoding to track cell fate specification from dopamine-patterned human ES cells

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Stem cell-based cell therapy provides an avenue for the treatment of neurodegenerative diseases and in particular for the Parkinson's disease (PD). Ventral midbrain (VM) patterned progenitors from pluripotent stem cells, such as human ES cells (ESCs), has been shown to be able to mature, innervate and functionally integrate into the brain of PD animal models, restoring synaptic connection and dopamine release. At the timepoint when the cells are transplanted they all express markers typical of dopamine neuron progenitors, yet the graft contains a number of different cell types when assessed 6 months after transplantation.
In this study, we aim to explore the lineage relationships between the progenitors and their mature progeny after transplantation in vivo in the PD rat model and after maturation in 3D organoid cultures in vitro. To perform a precise fate mapping, single cell viral vector barcoding was used for deconstructing the lineage diversification that emerges during neural cell development. In this method, each progenitor is tagged with a unique DNA barcode or barcode combination, allowing it to find their progeny after differentiation in vivo or in vitro. This study will provide us with the knowledge for understanding the sources of different cell populations present in DAergic grafts. The underlying molecular mechanisms revealed in thus progenitors fate specification will also guide the future development of cell therapy with precisely controlled cell differentiation and graft composition.

BASIC SCIENCE: Dopamine, receptors, and other neurotransmitters

P08.01

Retromer-mediated trafficking of the dopamine transporter in PD

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Parkinson's disease (PD) is a neurological disease characterized by the progressive loss of midbrain dopaminergic neurons and the accumulation of proteinaceous inclusions rich in α-synuclein. The axonal projections of those midbrain dopaminergic neurons provide extensive innervation to the striatum, with each neuron giving rise to ~400,000 pre-synaptic terminals. The biological function of these neurons orchestrates the demands for dopamine synthesis, release and reuptake, and trafficking of monoamine transporters, whilst handling dopamine's propensity to oxidation. During neurotransmission, presynaptic reuptake of dopamine is mediated by the dopamine transporter (DAT) and tightly controls the balance of extra- to intracellular dopamine levels. However, the specific mechanisms underlying DAT trafficking remain elusive.
Vacuolar protein sorting 35 (VPS35) is a core component of the retromer trimer required for endosomal protein trafficking. VPS35 engages VPS26 and VPS29 to form a cargo-selective-complex that recycles internalized cargo molecules. In 2011, the discovery of a missense mutation, Vps35 p.D620N, implicated retromer dysfunction in the pathogenesis of PD. Here we explore how retromer may regulate DAT trafficking.
Using co-immunoprecipitation of Vps35 from mouse midbrain, we reveal a novel association of DAT with the retromer complex. Validation of this interaction was achieved using an exogenous YFP-HA-DAT reporter construct. In contrast, Vps35 failed to co-immunoprecipitate serotonergic (SERT) and noradrenergic (NET) transporters, suggestive of a specificity for DAT by the retromer complex. Fluorescence immunohistochemistry and confocal microscopy analysis supported this association as DAT was observed to decorate Vps35 positive endosomes in the dorsolateral striatum of male mice. Further, utilizing a novel Vps35 p.D620N (VKI) mouse model, we show that at 3 months of age, VKI mice have a significant reduction in the total level of DAT by immunohistochemical analysis and ex-vivo biotinylation of living striatal slices. These differences occurred independent of changes in the cell-surface levels of the SERT, Tyrosine hydroxylase positive nigral neuron counts or terminal expression in striata (previously published). Consolidating our new findings with previously published data, we show considerable evidence that the retromer complex plays a fundamental and selective role in dopaminergic physiology and that expression of Vps35 p.D620N profoundly alters the trafficking itinerary of DAT likely through this novel interaction.

BASIC SCIENCE: Neuropharmacology

P09.01

Long-term suppression of levodopa-induced dyskinesia by sub-anesthetic ketamine is mediated by BDNF and changes in striatal dendritic spine morphology

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Amantadine, a weak N-methyl-D-aspartate receptor (NMDAR) antagonist, is the only FDA approved drug indicated for levodopa-induced dyskinesia (LID). However, amantadine is not universally effective and has side-effects warranting further investigation into alternative NMDAR antagonists. Ketamine, a well-established NMDAR antagonist with greater binding affinity than amantadine, has been utilized as a clinical anesthetic since 1970. Recently, it has been repurposed due to clinical trials demonstrating sub-anesthetic ketamine is well tolerated and effectively treats depression and chronic pain, two non-motor symptoms that impact Parkinson's disease (PD) patient's quality of life.
Our lab has demonstrated a long-term therapeutic effect of ketamine in 5 PD patient case studies with LID (Sherman et al., Case Reports in Neurology, 2016). In a preclinical model (Bartlett et al., Neuroscience Letters, 2016), we reported that established LID, measured by abnormal involuntary movements (AIMs), is reduced by a sub-anesthetic 10-hour ketamine infusion (20 mg/kg; 5x i.p. injection, 2-hours apart). Using this infusion paradigm, we showed at WPC 2016 that ketamine also suppresses the development of LID, including on days without ketamine (Bartlett, et al., Journal of Parkinson's disease, 2016). This data indicates ketamine has a long-term neuroplastic effect in LID, but its mechanisms remain unclear.
Here, unilateral 6-hydroxydopmaine-lesioned PD rats (n=10/group, 3 groups) were pretreated on Days 0 and 7 with either a 10-hour ketamine infusion, ketamine plus ANA-12, a brain-derived neurotrophic factor (BDNF) receptor tropomyosin receptor kinase B (TrkB) antagonist, or vehicle. Rats were primed with levodopa (6 mg/kg, i.p.) daily (Days 0–14) with AIMs scored every 3–4 days. On Day 14, ketamine treated rats had a 50% reduction in AIMs compared to vehicle. These sustained effects were reversed in rats co-treated with ANA-12. Rats were then euthanized and striatal sections were Golgi stained for dendritic spine analysis. The levodopa-induced 2-fold increase in multi-synaptic mushroom spines in the lesioned LID hemisphere was completely reversed by ketamine, and ANA-12 blocked this effect.

Combined, our data indicates BDNF release and subsequent changes in striatal dendritic spine morphology play a major role in ketamine's long-term anti-dyskinetic effects. Additionally, this data suggests ketamine as a novel, long-lasting therapy to suppress LID development.

P09.02

7,8-Dihydroxyflavone (TrkB agonist) prevented the neuroinflammation and neurodegeneration via acting on sulfiredoxin-peroxiredoxin axis in Parkinson's disease evaluated in-vitro and in-vivo

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Parkinson disease is (PD) a debilitating motor disorder affected million of the population worldwide. The underlying cause for the loss of substantial nigra pars compacta (SNc) neurons with several different theories have been implicated for the years but still, the actual fact is undetermined and vague. However, oxidative stress is being considered to be the most important contributing factor in neurodegeneration. With huge oxygen demand brain always remain prone to oxidative stress. To combat this oxidative stress the body has sets of endogenous antioxidants counteracting and managed the raised oxidative stress conditions. As the intolerable limit of radical species cause redox imbalance and resulting in pathogenesis leading neuroinflammation and neurodegeneration. Previous reports found with the involvement of sulfiredoxin-peroxiredoxin (Srx-Prx) axis role in carcinogenesis, cell proliferation, migration, and metastasis. This potential axis gets overexpressed in cancer but less express in the dopamine region of SNc and striatum. Earlier reports also suggested the peroxiredoxin (thiol-based peroxidase) isoforms if overexpress or knockout in animal or cells lead to altering the pathogenesis in PD. This peroxiredoxin with 6 isoforms serves an important function with peroxidatic activity and chaperone alike activity in hyperoxidized form (sulfonic acid; PrxSO3). The ATP and sulfiredoxin-1 (Srx-1) mediate as a key player for the restoration of reduced Prx with its peroxidatic activity in neutralizing the peroxides. For understanding the mechanistic approach we studied the effect of neurotoxins such as 6-hydroxydopamine (6-OHDA), MPP+ induced reactive oxygen species leading inflammation role in neuroblastoma and microglia cells. Moreover, we also investigated the effect of 7,8-dihydroxyflavone (7,8-DHF) on sulfiredoxin and peroxiredoxin axis. We utilized the potential Nrf2 activator (D3T; 3H-1,2-Dithiole-3-thione) we found the increased expression of sulfiredoxin-1 and with combination of 7,8-DHF provided the add-on effect that confirms 7,8-DHF role in increasing genes and protein expressions of Srx-1 and Prx (2,3,4,5,6) in cells and animal mouse model of MPTP. The tunnel assay also confirms the prevented death by 7,8-DHF in the striatum and nigral region of mice. Thus, TrkB agonist may be future drug candidate or adjunct in treating Parkinson's disease with multiple potentials of neurogenesis and augmenting the antioxidant status.

P09.03

Leucine-Rich Repeat Kinase 2 regulates Parkinson's disease levodopa-induced dyskinesia

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The gold standard for treatment of Parkinson's disease (PD) motor symptoms is the restoration of dopamine transmission with administration of the dopamine precursor levodopa. However, ~80% of patients develop abnormal involuntary movements, or levodopa-induced dyskinesias (LID), which constitute a major cause of disability and limit therapeutic efficacy. Evidence from in vitro and in vivo studies suggests that, when nigral dopaminergic neurons degenerate, levodopa treatment can cause LID by altering dopamine metabolism and inducing maladaptive neuroplasticity within the dorsal striatum.
LRRK2 protein has been associated with several key regulators of striatal medium spiny neuron (MSN) function that are involved in LID. LRRK2 mutations were shown to increase membrane presentation of dopamine receptor D1 (Drd1) and downstream signaling cascades. Overexpression of wild type LRRK2 negatively regulated PKA activity in MSNs in response to Drd1 activation, while LRRK2 knockout significantly increased PKA levels in striatal dendritic spines.
We hypothesize that disruption of LRRK2 levels via either inhibition of endogenous LRRK2 with short-hairpin RNA (shRNA) interference or PD-associated G2019S mutation will promote LID in the unilateral 6-hydroxydopamine (6OHDA) mouse model of PD. First, we generated AAV vectors to inhibit mouse LRRK2 (AAV-sh.LRRK2), and control vector (AAV.sh.Luciferase), and injected it into the dorsal striatum ipsilateral to the 6OHDA lesion in C57Bl/6 mice. We induced LID by administering a daily levodopa treatment for 3 weeks at increasing levodopa doses (3,6,12 mg/kg s.c.). We scored locomotor, axial, limb and orolingual LID, and surprisingly found that inhibition of striatal LRRK2 expression significantly increased LID scores by 40% compared to AAV.sh.Luciferase injected control mice. To test the influence of G2019S LRRK2 on LID, we 6OHDA lesioned G2019S LRRK2 knock-in mice and wild type mice as controls. Upon induction of LID as described above, we observed that G2019S LRRK2 significantly increases rotational behavior and locomotor LID, while decreasing limb-orolingual LID in dyskinetic mice. Interestingly, our data suggest that striatal LRRK2 may be a key regulator of the LID response to dopaminergic pharmacotherapy and also raises questions about the potential unintended effects of experimental therapies targeting LRKK2 inhibition on striatal function.

P09.04

Managing psychosis risk with pharmacotherapy: Help for patients, caregivers through nursing science & practice

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Psychosis in Parkinson's disease (PD) may occur as a pathology prior to diagnosis, as a mental health state, or may occur as a result of essential medicines in PD management. Although etiologies differ, the management of psychosis is neccessary for optimal health and functioning regardless of causation. Patients, their families and communities suffer when psychosis occurs and is endured, therefore it is critical that education occur for the broad benefit of public health. Professional nurse education rarely includes management of psychosis in PD, as either prescribers and/or patient/family/community educators. PD has a global presence and is a common major issue and/or comorbidity in any health care setting. Since professional nurses are key to public education in management of health issues, a project has been created as an interactive module, designed to prepare undergraduate and graduate professional nurses is presented. The outcomes of nurse education include goals of understanding the dynamics of psychosis in PD. The module includes anatomy, physiology of PD, "on and off" issues, traditional medicines, as well as pharmacologic advances are discussed to manage psychosis. To better prepare nurses upon

graduation to serve this population, this project will also include prescribing commonly used pharmacologic agents to prevent and reduce psychosis, regardless of cause, in a timely manner for both professional level and advance practice registered nurses. The outcomes projected include a better prepared nursing workforce, and most importantly, a PD community that is better served.

P09.05

A novel nanocarrier delivery system for curcumin and deferoxamine as a potential neuroprotective strategy for Parkinson's disease

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Introduction: In Parkinson's disease (PD) there is reduced glutathione levels alongside excessive free iron within dopaminergic, substantia nigra neurons. This can drive accumulation of toxic hydroxyl radicals resulting in sustained oxidative stress and catastrophic cellular damage. The antioxidant curcumin (CU) and iron chelators such as deferoxamine (DFO) can act as potential neuroprotective agents for PD as CU displays free radical scavenging properties and DFO may limit the availability of detrimental free iron. However, CU is unstable with low bioavailability and both compounds are unlikely to access the brain at therapeutic concentrations. Nano-carriers have demonstrated potential as targeted delivery systems to improve stability of labile molecules and increase delivery across membranes including the blood-brain barrier.
Objectives: This study aimed to develop miceller nanocarrier delivery systems for CU and/or DFO to counteract rotenone-induced changes in cell viability and oxidative stress in SH-SY5Y cells.
Methods: Nanocarriers of CU and/or DFO were prepared using the amphiphilic polymer, Pluronic F68 (P68) by modified thin film hydration alongside corresponding unloaded formulations. Particle size and drug loading were assessed using Zetasizer Nano and UV spectrophotometry, respectively. Nanoformulation toxicity and ability to counteract rotenone-induced reductions in cell viability were evaluated using MTT assays. TBARS assays assessed nanoformulation capacity to counteract rotenone-induced lipid peroxidation.
Results: All formulations demonstrated high drug loading (>60%) and nanocarrier size was <200nm. Cytotoxicity was not observed for any nanoformulation ≥80% (n=6). 100uM rotenone reduced cell viability by 38.5% ($p<0.0001$). 3h pretreatment with various concentrations of CU, DFO and combined nanoformulations significantly protected against rotenone-reduced cell viability (5uM CU ($p<0.0001$), 10uM CU ($p=0.001$), 100uM DFO ($p<0.0001$), 5uM CU + 50uM DFO ($p=0.003$), 10uM CU + 100uM DFO ($p=0.021$)). All nanoformulations significantly protected against rotenone-induced lipid peroxidation ($p<0.0001$) and were superior to free CU and/or DFO.
Conclusion: This study demonstrates for the first time the use of P68-based nanocarriers as a delivery system to formulate and deliver curcumin and/or DFO to counteract a cellular PD model. This strategy may thus provide a novel approach to fully utilise their therapeutic benefit for PD.

P09.06

Can Coenzyme Q10 and creatine slow the progress of Parkinson's disease?

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Objectives: This meta-analysis of randomized controlled trials (RCTs) analysis aims at providing class one evidence about the efficacy of Coenzyme (CoQ10) and creatine for neuroprotection against Parkinson's disease (PD). CoQ10 and creatine are two antioxidants that showed neuroprotective effects in animal models of PD. Both drugs were selected by the National Institute of Neurological Disorders and Stroke as possible disease-modifying agents for PD and subjected to evaluation in phase III clinical trials. However, clinical trials on both drugs showed controversial results regarding their efficacy.
Methods: We followed the guidelines of PRISMA statement and Cochrane handbook guidelines during the preparation of this meta-analysis. A computer literature search was performed through October 2018 to identify relevant RCTs. Outcomes of total Unified Parkinson's disease Rating Scale (UPDRS), UPDRS I, UPDRS II, and UPDRS III were pooled as standardized mean difference (SMD) or mean difference (MD) between two groups from baseline to the endpoint. Statistical heterogeneity was assessed by visual inspection of the forest plot and measured by chi-square and I square tests.
Results: Eight RCTS (CoQ10: five RCTs, n=981; and Creatine: three RCTs, n=1935) were included in this study. Neither CoQ10 nor creatine was superior to placebo in terms of: UPDRS total score (CoQ10: SMD -0.05, 95% CI [-0.10 to 0.15]; creatine: MD 1.07, 95% CI [3.38 to 1.25]), UPDRS III (CoQ10: SMD -0.05, 95% CI [-0.07, 0.17]; creatine: MD 0.62, 95% CI [2.27 to 1.02]), UPDRS II (CoQ10: SMD -0.10, 95% CI [-0.35, 0.15]; creatine: MD 0.03, 95% CI [0.81 to 0.86]), and UPDRS I (CoQ10: SMD -0.05, 95% CI [-0.10, 0.15]; Creatine: MD 0.03, 95% CI [0.33 to 0.28]).
Conclusion: This meta-analysis provides class one evidence that neither Coenzyme Q10 nor Creatine can slow the progress of PD or provide any symptomatic benefit for PD patients.

P09.07

The neuroprotective effect of epicatechin on hemiparkinsonism induced by MPP + in a rat murine model

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Introduction: Parkinson's disease (PD) is characterized by the death of neurons in the substantia nigra pars compacta (SNpc), leading to a significant reduction of the dopamine content in the caudate nucleus and putamen, causing clinical symptoms such as tremor and loss of postural reflexes. It has been documented that epicatechin (Epi) is the most abundant flavonoid found in plants (including Camellia sinensis and Theobroma cacao) and substantially improves oxidative stress in the various systems (liver, kidney and skeletal muscle) in a mouse model. In this work we investigated the neuroprotective effect of epicatechin on the striatum of the brain of rats while simulating a Parkinson's syndrome.
Objective: To examine the neuroprotective efficacy before and after treatment of epicatechin in the murine model of Hemi-Parkinson's induced by MPP+
Material and Methods: Male Wistar rats of 250–300 g from the UNAM's Faculty of Medicine were used. They were divided into two

groups A) pre-treatment and B) post-treatment. In group A), DMSO in 10% saline solution was administered, via intra-esophageal (IE) to the control rats, as well as treatments with 10% DMSO plus epicatechin (150 mg/kg of animal weight). After 5 hours, stereotaxic surgery was performed using MPP+ (7.5 µg/8 µl). In group B) stereotaxic surgery using MPP+ was performed. After surgery, 10% DMSO and saline (control group) and DMSO were administered at 10% plus epicatechin (indicated dose) IE. After 6 days, turn behavior, Western Blot and Immunofluorescence tests were performed.

Results: The turning behavior in the pre-treatment animals improved the with the epicatechin (***p<0.001) compared with the control group microinjected with MPP+. Likewise, the effect within the post-treatment animals was 13% fewer turns than the pre-treatment animals (16%). In the immunofluorescence and the Western Blot the decrease in TH activity was present in the control group, both in the striatum, and the substance nigra. It also reversed the dopaminergic decline and maintained the activity levels in the animals within the pre- and post-treatment group. Epicatechin is a possible neuroprotective target molecule against the acute symptoms, or the early stages of Parkinson's disease.

BASIC SCIENCE: Electrophysiology & functional imaging, optogenetics

P10.01

Hitting the brakes: Freezing of gait in Parkinson's disease derives from pathological activity in the subthalamic nucleus

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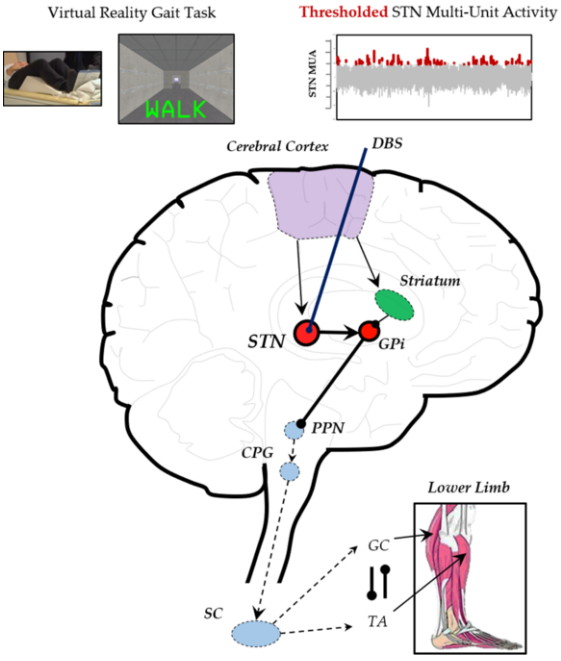
Freezing of gait is a poorly understood, highly debilitating symptom of Parkinson's disease (PD) that manifests as s sudden motor arrest often leading to falls. Traditional models of PD implicating dopaminergic denervation inadequately explain the pathophysiological mechanism of freezing, which occurs paroxysmally and in a variety of cognitive contexts. As such, current therapies are partially effective at best.

We collected intraoperative microelectrode recordings of subthalamic nucleus (STN) multiunit activity (MUA) from 8 patients with PD performing a validated virtual reality (VR) gait task during awake neurosurgical implantation of deep brain stimulation (DBS) electrodes. The intraoperative VR task consisted of a virtual corridor which subjects navigated using a set of footpedals (Figure 1).

We examined STN MUA firing rate during lower limb freezing events elicited by the VR task and compared these to periods of normal walking and volitional stopping. In addition, we analysed beta and theta frequency modulation of the STN signal and used Granger Causality Analysis to investigate whether pathological rhythms in the STN during freezing could be causative of concurrent pathological lower limb muscle firing recorded by electromyography.

We present evidence to support our original prediction that freezing episodes are associated with transient increases in STN MUA firing rate (Freeze=12.6±6.8; Walk=6.5±3.5; p=2.0x10-5). We further refine the pathophysiological mechanism underlying freezing by characterising the oscillatory dynamics of STN activity coincident with freezing. We found an increase in beta activity that peaked with freezing onset, and increased theta oscillations during freezing episodes and demonstrate a temporal chain of pathological activity from the STN to abnormal lower limb muscle firing characteristic of freezing. Finally, we interrogated the potential clinical utility of STN spiking activity by contrasting the pathological freezing signature with purposeful stopping.

Together, these results advance our understanding of the neurobiological basis of gait freezing in PD, highlighting the role of emergent STN activity. This work offers a step towards the identification of clinically useful biomarkers for novel therapeutic interventions such as closed loop adaptive DBS protocols.



P10.02

The role of LRRK2 at cortico-and thalamo-striatal synapses in the G2019S knock-in mouse model

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The striatum is the gateway to the basal ganglia: GABAergic spiny projection neurons (SPNs) receive converging glutamatergic inputs from the cortex and the thalamus, as well as dopaminergic modulation from the substantia nigra, and form the sole output pathways. Altered striatal circuitry and plasticity is implicated in numerous psychiatric and neurodegenerative disorders, including Parkinson's disease (PD). While mutations in the PD-linked LRRK2 gene perturb several cellular functions, the effects on striatal plasticity are unknown. We previously reported that the LRRK2-G2019S mutation increases glutamatergic transmission in cultured cortical neurons and striatal slices from young G2019S knock-in (GKI) male mice, suggesting a role in early pathophysiology. However, glutamatergic inputs from the cortex and thalamus differ

considerably in their striatal synaptic targets, NMDA/AMPA ratios, plasticity and vulnerability in PD, with a substantial loss of thalamic inputs in PD patients and animal models. Thus, we sought to examine whether the LRRK2-G2019S mutation has pathway-specific effects, using selective optogenetic activation of cortical or thalamic inputs while recording from SPNs in striatal slices from 2-month-old male GKI and wild-type (WT) littermates. We report that both pathways show greater initial glutamatergic release followed by rapid depletion, as evidenced by a decrease in light-evoked paired-pulse ratios and stability of responses over time. We further examined whether there were any input-specific differences in mGluR-dependant LTD, and whether these effects could be rescued by acute inhibition of LRRK2 kinase activity. While these are ongoing experiments, preliminary results suggest that the LRRK2 kinase inhibitor MLi2 may restore GKI paired-pulse ratios to levels observed in WT cells. This work extends the LRRK2 literature by demonstrating early pathophysiological changes in both cortical and thalamic evoked glutamatergic release, and examines the potential for therapeutic intervention by modulating LRRK2 kinase activity.

P10.03

Cortical response to open and closed-loop tactile cueing during walking and turning in Parkinson's

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Gait and turning impairments are common in Parkinson's disease (PD). Tactile cues delivered in open (OL) or closed-loop (CL) modalities may improve gait and turning in PD, but the underlying mechanisms are unclear. Evidence suggests that attention stemming from the pre-frontal cortex (PFC) may play a vital role in cue response. Examining how OL and CL cueing influences PFC activity in PD may allow greater understanding of mechanisms involved, which could help develop effective therapeutics. This pilot study examined PFC activity during walking and turning in response to OL and CL cueing in PD, and explored association between PFC activity and behavioral measures/cognitive function.
A mobile functional near-infrared spectroscopy device measured PFC activity during walking and turning in 25 people with PD (n=13 freezers, n=12 non-freezers. OFF medication). Participants performed 180° and 360° turns while walking, and a two minute walk under single and dual-task (AX-CPT) condition with and without OL (metronome-like vibration) or CL (bio-feedback vibration) tactile cues. The primary outcome was oxygenated hemoglobin (HbO2) at the PFC, which is a proxy for cortical activity.
PFC activity increased during a turn compared to prior-to a turn ($p<.001$), and was higher in the early phase (first 40sec) compared to late phase (last 40sec) of walking ($p<.001$) in PD. Interestingly, PFC activity did not change with the application of tactile cueing when walking (OL $p=.805$, CL $p=.258$) or turning (OL $p=.392$, CL $p=.934$) in PD, and it did not depend upon freezing status or task demands. Despite this, walking and turning significantly improved with both OL and CL cueing, specifically dual-task cost for step length improved (OL $p<.001$, CL $p=.003$) and turning slowed.
PFC activity did not relate to walking or turning performance. Importantly, a higher PFC activity when walking (single-task early phase; rho=.56, $p=.005$) and turning (prior-to 180° turn; rho=-.52, $p=.008$) was associated to better executive function (CLOX1 and TMT-A).
Our preliminary results suggest that both open and closed-loop cueing can improve behavioral measures of mobility in PD, without posing additional burden to the PFC. Future research is required to examine more brain regions and different cueing modality to provide greater understanding of cue response.

BASIC SCIENCE: Neurophysiology, functional imaging, human studies

P11.01

Dopamine transporter image of Gerstmann-Sträussler-Scheinker disease

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Objective: Gerstmann-Sträussler-Scheinker disease (GSS) is a rare genetic form of transmissible spongiform encephalopathy. A variety of symptoms including parkinsonism developed along with progressive ataxia in GSS. However, studies on dopamine transporter (DAT) image have never been reported in the literature before. We report DAT image of a woman with GSS showing parkinsonism.
Case: A 45-year-old woman was admitted for slowly progressive ataxic gait and dysarthria for 5 years. Cognitive decline developed one year prior to admission and gradually aggravated. In family history, her mother had similar clinical features and expired at her fifth decade. Gene study for spinocerebellar ataxia was negative. On examination, she had severe dysarthria to the point that most of words were not understandable. However, she could comprehend and obey simple command. She could not stand alone without assistance. She also had hearing difficulty. Finger-to-nose test showed severe ataxia in her both hands. Areflexia was noticed in lower limbs. Evaluation for parkinsonism was difficult because of cognitive decline and severe ataxia. However, mild rigidity was found in her both limbs.
MRI showed severe cerebellar atrophy but not cortical high signal intensity in DWI. PRNP analysis revealed a mutation in codon 102 proline to leucine (P102L). 129 codon showed methionine homozygote. DAT image showed mildly decreased uptake in tails of both striatum.
Conclusion: The DAT image showed mildly decreased uptake in tails of both striatum corresponding to the clinical features of mild parkinsonism. However, the typical pattern of dorsoposterior gradient which was commonly found in idiopathic parkinsonism was not observed. A larger studies will be needed to know the DAT uptake pattern in GSS.

P11.02

Transcranial direct current stimulation for limb-kinetic apraxia in Parkinson's disease – a randomized, double-blinded, sham-controlled trial

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Objective: To examine the effects of transcranial direct current stimulation on limb-kinetic apraxia(LKA) in Parkinson's disease(PD).
Background: Limb-kinetic apraxia is a commonly overlooked phenomenon in PD, characterized as difficulty performing precise and coordinated finger movements. To date, there are no established treatments for this phenomenon, and levodopa medication has been reported to have no effect.
Design/Methods: 28 PD patients completed the study. Patients were randomized to two groups; anodal or sham stimulation. For

patients assigned to active stimulation, anodal stimulation of the left posterior parietal cortex was performed using 2 mA current for 20 minutes. Patients receiving sham stimulation also underwent the session for 20 minutes. The investigators and patients were both blinded to group allocation. Both groups were instructed to perform repetitive manual tasks including buttoning and unbuttoning, handwriting and coin flipping following the stimulation session. The primary outcome measure was time performing sequential buttoning and unbuttoning, and several secondary outcome measures were obtained (e.g., Unified Parkinson's disease Rating Scale: UPDRS scores, resting motor threshold: RMT, time writing one's name 10 times, time flipping a coin using each hand, etc.).
Results: Mean age in the active and sham group were 73 and 72 years, respectively. Mean MMSE scores were 25 and 26, respectively. Mixed ANOVA was performed and a significant interaction was found between stimulation type and conditions (medication OFF, ON, tDCS immediate and post-tDCS 24 hours). Patients who received active (anodal) stimulation were found to have a significant decrease in sequential buttoning and unbuttoning times immediately following tDCS and at 24 hours, compared to the medication-OFF state (31% and 29% decrease, respectively). No statistically significant findings were found in the sham group.
Conclusions: Anodal tDCS of the left posterior parietal cortex, relevant in praxis, appears to be effective in ameliorating LKA in PD. Therefore, future long-term projects performing serial stimulation sessions seem worthwhile.

P11.03

Olfactory bulb atrophy in the earliest clinical stage of Parkinson's disease

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Objective: To investigate whether there is olfactory bulb (OB) atrophy in the earliest clinical stage of Parkinson's disease (PD).
Introduction: PD is characterized by motor and non-motor symptoms. Hyposmia has been reported to occur in the majority of early-stage PD patients, with deficits in odor detection, identification, and discrimination. Postmortem studies show that the OB is highly affected by Lewy bodies, the hallmark pathology of PD. However, whether there are OB morphological changes in early-stage PD is not clear. We hypothesized that there will be detectable OB atrophy in H&Y stage-1 PD patients.
Methods: Seventeen idiopathic stage-1 PD participants and 14 age/sex-matched HCs participated in this study. Smellthresholds and smell identification functions were obtained using OLFACT-C Olfactory Threshold Test, University of Pennsylvania Smell Identification Test (UPSIT), and OLFACT-C Olfactory Identification Test. Each nostril was assessed separately. The MRI study was conducted on a 3T scanner with a 64-channel head/neck coil. OB volumes of left and right sides were measured via manual segmentation by two raters blinded to patient status and olfactory scores. Analysis of OB volume was performed with both absolute and intracranial volume (ICV) normalized volume. Cross-cohort comparisons were conducted using ANOVA with multiple comparisons and age/sex as covariates in SPSS. The two sides were compared with paired t-tests.
Results: Scores of smell threshold and identification tests were significantly lower in stage-1 PD patients compared to those of HCs ($p<0.001$). Comparison of OB volumes revealed significant differences between the two groups when using absolute OB volume values (left: $p=0.036$, right: $p=0.014$, total: $p=0.014$) and ICV normalized volumes (left: $p=0.038$, right $p=0.019$, total: $p=0.014$). There were no significant differences between left and right sides in smell functions or OB volumes in either group.
Conclusion: Results from the psychophysical tests of smell functions demonstrate significant smell deficits in H&Y stage-1 PD patients. In alignment with reduced smell functions, OB volume was found to be reduced in the PD group. Our findings support our hypothesis that there is OB atrophy in the earliest clinical stage of PD. To further validate this finding, longitudinal studies are necessary.

P11.04

Vital paradigm shift for people living with Parkinson's

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"One cannot solve the problem at the same level that creates it." ~Albert Einstein
Parkinson's disease can cause much suffering for those living with it. It impairs people's physical abilities and their mental processes. People with Parkinson's cannot live life as they did before they were diagnosed. Their long-term future becomes dominated by the disease.
Too often, the medical treatments proposed for Parkinson's have only superficial results. They don't reach the deeper causes of the disease, and patients can suffer severe side effects.
In January 2018, members of the Sibu Parkinson Society underwent a two-day training session about the Chinese healing system Yellow Emperor's Inner Classic (YEIC), which dates back about 3,000 years.
According to YEIC, there are tell-tale signs well before major diseases develop. They can be summarised as a yin-yang imbalance.
YEIC sees a human being as an integrated whole, made up of several subsystems with linked functionalities.
Healing is focused on restoring these subsystems and functionalities. YEIC concentrates on the well-being of the person overall, not the disease that is manifested.
When the body's subsystems and functionalities are restored, a person's physical, mental, and emotional health all improve.
The paradigm shift involves changes in belief systems and practices.
1. The YEIC approach to diet is very different from western theories about nutrition. According to YEIC, the foods that we consume daily act as medicines for the bodily system's functionalities.
2. The concepts behind the qi (energy) therapies used in YEIC healing are very different from those on which western physiotherapy is based, although some of the practices are similar. The focus is on the movement of qi to improve the body's subsystems and their functionalities.
3. YEIC healing brings about a shift in people's emotions, their value and belief systems, and even their personality.
When YEIC practices become part of a person's daily life, his or her whole consciousness changes. People become more inspired and every cell of their body is energised. Healing becomes holistic.
People with Parkinson's who create this paradigm shift feel a difference within six months.
With YEIC, you become the master of your health issues, not their victim.

P11.05

Premovement betaband event-related desynchronization related to simple lower limb movement and simulated gait initiation in Parkinson's disease patients: MEG study

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Objective: To compare premovement event related desynchronization (ERD) between simple lower limb movement and simulated gait initiation in Parkinson's disease (PD) patients using Magnetoencephalography (MEG).
Background: It has been known that the beta-band (13–30Hz) desynchronization in motor-related cerebral cortex during motor preparation is modulated by the motor task. In this study, we compared premovement ERD between lower limb movement and simulated gait initiation in PD patients.
Methods: We enrolled PD patients without gait freezing, and the subjects were to take MEG on two tasks with right feet. In the first task, the task was simple ankle dorsiflexion (S(-)) similar to gait initiation, and in the second, simulated gait initiation was done with simple dorsiflexion (S(+)). Each task was examined in visual cued movement sequences independently. We performed the two tasks in medication-off state(M(-)) and medication-on state(M(+)), respectively. Gyroscope chips were attached to right toe to precisely detect movement onsets and artifacts. Visual cue was presented on the screen irregularly.
Time-frequency power plot were calculated for each tasks during the premovement period (the 2.0 seconds preceding S(-) or S(+) execution), and the corresponding beta-band ERD (beta-ERD) or beta-band synchronization (beta-ERS) power was represented. We chose the sensors near the contralateral supplementary motor, premotor and primary motor cortex.
Results: We analyzed data from 11 PD patients. During 0.6–0.0 sec prior to the movement onset, the maximum premovement beta-ERD values were statistically different in M(+) (-65.22±30.85% in S(-) vs. -82.36±50.71% in S(+), P=0.04, respectively), but not in M(-) (-53.45±18.53% in S(-) vs. -60.17±29.58% in S(+), P=0.35, respectively). Mean power of beta-ERD showed significant differences between S(-) and S(+) different in M(+) (-32.71±2.85% in S(-) vs. -47.02±27.68% in S(+), P=0.02) and not in M(-) (-20.50±7.16% in S(-) vs. -25.12±10.93% in S(+), P=0.85).
Conclusions: We found that the maximum or mean power in premovement beta-ERD activity was higher in S(+) than S(-) in the contralateral medial sensorimotor area in M(+). This result implicates that the beta-band power during premovement phase can reflect the intent of movement in PD patients in medication-on state.

CLINICAL SCIENCE: Symptoms, signs, features & non-motor manifestations

P12.01

Visuomotor training to music with learning choreography changes sensorimotor networks and weekly dance slows down disease progression as assessed by UPDRS and MMSE over 4-years

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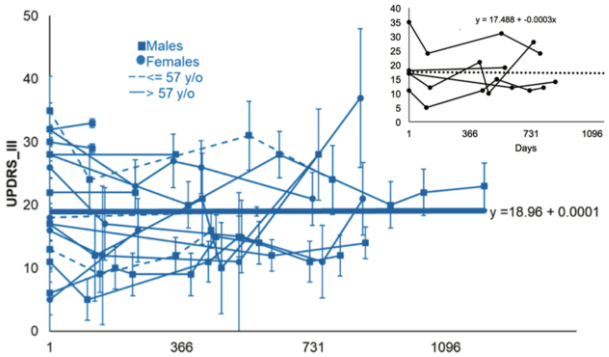
Purpose: Our research groups goals are to: (1) Develop a robust strategy to fight neurodegeneration, leveraging the brain's remaining plasticity through complex visuomotor enrichment, i.e. dance; (2) Develop putative neural mechanisms and predictive models which can be used to identify future biomarkers; (3) Collect longitudinal data.
Method: Using functional neuroimaging scans we studied 10 people with Parkinson's disease (PwPD) learning choreographed dance. For the next 4 years, we enrolled 110 subjects (n=67 PwPD) using rsEEG, UPDRS I-IV, MMSE, GDS and PANAS-X. These interim results discuss 10 (fMRI) and 16 (UPDRS I-IV) PwPD, drawn from a pool of participants we are longitudinally following. 16 PD-Dancers were H&Y=1.25 (SD=0.86), Age=68.73 (SD=8.41), Disease Duration=5.54 (SD=4.52) trained in 1.25-hour Dance for PD® classes. UPDRS III videos were scored by 7–8 MDS-trained raters and were averaged and plotted in the blue data in the figure. There was no disease progression in all four subscales of the UPDRS in our 16 PwPD: motor impairment across time in PwPD (blue data in figure, p=.817); daily living (p=.329), motor experiences of daily living (p=.540), and motor complications (p=.390). MMSE also showed no significant impairment. We used the Parkinson's Progression Markers Initiative (PPMI) to match our PD-Dancers longitudinally. A significant Group (PD-Dancers and PD-Controls) by Days interaction showed that PwPD who danced had less motor impairment (M=18.75) than PD-Controls (M=24.61) over time (p=0.049). PD-Controls showed normal motor impairment (subscale III) across time (p=0.009) but our PD-Dancers did not. PD-Dancers subscales I (p=0.005) and II (p=0.008) showed progression across time, whereas subscale IV showed no progression (p=0.365). Our interim longitudinal study results indicate the potential for dance to slow disease progression in PD. The brain regions involved were analyzed using a general linear model (p<0.001 BonfCor) bilateral auditory regions, supplementary motor cortex, parietal, prefrontal and subcortical regions (putamen, caudate and thalamic regions) and the subset black graph shows this progression. These findings suggest the benefits of weekly dance for PwPD as a supplement to a normal PD treatment regimen helps slow down disease progression.



P12.02

Randomized multicenter single-blind parallel-group trial to compare the efficacy of a Holter for Parkinson symptoms against other clinical follow-up methods

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Introduction: In the last few years, a number of research studies have been carried out for developing and validating portable technological devices for monitoring the motor manifestations of the Parkinson's disease (PD). The efficacy of such devices to enhance clinical control of the disease is unknown.
Methods: Randomized, single-blind, controlled trial. Neurologists from different Spanish healthcare centers will be randomly allocated to one of three study groups (1:1:1): A) therapy adjustment based on the information coming from STAT-ON, a inertial wearable device for monitoring PD motor symptoms commercialized by Sense4Care S.L., which their patients will be wearing for 7 days; B) therapy adjustment based on the information coming from a diary, where their patients will record motor fluctuations for 7 days; C) therapy adjustment based on the clinical information recorded during patients' visits. The recruitment period will last 12 months, during which inclusion of 330 patients is expected.
The efficacy of interventions will be measured through the time in Off (motor fluctuations diary), occurrence and intensity of dyskinesia (data from the Unified Parkinson's disease Rating Scale), occurrence and intensity of Freezing of Gait episodes (Freezing of Gait Questionnaire) and number of visits to the doctor for medication adjustment. In the assessment of efficacy results a double approach will be used: evaluation of superiority against group C and evaluation of non-inferiority against group A.
Results: The results of this study will provide information on the practical usefulness of the information processed by the STAT-ON wearable sensor, presented in a report generated by the corresponding application. Consequently, this study will analyze the convenience of adopting this technology in the clinical practice and future clinical trials.
Conclusions: This clinical trial has been designed to evaluate whether automated symptom-monitorization systems (holter for Parkinson) enhance the clinical control of patients with motor fluctuations. We expect to obtain the first results by the first half of 2020.

P12.03

Exploring the experience of wearing off in Parkinson's disease: A qualitative research approach

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Objective: To gain insights into how patients with PD communicate about wearing off via an in-depth analysis of patient descriptions of their experiences with this phenomenon.
Background: Wearing off in Parkinson's disease (PD) is characterized by the emergence of symptoms prior to scheduled doses of dopaminergic medication, that usually improve after redosing. While treatable, it has a significant negative impact on quality of life. Thus, its diagnosis is essential. Unfortunately, it may go undetected in many patients. Better understanding of how patients with PD communicate about wearing off is needed.
Design/Methods: A convenience sample of PD patients on levodopa therapy reporting wearing off was recruited. Qualitative exploration occurred in 2 phases. Phase 1 included 12 participants and consisted of moderator facilitated online journaling exercises for 1–2 hours/day for 3 days, while patients were either in the off- or on-medication state. A series of questions, interactive graphics, and images were presented to facilitate discussion and elicit detailed descriptions. Phase 2 involved in-depth semi-structured telephone interviews administered to 14 additional participants.
Results: Four main themes regarding the experience of wearing off in PD emerged (1) During wearing off, patients usually experience multiple motor and non-motor symptoms of varying levels of severity (2) Off symptoms can be triggered as well as mitigated by environmental/situational factors (3) PD patients have a rich language that enables them to understand, contextualize, and communicate about their experience of wearing off, including use of metaphors as well as technical medical terminology (4) The range of linguistic tools employed by patients to describe their wearing off symptoms vary dramatically between and within patients.
Conclusions: Wearing off is a complex, multidimensional phenomenon. Our findings shed light on the means of communication patients with PD employ to describe wearing off. These findings provide a starting point for devising interventions to improve physician-patient communication about wearing off.

P12.04

Complementary and Alternative Medicine (CAM) and over-the-counter therapies in Parkinson's: A simple algorithm and relatively inexpensive plan

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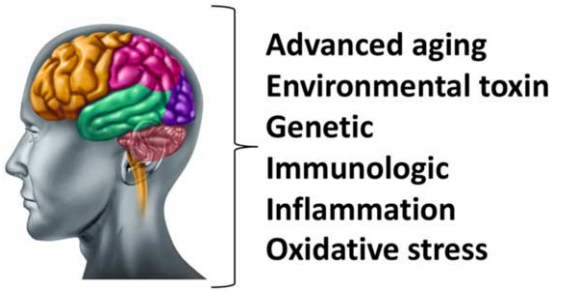
Parkinson's disease (PD) is a progressive degenerative nervous system disorder and is the second most common neurodegenerative disorder in the elderly population. The disease originates from the loss of dopamine-producing neurons in the substantia nigra in the brain, resulting in unregulated activity of the basal ganglia. The etiology of PD is still evolving; however, there is substantial evidence supporting the detrimental effects of neuroinflammation, environmental toxins, numerous genetic factors, changes in the cellular microenvironment (oxidative stress), innate and possibly adaptive immune systems, and advanced aging.
My plan consists of (i) traditional Parkinson's medication (Carbidopa/Levodopa and dopamine agonist); (ii) supplemented by a complementary and alternative medicine (CAM) approach, and (iii) fueled by exercise. My philosophy is simple because I truly believe there are steps I can follow to remain as healthy as possible, which include having a positive mindset to support this effort, and to accept the axiom of the harder I try the better I'll be.
My CAM strategy is relatively straightforward and based on the following scientific features: (1) does it counteract one of the proposed causes of Parkinson's as described above? (2) does it augment one of the biological mechanisms that could contribute to slowing progression of Parkinson's? (3) does the compound penetrate the blood brain barrier? (4) is there any published information in animal models or in human clinical trials? (5) Are the

compounds easy to take orally and relatively inexpensive. Based on the 5 points above, my CAM strategy consists of mannitol, resveratrol, taurine, N-acetyl cysteine (NAC), and S-acetyl glutathione. Also, daily exercise and adequate sleep are essential.



P12.05

Observed racial differences in Parkinson's disease in the Fox Insight cohort, an international internet-based study

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Background: Prior studies have suggested there may be important differences in the characteristics of Parkinson's disease (PD) in the African American (AA) population compared to Caucasians. Reported differences include: lower prevalence in the AA population; more advanced symptoms at diagnosis; and a greater frequency of dementia. All of these observations are based on relatively small population samples. Fox Insight, a large-scale, internet-based study, provides an opportunity to evaluate PD racial differences using a large database of patient-reported information.
Objective: To identify differences between White and AA patients using PD patient-reported demographics, motor symptoms, and non-motor symptoms.
Methods: Data was extracted from Fox Insight on October 11, 2018. Subjects that reported the diagnosis of PD and reported their race as either White or African American were included. Missing data was excluded from analysis. Student's t-tests, Chi-square, or Fisher's exact tests were used to compare all variables between African American and White PD patients. Statistical analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC).
Results: There were 15,793 White and 128 AA patients enrolled in the study at the time of data extraction. Several clinical features distinguished these populations. The AA patients more frequently reported a younger age of PD diagnosis ($p<0.0001$) and less frequently reported a family history of PD ($p<0.0014$). Freezing, hallucinations, vivid dreams, acting out dreams, and cognitive changes were more frequently reported by AA patients ($p<.01$ for each of these features). (Table 1)
Conclusions: Fox Insight provides a unique opportunity to explore features of PD in a large international population. Although the current sample size of Fox Insight is more than 15,000, AA patients are under-represented and make up less than 1% of the sample. This preliminary analysis suggests there are important differences: it appears that AA patients are diagnosed with PD at a younger age, more often lack a family history of PD, and more frequently have hallucinations, dream enactment, and cognitive changes when compared to White PD patients. Replication of these data in an independent sample is an important next step.

Table 1: Characteristics of White vs AA PD patients

	White	AA	p value*
Demographics			
Current age (SD)	65.34 (9.59)	60.69 (12.32)	<0.0001
Age at PD Diagnosis (SD)	60.00 (10.65)	55.54 (12.81)	0.0001
Family History PD			0.0014
Yes	3869 (28.0%)	11 (12.0%)	
No	8102	63	
Prefer Not To Answer	6	0	
Unknown	1861	18	
Non-motor symptoms in last month			
Hallucinations			0.0010
Yes	1475 (11.3%)	20 (22.5%)	
No	11565	69	
Vivid dreams			0.0094
Yes	4442 (34.1%)	42 (47.2%)	
No	8587	47	
Forgetting to do things/memory			0.0034
Yes	6322 (48.5%)	57 (64.0%)	
No	6719	32	
Acting out dreams			0.0004
Yes	4274 (32.8%)	45 (50.1%)	
No	8754	44	
Difficulty keeping train of thought			0.0014
None	5447 (42.7%)	28 (32.2%)	
A little	5147	30	
Somewhat	1457	17	
A lot	632 (5.0%)	11 (12.6%)	
Cannot do	56	1	
Prefer Not to Answer	10	0	
Difficulty following complex instructions			0.0068
None	8403 (65.9%)	50 (57.5%)	
A little	2845	16	
Somewhat	939	11	
A lot	421 (3.3 %)	7 (8.0 %)	
Cannot do	142	3	
Prefer Not To Answer	10	0	
Difficulty explaining several steps			0.0068
None	6660 (52.2%)	32 (36.8%)	
A little	3839	31	
Somewhat	1390	11	
A lot	712 (5.6%)	11 (12.6%)	
Cannot do	138	2	
Prefer Not To Answer	18	0	
Difficulty counting money			0.0055
None	10872 (85.2%)	65 (74.7%)	
A little	1257	11	
Somewhat	360	5	
A lot	158 (1.2%)	4 (4.6%)	
Cannot do	89	2	
Prefer Not To Answer	27	0	
Motor symptoms in last week			
Freezing			0.0008
0 (none)	8990 (68.9%)	45 (50.6%)	
1	2217	19	
2	897	14	
3	682	7	
4 (severe)	260 (2.0%)	4 (4.5%)	

*only p values <0.01 were included in table for the listed categories

Key: AA=African American; PD=Parkinson's Disease; SD=standard deviation

P12.06

Impact and perceptions of non-motor symptoms in Parkinson's disease as reported by people with Parkinson's (PwP) and their care partners: A pilot survey of the PMDAlliance

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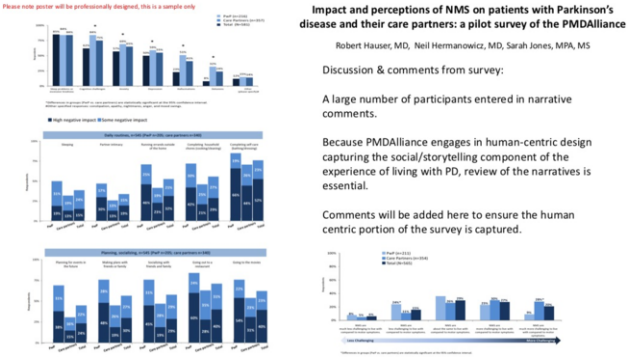
Parkinson and Movement Disorders Alliance (PMDAlliance), a nonprofit organization that promotes the daily health and well-being of people with PD and their care partners distributed a survey to better understand the perceptions, experiences, and educational needs of individuals with non-motor symptoms (NMS) of PD and their care partners. The survey was addressed to the total membership of the PMDAlliance (approximately N=3685). A total of

700 respondents completed the survey, either totally or partially. Of the 700 respondents, 54% were care partners and 41% were people/persons with Parkinson's disease (PwP). The remaining 5% were non–care partners/family members of PwP or "others."
Among the 700 respondents, 90% reported that PwP experienced NMS. Notably, a greater percentage of care partners reported that their PwP experienced NMS than did PwP (97% vs 80%). Overall, more than half of respondents (responses pooled for 581 PwP and care partners) reported sleep problems or excessive tiredness (84%), cognitive challenges (75%), anxiety (65%), or depression (55%) among PwP (ie, reported by PwP themselves or their care partners). Respondents also reported a high prevalence of hallucinations (41%) and delusions (24%) among PwP (ie, reported by PwP themselves or their care partners). There were differences in reported NMS prevalence in PwP between care partners and PwP, with care partners reporting higher prevalences across all symptoms. The differences in reported NMS prevalence by care partners (357 respondents) and PwP (216 respondents) were statistically significant for cognitive symptoms (84% vs 62%), anxiety (69% vs 65%), depression (59% vs 55%), hallucinations (51% vs 23%), and delusions (32% vs 8%) Among respondents with NMS experience, as PwP or care partners (579 respondents), the onset of NMS occurred within the first 3 years after PD diagnosis for more than half (53%), and within the first 5 years after diagnosis for 72%. The reported onset of NMS appeared to be largely similar for affected PwP, whether reported by them or by their care partners.



P12.07

A fitbit for Parkinson's?
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After being diagnosed with Parkinson's a couple of years ago and being in the lucky situation of working at CERN, the European Laboratory for Particle Physics – a place with lots of engineers and technicians, who relish a challenge – my colleagues and I were surprised to find that a simple personal wearable device to monitor the symptoms of Parkinson's 24/7 was not available. At least a device like that would make it possible for the patient to keep track of how his or her own disease develops. There are already a few such devices available but they are all only available from very few neurology clinics and thus only to the very few patients frequenting those few clinics. We would like to make them available to all Parkinson's patients.
Given that most Parkinson's patients are above 65 years of age and hence perhaps not very tech savvy, the device should be made as simple to operate as possible and it should be easy to retrieve the data and visualize it.
We believe the time to make such a wearable device is now. The development of much better batteries and better and less power hungry sensors, memory and e-ink screens allows us to build a device, which will only need to be charged every 14–21 days thus also allowing tracking of sleep related symptoms. The sensor package consists of accelerometers, gyroscopes and magnetometers. Battery lifetime is extended by only downloading the data when the device is connected for recharging. The device will also have medicine reminders and a button to record the exact time the pills were taken. This could also be used to make the patient do certain exercises that will help in monitoring the progression of typical symptoms other than just tremors. If the patient allows it, the data could also be added to a large database where machine learning algorithms could try to analyze the data for connections hither here never seen. This might aid us in learning more about the disease and perhaps help in the quest for a cure.

P12.08

Chief complaints of de novo patients with Parkinson's disease
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Objective: Patients are required to see a doctor for early diagnosis of Parkinson's disease.
We discuss what kind of symptoms the patients have with feeling abnormal for their visit.
Methods: We examined chief complaints of our outpatients with de novo Parkinson's disease between April 2015 and October 2018. They were diagnosed according to UK brain bank criteria.
Results: There were total 334 patients (142 men and 192 women). Their chief complaints were classified as follows: (i) those associated with motor symptoms of Parkinson's disease, (ii) abnormalities attributable to motor symptoms, (iii) non-motor symptoms, (iv) those for other diseases, which included 213 patients (63.8%), 40 patients (12.0%), 63 patients (19.2%), 134 patients (3.9%), respectively. Tremor was the most common complaint of motor symptoms, observed in 107 patients (19.2%). Other complaints in (i) included gait disturbance (63 cases), bradykinesia (11), frequent fall (8), postural disturbance (6), poor hand movement and dysgraphia (6), dysarthria or dysphagia (6), gait festination (4 cases), and freezing (2). In (ii), complaints were shown as unsteady walking (26), weakness in hands and legs (8 cases), light-headedness (2), and body stiffness (2). Non-motor symptoms in (iii) consisted of forgetfulness (15), numbness in hands and feet (12), headache (9), pain in hands, feet and hips (8), fatigue (5), blood pressure fluctuation (4), difficulty in concentrating (3 cases), sleep talking (3), syncope (2), restless legs (1), and apathy (1). Patients in (iv) had symptoms such as cervical spondylosis (4), vertigo (3), polyneuritis (2), migraine (2), transient ischemic attack (1), Bell's palsy (1), and hemifacial spasm (1).
Conclusion: Approximately 75% of patients' complaints involve motor symptoms or related disorders, with high percentage of 50% for tremor and gait disturbance. On the other hand, 20% of patients present with non-motor symptoms. Therefore, motor symptoms are suspected even in patients with a non-motor symptom as a chief complaint. It is also required that doctors consider Parkinson's disease in the daily medical care because they may detect it in patients showing symptoms of other diseases.

P12.09

Eye problems experienced by people with Parkinson's disease – Influence of double vision on activities of daily living

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Introduction: The purpose of this report is to show the eye problems experienced by people with Parkinson's disease, especially the presence and duration of double vision(DV), and the impact on daily life.
People with Parkinson's disease experience various eye-related problems such as difficulty in eye movements, DV, blurred vision, blepharospasm. DV is one factor that interferes with activities of daily living. However, in Japan it is not fully recognized.
Method: We conducted a questionnaire survey on 42 persons using day service center specialized in Parkinson's disease. The question was 20 items such as "Do you have DV?", "Does DV occur at a certain time?", "What is troubling with DV?", "Does DV also occur when viewing with one eye?" and so on.
Result: 16 people out of 42 responded that they had DV. And 9 out of 16 responded to all items.
1) Presence or absence of DV: 3 answered "always there" and 6 "sometimes".
2) Does DV occur at a certain time: 2 answered "constant", 5 were "constant",2 were "not quite constant".
3) What is troubling with DV: 5 of them answered "It is hard to see television", 2 were "hard to work at hand", 1 were "Because the eye movement is bad, I will stare at one point", 1 were "no particular".
4) Does DV also occur when viewing with one eye: 2 answered "Yes", 4 were "No" and 3 were "I do not know."
Discussion: 16 people in 42 were conscious of DV, and as a result of the investigation of 9 people, it became clear that the time for DV is approximately constant for 7 people. This indicates that medication time and DV are related. Many also appealed that DV was a problem when watching TV images. In the future, it is necessary to study in detail the relationship between DV and medicinal effect, more detailed difficulty in everyday life.
In addition, 2 out of 9 respondents said "DV occurs even with one eye alone." This indicates the necessity of considering ocular organic problems such as astigmatism.

P12.10

What emotional prosodies tell us about early-onset Parkinson's disease

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Previous study indicated that people with Parkinson's disease (PD) impairs the identification of emotions. Deficit in recognition of emotions in PD might be related to the onset-differences of PD, where a progressive neurological manner with the decline in emotion recognition is suggested.
The purpose of the present study set out to investigate where the ability in emotion recognition is affected in either early-onset and typical-onset Cantonese-speakers with PD and to test their potential difference in the ability of emotion recognition in four specific emotional valences (happiness, sadness, anger, and neutral).
Method: Sixty Cantonese-speaking participants were recruited into three experiment groups (20 participants with early onset of PD, 20 participants with typical-onset of PD and 20 participants from normal population). Four emotions (happiness, sadness, anger, and neutral) were presented randomly in two conditions: (1) congruent and (2) incongruent visual-auditory integration. The participants were instructed to watch photos of facial emotional expressions presented by the respective eye region of a model, and heard the vocal emotion presented concurrently. They were required to choose a name of emotion from multiple-choice task that are the most relevant to what they heard from the visual-auditory integration.
Results: Both PD groups were less accurate to recognize vocal emotion of speakers presented in visual-auditory integration, but no onset-differences were showed in our results. The result align with previous studies that the presence of PD decreased the accuracy in emotion recognition. By conducting between-group analysis of individual recognition of emotions, early-onset-PD outperformed typical-onset PD in recognizing happy and angry vocal emotion from visual-auditory integration, where they demonstrated similar performances in recognizing sad and neutral vocal emotion from visual-auditory integration.
Our study confirmed PD impaired the vocal emotions recognition. However, early-onset PD preserved ability to recognize positive valences (happiness and anger) while typical-onset PD experienced deficits in vocal emotion recognition for all emotion states.

P12.11

Communication about of OFF periods in Parkinson's disease: A survey of physicians, PwP and carepartners

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Background: OFF periods impair quality of life of patients with Parkinson's disease and are often amenable to treatment. Optimal treatment decisions rely on effective communication between physicians, PwP and carepartners regarding this highly variable and complex phenomenon. Little is published in the literature about communication about OFF periods.
Methods: Informed by interviews with physicians, PwP and carepartners we designed questionnaires for each group. We surveyed these parties using an online platform to investigate the frequency, content and ease of communication about OFF periods and barriers and facilitators of communication with physicians.
Results: 50 movement disorder neurologists, 50 general neurologists, 442 PwP and 97 carepartners participated. A free-flowing dialogue is the mainstay of communication according to all parties. Motor aspects of OFF periods are discussed more frequently than non-motor aspects (90% vs <50% according to both general neurologists and movement disorder neurologists). The most common physician-reported barriers to communication are patient cognitive impairment, patient difficulty recognizing OFF periods and poor patient understanding of OFF periods' relationship to medication timing. The barriers most commonly cited as major by PwP were that they perceived OFF periods to be part of the disease (i.e., not a clinical aspect that could be improved by a physician), variability of symptoms, and difficulty in describing symptoms. The most commonly described communication facilitator (by physicians) was the input of a caregiver. Positively viewed but less commonly used facilitators include pre-visit questionnaires or diaries, digital apps or wearable devices to monitor fluctuations. The majority of PwP and carepartners identified a free-flowing dialogue with their physicians and having an agenda as helpful facilitators of communication about OFF periods which they already use. The majority of both groups felt that keeping a diary and pre-visit questionnaires were potentially helpful facilitators that were not currently in use.

Conclusions: Perceived barriers and facilitators to communication about OFF periods are different between health care providers and receivers of health care. Modifiable barriers and facilitators that could be implemented were identified by both groups. Future research should develop and test strategies based on this input to optimize communication and thus clinical care for this common and debilitating problem.

P12.12

Experience and impact of OFF periods in Parkinson's disease: A survey of physicians, PwP and carepartners

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Background: OFF periods impair quality of life in patients with Parkinson's disease (PwP) and are often amenable to treatment. Optimal treatment decisions rely on assessing the impact of these periods on PwP and their carepartners. Little is known about the impact of OFF periods on their daily lives. Methods: Informed by interviews with neurologists, PwP and carepartners, we designed questionnaires for each group. We surveyed these parties to investigate the breadth of OFF period symptoms, the impact of individual symptoms, of OFF periods and the impact on various aspects of their lives.
Results: 50 general neurologists, 50 movement disorder neurologists, 442 PwP (median disease duration 5years; median age 66) and 97 carepartners (median age 64) participated. The most common OFF symptoms reported were stiffness, slowness and changes in gait in both PwP and carepartners Across all symptoms, a higher proportion of carepartners than PwP reported each symptom. A minority of general neurologists and movement disorder neurologists recognized pain, sweating and anxiety as possible symptoms of OFF periods. The three OFF symptoms most frequently designated as having great impact by PwP were changes in gait, slowness in movement, and stiffness. In contrast to patient responses, carepartners most frequently rated cognitive impairment as having great impact. The aspects of life most commonly rated by PwP as severely impacted were physical activities, household tasks, leisure/hobbies and employment. Carepartners most frequently cited their own mood, leisure activities, freedom to leave the home and household tasks as severely affected.
Conclusions: OFF periods affect a broad range of the daily lives of PwP and carepartners. In PwP with relatively short (less than 10 years) disease duration, motor symptoms of OFF periods predominate in impact, however non-motor symptoms are also rated as impactful, particularly by carepartners. Education is needed for neurologists regarding the non-motor aspects of OFF periods. The importance of involving carepartners in the assessment regarding OFF periods is supported by the higher frequency of symptom reporting by carepartners, and the significant impact on many aspects of their lives.

P12.13

Attitude of older patients with Parkinson's disease towards deprescribing: A pilot study

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Objective: There is limited understanding on how older patients with Parkinson's disease (PD) perceive their medication. We wish to assess the older patients' attitude towards deprescribing of inappropriate medications using the Revised Patients' Attitudes towards Deprescribing' (rPATD) tool and determine the suitability of the questionnaire for use in this cohort.
Methods: An anonymous survey was completed by participants with PD who attended a public health talk in November 2018 organised by the local support group. All participants were asked to complete the rPATD for older patients. Data were collected on sociodemographic characteristics and clinical data such as comorbidity and polypharmacy, and the main outcome was older patients' willingness to deprescribe inappropriate medications.
Results: A total of 18 patients completed the survey. The median age of participants is 64 years (56–73 years). Of these, 55.6% were men and were taking a median of 5 (IQR: 3–8) medications and supplements daily. Overall, only two-third of participants (n=12; 66.7%) were satisfied with the medications they were taking; and a significant number of participants (n=13; 72.2%) were willing to stop one or more of their medications if possible and agreed by their doctors. This willingness was correlated with seven items of the rPATD, including a strong correlation with the overall satisfaction of patients with the medications taken.
Conclusion: Many older patients with Parkinson disease have shown their willingness to reduce one or more of their medications if their doctors said it was possible. Healthcare providers should be proactive in discussing and evaluating potentially inappropriate medications for better clinical decision making.

P12.14

Motor and non-motor symptoms more disturbing for people living with Parkinson's disease in Brazil: AMPARO's study

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Although the motor symptoms are the main feature of Parkinson's disease (PD), currently it is well known that the several other cognitive, emotional and autonomic alterations are part of disease. However, the perception about the impact of this alterations on the quality of life according to people living with PD and their care partners has been little studied. AMPARO network is part of FAPESP's Research, Innovation and Dissemination Center for Neuromathematics (http://neuromat.numec.prp.usp.br/) has the main purpose to built to establish a common understanding of challenges persons with Parkinson's disease face in Brazil and to have an impact on clinical policies and research projects associated to this disease.
To investigate the perception of people with PD and their care partner living in five different Brazilian regions about the more disturbing alteration associated to PD among the members of AMPARO network.
Participated this study 180 PPD living in Brazil, mean age of 63.2 years, 120 care partners. After becoming a member of AMPARO by internet, the people were invited to answer a survey. The surveys were elaborated by an interprofessional team specialized in movement disorders based on clinical experience and scientific evidences in PD.
The analysis of the results showed that, according to people with PD, the most disturbing symptom associated to PD were slowness in movement/muscle rigidity (36.59%); tremor (12.20%); lack of balance (10.98%), while the most distressing alteration in daily living were maintain quality sleep (31.71%); community walking e (28.05%); wear clothes and footwear (17.07%). On the other hand, according to the care partner, the more challenger task is to offer the emotional support for people with PD (49.28%), followed by help during the shower (10.14%) and to manage the medication schedule (5.80%)

Among the 14 symptoms experienced by people with PD, although the four more disturbing of them were associated to motor symptoms, several non-motor symptoms were also cited. More interesting, the most distressing of them was sleep disfunction according to people with PD, and the emotional alterations according to care partners.
These results reinforce the crucial role of interprofessional care to improve the quality of life for people with PD and their care partners.

P12.15

Risk factors for the development of cognitive impairment in Parkinson's disease

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Introduction: Cognitive decline is a common nonmotor feature of Parkinson Disease (PD). We analyzed data from the Parkinson's Foundation Quality Improvement Initiative (QII) to identify potential risk factors for the development of cognitive decline in PD.
Methods: Subjects enrolled in the Parkinson's Foundation (QII) are followed annually and subjects who developed cognitive decline were compared to those who did not. Cognitive impairment was defined as scoring in the lowest quartile in both delayed recall of 5 words (<3 words) and verbal fluency (<15 animals in 1 minute). Individuals with a diagnostic certainty of PD less than 90%, those missing delayed recall of 5 words/semantic verbal fluency values, those having less than 2 visits, and those who were defined as cognitively impaired at first visit were excluded. This left 5,180 subjects (out of a total of 11,920) included in the analysis. Variables examined included: age, sex, race, obesity (BMI=30), level of education, depression, diabetes, hypertension, and level of exercise. Logistic regression analysis was performed to estimate adjusted odds ratio (AOR) and 95% confidence intervals of risk factors.
Results: Patients with lower cognitive function (P<.0001; AOR=5.0 for decrease of 1.0 in average z-score of delayed recall and verbal fluency), presence of depression (p=0.0036; AOR=2.5), older age (p=0.011; AOR=1.5 for increase of 9.2 years), and lack of exercise (P=0.0001; AOR=1.5) at the first visit had significantly higher possibility to be cognitively impaired at the second visit.
Conclusion: Lack of exercise and depression represent potential modifiable risk factors for the development of cognitive impairment in Parkinson's disease. Vascular risk factors (hypertension, diabetes, and obesity) recognized as risk factors for Alzheimer's disease do not appear to be an independent risk for the development of cognitive decline in PD.

P12.16

A wireless brain-spine interface alleviating gait deficits in a non-human primate model of Parkinson's disease

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Objective: While levodopa and deep brain stimulation alleviate most of the symptoms associated with Parkinson's disease (PD), axial gait disorders are less responsive to these treatments. Impairments include short and slow steps, balance deficits and freezing of gait. Using MPTP-treated non-human primates, we studied the impact of a brain-spine interface on alleviating axial gait deficits observed in PD.
Background: We have established a mechanistic and technological framework that guided the design of electrical spinal cord stimulation protocols engaging extensor and flexor muscle groups. We created an interface that linked gait events decoded from leg motor cortex activity to spatially selective stimulation protocols that reinforced the movements associated with these events.
Methods: Three MPTP macaques were implanted with the wireless brain-spine interface. Recordings of multi-unit activity from the left and right leg motor cortex were used to detect neural states related to flexion and extension movements of both legs while the animal walked freely overground or over a horizontal ladder. The detection of these gait events triggered the delivery of spatially selective electrical stimulation protocols that reinforced the extension and flexion movements of the legs. Stimulation protocols were delivered using an implantable pulse generator with real-time triggering capability that was connected to a custom-made electrode array. The electrode layout was based on a computational model that estimated optimal locations to target the dorsal roots of each lumbar spinal cord segment.
Results: The three MPTP-treated monkeys exhibited moderate to severe axial gait deficits, including short and slow steps, balance deficits, freezing of gait, and poor precision of paw placement when traversing the horizontal ladder. The brain-spine interface instantly alleviated these deficits, allowing the monkeys to increase their walking speed, improved their balance and regained coordinated gait patterns. Moreover, the brain-spine interface enabled the monkeys to regain the ability to position the paws precisely on the rungs of the horizontal ladder.
Conclusion: These preliminary results illustrate the ability of the brain-spine interface to alleviate axial gait deficits and restore visuomotor control of leg movements in MPTP-treated non-human primates. These findings open promising avenues for targeting gait deficits in people with PD, which are still resistant to current treatments.

P12.17

Characterizing stepping responses using an instrumented pull test in people with mild Parkinson's disease

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Background: Postural reflexes are commonly intact in people with mild Parkinson's disease (PD). However, changes in postural control are known to occur early in PD, when balance is considered normal. To assess postural reflexes, clinicians typically employ the 'pull test' to grade corrective responses to a backward perturbation at the shoulders. Recent studies suggest levodopa does not improve step responses following this perturbation. Objective measurement of balance using an instrumented version of the clinical pull test could capture early abnormalities in postural responses, detect changes in response to medication, and account for force variation during the test administration.
Objective: To characterize stepping responses and the effects of levodopa in people with PD using an instrumented pull test.
Methods: Seventeen participants (age 58.5±9.1; 11 males) with mild PD (Hoehn and Yahr = 2) were recruited and assessed OFF and ON levodopa. Postural responses were quantified using an instrumented pull test. An examiner manually administered thirty five backward pulls, with pull force measured. Stepping responses were captured using motion tracking with sensors attached at the trunk and ankles. Initial step length, step reaction time (time between onset of trunk displacement and initial foot lift off), and retropulsion (posterior displacement between first foot lift off and landing of the final foot arresting movement) were recorded. The first five practice trials were excluded from analysis. To determine the effects of pull force and medication on stepping, linear mixed models analysis was conducted.
Results: Initial step length was greater OFF-levodopa compared to ON (mean difference 29 mm, $p<0.001$). Retropulsion was greater OFF-levodopa compared to ON (mean difference 55 mm, $p<0.001$). There was no difference in step reaction time ($p=0.573$). Increased peak pull force was associated with larger initial step length ($b=0.171$, $p<0.001$) and retropulsion ($b=0.864$, $p<0.001$).
Conclusion: People with mild PD demonstrate subclinical differences when stepping in an instrumented pull test, suggesting aspects of stepping may be levodopa responsive. Examiner peak pull force influenced size of stepping, which explains why reliability has been a confounder during clinical pull test administration.

P12.18

Characteristics of swallowing dysfunction by video-fluoroscopic swallowing study in Parkinson's disease

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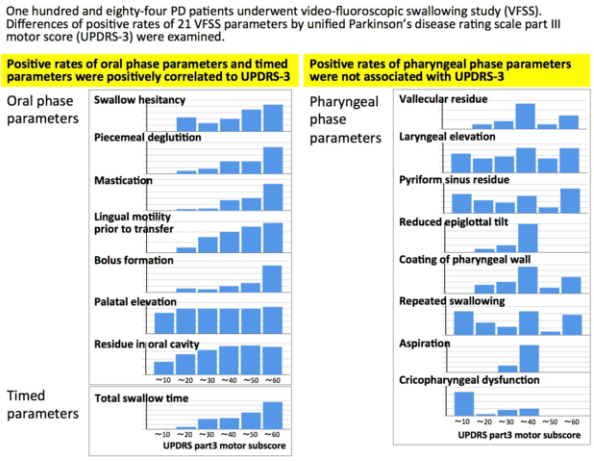
Introduction: Dysphagia is a serious complication in the advanced stage of Parkinson's disease (PD) and the most common cause of death is subsequent aspiration pneumonia. We formerly analyzed 21 video-fluoroscopic swallowing study (VFSS) parameters, and created a VFSS severity scale for PD (PDVFS) which predicted subsequent aspiration pneumonia, although the pathophysiology of dysphagia in PD remains unknown. Swallowing system is composed from oral and pharyngeal phases. In this study, to clarify the characteristics of dysphagia in PD, we analyzed the association between parkinsonism and these 21 VFSS parameters in dividing these phases.
Methods: We enrolled 184 PD patients who underwent VFSS because of suspected dysphagia. Twenty-one VFSS parameters, which were previously demonstrated as significant predictive factors for subsequent development of aspiration pneumonia within six months of the VFSS, were adopted for this study.
Associations between positive rates of oral-phase, pharyngeal-phase or timed parameters and unified Parkinson's disease rating scale part III motor score (UPDRS-3) were examined.
Results: Positive rates of VFSS parameters of oral phase (e.g. piecemeal deglutition, mastication, lingual motility prior to transfer, and bolus formation) and total swallow duration were positively correlated to UPDRS-3, however those of pharyngeal phase (e.g. vallecular residue, laryngeal elevation, pyriform sinus residue, reduced epiglottal tilt, coating of pharyngeal wall, repeated swallowing, aspiration, and cricopharyngeal dysfunction) were not associated with UPDRS-3.
Conclusion: The results of this study suggest that dysphagia in PD in oral-phase swallowing, is mainly due to parkinsonism. However, in pharyngeal-phase dysfunction in PD patients with dysphagia, there may exist different mechanisms other than parkinsonian motor symptoms.



P12.19

Clinical characteristics of Parkinson's disease in Sanglah General Hospital Denpasar Bali 2015–2018

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Parkinson's disease (PD) is the second most common neurodegenerative disease. About 5 to 10% of people worldwide suffering Parkinson's disease with initial symptoms that appear before 4th decade of life. Indonesia, with population of 210 million people, around 200,000–400,000 people suffered from PD, ranging from 18 to 85 years old with median of 50, and men are more affected than women. We conducted descriptive study to determine the characteristics of Parkinson's disease with various age-onset, clinical symptoms, complications and the burden of the resulting morbidity. Data was collected using consecutive-sampling from the medical records of patients diagnosed with PD at Sanglah Hospital Denpasar. This study involved 43 samples consisting of 29 Indonesian Citizens and 3 Foreign Citizens, age ranging from 21 to 87 years old. Men more frequent than women. The most common risk factors are vascular disease, with the dominant clinical symptoms being rigidity and tremor, and mostly in stages 2 and 3

based on Hoen & Yahr Criteria. Complications were found on 28 subjects with cognitive impairment being the most frequent.

P12.20

Survey to understand the impact of Parkinson's on the individual with the condition and their spouse/partner/loved ones – Compiled and developed by Team Spark for Rallying to the Challenge 2018, Grand Rapids Michigan

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The agenda for the annual Rallying to the Challenge conference, Van Andel Research Institute (VARI), Grand Rapids, Michigan, is devised and delivered by people with Parkinson's (PwP) in tandem with Grand Challenges. In the 3 months prior to the conference, the Parkinson's community is surveyed around a topic of relevance. The surveys are analysed with the findings presented at Rallying. Focus groups then meet to identify tools and practical approaches to address the findings. The theme of this year's meetings was non-motor symptoms. In an attempt to bring the patient/support person voice to the issue, members of Team Spark, Rallying's local support team, designed and compiled a survey aimed at understanding the impact of Parkinson's on the individual with the condition and their spouse/partner/loved ones (partners).
Methods: A short symptom questionnaire already used by Team Spark formed the basis for a larger survey to identify the impact of Parkinson's on both the PwP and their partners in 5 domains: Mood & Behaviour; Fatigue & Sleep; Thinking, Memory & Perception; Autonomic, Gastrointestinal & Sensory and Motor Symptoms.
Through 3 focus groups held at VARI, the survey was expanded into two parallel sections; one for the PwP and the other for the partner allowing the findings to be compared and discussed.
The online survey was distributed online via Parkinson's Movement, Health Unlocked/CPT in person via Team Spark, Michigan Parkinson's groups and the Rallying database. Print versions were also available triggering 210 responses. These were analysed from the perspective of the PwP, and compared with responses by spouses/partners/loved ones. There was accurate reporting of symptoms between spouses/partners/loved ones, with a very wide range of symptoms being defined as moderately to very troublesome.
Conclusions: The focus groups revealed a need to identify ways of raising sensitive issues such as mental health and cognition with a balance of tact and respect – and called for a tool to support communication prompting when and how to ask for help, and how to raise difficult topics proactively in a supportive and sensitive way.

P12.21

Concentration, easily overlooked orthostatic intolerance, its influence on early Parkinson's disease patients

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Background: Orthostatic intolerance is cardiovascular dysautonomia that includes diverse symptoms. Because it incorporates nonspecific symptoms such as impaired concentration, in clinical practice, physicians sometimes fail to address such issues in their time-limited appointment with the patients. Blunted cognition during orthostasis may affect various aspects of general status in PD and its clinical impact on early PD is not clarified.
Objective: This study is aimed to investigate the occurrence and effect of impaired concentration during standing, on quality of life in de novo Korean PD patients. We also looked for contributing factors that influenced the incidence of orthostatic concentration trouble.
Methods: In this study, we enrolled 124 newly diagnosed PD patients. They received structured clinical interview and examination. Their overall motor status was assessed by modified Hoehn and Yahr stage (mHYS) and non-motor symptoms were evaluated with Non-Motor Symptoms Scale (NMSS). Patient's mood was estimated with Montgomery-Asberg depression rating scale (MADRS). Their disturbed concentration was evaluated with Orthostatic Hypotension Questionnaire (OHQ). Quality of life was measured using the Parkinson's disease Quality of Life 39 (PDQ-39). The relationships between loss of concentration and each scale were investigated. We also measured patient's blood pressure during supine and upright position with tilt table to look for supine hypertension (SH) and orthostatic hypotension (OH). We weighed which factors independently contributed to the blunted cognition during osthostasis.
Results: The mean age of enrolled patients was 70.1±8.9 years old. Their median disease duration was 12 months and median modified Hoehn and Yahr stage was 1.5. Among the study population, 76 (61.3%) patients responded to have trouble in concentration. They had steeper blood pressure fall during orthostasis. Their OHQ Part 1–5 (trouble concentrating subscale) score was positively associated with NMSS, MADRS, PDQ-39. Among BP variability, only OH without SH was independently correlated with episodes of disturbed concentration in PD.
Conclusions: Concentration problem during standing is frequent finding in early PD. It influences negatively on non-motor burden, mood and quality of life in PD patients. Only OH was independently correlated with incidence of disturbed concentration. Such findings complicate treatment but provide valuable information in dealing early PD.

Association between Trouble concentration (OHQ Part I-5) and NMSS, PDQ-39 and MADRS

		NMSS			PDQ-39 index				MADRS	
		Cardiovascular	Attention/ Memory (KNMSS)	NMSS Sum	Mobility	ADL	Cognition	PDQ-39 Summary index	Concentration	MADRS Sum
OHQ Part I-5	Correlation Coefficient	.358	.550	.583	.292	.261	.541	.424	.686	.549
	P value	< 0.001	< 0.001	< 0.001	.001	.004	< 0.001	< 0.001	< 0.001	< 0.001

* Spearman partial correlation analysis, adjusted for age and disease duration

CLINICAL SCIENCE: Progression & prognosis

P13.01

Ambulatory inertial sensors in Parkinson's disease: Exploring the objective characterization of motor disability with Timed Up and Go test

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Objective: To explore the applicability of an ambulatory inertial sensor (G-walk) to characterize gait function during the Timed Up and Go (TUG) Test under three different conditions.

Background: In Parkinson's disease (PD), the current lack of both reliable and feasible biomarkers of gait function and mobility limits the objective characterization of motor ability, clinical progression, and responsiveness to treatments. Current assessments of motor function rely on a clinicians' subjective judgement and/or the patient's self-reported questionnaires, which are not sensitive in capturing subtle changes over time and restrict comparability across raters. Ambulatory inertial sensors allow for non-invasive, wireless transmission of accurate quantitative data and therefore, may represent a useful tool in ambulatory settings.
Design/Methods: Nineteen (19) PD patients (H&Y <4) and 10 age-matched controls (CTRL) were consecutively enrolled to undergo inertial TUG (iTUG) testing under three experimental conditions: normal walking (iTUGnorm), dual task walking (iTUGcog), and at maximum speed (iTUGfast). The time needed to complete each test was sub-divided into six distinct phases quantified by the sensor: sit-to-stand (1), forward gait (2), mid-turn (3), return gait (4), end-turn (5) and stand-to-sit (6). Other assessments included UDPRS Part III, MoCA, depression, fatigue, Benton and Rey–Osterrieth visual tests.
Results: A total of nineteen PD patients and ten CTRLs completed all assessments. PD patients were divided into mild (H&Y=2, n=12) and moderate (H&Y=3, n=7) disease severity. One-way-ANOVA and correlation analysis were performed. Different patterns of kinematic performance were observed (figure 1.A and 1.B). In PD, iTUG correlations were found with cognitive function, visual performance and motor severity, while in CTRLs there was only a correlation with motor performance only. iTUGfast performance seemed more sensitive experimental condition when PD was stratify by severity (figure 1.B).
Conclusion: iTUG assessed by an ambulatory inertial sensor is a quick, sensitive and feasible tool for objective measurements of functional mobility in PD. Utilizing validate tests for mobility and gait under different stress conditions can provide distinct information of gait function and mobility. Future longitudinal studies are warranted to better characterize the sensitivity to disease progression and the potential for monitoring and optimizing therapeutic interventions in this patient population.

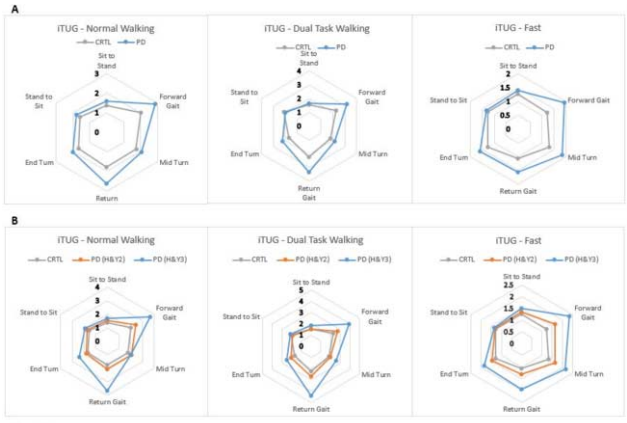

Figure 1: Radar charts representing six sub-sections of the inertial Timed Up and Go (iTUG) test measured by G-Walk. iTUG was performed under three different conditions: *normal walking*, *dual task walking* and, *at maximum speed*. The distance to the center of the radar represents time (seconds). **A:** Time performance comparison between controls and Parkinson's disease (PD). **B:** Time performance comparison between controls and PD severity (PD mild: H&Y≤2; PD moderate H&Y=3).

P13.02

Has the change in treatment for thirteen years changed the subjective symptoms of Parkinson's disease?
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The number of patients with Parkinson's disease (PD) would increase with the aging in Japan.
Objective: We would like to know the changes in subjective symptoms to support the patient's recuperation in the development of the medicine.
Methods: We did a comparison of the year 2004 and 2017 using questionnaire. The questionnaire was sent in January 2017. This resulted in a total of 353 patients with PD (163 males, 190 females) that were included in the analysis. Once as well the resulted in a total of 194 patients with PD (88 males, 106 females) that were included in the analysis. The ratio and average of the group were compared. And We reported odds ratios (OR) and 95% confidence intervals (CI) from multivariable logistic regression models.
Results: The average age was 69.0±7.8 in 2004, and 73.1±7.6 in 2017. The incidence of tremor (OR 1.08, 95%CI 1.05–1.11), rigidity (OR 0.63, 95%CI 0.42–0.95), postural instability (OR 0.53, 95%CI 0.32–0.87) and Akinesia (OR 0.57, 95%CI 0.37–0.90) had been improved in 2017. For a subjective to treatments were getting better. There were wishing to treat iPS cells (62.0%).
Conclusions: In the future, we need to examine the symptoms. The reason for proportion of the elderly people to the whole society increases, and the contribute reason why the elderly person's chance to participate in the society may increase. However, PD patients in an aging society would be more required to consider not only diseases but also problems caused by aging.

P13.03

What factors predict hospital admissions in community-dwelling people with Parkinson's?
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Background: People with Parkinson's (PwP) are more likely to be admitted to hospital, on average have a longer admission and are more likely to have a hospital related complication during their stay. Previous studies have looked at the reasons for hospital admission in PwP, however few have looked at baseline factors that could precipitate hospital admission in the Parkinson's population.
Methods: This study was nested within the prospective, longitudinal Northumbria Care Needs Project. The study included all patients with a diagnosis of Parkinson's or Parkinson's disease with dementia (PDD) of Hoehn and Yahr stage III-V11 and those with Parkinson's plus syndromes. Baseline data included demographic and clinical data, examining motor and non-motor symptoms, and Quality of Life. Data on hospital admissions across a two-year period were collated from a review of clinical records. Admissions for any causes were recorded but elective admissions were excluded. Data collected included total number, dates and duration of admission.
Results: One hundred and sixty two patients (99 males and 63 females) consented to be part of the study and had baseline data collected. The mean age was 73.9 years (SD 7.80, range 52–90), with 99 (61.1%) males. One-hundred and forty-two PwP (87.7%) had a diagnosis of Parkinson's, 10 (6.2%) had PDD, 5 (3.1%) MSA and 5 (3.1%) PSP. Seventy-one PwP (43.8%) had at least one

hospital admission and 17 patients (10.5%) had 3 or more admissions to hospital. Those admitted to hospital had poorer cognition, more non-motor symptoms, poorer quality of life, slower timed-up-and-go test scores and more abnormal swallow. Dizziness, cognitive impairment, anxiety and gait dysfunction were independent risk factors following multivariate analysis. PwP who lacked support from family or close friends were also more likely to be admitted to hospital.
Conclusions: Our study looked at a large number of potential risk factors for hospital admission and emphasises the importance of non-motor symptoms in predicting admission. The factors identified are all potentially modifiable. A cost-benefit analysis of the potential for the costs of early stage preventative care input and prospective long-term care planning to be offset by reduced use of hospital services in later stage disease is merited.

P13.04

Intestinal microbial diversity and Parkinson's disease severity
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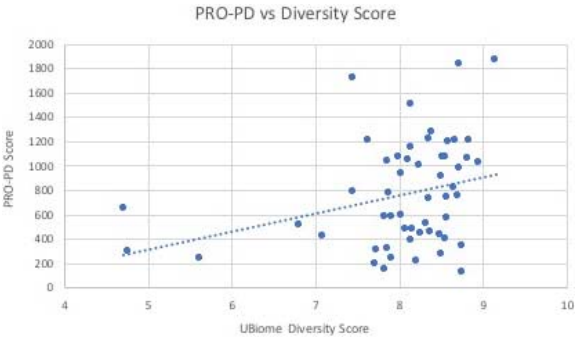
Background: There is growing awareness that intestinal bacterial microbiome is different in Parkinson's disease (PD) compared to controls. In the general population, high microbial diversity is associated with decreased incidence of disease. Similarly, recent studies are showing lower intestinal diversity in PD compared to controls. While bacterial diversity may offer protection against development of disease, it is not known whether microbial diversity is associated with symptom severity.
Objective: The goal of this study was to evaluate whether microbial diversity was associated with severity of PD symptoms.
Methods: 16S sequencing was performed by UBiome on 54 consecutive individuals with PD. Simpson's Diversity Index was used to assess microbial diversity by looking at the number of species present and the relative abundance of each species. Diversity scores ranged from 0–10, with 10 implying the most diverse microbiome and 0 the least diverse. The PRO-PD was used as the primary outcome measure of patient reported symptom severity. For constipation, patients rated the severity of that symptom using a slider bar ranging from 0–100, with 0 representing healthy, daily bowel movements and 100 representing severe constipation.
Results: Although these results did not reach statistical significance, lower diversity scores were associated with fewer reported PD symptoms and less constipation. After adjusting for age, gender, and years since diagnosis, the average PRO-PD score worsened by 121 points for every 1-point increase in Simpson's Diversity Index (121.17; P=0.084).
Conclusions: Simpson's Diversity Index did not correlate with constipation or patient-reported PD symptom burden. While prior studies suggest diversity may offer protection against the development of PD, these data suggest microbial diversity is not associated with disease progression. As more microbiome mapping is becoming readily available to the public, providers should be prepared to review with patients the limited value of the data they are being given as it relates to disease severity.



P13.05

Role of complex Parkinson's clinic in movement disorder clinic
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Introduction: Majority of patients attending our movement disorder clinic have a time slot of 20 minutes for consultation. For a complex Parkinson disease (PD) patient and carer this may be insufficient. Many patients in complex stages of PD are older and have various non-motor, cognitive and motor symptoms needing longer consultation to decide an appropriate management.
Methods: Our Movement disorder clinic have over 700 patients and over 500 of these are PD. Nearly 100 of these patients are complex either due to cognitive problems and/or motor fluctuations as well as multiple non-motor symptoms (NMS).
In April 2018 our clinic team changed frequency of one weekly routine clinic to monthly complex clinic, seeing only 5 patients with 45 minutes slots, combining consultations to strengthen our decision making, improving management and learning.
Patients attending this clinic were selected by a team member and all were under routine follow up otherwise. Most patients booked into this clinic were seen once and transferred back to routine follow up clinic.
We collected demographic data, medication use, motor and NMS, assessment of cognition, advance therapy, management of multiple drug regimen for PD, driving, mobility, falls, bowel & bladder management, sleep issues, drug related side effects, autonomic dysfunction, wt.loss.
Results: 26 patients were seen in 5 clinics. All patients were seen together by 2 consultants and PD nurse specialist.
Mean age of patients 69.8yrs, 17 male. Mean duration of PD was 11.1 yrs. Mean H&Y 3.4. 15 patients had dyskinesia and all wearing off. Mean NMS were 2.4.
Mean nos. of anti-Parkinson's drugs were 3.2 (2–5). All patients were on Levodopa, additionally 9 were on long acting D-agonists, 7 on MAOB inhibitors, 11 on COMT inhibitors.
12 patients were on advance treatment (Apo go), one on Duo dopa (LCIG), one had DBS.
7 patients were on either Rivastigmine or Memantine, 3 were on Quietiapine
[N.B. List of NMS with frequency and clinic benefits to be provided in poster]
Conclusion: Patients with complex stage of PD have multifocal management requiring more time and multidisciplinary approach in the clinic. These can only be addressed with longer clinic consultations and joint approach to improve communication.

P13.06

Tracking freezing of gait in Parkinson's disease: A model identification objective method for predicting and preventing FoG episodes in PD

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Introduction: Parkinson's disease (PD) is a neurodegenerative-disease which is characterized by the convolution of cardinal motor-symptoms. The main-cause of PD is a loss-of- dopaminergic, sub-cortical-neurons, which leads to motor-impairments [1]. To validate the severity-of frequency of gait (FoG) presently, clinicians use patient-questionnaires such as the new-FoG-Questionnaire (NFoG-Q)[2] that rely-on-patient self-report. There is a growing need to develop automated methods for detecting FoG, with ultimate-goal of being able not only to determine but also to predict and prevent episodes of FoG. In-this-connection, we developed a new-method which automatically detects the onset-and-duration of FoG in PDs in the given interval-of-time (real-time), employing inertial-sensors.
Methods: In this study, we develop-new-methods to automatically-detect the onset/duration of FoG in PD-patients in real-time, employing inertial-sensors. We first-build a physical-model that describes trembling-motion during the FoG-events. We then design a generalized likelihood-ratio-test framework-to-develop a two-stage detector-for-determining zero-velocity and trembling-events during-gait. Thereafter, to filter-out-falsely detected-FoG-events, we develop a point-process-filter that combines the output-of-the-detectors with information about the speed-of-the-foot, provided by a foot mounted inertial-navigation-system. We computed the probability of FoG by using the point-process filter to determine the onset/duration-of-FoG event. Finally, we validate the performance-of-proposed system-design using real-data gathered from PD cases (while on gait tasks). We compare our results with an existing method that uses accelerometer-data.
Results: The results indicate that our method yields 81.03% accuracy in detecting FoG events and a threefold decrease in the false alarm rate relative to the existing method.
Conclusions: We introduced a new system-design to address the problem-of-finding of FoG using inertial-sensors. Future-plan is to develop an adaptive-design-framework which learns the system-parameters based on Fog-events and dynamically adjusts the model-parameters. Development of a valid, reliable, and dynamic-method of real-time identification-of-FoG is critical to better-understand patterns and frequency of FOG in daily life. Significance: An enhanced-understanding of FoG may lead to development of novel-treatment-approaches to address FoG-events in real-time.
References:
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P13.07

Role of microelectrode recording (MER) in accurate targeting subthalamic-nuclei (STN) deep brain stimulation (DBS) in Parkinson's disease

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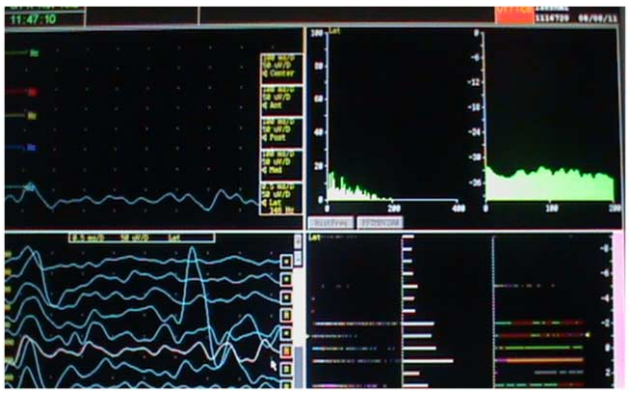
Objectives: Parkinson's disease (PD) is a neurodegenerative disease, is caused by damage to the central-nervous-system(CNS). PD is characterized by combination of cardinal motor-symptoms: tremor, Bradykinesia, rigidity, and postural-instability. Despite all of the studies-on-PD, the formation-mechanism of its symptoms remained-anonymous. It is still not obvious why damage only to the substantia-nigra-pars-compacta(SNpc), a small part of the brain, causes a wide-range-of-symptoms. Moreover, the causes-of-brain-damages remain to be fully-elucidated. The purpose is to study the role of microelectrode-recording (MER) and correlation of MER with the final-tract chosen during-bilateral STN-DBS performed at a specialised centre in South-India.
Methods: 46 patients were included in this study. Ethical-clearance was obtained from the institute. The mean-age was 58.1+9.1 years, mean-disease-duration(8.8+3.64yrs), mean-UPDRS-score in 'off'/'on' state was('52.7+10.6'/'13.4+5.0'). 5 Channel-Medtronic Lead-Point-MER is done in all PD-patients.
Results: Mean number of 5 multiple-channels in which STN-MER was detected right-side=3.5+1.1, left-side=3.6+1.04. The 92sides were computed and concordance-rate with most-finer-signal and maximum-width of signal-recording were and combinations were analyzed. Final-channel selected were central in 39/92-42.3%, Anterior in 31/92-33.7%, Medial in 15/92-16.3%, Posterior 4/92-4.3%, and Lateral in 3/92-3.2%. Concordance with highest recording (with the track chosen) was seen in 58.7%, mean-maximum length-of-recording was 5.3 + 1.3 mm, maximum-length-of-STN was in the chosen-track in 48%, and Concordance with either highest recording or maximum-length was noted in 64%. In 28-patients, the final-tract did not correspond either to the tract with highest-recording or maximum-width-of-MER. 13had central-tract, 8had anterior, 7had medial-tract as final-tract, Mean-length of MER in these-channels was 2.3+1.8mm. 93.48% of patients showed STN-recording in the final-channel-chosen. Absence-of any recording-from-STN in the final-tract selected was noted in 6/92-6.52%(0.0652). Out of six-patients, one had no MER-recording in any of five-channels and lead was placed in central-channel. 2patients had medial,2anterior and 2central-channels as their final-tract(selected based on macrostimulation).
Conclusions: In our study, we find that MER-gives proof-of-correct-positioning-of-electrode ensures accurate-detection of STN precincts its exact-coordinates in a more objective-way. MER-enhances safety, accuracy and efficacy-of-DBS electrode-implementation. Thus, MER-corroborates presence-of-abnormal STN-neurons. Unperturbed-MER-definitely can confirm the clear position-of-electrodes and bolsters the confidence of the neuroscientists-neurologists-neurosurgeons that they are in the right-target. Availability of MER-results in a vast-data regarding functioning-on-neurons situated-deep in the brain may further-help in unraveling-mysteries-of-brain.



P13.08

A cross-sectional natural history of Parkinson's disease as reported by >10,000 patients

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There has been no systematic research to characterize the course of neurological disease as reported directly by patients. Using natural language processing (NLP), expert clinical curation, and machine learning (ML), we analyzed the Patient Reports of Problems (PROP) from Parkinson disease (PD) patients who volunteered to answer in their own words: (1) What bothers you the most about your PD? and (2) In what way does this problem affect your daily functioning? Participants were also asked to reply to what bothers them the 2nd most, up to 5 bothersome problems. From February-August 2018, >10,000 consenting patients worldwide entered their verbatim PROP replies, age, and date of PD diagnosis by computer keyboard (about 40% used mobile/tablet devices) on the Michael J Fox Foundation (MJFF) FoxInsight.org research platform, with an ongoing accrual rate of about 1,000 new patients/month.

Using NLP-derived and clinically-curated terms, motor and non-motor symptoms were classified with respect to age and 0–10 years since diagnosis. Motor and non-motor symptoms constituted 60% and 40% respectively of patient-reported problems: Tremor was reported at all disease durations; Rigidity and Bradykinesia were more frequent with increased duration of PD; Postural Instability (imbalance, unsteadiness) was reported early within 0–3 years of diagnosis, and was more common with age of the patient and longer duration of PD. Sleep, Pain, Mood and Cognition problems were more frequent with increased duration of PD. Fatigue symptoms were similar across duration of PD and age. Constipation was more frequent with increased age and duration of illness. These relationships will be illustrated by 3-D videos.

The PD-PROP represents the largest compilation of patient-reported verbatim problems for any neurological disorder. The verbatim patient reports and application of NLP/ML techniques show utility in capturing bothersome problems and provide a cross-sectional natural history of PD from the perspective of patients – to be further informed as patients are invited every six months to update their PROP replies and longitudinal data accrue. The PD-PROP can be further customized to develop fit-for-purpose clinical outcome assessments applicable to clinical trials. De-identified PROP data are being made available to scientists for analysis by the MJFF.

P13.09

Motor subtype change in Parkinson's disease: A retrospective study

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Background and Objective: There has been substantial debate regarding if the motor subtypes of Parkinson's disease represent different stages of disease or different diseases at all, with evidence being inconclusive. In our country, there have been scarce reports on the topic. Therefore, we performed a retrospective analysis to find out the prevalence of subtype change, its pattern and clinical correlates.

Methods: Cases were selected from the movement disorders clinic database (2014 to 2017). Initial motor subtype was registered as the predominant impairment at onset in: tremor-dominant (TD), Non-Tremor-Dominant (Non-TD) including rigidity/bradykinesia(R/B), postural instability/gait disorder (PIGD). Actual subtype was assessed with MDS-UPDRS part III subscores in: TD, and Non-TD as the sum of PIGD, and indeterminate (IND) subytpes. Motor subtype change was registered. We compared variables between subtype change groups.

Results: Of 105 patients with PD, male (67.6%; n=71), mean age 60.3±11.9 years; age at onset 54.7±12.8, and disease duration 7.2±5.4 years. Mean Hoehn &Yahr (H&Y) 2.4±0.9. TD was the most frequent initial subtype (62.9%; n=66), yet the most common actual subtype was PIGD (56.2%; n=59). Change of motor subtype in 55% (n=58) patients, the most common from TD to Non-TD (57%, n=34), the most frequent of which was TD to PIGD (88%, n=30). We found significantly higher mean H&Y stages either in the No change, and TD to Non-TD group than in the Non-TD to TD when comparing means (2.5±0.9 and 2.6±1.0, vs 2.0±0.6; p=0.008), and stages (mild-moderate-severe, p=0.006); also higher prevalence of hypertension in patients without change (40.4% vs 15.7% vs 25.0%; p=0.037). We found no significant difference in age at onset or disease duration.

Conclusion: We found a significantly higher proportion of moderate to severe disease in patients with no change of subtype, and in those with change from TD to Non-TD, without difference in age at onset or disease duration, which suggests change isn't simply progression of disease.

	No change n= 47	TD to Non-TD n= 34	Non-TD to TD n= 24	P
Male gender	31 (66.0)	25 (73.5)	15 (62.5)	0.641
Age	61.3 ± 10.9	58.1 ± 13.2	61.3 ± 12.1	0.619
Hypertension	19 (40.4)	5 (14.7)	6 (25.0)	0.037
Age at onset	55.1 ± 11.9	52.9 ± 13.9	56.7 ± 12.9	0.573
Duration	6.0 (1.0 - 20.0)	6.0 (1.0 - 21.0)	4.0 (1.0 - 23.0)	0.351
Hoehn & Yahr				
Mean	2.5 ± 0.9	2.6 ± 1.0	2.0 ± 0.6	0.008
Mild (1-2), n (%).	23 (48.9)	15 (44.1)	20 (83.3)	0.006
Moderate (3), n (%).	20 (42.6)	13 (38.2)	4 (16.7)	
Severe (4-5), n (%).	4 (8.5)	6 (17.6)	—	
0, Asymptomatic	1 (2.1)	—	—	0.060
1, Unilateral involvement.	4 (8.5)	4 (11.8)	5 (20.8)	
2, Bilateral disease without impairment of balance.	18 (38.3)	11 (32.4)	15 (62.5)	
3, Bilateral disease with impaired postural reflexes.	20 (42.6)	13 (38.2)	4 (16.7)	
4, Severe disease, but still able to walk or stand unassisted.	4 (8.5)	5 (14.7)	—	
5, Confinement to bed or wheelchair unless aided.	—	1 (2.9)	—	

PIGD, Postural Instability/Gait Disorder.

CLINICAL SCIENCE: Behavioral disorders

P14.01

Parkinsonism in association with dihydropteridine reductase deficiency

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We report a 16-year-old man with disorders of tetrahydrobiopterin metabolism due to DHPR deficiency. He revealed moderate mental retardation, parkinsonism, and spastic paralysis with levodopa and 5-hydroxytryptophan (5-HTP) supplementation from age 2 months. Brain magnetic resonance imaging (MRI) showed high intensity areas in bilateral frontal and posterior deep white matters on fluid-attenuated inversion recovery (FLAIR). Coronal FLAIR image showed high signal in bilateral pyramidal tracts. Single photon computed tomography (SPECT) imaging of the dopamine transporter was normal. This imaging indicates no dopaminergic cell loss. Our patient had no motor fluctuations or dyskinesias. Our case report suggests that early diagnosis and replacement therapy with levodopa and 5-HTP might have protective effects on brain neurons during development.

P14.02

Lewy body dementia prevalence and acetylcholinesterase inhibitor use in Florida

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Objective: To characterize the LBD population in Florida using a statewide Patient Centered Outcomes Research Institute (PCORI)-funded clinical data research network, OneFlorida Clinical Research Consortium (CRC).
Background: Lewy body dementia (LBD) is the second most common dementia in the United States, however there is limited information about the characteristics of this patient population. Cholinesterase inhibitors are generally considered standard of care in LBD, but the frequency of use is not well reported.
Methods: Patients in the OneFlorida CRC with an ICD-9-CM 331.82 or ICD-10CM G31.83 diagnosis code during at least 1 encounter from January 2012 through March 2018 were included. Prevalence was calculated by comparing to the whole OneFlorida CRC sample and stratified by age group. The gender distribution of LBD in Florida and racial/ethnic demographics were assessed. Frequency of acetylcholinesterase inhibitor use was assessed using prescription information (RXCui code).
Results: Approximately 3700 individuals with a diagnosis of LBD between 2012 and 2016 were identified. Among 7 million patients in the One-Florida CRC the prevalence of LBD was 0.05%. Males accounted for 55.7% of individuals diagnosed with LBD. LBD was most commonly diagnosed in individuals identifying as white (77.6%), followed by African American/black (10.8%) and Asian (1.1%). Almost 19% of the population identified as Hispanic. Less than half of individuals with LBD in Florida received a cholinesterase inhibitor during the examined period. Donepezil was most commonly prescribed (23.8%), followed by rivastigmine (11.5%), and galantamine (1%).
Conclusions: LBD is diagnosed in individuals in Florida across racial-ethic categories. African-Americans account for a lower percent of LBD cases than the proportion of African-Americans in Florida (16%), suggesting that LBD may be underdiagnosed in this population. The male predominance seen is consistent with other population-based studies in LBD. Fewer than half of individuals with LBD received a cholinesterase inhibitor trial, a clear area to target improvement.

CLINICAL SCIENCE: Cognition/Mood/ Memory

P15.01

Action observation affects hand movement amplitude more than simple cues in Parkinson's

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Objectives: Although visual cues can facilitate aspects of gait in people with Parkinson's (e.g., step length), these cues may be less helpful for manual actions, and may not have lasting effects. Observation of human movement activates neural structures involved in action execution and may provide a more powerful stimulus for movement. Action observation has been found to facilitate hand movements in Parkinson's, and intervention studies suggest that action observation training may improve gait and increase functional independence. However, action representation may be altered in Parkinson's, and there may be an increased reliance on visual mechanisms, so it is unclear whether human movement is more effective than simple visual stimuli for people with Parkinson's.
This study aimed to (i) compare effects of observing human movement vs. a simple moving cue on hand movements in people with Parkinson's and a control group, and (ii) explore mechanisms of action representation by analysing eye movements during observation.
Methods: Participants with idiopathic Parkinson's (N=22; Hoehn & Yahr stage 1–3) and healthy age-matched controls (N=23) observed and imitated videos of simple sequential movements, depicted by either a human hand or a simple shape. Motion tracking was used to measure effects on the speed and amplitude of hand movements, and eye gaze was recorded to explore mechanisms of attention and prediction.
Results: Both groups exhibited increased modulation of movement amplitude when observing the human hand than with the simple cue. Participants made larger saccades and fixated the movement end-point later when watching the shape, suggesting closer tracking of the hand.
Conclusions: These results indicate that both people with mild to moderate Parkinson's and healthy older adults modulate their hand movements to a greater extent in response to human action than simple moving cues, and may observe human movements more closely. This suggests that action observation could provide an effective tool for rehabilitation of manual tasks via activation of sensorimotor networks.

P15.02

Psychiatric morbidity in Parkinson's disease in northeast region of Romania

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Background: PD is the second most common chronic neurodegenerative condition in older people. The prevalence of PD in different countries have varied widely, around 1% in people aged above 65 years. Motor symptoms are just the "tip of the iceberg" of clinical manifestations of PD. Besides motor symptoms, PD is characterized by many non-motor symptoms, which include cognitive decline, psychiatric disturbances (depression, psychosis, and impulse control), sleep difficulties, autonomic failures (gastrointestinal, cardiovascular, urinary, thermoregulation) and pain syndrome.
The aim of this study was to evaluate the psychological and psychiatric disturbance of Parkinson disease patients and the statistical bilateral correlation between duration, severity, gender, the age of the patient and this manifestation.
Method: our prospective and observational study consisted in a sample of 94 consecutively evaluated subjects with Parkinson disease in our neurological service between 1 Jan 2017 – 1 nov 2018. The patients were investigated by clinical examination, neuropsychological test (Montreal cognitive assessment –MOCA Global Assessment of Functioning – GAF scale, Hamilton Depression Rating Scale – HAM-D, Questionnaire for Impulsive-compulsive Disorders in Parkinson Disease rating scale QUIP-RS, brain computed tomography. Statistical analysis by One Way ANOVA.
Results: Over 60% of patients have cognitive impairment and 84% depression. Only 23% of them have compulsive impulsive behavior (punding, >sexual).
The level of education, gender, age, duration of the illness, severity, the treatment seems to have an influence in appearance and evolution of psychiatric manifestation.
We find a correlation between depression end duration of illness (p=0,08), a fluctuation of cognitive performances related to age and treatment (p=0,019) compulsive-impulsive manifestation related to age and duration of illness (p=0,024).
Conclusion: This data suggests that psychiatric morbidity is highly prevalent in patients with PD. In advanced PD, non-motor symptoms dominate the clinical picture and are associated with severe disability, impaired quality of life. Further studies are required to evaluate the efficacy of various measures for management with the multidisciplinary approach of psychiatric morbidity in patients with PD.

P15.03

Measuring salivary cortisol levels in person with Parkinson's disease

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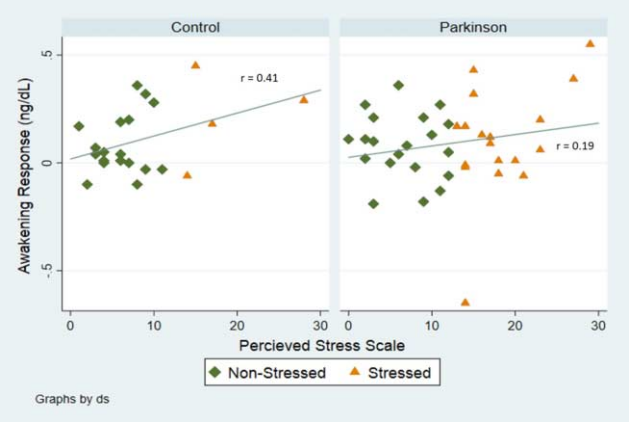
Background: Psychological stress is known to exacerbate the symptoms of Parkinson's disease (PD) and in animal models is deleterious to the nervous system. Increased stress may contribute to the development of and faster disease progression in PD. Salivary cortisol is an objective measure of stress and corresponds with serum cortisol, however it is not well characterized in PD. Better characterization could assist in future studies examining the interplay of psychological stress and stress reduction in PD.
Objective: To better characterize the relationship between salivary cortisol and psychological stress in persons with PD.
Methods: Saliva samples were obtained at home at four times: immediately upon awakening, 30 minutes after that, at noon, and right before bedtime. Cortisol was averaged across all three days for each time point. Data were first inspected to ensure there were no cortisol outliers and extreme outliers (>3 standard deviations) were deleted. Awakening Response was computed by taking 30-minutes after awakening (AM2) – awakening (AM1).
Results: We analyzed salivary cortisol in 62 subjects in four groups – high (n=4) and low stress (n=22) controls and high (n=18) and low stress (n=20) persons with PD. Stress categories were defined by the Perceived Stress Scale (PSS)=13. Participants were well matched in regard to age and gender. Subjects with PD had similar disease severity between the stressed and non-stressed groups. Average cortisol levels were highest in the stress controls, followed by stressed PD, with lowest levels in non-stressed PD and controls – however due to large variability these differences were not statistically significant. Perceived stress scale correlated strongly with anxiety and depression scales. All the mood scales had at least a trend towards significant correlation with the cortisol awakening response but this relationship was consistently more robust in controls compared to persons with PD.
Conclusions: Persons with PD appear to have similar pattern of diurnal variation in cortisol levels as persons with out PD. However it also appears that cortisol may be less reactive to stress in persons with PD and does not appear to correlate as strongly with measures of stress, and mood.



P15.04

Age-related cognitive effects of SIRT6 overexpression: Emerging role of astrocytes

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The increased in human lifespan poses many challenges, among them age-related neurodegenerative diseases such as Parkinson's disease. Mice overexpressing the NAD+ dependent deacylase, SIRT6 have been associated with increased health and longevity. SIRT6 regulates diverse cellular functions such as transcription, genome stability and metabolic related pathologies such as obesity. Here, we investigate the role of SIRT6 in cognitive and behavioral

functions in aged mice. Young and old of wild type (WT) and SIRT6 overexpressing mice (MOSES mice) were examined using a battery of behavioral tests. In comparison to aged WT littermates, MOSES mice have significant improved spatial memory performance. Immunohistochemistry of the hippocampus and cortex showed a significant increase in early neurogenesis and astrocytes' number and a significant reduction of apoptosis and DNA damages in aged MOSES mice. RNA expression analyses of the hippocampus of aged mice revealed an increase in the RNA editing enzyme ADAR. Examination of more than 5000 RNA editing sites in the hippocampus of young and old, WT and MOSES mice found a young-like editing status in hundreds of sites in old MOSES mice, including genes which are tightly involved in learning and memory processes. Altogether, these findings show that SIRT6 is a key regulator of memory and suggest it as a potential target for treating age related cognitive decline.

P15.05

Cognitive associations with comprehensive gait and balance measures in Parkinson's disease

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Objective: Gait and balance disorders are a cardinal feature of Parkinson's disease (PD) that lead to increased fall risk and reduced quality of life. Gait and balance are no longer considered automatic tasks and are dependent on cognitive control. However, the extent to which specific gait and balance characteristics are related to cognition in PD remains unclear. Furthermore, associations between gait and cognition and balance and cognition have not been assessed within the same cohort. We aimed to determine which particular gait and balance characteristics are related to cognitive function and how they differed in an analysis from the same cohort.
Methods: One hundred and ninety nine people with PD were recruited to the Pacific Udall Center (PUC; VA Puget Sound/University of Washington, Seattle; Oregon Health & Science University/Portland VA Medical Center, Portland; and Stanford University). Comprehensive gait measurements were collected over a two-minute continuous walk with 180 degree turns and comprehensive balance measures were collected during a 60-second quiet standing task. Gait and balance measures were collected using six inertial sensors (APDM, Inc.). Four domains of cognition were assessed: global cognition, frontal-executive attention, learning and memory, and visuospatial function. Correlations and multivariate linear regression were used to determine independent associations, controlling for age, gender, years of education, disease duration, disease severity (MDS-UPDRS III), and site.
Results: Gait domains of pace/turning and variability were most strongly associated with frontal-executive function. The strongest associations were demonstrated between the performance on the Stroop task with both turn duration (β.439, p<.001) and stride length (β.334, p<.001). In contrast, balance domains of sway and jerkiness were most strongly associated with visuospatial function assessed by the Judgement of Line Orientation (β -.276, p<.001).
Conclusions: Different gait and balance domains were associated with specific types of cognitive domains. The observed relationships between gait or balance with cognitive functions suggests shared cerebral cortical circuitry for mobility and cognitive functions. These findings suggest that depending on the mobility deficit, therapeutics should be tailored in order to improve gait and balance and ultimately reduce falls.

P15.06

How does Parkinson's affect gesture and communication about spatial information?

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Objectives: Visuospatial processing is affected in Parkinson's with reduced performance on tasks involving spatial working memory, visuospatial construction, and spatial navigation. Visuospatial cognition is critical for the general production of gestures, which arise from spatial and motor cognitive representations. Furthermore, people gesture particularly frequently when describing spatial information. However, little is known about changes to gestures depicting spatial information in Parkinson's. We aimed to characterise how Parkinson's affects the ability to gesture about space.
Methods: 37 people with mild-to-moderate Parkinson's [mean (SD) age=65.00 (7.3), 12 female] and 33 age matched controls [age=66.00 (6.0), 21 female] were video-recorded as they described their house layout to a listener, who sketched a floor-plan based on the description. The descriptions were transcribed, and gestures depicting spatial information related to the house layout were coded for whether they contained the following spatial information: a. location/position, b. direction, c. size d. shape.
Results: The overall rate at which people gestured did not differ between the Parkinson's [mean (SD) gestures/100 words=9.92(6.4)] and control [11.3 (6.87)] groups. However, the content of the gestures depicting spatial aspects was altered. People with Parkinson's produced simpler gestures [1.39 (.34) spatial information per gesture] than controls [1.64 (.37)]. Furthermore, people with Parkinson's gestured significantly more about direction than controls, whereas controls gestured significantly more about shape and size.
Conclusions: People with mild-to-moderate Parkinson's gestured as often as controls, replicating our previous findings. This suggests that co-speech gestures could be considered within strategies to improve and maintain communication in Parkinson's. However, the Parkinson's group made fewer complex gestures and there were clear differences in the type of spatial information conveyed. We are currently conducting follow-up analyses to test what may motivate these differences in depicting spatial information, with a focus on the cognitive operations and mental representations underlying gesturing in PD.

P15.07

Analysis of sub-threshold errors reveals no deficit in response inhibition in mild to moderate Parkinson's

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Background and Objectives: Successful motor inhibition relies on the fronto-striatal circuits affected by Parkinson's disease. However, previous studies examining response inhibition in Parkinson's have

produced conflicting findings, and it remains unclear whether and how Parkinson's may affect control over actions. Here, we measured continuous response force to provide a sensitive measure of response activation and control to examine sub-threshold action control deficits (i.e. partial errors) without the need for brain imaging.
Methods: 25 people with mild to moderate Parkinson's (8 female, mean age 63.84, mean UPDRS III 26.64) and 23 healthy control participants (11 female, mean age 68.91) completed two common tasks assessing response inhibition and conflict: the Stop Signal Task and the Simon Task.
Results: No significant differences in response inhibition were found for either group in either task. In both participant groups, sub-threshold partial errors in response force were detected on approximately 27–28% of otherwise correct (according to the button press) stop trials on the Stop Signal task, and 10–12% of otherwise correct incongruent trials in the Simon task. Moreover, further examination of the temporal dynamics of these effects (using delta plots and conditional accuracy functions) yielded no reliable evidence of any group differences.
Conclusions: We found no significant group differences in motor inhibition even with sensitive methods of response measurement and analysis. This may suggest that there is no deficit in behavioural response inhibition in mild to moderate Parkinson's, contrasting with some previous literature. We discuss our findings in the context of the heterogeneity of Parkinson's, and the difficulties of behavioural and experimental patient research.

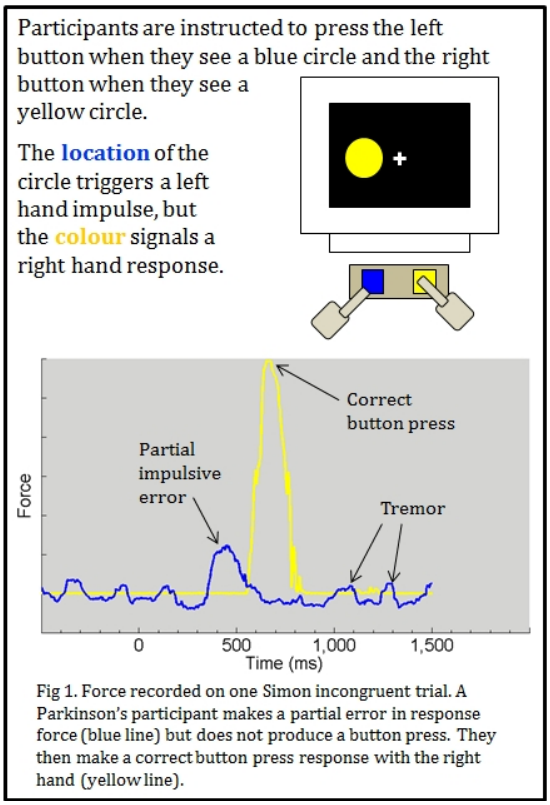

Fig 1. Force recorded on one Simon incongruent trial. A Parkinson's participant makes a partial error in response force (blue line) but does not produce a button press. They then make a correct button press response with the right hand (yellow line).

P15.08

Lessons from the cognitive rehabilitation program of the Parkinson Foundation of Colombia
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Two hundred years have happened since James Parkinson described the Parkinson Disease in <>. At that time the emphasis had been placed on the motor triad of bradykinesia, rigidity, and resting tremor. However, over the past decade, research studies have described the substantial cognitive changes that could occurred from early stages to last stages of PD. The characterization of the cognitive profile in PD point out the difficulties in memory, executive functions, problem solving and visuospatial abilities, as well as a more generalized cognitive impartment in the Parkinson's disease Dementia (PD-D). Thus, cognitive dysfunction in PD can be classified as being either domain-specific, for which the severity of the impairment does not fall under the established criteria for dementia, or as a being severe enough affecting various cognitive domains and daily life activities, fulfilling with dementia criteria. It does not mean that all of the patients with PD should develop a MCI (Mild Cognitive Impairment)/PD-D. Therefore, according to the necessity of patients with PD and their families, we build a Cognitive Rehabilitation Program with the following criteria: 1) Group building: Cognitive Screening to organize patients in regard with the Cognitive performance (PD without MCI, PD-MCI, PD-D; 2) Cognitive Program Setting: Three Cognitive Domains (Attention, Memory and Executive Functions), 3) Performance Tracking. After four years of a hard labor with hundred of patients, we learned in the Parkinson Foundation of Colombia the following lessons to rebuild our Cognitive Rehabilitation Program: 1) Outcome Time: brain is not too different from body, nobody becomes fitness in a month; 2) Cognitive Profiles: there is not one PD Profile, it changes through the time; 3) Performance Tracking: avoid retest effects; 4) Cognitive Program Setting: Integral Program works better than a Single Domain Program; 5) Mood Disorders and Anxiety Disorders: Depression and Anxiety disorder affect Cognitive Performance, mental health support is necessary; 6) Misconceptions about Aging: Aging bias affect cognitive performance and subjective assessment of cognitive functioning.

P15.09

Investigating cognition in clinical routine in people with Parkinson's disease
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Background: In our rehabilitation clinic the Short Orientation and Memory Concentration Test (SOMCT) is used as a quick test of cognitive functions. In addition, when cognitive decline is clinically suspected, patients are assessed with the Mini Mental State Examination (MMSE) before extensive neuropsychological assessment is conducted. Reports in the literate show that the Montreal Cognitive Assessment (MoCA) is more sensitive to detect impairment in Patients with Parkinson's disease (PwPD), especially in the early stages of the cognitive decline.
Aim: To investigate whether MoCA or MMSE are better suited to assess cognitive decline in clinical practice to detect early signs of cognitive impairment in PwPD who show normal scores in SOMCT.
Methods: we investigated 46 patients with SOMCT, MMSE and MoCA between April and October 2018 as part of our clinical routine. 3 patients were excluded from analysis due to diagnosis of Atypical Parkinson's disease. Demographic data of 43 PwPD:

- Gender: 33 males, 10 females
- Age: average 73,91 years (range 48–83)
- Hoehn & Yahr stage: average 2,74 (range 1,5-5, median: 3)
- Time since diagnosis: average 9,58 years (range 0–25)
- Subtypes of IPS: tremor-dominant: 3, akinetic-rigid: 18, mixed type: 22

Results: Of the 43 PwPD investigated with:

a) SOMTC, 29 were classified as normal (0–6 points), 14 as impaired (>6 points).
b) MMSE, 18 were classified as normal (27–30), 25 as impaired (<27).
c) MoCA, 4 were classified as normal (27–30), 39 as impaired (<39).

Additional details are shown in tab. 1.
Due to the small numbers per subgroup, no further analysis according to age, gender, subtype of PD or years since diagnosis was made.
Conclusion: These results indicate that in our sample of PwPD the MoCA is more sensitive to detect cognitive decline, in particular in PwPD who have a normal SOMCT score. It is evident that this cannot substitute in-depth neuropsychological testing.

Tab. 1.	No. of PwPD		No. of PwPD		No. of PwPD
SOMCT normal scores (0-6)	29	MMSE normal scores	16	MoCA normal scores	4
		MMSE =/<26	13	MoCA =/<26	23
SOMCT impaired (>6)	14	MMSE normal scores	2	MoCA normal scores	0
		MMSE =/<26	12	MoCA =/<26	16

P15.10

Mild cognitive impairment (MCI) subtypes after deep brain stimulation (DBS): Role of pre-operative diagnosis
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Objective: Relatively little is known about the impact of mild cognitive impairment (MCI) on the outcome of deep brain stimulation (DBS) and whether DBS increases risk of MCI. The purpose of this study was to examine cognitive outcome among persons with Parkinson's disease (PD) who did and did not have MCI before subthalamic (STN) or pallidal (GPi) DBS. Specifically, the primary question of interest was whether persons with pre-surgical single domain MCI were more likely to develop multi-domain MCI after DBS than persons without MCI.
Methods: Neuropsychological evaluation using at least two tests per each of five domains (attention, executive function, language, visual perception, and memory) was carried out before and about nine months after surgery. The International Parkinson and Movement Disorder Society (MDS) criteria (Level II) were used to identify MCI and to subtype MCI into 4 categories: single domain amnestic and non-amnestic and multi-domain amnestic and non-amnestic. 125 persons underwent unilateral or bilateral STN or GPi DBS awake using microelectrode recording, or using direct anatomical targeting under general anesthesia.
Results: Almost half of the persons had MCI before surgery, the majority of them having multi-domain MCI. After surgery, about one third of people developed MCI anew. The proportions developing MCI anew were similar after STN and GPi surgery but all cases occurred after bilateral surgery or surgery on the dominant, left hemisphere. Persons without MCI or single domain MCI before surgery were similarly likely to develop multi-domain MCI after surgery, with about one quarter to one third of persons with no or single domain MCI developing multi-domain MCI after STN or GPi DBS.
Conclusions: In our series of patients about a third developed MCI anew. Most of the MCI was of the multi-domain subtype indicating that mild declines had occurred in several domains of cognition. The absence or presence of single domain MCI before surgery was unrelated to the odds of developing multi-domain MCI. Instead, all declines occurred after bilateral or dominant hemisphere surgery.

P15.11

Facial emotion recognition in Parkinson's disease: Impact of presentation time and levodopa
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Facial emotion recognition (FER) is an important component of social interactions. In this study, we hypothesized that the deficit in FER in Parkinson's disease (PD) is more pronounced when the presentation time is short and that this may be caused by a narrowed visual scanning area. Furthermore, we investigated whether levodopa intake improved FER.
25 PD patients and 24 age-matched healthy controls without signs of depression performed an emotion identification task which consisted of 56 static photographs. 8 pictures of each of the six basic emotions anger, fear, happiness, surprise, sadness as well as 8 neutral faces were displayed with a presentation time of either 500 ms or 5000 ms in a randomized order. Eye movements were recorded using the Eyelink 1000 plus eye-tracker.
Within-groups comparision revealed that both, PD and HC, executed an increased number of errors in the short, compared to the long FER task.
PD patients in off medication state obtained a lower overall FER score than HC solely in the short task (500 ms; $p<0.05$), while there was no difference between the groups in the long task (5000 ms).
Regarding specific emotions, the only, but highly significant difference between PD and HC was found in the identification of shortly presented sadness ($p<0.001$). Levodopa intake tended to improve both the short total and sadness score, however, without reaching statistical significance. The total FER score correlated with the motor performance assessed with MDS-UPDRS part III in on medication state.
Additionally, results of eye movement analysis will be shown.
In conclusion, PD patients show a deficit in the recognition of facial emotions, in particular of sadness, when displayed briefly. This may have an impact on social life since fleeting emotional expressions may be crucial in understanding and empathizing with conversational partners.

CLINICAL SCIENCE: Sleep disorders/ Fatigue

P16.01

Circadian rhythm and sleep disorders in α-synuclein-propagation model mouse
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The intracellular accumulation of α-synuclein is the hallmark of α-synucleinopathy. REM sleep behavior disorder (RBD) is now recognized as the prodromal stage of α-synucleinopathy. The causal relationship between protein accumulation and the early phenotype as sleep disorder is unclear. To ask the question we investigate sleep condition and the circadian rhythm in α-synuclein propagation model mouse. Aggregated α-synuclein fibrils (PFFs)

spread to cortical layers and midbrain in mouse brain in a prion-like fashion. We identified some changes in circadian rhythm and sleep architecture in the process of α-synuclein propagation in mouse. We discuss the potential role of α-synuclein in neuronal network during REM sleep and the possible sleep/circadian-targeted therapy against α-synucleinopathy.

P16.02

The effect of DUODOPA treatment in advanced Parkinson's disease on sleep quality and sleep disorders

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Sleep Quality (SQ) in advanced Parkinson's disease (aPD) are among the most challenging non-motor symptoms of the disease. The Quality of Life (QoL) and the sustainable condition for daily life are affected by SP.
PD and SP are all involved at brainstem and basal ganglia. The related neurotransmitters e.i. PD is dopamine, but also we know that the cholinergic and serotonergic systems are all involved in aPD and sleep.
PD is highly complex and heterogeneous in its presentation. QoL is affected in time.
SQ includes insomnia, excessive daytime sleepiness, sleep disordered breathing, Willis Ekbom Syndromes, REM Sleep behavior disorders. And all the problems with SQ are involved in some extend in aPD.
We included 23 patients with aPH who were applied DUODOPA treatment in this study. PSG was performed in each patient just before the intervention and after 6&12 mo. Sleep architecture, SQ and sleep disturbance scales were also completed in each patient.
The study was carried out from May 2014 to November 2018. 13 males, 10 female patients with DUODOPA were studies with Hoehn Yahr Scale, UPDRS I – V scores, PDQ39, PDSS-2, MMSE, COPE, Epworth Sleepiness Scale, Beck Anxiety Inventory.
Median age for PD initiation was 55,04±5,37 and DUODOPA application age was 64,3±3,89 y.
The best improvement was achieved in Sleep Fragmentation (72%) and turning in bed from side to side (81%). The decrement in Nocturnal dystonia was 41%. Nocturnal micturition decreased by 35%. Diurnal well-being and improvement at Fatigue was around 54%. The sleep latency decreased by 37%. The score for REM Sleep Behavior disorders decreased with 30%.
Shortly, DUODOPA treatment in aPD improves the Sleep quality and Daily Life activity scores positively.

P16.03

Inverse association between objective sleep quality and early morning akinesia in patients with Parkinson's disease: Cross-sectional analysis of the PHASE study

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Introduction: Sleep problems are the most important non-motor symptoms in Parkinson's disease (PD). Slowness or stiffness in the early morning (early morning akinesia) is a major troublesome among a wide spectrum of motor and non-motor wearing-off symptoms, regardless of anti-parkinsonian medication. Some reports suggested an association between early morning akinesia and sleep quality measured using questionnaires; however, the association between objectively measured morning activity and sleep quality has not been studied.
Methods: In the present cross-sectional study of 157 PD patients (mean age, 71.4 years), we measured objective physical activity using an actigraph on the non-dominant wrist for 7 consecutive days. Low morning physical activity was determined as <100 counts/min in 2-h after rising. Five actigraphic sleep parameters were determined using objective data (sleep status and sleep onset and termination) and self-reported data (bedtime and rising time) as follows: sleep efficiency (SE); wake after sleep onset (WASO); sleep onset latency (SOL); total sleep time (TST); and fragmentation index (FI).
Results: Mean duration in low morning physical activity was 55.7 min (SD, 23.8). Means in sleep parameters were described as follows: SE, 72.1% (SD, 13.6); WASO, 104.7 min (57.9); SOL, 2.5 log min (0.9); TST, 343.6 min (104.0); and FI, 3.5 (3.4). In multivariable linear regression models adjusted for potential confounders, such as age, gender, Hoehn-Yahr stage, daytime physical activity levels, BMI, smoking and drinking status, socioeconomic status, hypertension, diabetes, sleep medications, levodopa equivalent dose, and REM sleep behavior disorder symptoms, Significant associations between objective sleep quality and low morning physical activity duration were observed (SE per %: β, -0.396; 95% CI, -0.609 to -0.184; P<0.001; WASO per min: β, 0.057; 95% CI, 0.004 to 0.110; P=0.034; SOL per log min: β, 6.138; 95% CI, 2.671 to 9.605; P=0.001; and FI per unit; β,1.049; 95% CI, 0.196 to 1.902; P=0.016) but not TST (P=0.84). These associations were consistent with the results using different cut-off values of physical activity (50 counts/min) and duration (1-h after rising).
Conclusions: Objectively measured sleep quality was significantly associated with early morning akinesia in PD patients. Sleep therapy might be a clinical option for early morning akinesia.

P16.04

Tele-monitored tDCS (Tele-tDCS) for Parkinson's disease related fatigue

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Background: Fatigue is one of the most prevalent and under-assessed non-motor symptoms in PD. Transcranial direct current stimulation (tDCS) is a portable non-invasive brain stimulation device that utilizes low current to alter brain activity. We designed a tele-monitored tDCS (tele-tDCS) protocol to assess feasibility, safety and explore the therapeutic potential of tele-tDCS for Parkinson's disease (PD) related fatigue. We utilized a live video-conferencing platform and specifically designed equipment.
Methods: Preliminary analysis of eighteen PD patients, age 35–89 that participated in a double-blind, randomized, sham-controlled study. Each participant completed 10 tDCS sessions (20-minute, 2.0-mA, bi-frontal DLPFC montage, left anodal), over a span of two weeks. After completion, 10 additional open-label sessions were offered. Tolerability, safety, and compliance were evaluated. Preliminary clinical effects were measured with the Fatigue Severity Scale (FSS).
Results: Seventeen participants completed 330 tele-tDCS sessions; one subject chose not to complete the 10 optional sessions. Tolerability of 2.0 mA stimulation with = 6 on the Visual Analog Scale for Pain (VAS-Pain) was 100%. Systematically recorded side effects were comparable with previously published studies using conventional tDCS (in-lab). No serious adverse events were reported. Compliance was 100% as subjects completed all required visits with no attrition or interruptions. Preliminary fatigue

clinical effects of 10 sessions showed a significant decrease of FSS only in real-tDCS (mean 16% decrease in FSS, p=0.05); however, there was no significant difference between groups. Further analysis of 20 real-tDCS sessions in nine subjects showed a further decrease in FSS (mean 27%; p=0.013).
Conclusion: At-home tele-tDCS therapy is safe and well tolerated by PD patients, with the advantages of ease of recruitment and subject compliance. Acceptability was achieved by easy setup and intuitive design of the device. At-home tele-tDCS therapy shows potential to remediate fatigue symptoms in PD, especially after 20 sessions. The small sample size limits efficacy conclusions. Our paradigm may be influential in designing future studies that will facilitate clinical trials with a larger subject population and extended trial duration.
Sponsor: Parkinson's Foundation
Grant# 17-A0-00-007749
Poster presented at Neuromodulation Conference & NANs Summer Series; 2018 August 24–26; New York, NY.

Figure 1: Tele-monitored tDCS (tele-tDCS) setup including the tDCS device, head strap and the videoconferencing platform.

P16.05

The potential value and insight mobile lifestyle tracking apps can give into the effects of fatigue in Parkinson's disease
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Background: A series of market research surveys were completed in 2015 and 2018 by members of the Parkinson's disease community. These surveys revealed that fatigue was a major unaddressed problem. The aim of this poster is to illustrate how fatigue relates to other motor and non-motor symptoms of fatigue identified from the lifestyle tracking application uMotif', and their '100 for Parkinson's' study. The uMotif app contains 5 fixed motifs (Sleep quality, Exercise, Healthy eating, Mood and Stress) and 5 motifs that the user can select to track. The dataset includes 1114 People with Parkinson's (PwP) and 1536 individuals without a Parkinson's diagnosis. Of these 46% of the whole sample selected Energy which is how fatigue was tracked, as a key motif, some participants completed the uMotif every day and some were less frequent users.
Method: As a proof of principle exercise, we identified seven participants with varying disease duration, ranging from a few months to a decade. The uMotif app required participants to score the 10 motifs on a scale between 1 and 5. The daily tracking patterns of these 7 individuals were plotted as a means of illustrating the more fine grained insights into fatigue, which can be gleaned from daily symptom tracking over a week.
Results: The exercise revealed interesting starting points for hypotheses that can be tested in the future, and speaks to the promise and intrinsic value of daily longitudinal symptom tracking.
Conclusion: In our poster we intend to highlight that a number of lifestyle factors influence fatigue levels, which PwP tell us impacts on quality of life and should become a research priority. This poster will also highlight the idiosyncratic nature of PD in that it will show that PwP experience a range of different symptoms, which can vary dramatically from day to day. PwP cannot be clustered into a group, we need to treat PwP as individuals each with a unique set of symptoms.

P16.06

Bright light therapy does not alter the sleep/wake cycle when treating circadian based sleep disorders in Parkinson's disease: A study by The Bronowski Innstitute, Australia
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Insomnia is a major problem for Parkinson's disease patients. While numerous soporific drugs are implemented to address this problem, side effects are common making drug related treatments problematic. Alternatively, bright light therapy improves sleep in patients suffering from circadian based sleep disorders and in particular patients with Parkinson's disease. However, little is known about any potential side effects that light therapy might posess, particularly in regard to the function of light as a "zeitgeiber" that can adversely affect circadian rhythms. In a retrospective study we examined the effect of bright light therapy on the sleep/wake phase to determine if bright light therapy altered the sleep/wake cycle in Parkinson's patients that reported improvement in sleep. Assessment of 109 patients receiving bright light therapy prior to retiring for up to 15 years revelled that little or no alteration of the day/night cycle in these patients occurred. While it was not the subject of the present study to examine drug and light combinations, the present study shows that bright light repairs disturbed sleep in Parkinson's disease patients without phase advancing the circadian rhythm.

CLINICAL SCIENCE: Diagnosis (differential, accuracy)

P17.01

Longitudinal study of subjects with prodromal signs of Parkinson's disease
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Introduction: Future disease modifying therapies against Parkinson's disease (PD) should preferably be initiated at an early disease stage, before the appearance of characteristic motor symptoms. However, due to the lack of biomarkers, our ability to

detect prodromal PD is limited. The objective of this project is to study the prodromal phase of PD.
At autopsy, PD brains usually display Lewy bodies, intracellular aggregates of α-synuclein (α-syn). Several studies have suggested that toxic oligomeric forms of α-syn are increased in PD cerebrospinal fluid (CSF). Moreover, it has been shown that phosphorylated α-syn is present in peripheral nerves in skin biopsies from PD patients. In addition, a recent study suggests that such α-syn forms are present also in skin biopsies from subjects with idiopathic REM sleep behavior disorder, a prodromal risk factor of α-syn-related disease. How such α-syn skin deposits develop over time is not known.
Method: This is a cohort study following patients with prodromal and manifest PD, dementia with Lewy bodies, Alzheimer's disease and healthy controls with 30 subjects in each group. The study participants will be subjected to an extensive test battery including annual follow up neurological testing, cognitive testing, motor testing, self-assessment rating scales, neuroimaging investigations with MRI and PET (11C-PE2I), laboratory testing of cerebrospinal fluid, blood and saliva as well as analyses of skin biopsies for presence of various α-syn forms. Four 3 mm skin biopsies are taken in pairs from four locations (cervical spine and lower extremities, bilaterally) under local anesthesia. PET scans are performed twice during the course of the study.
Conclusion: The first subjects will be enrolled in december 2018. A detailed description of the study design and the first experiences, including some preliminary results, will be presented.

P17.02

Automated immunohistochemical detection of skin depositions of pathological α-synuclein in idiopathic rem sleep behavior disorder and parkinsonism
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Objective: The goal of this study was to employ a novel highly sensitive dual-stain immunohistochemical (IHC) assay in the assessment of cutaneous pathological α-synuclein (αSyn) depositions in patients with idiopathic REM sleep behavior disorder (iRBD), Parkinson's disease (PD), atypical parkinsonism and controls.
Background: Development of therapeutic agents for PD is hampered by a lack of diagnostic tests that accurately identify patients with PD, especially early PD. While the definitive diagnosis of PD can only be made at autopsy upon demonstration of pathological central nervous system αSyn, recent findings suggest that detection of pathological αSyn deposition in skin biopsies can be used to identify patients with PD during life.
Methods: Formalin-fixed, paraffin embedded paravertebral C7 area skin punch biopsies of 79 subjects (28 iRBD, 20 PD, 10 atypical parkinsonism, 21 controls) were bisected. A single slide from each bisected block was analyzed for pathological αSyn on the automated BenchMark ULTRA system using a novel chromogenic dual-stain IHC assay that enabled high contrast visualization of pathological αSyn.
Results: With two slides from one skin biopsy area per subject, pathological αSyn was observed in 60% of PD, 71% of iRBD, 20% of atypical parkinsonism, and 5% of control subjects. Full results based upon extensive sectioning of tissue blocks will be presented.
Conclusions: A novel IHC assay was developed to detect αSyn pathology associated with PD in the peripheral tissue with high sensitivity and specificity. This tool has the potential to be developed into a diagnostic assay for synucleinopathies and selection of patients for clinical trials targeting aggregated αSyn
Prior presentations: The development of the dual-stain immunohistochemical (IHC) assay for pathological αSyn as well as proof-of-concept data were presented in two posters at the International Congress of Parkinson's disease and Movement Disorders (MDS) in October 2018. Data will also be shown at the International Conference on Alzheimer's and Parkinson's Disease (AD/PD) in March 2019.

P17.03

Clinical significance and usefullness of superficial reflex for diagnosis of Parkinson related disorders: Oldies But Goodies
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Background: Palmomental reflex (PMR) and Rossolimo reflex (RSR) are considered as primitive reflexes, which has been regarded as correlates of frontal release. However, the exact significance is still debated since they have been consistently shown in healthy subjects.
Objective: Primary aim of this work consists in assessing the exact prevalence and value of the PMR and RSR as a neurological examination following with routine image diagnostic technology for neurological disorders especially for Parkinson related disorder (PRD).
Materials and methods: 4,350 out/inpatients of neurological disorders were performed with full neurological examination including PMR and RSR from 2004 to 2018 in Omuta National Hospital and Kochi Medical School Hospital. We have analyzed the correlation between the result of PMR/RSR and final diagnosis according to the common criteria.
Result: (1) PMR and PRD. Of 4,350 patients, 540 cases (12.4%) showed positive PMR reflex and 39 (0.9%) showed lateralized difference of PMR. Out of 39 cases, 17 included Parkinsonism (4 Dementia with Parkinson disease, 3 Multisystem atrophy, 3 Corticobasal degeneration, 2 Parkinson disease (PD), 2 Progressive supranuclear palsy (PSP), 2 Dementia with Lewy body disease (DLB), 1 unknown), 11 were multiple cerebral infarction, 4 were encephalopathy/encephalitis, 3 were ALS, 2 were brain tumor and 1 case of hemifacial palsy. Statistical significance was observed in these disorders ($p<.05$).
(2) RSR and PRD. Of 1,440 patients, 152 cases (10.6%) showed abnormal PMR reflex. Statistical significantly with abnormal RSR ($p<.05$) are observed in 3 cases of dementia with multiple cerebral infarction (DMCI), 21 case of encephalopathy, 4 cases of FTD/ALS complex, 27 cases of Parkinson disease, 10 cases of MSA-P and 5 cases of FTLD.
Discussion: Though the sensitivity is low, the positive PMR and/or RSR show high specificity for detection of not only dementia with multiple cerebral infarction, but also PD related disorders.

CLINICAL SCIENCE: Co-morbidities

P18.01

Impaired cerebral blood-flow self-regulation in patients with Parkinson's disease: Association with leukoaraiosis. A pilot study from northeast Mexico

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Background and Objective: Parkinson's disease (PD) is the second most frequent neurodegenerative disease, although deemed to be associated with, its relationship to cerebral vascular disease (CVD) remains unexplored. Vasoreactivity, as measured by transcranial Doppler ultrasound (TDU), is a non-invasive marker of cerebrovascular pathology. Leukoaraiosis(LA) consists of diffuse and confluent white matter hyperintensities on magnetic resonance, the result of vascular damage and associated with other vascular risk factors. Both have been assessed in PD-independently-with conflicting results. Therefore, we designed a study to explore the relationship between impairment of cerebral vasoreactivity and degree of LA in PD.
Design/methods: Transversal study. Patients with PD diagnosis were recruited from the movement disorders clinic. Transcranial Doppler ultrasound was performed before and after 5-minute 7% carbon dioxide (CO2) inhalation; vasoreactivity (VR) was defined as the change in cerebral blood flow velocity. Magnetic resonance imaging (MRI) with FLAIR sequence was performed, and LA was graded according to the Fazekas scale (1–3).
Results: 19 patients with PD were recruited, 79% (n=15) male, mean age of 57.0±13.2 years, mean disease duration 5.7±4.9 years, and mean Hoehn & Yahr stage 1.6±0.8. Vasoreactivity was absent in 79% (n=15), with a median change of -6.3±104.2. LA was present in all patients, most frequent grade being Fazekas 1 (68%, n=13). Among the patients with loss of vasoreactivity, Fazekas 1 was present in 73% (n=11). A linear regression analysis was performed in search of predictive factors of loss of vasoreactivity, with LA achieving statistical significance (OR -41.6, 95% CI: -68.2 — -15.0, p=0.005), along with disease duration and age of onset (Table 1).
Conclusion: In patients with Parkinson's disease, leukoaraiosis it's associated with loss of cerebral self-regulation, further studies are required to fully explore the relationship between cerebral vascular disease and Parkinson's disease. Our results are preliminary, as patients are still being recruited.

Table 1 — Linear Regression Analysis

	SE	Beta	T	B	95% CI		P
Fazekas Scale	12.1	-0.9	-3.4	-41.6	-68.2	-15.0	0.005
Disease Duration	3.5	2.5	3.1	11.0	3.2	18.8	0.010
Time from Diagnosis	4.1	-1.9	-2.5	-10.1	-19.1	-1.1	0.030
NMSS Score	0.1	-0.3	-1.4	-0.2	-0.5	0.1	0.183
MoCA Score	1.0	-0.2	-0.9	-0.8	-2.9	1.2	0.394
Levodopa Equivalent Daily Dose	0.0	0.1	0.3	0.0	-0.0	0.0	0.780
Hoehn & Yahr	7.6	-0.1	-0.2	-1.4	-18.0	15.2	0.855

Dependent Variable: Mean Vasoreactivity (CBF change).

P18.02

Women with Parkinson's disease: Vision and reading

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Person with Parkinson, Hermiston, OR, USA

One hundred women with Parkinson's disease were surveyed via social media. Demographic data collected included age, education level and status concerning deep brain stimulation surgery. Subjects chose from a selection of physical eye symptoms and visual concerns. They were then asked to report if they had difficulty reading, and if so what types of reading materials were problematic. Further queries included their report of vision or reading concerns to PD health providers or Vision health providers. Approximately 33% of respondents chose to provide additional comment to their answers.

P18.03

Utilization of the emergency department (ED) in Florida among patients with Parkinson's disease (PD)

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Objective: To characterize emergency department visits in patients with Parkinson's disease before and after their diagnosis using a statewide Patient Centered Outcomes Research Institute (PCORI)-funded clinical data research network, OneFlorida Clinical Research Consortium (CRC).
Background: Approximately 20% of US adults seek care at the emergency room annually. Prior studies have reported patients with PD were hospitalized more often than age matched controls and have higher hospital related complications. There is limited information about the frequency of ED visits in patients with PD before and after diagnosis along with prodromal symptoms of PD resulting in ED visits. Given that the cumulative hospital encounters can increase care burden, costs, and morbidity we aim to assess the frequency of these visits and identify the commons causes of these visits.
Methods: Patients in the OneFlorida CRC with an ICD-9-CM 332.0 or ICD-10-CM G20 diagnosis code during at least 1 encounter from January 2012 through June 2017 and at least 1 emergency department visit before or after the PD diagnosis were included. Frequency of ED visits before and after diagnosis were assessed. Diagnosis codes among all ED encounters were assessed.
Results: 1925 individuals with a diagnosis of PD between 2012 and 2017 were identified who had at least one ED visit within 2 years before or after the diagnosis. The frequency of ED visits increased in the 2 years post diagnosis compared to the number of visits before the diagnosis. The top reasons for visits were cardiovascular disease (including hypertension, hyperlipidemia, or diabetes) falls, urinary tract infection, and gastroesophageal reflux.
Conclusions: Patients with Parkinson's disease had increased frequency of visits to the emergency department after the diagnosis, and the most common cause for these visits pre-diagnosis and post-diagnosis was hypertension followed by additional cardiovascular risk factors.

P18.04

Profile of the patient attending for the neurological center specialist in Parkinson's disease: CENPAR, Santiago Chile

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CENPAR, Santiago, Metropolitana, Chile

Objective: To identify characteristics of people with Parkinson's disease to develop an initial profile that allows them to meet their needs in a country in Latin America such as Chile where there is little information and a geography that limits as is the case of the Andes mountain range, the desert, Pacific Ocean, islands and the Antarctic.
Method: This is a retrospective descriptive study obtained from the admission of patients with Parkinson's disease (PPD). A random sample of 258 people admitted between 2017- 2018 is collected. The lack of information is excluded. To determine the profile variables of sex, age, years with Parkinson's disease, type of schooling, type of wealth, place of residence and type of medication for Parkinson's are analyzed.
Result: The distribution shows that 46% PPD are women and 54% men, the correlation is no relationship to sex and PD (0,06). The average age is 68 years; 13% are aged 80 to 89; 37% 70 to 79 years old; 28% 60 to 69 years old; 15% 50 to 59 years old; 7% less than 49 years old. 78% are 60 years old or older. Years of diagnosis PPD 56% 10 15 years. When analyzing the type of schooling, 40% have University studies; 14% technical; 4% complete schooling (12 years); 18% do not complete schooling (<12 years); 25% no school. The level of wealth is 54% medium to low with health system FONASA(public); 32% medium to high with ISAPRE(private); 14% other. The locality 74% come from the Metropolitan Region; 24% come from different regions; 2% comes from other countries in America. 1% ingest only levodopa; 10% levodopa and another; 28% only prolopa; 42% Prolopa and other; 19% other medicines for Parkinson's.
Conclusion: The patient who attends CENPAR is occasionally male, over 60 years of age who has between 0 and 5 years of diagnosis, professional, with a medium to low level of wealth with Fonasa public health system, coming from the Metropolitan Region, ingests prolopa and other neurological medications.

	Nº PPD	PERCENT
Woman	119	46
Man	139	54
AGE		
30 to 59	57	22
60 or more	201	78
YEAR OF MEDICAL DIAGNOSTIC		
0 to 5 years	144	56
6 to 10 year	57	22
11 to 15 year	36	14
>15	21	8
EDUCATION LEVEL		
University (13 years or more)	103	40
Tecnic (13 years or more)	36	14
Complete (12 years)	10	3
Incomplete (11 or less)	45	18
No school	64	25
MEDICATION		
Levodopa	3	1
Levodopa+other	26	10
Prolopa	72	28
Prolopa+other	108	42
Other	49	19
PENSION SYSTEM		
Fonasa	139	54
Isapre	82	32
other	37	14
LOCATION		
Metropolis	191	74
Other city	63	24
Forein	4	2

P18.05

Clinical correlates of carotid intima media thickness in Parkinson's disease: A pilot study from northeast mexico

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Objective: To determine the clinical correlates of carotid intima media thickess in patients with idiopathic Parkinson's disease.
Background: Subclinical cardiovascular disease has been suggested to influence the phenotype and course of Parkinson's disease (PD), making the identification of risk factors of paramount importance[1, 2]. Carotid Intima Media Thickness (CIMT), is a non-invasive marker of subclinical atherosclerosis, that in PD patients has been associated with disease severity[3], and decreased survival[4].
Design/Methods: Transversal analytical study. Patients with PD diagnosis were recruited from the movement disorder outpatient clinic. CIMT was measured as the mean average of bilateral common carotid artery along 20mm; disease was evaluated with severity (Hoehn & Yahr), cognitive (MoCA), motor (MDS-UPDRS III), non-motor (NMSS) and quality of life (PDQ8) scores. Bivariate correlations were sought between CIMT and previously mentioned variables, and for those with significant moderate-strong correlation, multiple linear regression analysis was performed using CIMT as dependant variable. A $p<0.05$ was deemed as significant.
Results: Eighteen patients were included, 53% female, mean age 58.3±9.0; most common comorbidities were hypertension (50%, n=9), diabetes (17%, n=3), hyperlipidemia 3 (16%), and active smoking (17%, n=3). Mean CIMT was 0.656±0.130 mm. We found significant correlations with age, and age at onset (strong, positive), PDQ8 (strong, negative) and MoCA (moderate, negative), and a non-significant trend with MDS-UPDRS III (moderate, negative). Regression analysis found for age (positive), age at onset and MDS-UPDRS III score (negative) as significant predictive variables for CIMT. Details are given in table 1.
Conclusions: In Parkinson's disease, CIMT correlates with age at onset, as it increases with younger ages; suggesting subclinical atherosclerosis might be involved in the onset of disease. Although CIMT seems to have a protective effect on motor severity, larger studies are required to determine the effect of cardiovascular disease on PD. Our results are preliminary, as patient recruitment is ongoing.

Table 1. Correlation and regression anaylsis for carotid intima media thickness.

		Bivariate Correlation[a]		Stepwise multiple linear regression[d]					
	Mean ± SD	CIMT	p	SE	β	t	OR	95 % CI	P
Age (years)	58.3 ± 9.0	0.798[b]	**<0.001**	0.004	1.304	5.4	0.019	[0.011 — 0.026]	**<0.001**
Duration (years)	6.5 ± 4.4	0.355[b]	0.148						
Age at onset	51.8 ± 9.1	0.618[b]	**0.006**	0.004	-0.651	-2.6	-0.009	[-0.017 — -0.002]	**0.021**
Hoehn & Yahr	1.8 ± 1.0	-0.092[c]	0.718						
Schwab & England	83.1 ± 18.2	0.283[c]	0.287						
MDS-UPDRS III	35.8 ± 22.9	-0.442[b]	**0.066**	0.001	-0.416	-3.5	-0.002	[-0.004 — -0.001]	**0.004**
MoCA	25.9 ± 6.3	-0.233[b]	0.368						
NMSS	37.5 (190)	-0.425[c]	**0.079**						
PDQ8	5.0 (19.0)	-0.582[c]	**0.011**						
Years with levodopa	5.9 ± 4.5	0.317[b]	0.269						
Levodopa (mg/day)	526.9 ± 195.7	-0.018[b]	0.952						
LEDD	656.0 ± 239.3	0.262[b]	0.193						

LEDD: Levodopa Equivalent Daily Dose. SD: Standard Deviation. CIMT: Carotid Intima Media Thickness. SE: Standard Error. OR: Odds Ratio. CI: Confidence Interval.
[a]Correlation coeficient: [b]Pearson, [c]Spearman.
[d]Variables entered in the model: CIMT as dependent variable. Age, Age at onset, MDS-UPDRS III, NMSS, PDQ8 scores, as predictive variables.

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CLINICAL SCIENCE: Biomarkers

P19.01

Dopamine buffering capacity measured by phMRI as a novel biomarker of disease progression in PD

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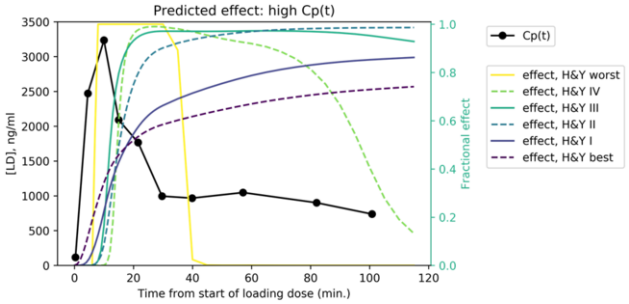
We present a novel brain imaging method for objectively quantifying disease severity in Parkinson disease (PD), called levodopa pharmacological fMRI rapid quantitative pharmacodynamic imaging. The novel method is based on the well-known clinical observation that the benefit from a dose of levodopa wears off more quickly as PD progresses. The body responds as if the levodopa in the plasma filled a reservoir and then slowly leaked out to produce benefit. With disease progression, even though the same amount of levodopa circulates in the blood, the benefit wears off much faster, as if the reservoir had become leakier. Biologically, the reservoir may represent the diminishing buffering capacity of ascending dopaminergic axons as midbrain dopamine neurons die off. The wearing off of benefit after a given dose has been quantified by a mathematical model that postulates a central effect compartment (reservoir) whose concentration of levodopa directly determines the clinical benefit. The buffering capacity in this model can be characterized by a single number, the effect site rate constant Ke, which can be computed from serial measurements of both plasma concentration and the effect of the drug. Such modeling has been done previously for clinical effect (tapping speed). Unfortunately, clinical measurements are influenced by confounding factors such as patient fatigue. A direct, objective brain measure of response to LD may reduce this added variance. This new method proposes to measure the effect based on the timing of the known metabolic and blood flow response of several brain regions to exogenous levodopa. These effects are robust and can be quantified without ionizing radiation using arterial spin labeling (ASL) perfusion MRI. Here we present simulation studies based on published clinical dose-response data and our experience with intravenous levodopa infusion. As shown in the figure, predicted time-effect curves differ substantially based on clinical severity. These simulation results support the feasibility of levodopa phMRI rapid quantitative pharmacodynamic imaging to measure the severity of dopamine denervation objectively and simultaneously in various brain regions. We also will present images from our ongoing pilot study using this method.

Support: Michael J. Fox Foundation and Washington University Medical Center's East Building MR Facility.



P19.02

Polymorphisms of ACMSD-TMEM163, MCCC1 and BCKDK-STX1b are not associated with Parkinson's disease in Taiwan

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Previous genome-wide association studies in Caucasian populations suggest genetic loci in amino acid catabolism may be associated with Parkinson's disease (PD). However, these genetic-disease associations were limitedly reported in Asian populations. Herein, we investigated the effect of 3 top PD-associated genetic variants in Caucasians listed on the top risk loci identified by meta-analysis of genome wide-association studies in PDGene database, including aminocarboxymuconate semialdehyde decarboxylase (ACMSD)-transmembrane protein 163 (TMEM163) rs6430538, methylcrotonoyl-CoA carboxylase 1 (MCCC1) rs12637471, and branched chain ketoacid dehydrogenase kinase (BCKDK)- syntaxin 1B (STX1B) rs14235, by genotyping 599 Taiwanese patients with PD and 598 age-matched control subjects. PD patients demonstrate similar allelic and genotypic frequencies in all tested genetic variants. These ethnic discrepancies of genetic variants suggest a distinct genetic background of amino acid metabolism between Taiwanese and Caucasian PD patients.

P19.03

The diagnostic and therapeutic potential of miR-153 and miR-223 in Parkinson's disease

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Dysregulated microRNA (miRNA) is thought to play a major role in developmental brain disorders, normal aging and various neurodegenerative conditions, including Parkinson disease (PD). These short noncoding RNA species bind to the 3' untranslated region (3'-UTR) of target genes, resulting in targeted mRNA cleavage or degradation and protein translation repression. A recent study employing miRNA microchip assays on HMOX1- and sham-transfected primary rat astroglia showed that altered expression profiles of salient miRNAs and their mRNA targets contribute to neural damage accruing from the overexpression of glial heme oxygenase-1 (HO-1). HO-1, a stress protein that catalyzes the conversion of heme to biliverdin (which is subsequently converted to bilirubin), carbon monoxide and free ferrous iron, has been implicated in the pathogenesis of PD. The advent of the parkinsonian transgenic GFAP.HMOX1 mouse, engineered to overexpress the human HO-1 gene (HMOX1) in the astrocytic compartment between 8.5 and 19 months of age, has facilitated our investigation of key miRNAs implicated in the etiopathogenesis of PD. The latter include miRNAs impacting neurodegenerative processes (oxidative stress; apoptosis; autophagy; reelin expression) and, more specifically, the hallmarks of PD (dopaminergic neuronal function and survival; α-synuclein aggregation). Downstream of HO-1 overexpression, miR-153 and miR-223 were found to directly regulate α-synuclein mRNA and protein both in vivo and in vitro. MiR-153 and miR-223 were significantly downregulated in GFAP.HMOX1 basal ganglia, correlating with increased α-synuclein mRNA and protein. Additionally, serum concentrations of both miRNAs progressively declined in the wild-type (WT) and GFAP.HMOX1 mice between 11 and 19 months of age. At each time point surveyed, circulating levels of miR-153 were significantly lower in the TG animals compared to WT controls. Moreover, in a diagnostic trial, miR-153 and miR-223 were similarly significantly decreased in the saliva of human PD subjects compared to age-matched, healthy controls. These findings underscore HO-1-mediated perturbations in brain and peripheral miRNA expression profiles as a driver of PD neuropathology and implicate glial HO-1, miR-153 and miR-223 as potential diagnostic markers and targets for disease-modifying therapy in this condition.

P19.04

Lipid analysis of CSF from Parkinson's disease patients with and without a LRRK2 mutation

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Missense mutations in leucine-rich repeat kinase 2 (LRRK2) increase the enzyme's catalytic kinase activity and contribute to an increased risk of developing Parkinson's disease (PD). Drugs that can block the activity of LRRK2 are in advanced stages of development and have recently passed early phase 1 safety trials in healthy individuals. To facilitate further clinical translation, it is becoming increasingly desirable to have a biomarker readout that demonstrates that LRRK2 inhibitors are effective in the brain. However, at present, no such validated central biomarker exists, and robust imaging agents have not been developed. In this study we have assessed the extent to which lipids are altered in cerebral spinal fluid (CSF) from participants with and without the most common LRRK2 G2019S mutation. CSF was obtained from the Michael J Fox Foundation LRRK2 clinical cohort consortium (n=89). Groups comprised of controls, idiopathic PD and both asymptomatic and symptomatic LRRK2 G2019S mutation carriers. Lipids were extracted from CSF using a chloroform-methanol extraction, and high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS) was used to detect, identify and compare the relative abundance of lipid species (employing internal standards). A total of 369 different lipid species across 27 lipid classes were identified. The abundance of 12 lipid species was significantly increased when subjects with a LRRK2 mutation were compared to participants without a LRRK2 mutation. Interestingly, in

idiopathic PD participants, ~20 lipid species were significantly decreased in abundance compared to both the control, and PD participants with a LRRK2 mutation. These results implicate LRRK2 in lipid homeostasis and further suggest that lipid species are altered in the CSF of PD patients. Further work is required to confirm lipid identifications and to determine if the altered lipid species identified have potential as biomarkers for PD.

P19.05

Evaluation of fungal markers in Parkinson's disease

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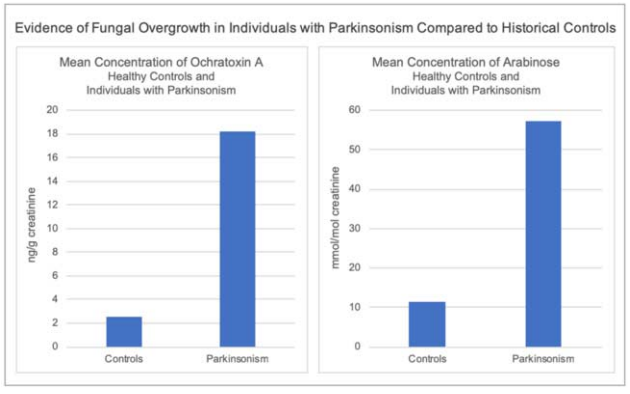
Background: Ochratoxin A (OCA) is ubiquitous neurotoxic mycotoxin. Several studies have demonstrated OCA results in depletion of striatal dopamine, oxidative stress, death of dopaminergic neurons, and clinical parkinsonian syndrome that responds to levodopa in animal models. The presence of OCA in people with parkinsonism (PwP) has never been evaluated.
Objective: The goal of this study was to evaluate the prevalence of elevated ochratoxin A and other fungal markers in a cohort of PwP and evaluate whether there is a correlation with Parkinson's disease severity.
Methods: OCA and organic acids indicative of intestinal fungal overgrowth were measured in the urine of 62 consecutive PwP. PD severity was measured by PRO-PD. Laboratory reference ranges were used as historical controls.
Results: Laboratory reference ranges for OCA, based on 100 healthy adults, had a mean of 2.5 (range: 0–11) ng/g creatinine. In our sample of PwP, the mean concentration of OCA was 18.2 (range: 0–418) ng/g creatine. 66% of the cohort showed elevated OCA values above the 95th percentile. For the other fungal markers, only arabinose appeared pervasive. Laboratory reference ranges for arabinose, based on 300 healthy adults, had a mean of 9 (range: 0–20) mmol/mol creatinine for males, and a mean of 14 (range: 0–29) mmol/mol creatinine for females. In our sample of PwP, the mean concentration of arabinose was 57 (range: 15–156) mmol/mol creatinine. 90% of the cohort showed elevated arabinose values above the 95th percentile.
Conclusions: These data support the hypothesis that PwP are more likely to harbor fungus, as measured by an above average excretion of fungal metabolites. Given that OCA has been shown to cause a levodopa-responsive parkinsonian syndrome in lab animals, further research into the role of fungal byproducts as a potentially causative factor contributing to parkinsonian syndrome is warranted. If these data prove reproducible, the next steps will be to identify the source of fungal infection and determine whether eradication of fungus and its metabolites will improve PD outcomes in those already diagnosed.



P19.06

Prospective investigation of metabolomics and Parkinson's disease

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Objective: To identify plasma metabolomic biomarkers associated with incident development of Parkinson's disease.
Methods: Using a prospective, nested case-control study within the Nurses' Health Study (NHS), the Health Professionals Follow-up Study (HPFS), and the Cancer Prevention Study II Nutrition Survey Cohort (CPS-IIN), we conducted a global, non-targeted metabolomics investigation. After risk-set sampling a control for each case, matched with respect to age, sex, cohort, time of blood collection, and fasting status at blood collection, we profiled plasma metabolites using liquid-chromatography mass spectrometry. We used conditional logistic regression to evaluate each identified metabolite's association with PD and additionally used L1-penalized logistic regression to investigate whether pre-diagnostic metabolomic profiles could differentiate PD cases from controls.
Results: Across these cohorts, we identified 567 cases of Parkinson's disease for whom a blood sample had been collected prior to diagnosis. Overall, a total of 22 out of 286 metabolites were associated with PD ($p<0.05$). Notably, of these 22 metabolites, 21 had an inverse association with PD status. Protective associations were observed for urate and metabolites involved in caffeine metabolism. In analyses stratified by length of time between blood collection and PD diagnosis, 11/286, 31/286, and 3/286 metabolites were associated with PD among those for whom blood was respectively collected <60 months, 60–179 months, or 180+ months prior to diagnosis. After correction for multiple testing, none of these associations remained statistically significant. Preliminary attempts at using L1-penalized logistic regression to develop a model to predict PD status using metabolite values have had limited success.
Conclusions: To date, we are unable to reliably distinguish PD cases from controls using metabolomic data from prospectively collected blood samples. Despite this, the results of our single-metabolite analyses support findings on previously established risk factors, caffeine consumption and urate, and indicate that some broad but ill-defined metabolic dysregulation may characterize the pre-diagnostic period of PD.

P19.07

Parkinson's patients possess abnormal blood monocytes and changes in soluble biomarkers

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Immunopathogenesis seems to play an active role in Parkinson's disease (PD) progression with peripheral immune cells contributing to the neurodegeneration. A better understanding of the immune changes during PD, might allow to design immunomodulatory therapies and define biomarkers. Our previous data suggest a relevant role of peripheral monocytes/macrophages, specifically those expressing CD163. Therefore, we aim to investigate how PD affects the peripheral monocyte populations and their ability to respond to α-synuclein (α-syn). Furthermore, we aim to develop a biomarker panel for PD progression, by measuring various soluble molecules in serum and CSF from different stages PD patients using 40-plex mesoscale and ELISAs.

Peripheral mononuclear cells (PBMCs), serum, and CSF were obtained from PD patients and age- and gender-matched healthy controls at the Hertie Biobank, Germany. PBMCs were cultured for 2 hrs (untreated) or 24 hrs (untreated, stimulated with LPS, monomeric-, or fibrillar α-syn) followed by flow cytometry and measurement of cytokines, and shed sCD163 in the culture supernatants. We are also in the process of measuring sCD163 and 40 different cytokines, chemokines, and vascular injury markers in the serum and CSF.

PBMCs from PD females were less viable compared to cells from the control group, suggesting exhausted immune cells. After 24 hrs in culture, a new immature CD14+/HLA-DR^{-} monocyte population arose in the PD females, indicating an attempt to compensate for the dying/exhausted cells. PD patient cells were less responsive to stimulations since only the control group had a significantly reduced CD14+, HLA-DR+, and CD163+ cell frequencies and expression levels after LPS and/or fibrillar α-syn stimulations. Gender discrepancy was observed for some parameters. Furthermore, opposite to controls, PD cells failed to produce IL-6 and the anti-inflammatory cytokine IL-10, as well as IL-13, important for antibody production, in response to stimulations. Interestingly, sCD163 culture shedding was also significantly decreased in the PD group.

In conclusion, PD patients have immature monocytic cells with low viability, reduced responsiveness to stimulations, and reduced in vitro shedding of sCD163, suggesting modified monocytic populations. Our ongoing studies will reveal disease progression-associated changes in soluble molecules in serum and CSF, suitable for a novel biomarker panel.

P19.08

Network models of Parkinson's disease during Subthalamic-Nuclei Deep Brain Stimulation (STN-DBS): An investigation of neural activity in PD

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Introduction: Parkinson's disease (PD) is a chronic neurodegenerative disease characterized by cardinal-motor hallmark symptoms. It is associated with pathological, oscillatory-neural-activity(ONA) in the basal-ganglia(BG). Deep brain stimulation(DBS) is often successfully used to treat-medically refractive Parkinson's disease. However, the selection-of-stimulation-parameters are based on qualitative-assessment-of-the-patient, which can result in a lengthy-tuning-period and a suboptimal-choice-of-parameters.

Purpose: This study explores fourth-order, control-theory-based computational-simulation-models of oscillatory-activity in the BG-circuitry.

Methods: Describing function-analysis is applied to study possible-mechanisms for the generation-of-oscillations(GoOs) in interacting nuclei and to investigate the suppression-of-oscillations (SoOs) with high-frequency-stimulation. The theoretical results for the suppression-of-oscillatory-activity(SoOA) obtained using fourth and second-order computational-simulation-models (CSM) are optimized to fit clinically-recorded local-field-potential(LFP) data obtained from PD patients with implanted DBS. Close-agreement between the power-of-oscillations(PoOs) recorded for a range of stimulation-amplitudes is observed (R2=0.69–0.99). To verify behavior-of-simulation-model in comparison to the physiological-system, the model-parameters of the fourth-order reduced series-model (Fig's.1,2) were optimized to fit clinical-LFP-data. The data gathered from neurology,NIMS-hospital(Hyderabad,South-India) from 46 patients advanced idiopathic Parkinson's disease. All patients gave their informed-consent to participate/take-part in the study approved by the ethical-committee.

Results: The results suggest that, behavior of the system and suppression of pathological-neural-oscillations with DBS are well described by the macroscopic-models presented, second-order model is sufficient to model the clinical-data, without the need for added complexity.

Conclusions: Computational simulation models of the cortico-basal-ganlia-circuitry thalamocortical network that capture the key-features of the physiological-system in order to produce a faithful-representation of the dynamics, while remaining analytically-tractable, are mainly/mostly-valuable. Results demonstrate that second and fourth-order series-models provide close agreement between the model-output and clinical-data. Thus second-order model is ample to represent-the-system, with the added-complexity of the fourth-order-model, in this case, unnecessary. The agreement-observed offers the possibility that the model could be translated to a clinical-tool to assist in DBS parameters-selection. The model could possibly be tuned to represent an individual-patient's pathological-state using a biomarker of PD. The analytically tractable theoretical-analysis established here can readily be extended to higher-order-models also, thus providing a valuable-framework with which to examine/test new models of this-type. Significance: Describing the system-behavior with computationally-efficient-models could aid in the identification-of-optimal-stimulation-parameters for patients in clinical-environments.

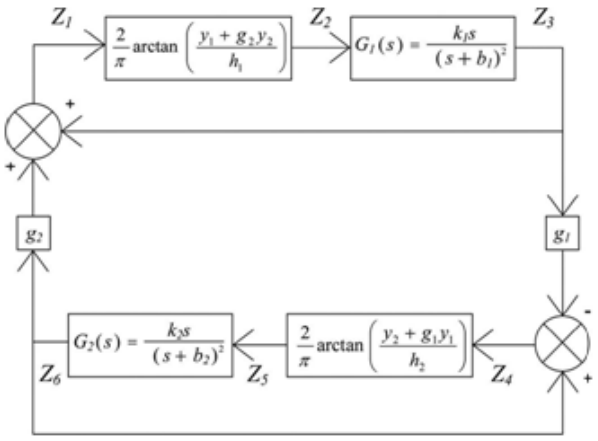

Fig. 1 Schematic diagram of the fourth-order series model (with feedback) representing neural synchrony in two interconnected second-order loops. The two networks are coupled through g_1 and g_2. For excitatory-excitatory coupling (+/+) $g1 = -g2 > 0$. For excitatory-inhibitory (+/-) coupling $g1 = g2$.

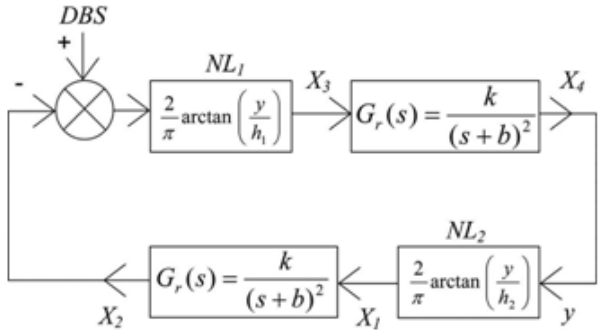

Fig. 2 Schematic diagram of the fourth-order model of neural synchrony comprised of a series connection of two second-order models of synchronous activity. For notational simplicity, the nonlinear element in the first nuclei is labeled as NL_1 and in the second nuclei similarly termed NL_2. The DBS is applied additively at the input to NL_1.

P19.09

Effectiveness of lead point using microelectrode recording for finding the subthalamic-nuclei deep brain stimulation in Parkinson's disease (geometry of electrode implantation)

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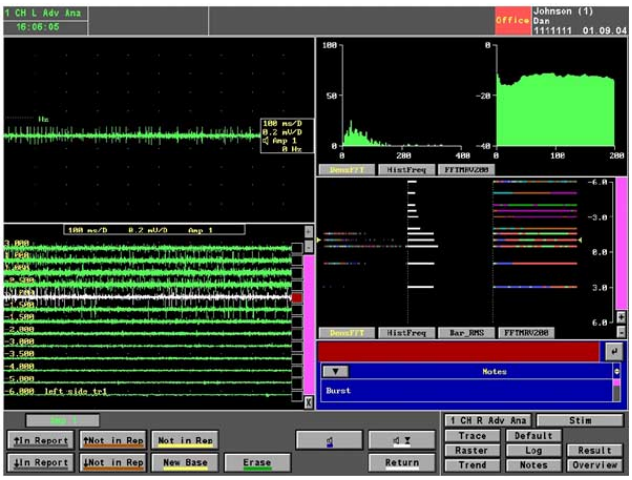
Introduction: Microelectrode recording (MER) techniques are often used in DBS stereotactic-functional-neurosurgery to give physiological-localization in conjunction with initial targeting by magnetic resonance imaging (MRI) [1]-[2]. MER with subthalamic-nuclei deep-brain electrical stimulation(STN-DBS) gives exact delineation of subcortical-structures (STN, GPeGPi, and thalamic-nuclei), for the treatment of a variety of neurodegenerative-diseases. Neural-recordings from these structures have added considerably to our understanding of basal-ganglia (BG) pathophysiology in patients with (idiopathic) Parkinson's disease (PD).

Objective: To study the effectiveness of lead-point with MER in finding STN-DBS, MER-signal-recordings with bilateral-STN-DBS for STN-localization in patients with idiopathic PD, and to improve functional-stereotactic microelectrode-localization-of small deep brain structures by developing and evaluating MER system with DBS-microelectrodes.

Methods: Forty-six patients (had 6 years disease-duration, good response to L-dopa, normal-cognition, able to walk-independently "ON" state in drug) with diagnosis-of-PD as per United-Kingdom-Parkinson-disease-society brain-bank-criteria/UPDRS scale were included in this-study. All the patients were willing-to-undergo the procedure and fulfilled-above-criteria. Patients who were wheelchair/or bed-bound, had cognitive-impairment(CI)/or-dementia or severe-psychiatric-disturbances were excluded. Surgery was planned using CRW-frame with MRI-protocol using 5channels (Framelink-software). Microelectrode recording was performed in all patients extending from 10mm above target to 10mm below STN-calculated on MRI. Final-target-selection was based on the effects and side-effects of macrostimulation and confirmed by post operative-MRI. STN is identified by a high-noise with a large-baseline and an irregular-discharge with multiple-frequencies. Intra-operative-microelectrode-recording was performed in all 5channels. Figure-shows the microelectrode-recording which is obtained-from-STN.

Results: Forty-six patients with their mean-age of 58.1±9.1 years, mean disease-duration of8.8±3.64 years were included. Prior-to-implantation, mean UPDRS score in "OFF" state was 52.7±10.6, "ON" state was 13.4±5.0. STN microelectrode-recordings were detected in a mean of 3.5±1.1 channels on right-side, 3.6±1.04 on left-side. Final-channel selected were most commonly central seen in 42.3% followed by anterior in 33.7%. Concordance-of-final-track with the channel having the highest-recording was 58.7%, with the channel-showing maximum-depth-of-recording was 48% and with either was 64%. Absence of any recording in the final-tract chosen was seen in 6.52%, in these patients the tract was chosen based on stimulation-results. Depth of microelectrodes was identified by microelectrode-recording in 75.6%.

Conclusion: MER is valuable to classify and confirm the tract in which DBS electrodes are positioned and is significant in finding the depth-of-electrodes-placement.



P19.10

Characterizing STN-DBS local field potential oscillations in Parkinson's disease intraoperatively using microelectrode recording

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Background: There is a growing interest in the nature of local field potentials (LFP) behavior gathered from the microelectrode recordings of subthalamic-nuclei (STN) with deep brain stimulations (DBS) of advanced idiopathic Parkinson's disease (PD) patients who underwent DBS stereotactic functional-neurosurgery. This is energized by the data that oscillatory-activity in the beta band frequency is unduly synchronized and sturdy in these patients and that these link to lack-of-dopamine in basal-ganglia (BG) parallel-circuit. Hence, power of beta-activity is correlated with the motor impairment in PDs and the changes in motoric-symptoms rigidity and Bradykinesia. The origin of these activities in STN area has been explored using microelectrode recordings (MER) intraoperatively. We focus and explore the spatial topography and movement related reactivity of spectral-features recorded directly from bilateral STN-DBS electrodes in eight 46 patients with advanced idiopathic Parkinson's disease.
Objective: This study aims to use the behavioral activities acquired from deep brain stimulation (DBS) microelectrode recordings (MER) to address the focality and distinct nature of the STN-LFP activities of different frequencies.
Methods: Preoperative and intraoperative functional Magnetic Resonance Imaging (fMRI) were recorded from advanced idiopathic Parkinson's disease (PD) patients who underwent DBS in the STN-LFP acquisition with MER at rest and during cued-movements. Signatures were reconstructed and visualized in three dimensions using the effectiveness of lead point with DBS to establish the coordinates of contact. The resting spectral power and movement-related power modulation of LFP-oscillations were estimated.
Results: Both STN-LFP activities acquired – recorded at rest and its modulation by movement had focal maxima in the alpha (α) beta (β) and gamma (γ)-bands. The spatial-distribution of α-band activity and its modulation was significantly different due to that in β-band. Also, there were significant differences in the scale and timing of movement related modulation across frequency band.
Conclusion: STN-LFP activities within specific-frequency-bands can be distinguished by spatial topography and pattern-of-movement related-modulation.
Significance Evaluation of the frequency, focality and pattern-movement related-modulation of STN-LFP discloses heterogeneity of neural-population-activity (NPA) in this area. Potentially this could be leveraged to intraoperative targeting finesse-skill and postoperative contact choice.

P19.11

The Accelerating Medicine Partnership in Parkinson's disease (AMP PD) – a data biosphere to support discovery research and broad data sharing

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The Accelerating Medicines Partnership (AMP) is a public-private partnership between the National Institutes of Health (NIH), the U.S. Food and Drug Administration (FDA), biopharmaceutical companies and non-profit organizations. Managed through the Foundation for the NIH (FNIH) the goal of AMP is to transform the current model for developing new diagnostic and treatments by jointly identifying and validating promising biological targets. In 2018, through FNIH, an AMP partnership between the National Institute of Neurological Disorders and Stroke (NINDS), the Food and Drug Administration (FDA), GSK, Pfizer, Sanofi, Celgene, Verily and the Michael J. Fox Foundation (MJFF) was launched for Parkinson's disease (PD). The research plan proposed for AMP PD encompasses a deep molecular characterization and longitudinal clinical profiling of PD patients. The proposal includes open data sharing of molecular and clinical data to enable dissection of new targets, disease subtypes, and the identification of predictive markers for disease progression and disease prognosis. AMP PD will utilize well characterized cohorts with existing biosamples that were collected under a common protocol. The cohorts represent over 3,364 PD participants and 1,709 healthy controls at baseline and an overall biorepository collection of 3,313 CSF samples, 15,530 RNA samples, 10,392 plasma samples, and 4,000 DNA samples. The cohorts include the Michael J. Fox Foundation Parkinson's Progression Marker Initiative (PPMI), the NINDS/MJFF BioFIND study, the NINDS Parkinson's disease Biomarkers Program 14081408(PDBP) and the Harvard Biomarker Study (HBS).
Stage 1 of AMP PD focuses on whole genome sequencing of 5,073 genomes, and whole transcriptome RNA sequence analysis of over 7, 700 blood-derived RNA samples. Raw and processed DNA and RNA sequence data will be available through the AMP PD Knowledge portal developed by Verily and the Broad Institute. Extensive clinical phenotypic data is already available for all subjects. Stage 2 will enable the development and integration of extracellular RNA, proteomic and metabolomic datasets, with the use of an adaptive design that is sensitive to advances in technology and inclusive of common discovery and replication cohorts for platform validation. AMP PD offers a unique opportunity to advance the PD biomarker field into a new era of large, genome-scale analyses using robust analytical platforms.

P19.12

Biospecimen and clinical resources within the NINDS Parkinson's disease Biomarkers Program (PDBP)

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The NINDS Parkinson's disease Biomarkers Program (PDBP) is a longitudinal natural history study with the goal of improving clinical trial design for Parkinson's disease (PD) and related disorders. Established in 2012, the program is comprised of four core features: 1) Standardized longitudinal clinical data and biosample collection from PD subjects (idiopathic and familial) and healthy controls, harmonized with complementary PPMI and BioFIND (supported by the Michael J Fox Foundation for Parkinson's Research) biomarker cohort efforts. The NINDS PDBP recently expanded to include participants with Atypical Parkinsonisms and other movement disorders (e.g. Multiple System Atrophy, Corticobasal Degeneration, Progressive Supranuclear Palsy, Essential Tremor), as well as five active clinical studies on Lewy Body Dementia (LBD) with an enrollment goal of 680 participants characterized with multimodal imaging. 2) Laboratory-based biomarker discovery and replication studies utilizing platforms such as whole genome sequencing (WGS), transcriptomics, methylation profiling, digital immunoassays, and exosomal characterization. These studies include longitudinal follow-up and independent replication of candidate biomarkers. Recently, the PDBP has expanded to support biomarker research in cutting-edge telemedicine and mobile health technology. 3) PDBP biospecimens banked and distributed to the research community

through the NINDS Biomarkers Repository (BioSEND) at Indiana University. New efforts in 2018 include collection and banking of PBMCs at the NINDS Human Cell and Data Repository (NHCDR) at Rutgers University to generate fibroblasts and iPSCs. 4) The PDBP Data Management Resource (DMR) infrastructure provides broad sharing and access to de-identified clinical data and associated biospecimens. With this multifaceted approach, the PDBP serves as one of the most comprehensive and long-ranging datasets enabling PD and PD-related biomarker research. Detailed information regarding PDBP projects, how to participate in PDBP studies, as well as how to query for clinical data and access biospecimens can be found on the PDBP website (https://pdbp.ninds.nih.gov).

CLINICAL SCIENCE: Pharmacological therapy

P20.01

The complement receptor C5aR1 is a co-factor for α-synuclein mediated NLRP3 inflammasome activation in microglia

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Chronic neuroinflammation driven by activation of the innate immune system is a key trigger of dopaminergic neuronal loss in Parkinson's disease (PD). Two innate immune systems that are linked to brain pathologies are inflammasomes and the complement system. We recently demonstrated that microglial NLRP3 inflammasome activation is triggered by α-synuclein aggregates leading to caspase-1 cleavage, and IL-1β secretion in preclinical models of PD. In the current study, we investigated whether complement signalling also underpins activation of microglial NLPR3 inflammasomes in PD. We first demonstrated that the receptor for complement activation fragment C5a, C5aR1, was expressed on activated microglia in postmortem PD brains. Primary microglia were then purified from C57BL/6 mice and primed with LPS, prior to stimulation with fibrillar α-synuclein to induce inflammasome activation. α-synuclein induced a delayed activation of NLPR3 inflammasomes, leading to caspase-1 cleavage, ASC speck formation, mature IL-1β secretion and dramatically increased C5aR1 expression. This response was markedly reduced in microglia isolated from C5aR1-deficient mice. Pharmacological inhibition of C5aR1 using two distinct antagonists was similarly able to diminish α-synuclein-mediated inflammasome activation. Furthermore, C5aR1 was also required for full activation of microglial inflammasomes mediated by other NLPR3 activators such as ATP. Administration of purified C5a alone to primed microglia was able to induce inflammasome activation, although not to the extent of α-synuclein. In support of these in vitro findings, AAV-overexpression of α-synuclein in the brains of mice dramatically increased C5aR1 expression in microglia. Finally, we demonstrated that fibrillar α-synuclein could activate complement directly in human plasma, and C5a was upregulated in post-mortem patient CSF and serum, providing support for this pathway in human PD pathology. Taken together, our results suggest that C5aR1 is essential co-factor in microglial NLRP3 inflammasome activation. Therapeutic targeting of C5aR1 could, therefore, be a viable strategy to reduce microglial-mediated neuroinflammation, to slow disease progression in PD and other neurodegenerative disorders.

P20.02

Validating levodopa equivalent dose conversion table in advanced Parkinson's patients on polytherapy

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Converting the dosages of different anti-parkinsonian drugs into a levodopa equivalent dose (LED) eases switching between drugs in individual patients, allows quantifiable longitudinal follow up for patients under changing drug regimens, and streamlines the interpretation of clinical study outcomes. Different conversion factors for LED were previously suggested by studies based on either theoretical considerations or on head-to-head clinical comparison of drug pairs. These studies overlooked the complex nature of real-life poly-drug regimens and the possibility that LEDs of different drugs are not linearly additive. To establish a set of conversion factors that is based on a real-life polypharmacy data in advanced Parkinson's disease, we analyzed retrospectively the pre-surgery drug dosages of 206 patients who underwent deep brain stimulation surgery between 2006 and 2018 at a single referral center. We hypothesized that the optimal set of conversion factors would minimize the coefficient of variation of total LEDs calculated over the entire population. We used a computerized optimizing tool to analyze multiple sets of conversion factors. The most optimal set was perfectly correlated (Pearson's r=1) with the commonly used set of conversion factors, that was calculated based on the arithmetic mean of previously suggested values. We concluded that real-life data from poly-drug regimens of patients with advanced Parkinson's support the currently used conversion factors for LED.

P20.03

Istradefylline, an adenosine A2A receptor antagonist, as adjunct to levodopa in Parkinson's disease (PD): A safety analysis of eight randomized controlled trials and four open-label long-term studies

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[2] IRCCS San Raffaele Pisana, Rome, Italy
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Objective: To examine safety results from pooled analyses of placebo-controlled and open-label long-term studies of istradefylline plus levodopa in patients with PD experiencing motor fluctuations.
Background: Istradefylline, a selective adenosine A2A receptor antagonist, acts via the indirect basal ganglia outflow pathway. In 2013, doses of 20 and 40 mg/day were approved in Japan as adjunctive treatment to levodopa-containing products in adults with PD experiencing wearing-off phenomena. In placebo-controlled studies, istradefylline (20 and 40 mg/day) reduced OFF-time and increased ON-time without troublesome dyskinesia, relative to placebo.
Design/Methods: Safety was evaluated in eight randomized, placebo-controlled double-blind 12- or 16-week phase 2b/3 studies

and four open-label long-term studies. Patients with PD experiencing motor fluctuations during treatment with levodopa-containing products and possibly other standard anti-Parkinson medications received adjunctive istradefylline or placebo. Assessments included treatment-emergent adverse events (TEAEs), physical (including neurologic) examinations, vital signs, weight, laboratory tests, and electrocardiograms.
Results: Placebo-controlled studies included patients receiving istradefylline (10–60 mg/day, fixed-dose, no titration; n=2073) or placebo (n=1010). TEAEs occurred in 72.4% of istradefylline-treated patients and 65.4% of placebo-treated patients. Dyskinesia was the most frequently reported TEAE (istradefylline 18%; placebo 10%). Other TEAEs occurring in >5% of istradefylline-treated patients included nausea, dizziness, and constipation. TEAEs led to similar treatment discontinuation rates between the istradefylline (6.5%) and placebo (5.2%) groups, with discontinuation rates due to dyskinesia of 1.3% and 0.7% (istradefylline and placebo, respectively). In long-term open-label studies (n=1893), patients received istradefylline for a median 53.3 weeks, with 62% treated for =1 year. The pattern of TEAEs during long-term treatment was similar to short-term treatment, with no additional adverse drug reactions identified.
Conclusions: Istradefylline offers an A2A receptor-mediated, nondopaminergic mechanism for patients with PD on levodopa and other conventional PD medications and was well-tolerated by patients with PD, with an acceptable safety profile.
Study supported by: Kyowa Kirin Pharmaceutical Development, Inc.
Previous presentation: Abstract/poster presentation submitted to AAN Annual Meeting; May 4–9, 2019; Philadelphia, PA

P20.04

A pooled analysis for 8 randomized controlled trials of istradefylline, an adenosine A2A receptor antagonist: Efficacy as adjunct to levodopa in Parkinson's disease (PD)
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Objective: Pooled efficacy analyses of eight randomized, placebo-controlled studies of istradefylline combined with levodopa in patients with PD and motor fluctuations.
Background: Istradefylline, a well-tolerated selective adenosine A2A receptor antagonist, acts via the indirect basal ganglia outflow pathway. In 2013, doses of 20 and 40 mg/day were approved in Japan as adjunctive treatment to levodopa-containing products in patients with PD experiencing wearing-off phenomena.
Design/Methods: Istradefylline was evaluated in patients with PD who concomitantly received levodopa with carbidopa or benserazide and experienced motor-response fluctuations. Eight 12- or 16-week randomized, placebo-controlled, double-blind phase 2b/3 clinical studies were conducted globally (n=3245 randomized in total); change in OFF-time in daily, patient-completed 24-hour ON/OFF diaries provided the primary endpoint. All studies were specifically designed to have common methodology. Pooled analysis results from once-daily oral istradefylline (20 and 40 mg/day) and placebo, evaluated using a mixed-model repeated-measures approach (including study as a factor), are presented.
Results: The pooled analysis included 2719 treated patients (placebo, n=992; 20 mg/day, n=848; 40 mg/day, n=879). At week 12, OFF-hours/day with 20 and 40 mg istradefylline were reduced (LS mean difference from placebo in reduction from baseline [95% CI], -0.38 [-0.61, -0.15] and 0.45 [-0.68, -0.22], respectively). ON-hours/day without troublesome dyskinesia increased from baseline with istradefylline compared with placebo (LS mean difference from placebo [95%CI], 20 mg, 0.40 [0.15, 0.66]; 40 mg, 0.33 [0.08, 0.59]). Five studies showed statistical improvement with istradefylline over placebo for OFF-time. Istradefylline was well-tolerated, with an average completion rate of 89% across all 8 studies. Dyskinesia was the most frequent adverse event (8% higher incidence with istradefylline than placebo). Other secondary outcomes will also be presented.
Conclusions: Istradefylline offers an adenosine A2A receptor-mediated, nondopaminergic mechanism for patients with PD on levodopa with motor fluctuations. Istradefylline significantly improved OFF-time and ON-time without troublesome dyskinesia in the pooled analysis of eight studies, as well as in five individual trials.
Study supported by: Kyowa Kirin Pharmaceutical Development, Inc.
Previous presentation: Abstract/poster presentation submitted to AAN Annual Meeting; May 4–9, 2019; Philadelphia, PA

P20.05

Efficacy and safety of apomorphine sublingual film for the treatment of "OFF" episodes in patients with Parkinson's disease: A phase 3, double-blind, placebo-controlled trial
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Most patients receiving chronic levodopa treatment for Parkinson's disease (PD) develop motor fluctuations with "OFF" episodes. A previous phase 2 study suggested that apomorphine sublingual film (APL) is efficacious for treatment of individual "OFF" episodes. This phase 3, double-blind, placebo-controlled study evaluated the efficacy and safety of APL as an acute, intermittent therapy for "OFF" episodes in patients with PD. Adult patients with PD and =1 "OFF" episode per day while on stable doses of levodopa/adjunctive PD medications received increasing doses of APL (10–35 mg) in an open-label titration phase until a FULL "ON" response was achieved. Patients were randomized to placebo or APL at the dose determined during titration for 12 weeks. The primary endpoint was change from predose to 30 minutes postdose in MDS-UPDRS Part III Motor Examination score at week 12. The key secondary endpoint was the percentage of patients with a self-rated FULL "ON" response within 30 minutes at week 12. In total, 109 patients who completed the open-label titration phase were randomized in the double-blind treatment phase (APL=54, placebo=55). Least squares mean (± standard error) change from predose to 30 minutes postdose in MDS-UPDRS Part III at week 12 was –11.1±1.46 with APL and –3.5±1.29 with placebo (difference, –7.6 points; P=0.0002). Separation from placebo was seen as early as 15 minutes and persisted up to the 90-minute timepoint. The self-rated FULL "ON" response rate within 30 minutes postdose at week 12 was significantly higher for APL versus placebo (35% vs 16%;

P=0.0426). The most common APL-associated, treatment-emergent adverse events (TEAEs) were nausea (28%), somnolence (13%), and dizziness (9%); the most common oral TEAE was oral mucosal erythema (7%); most TEAEs were mild and reversible upon treatment discontinuation. APL was an efficacious and well-tolerated treatment for the acute, intermittent management of "OFF" episodes associated with PD.

P20.06

Mavoglurant (AFQ056) for the treatment of levodopa-induced dyskinesia in patients with Parkinson's disease: A meta-analysis of 485 patients' data

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Introduction: Mavoglurant (AFQ056), a selective mGluR5 inhibitor, was developed to treat LID by decreasing the glutamergic signaling in the striatum. However, clinical trials showed inconsistent results regarding the efficacy of Mavoglurant in treating LID in patients with Parkinson's disease (PD).
Methods: A computer literature search of PubMed was conducted till July 2017. We selected relevant randomized controlled trials comparing Mavoglurant to placebo. Data were pooled in the Meta-analysis model using Review Manager software.
Results: Five RCTs were pooled in the final analysis. The overall mean changes in off-time and on time did not favor either of the two groups (MD -0.27 hour, 95% CI [-0.65 to 0.11]) and (MD 0.29 hour, 95% CI [-0.09 to 0.66]) respectively. The mean difference in LFADLDS from baseline to endpoint did not favor either of the two groups (MD -0.95, 95% CI [-1.98 to 0.07]. On the other hand, the pooled mean difference of change in the mAIMS favored the Mavoglurant group than the placebo group (MD -2.53, 95% CI [-4.23 to -0.82]). The pooled mean difference of change in the UPDRS-IV and UPDRS-III did not favor either of the two groups (MD -0.41, 95% CI [-0.85 to 0.03]) and (MD -0.51, 95% CI [-1.66 to 0.65]) respectively.
Conclusion: Current evidence does not support the use of Mavoglurant for the treatment of LID in PD.

P20.07

Natural Product, DP, confers neuroprotective effects in cell and worm assays via the HIF1α pathway

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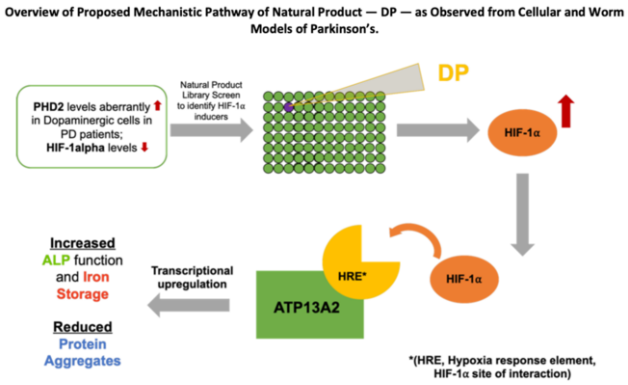
Objective: Research in our lab focuses on studying key therapeutic mechanisms for intervention in Parkinson's disease (PD). Hypoxia Response Factor 1 alpha (HIF1α) is known to induce neuroprotective pathways but is inhibited by Prolyl Hydroxylase Domain 2 (PHD2) which is aberrantly increased in PD brain tissues. We recently identified ATP13A2, a p-ATPase mutated in a young-onset form of PD (Kufer-Rakeb Syndrome), as a downstream HIF1α target. The function of ATP13A2 is not completely understood but it is hypothesized to aid in maintaining iron homeostasis and in the autophagic lysosomal pathway (ALP), an important mechanism for clearance of misfolded proteins including α-synuclein. α-synuclein aggregation within the Substantia Nigra leads to dopaminergic cell death associated with PD.
Methods: To explore HIF1α's therapeutic potential, we initiated a search for natural product compounds capable of significantly inducing HIF1α protein levels. Utilizing a high-throughput screening approach in human neuronal SHSY5Y cells, a top hit — DP — was found to result in an 8-fold induction of HIF-1α. DP was tested in a cellular model of paraquat toxicity. It was further tested in C. elegans models of PD — UA44, which involves over-expression of human α-synuclein within dopaminergic neurons leading to age-induced dopaminergic cell loss, and NL5901, which involves over-expression of α-synuclein in muscle cells leading to age-induced paralysis.
Results: Our results show that DP confers significant protection against paraquat toxicity as well as in the UA44 and NL5901 worm models. DP also significantly induced ATP13A2 protein levels in differentiated SHSY5Y cells, as well as an ATP13A2 worm homolog, capt-3, in wild-type worms (N2.)
Conclusion: The abrogation of cellular paraquat toxicity and improved health of UA44 and NL5901 worms suggests that DP is capable of preventing neuronal cell death in the latter models likely via clearance of protein aggregates. Our work currently involves elucidating DP's mechanism of action, specifically its biochemical target, and its potential role in the HIF-1α-ATP13A2 pathway.



P20.08

Comparative adherence rates of antipsychotic therapies in patients with Parkinson's disease psychosis within the United States

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Introduction: Parkinson's disease (PD) affects an estimated 1 million persons in the United States (US), with an annual incidence of 60,000 cases. Approximately 50% of PD patients develop psychosis (PDP) during the course of the disease. Antipsychotics (APs) are often prescribed off-label for PDP patients. Pimavanserin is the only treatment approved in the US for PDP (since May 2016). Since pimavanserin is new, there are no comparative treatment-pattern studies to evaluate adherence rates of pimavanserin with other antipsychotics (APs).
Methods: A retrospective claims database study was conducted to identify commercial and Medicare members with =1 claim for aripiprazole, olanzapine, pimavanserin, quetiapine (any, and low-dose [12.5–100 mg]), or risperidone from June 2016 to June 2017. The first claim was the index date. Patients had continuous insurance enrollment for 12 months pre-index and =6 months post-index. Patients in AP cohorts other than pimavanserin had =2 PD diagnoses (on index date and/or pre-index). Post-index adherence rates were measured with medication possession ratio (MPR, adherence during treatment time) and proportion of days covered (PDC, adherence during the post-index period). Patients with PDC=70% were considered adherent.
Results: The sample included 915 patients with mean age 76.9 years (standard deviation 8.2) and 54% male. Patients prescribed

pimavanserin had the highest mean PDC (0.68 versus 0.34–0.56; all p=0.002) and the highest percentage of patients with PDC=0.70 (66.7% versus 18.2%–43.1%; all p=0.002). Patients prescribed pimavanserin had higher mean MPR (0.86 versus 0.74; p<0.001) and a higher percentage of patients with MPR=0.70 (87.2% versus 64.0%; p<0.001) than patients prescribed low-dose quetiapine (12.5–100 mg/day). Patients on pimavanserin also had the highest mean percentage of post-index days at minimum mean daily dose (56.3% vs. 27.4–32.4%; p<0.001) and the lowest incidence rate per 365 days for a gap in therapy (0.59 vs. 1.28–2.98; p<0.001) than other cohorts.
Conclusion: Patients prescribed pimavanserin had better adherence as measured by PDC and gap in therapy than all other cohorts, showing for the first time real-world utilization differences of APs among PDP patients via a large US administrative claims database.

P20.09

THOR 201: A proof-of-concept study assessing safety, tolerability, pharmacokinetics and pharmacodynamics of L-dopa delivered by Impel's Precision Olfactory Delivery (PODTM) to Parkinson's disease patients in a morning OFF episode (in the presence of dopa decarboxylase inhibitor)
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Objective: Impel NeuroPharma has developed the patient-friendly, self or caregiver actuated Precision Olfactory Delivery (IMPEL PODTM) device to achieve consistent upper nasal cavity drug delivery, rapid systemic uptake and higher bioavailability relative to standard nasal sprays. This study with L-dopa for treatment of morning OFF episodes of Parkinson's disease (PD) assessed safety, tolerability, pharmacokinetics (PK) and pharmacodynamics of L-dopa administered with a dopa decarboxylase inhibitor (DCI).
Background: As PD progresses, the brain requires more frequent and higher doses of L-dopa, yet still patients suffer disabling OFF episodes due to L-dopa (the "platinum" standard treatment for PD1) plasma fluctuations. INP103 is a drug-device combination product of a novel formulation of L-dopa delivered to the upper nasal cavity by the POD device.
Methods: A randomized, placebo controlled, single dose study was conducted in L-dopa-responsive PD patients in a morning OFF episode at 5 Movement Disorder Clinics with safety, tolerability and PK blood collections for 2 hours post dosing and repeated MDS-UPDRS assessments. INP103 at 35 mg, 70 mg and 140 mg per dose were assessed, pre-dosed 60 minutes ahead of test dosing with oral DCI (benserazide).
Results: To date, 2 cohorts have completed dosing. Blinded, drug related TEAE data from 12 active and 4 placebo dosed subjects revealed single episodes of: hypertension, sinus dryness, foggy head, mucus back of nose/throat, sneezing + coughing, drowsiness and nasal irritation and 2 episodes of headache. All AEs were mild, self-limiting and most lasted less than 1 hour. There were 3 (blinded) reports of slight post dosing dyskinesia in cohort 1, but no reports in cohort 2.
Conclusions: Satisfactory safety and tolerability results have allowed for 3 escalating doses of INP103 to be administered to PD patients in morning OFF episodes, with detailed collection and analysis of PK and pharmacodynamic data ongoing.

P20.10

Dopamine agonists in advanced Parkinson's disease: Data from a large cohort of Romanian patients
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The objective was to describe dopamine agonists (DA) usage in a large group of consecutive patients with advanced Parkinson's disease (APD) with or without dyskinesia, that received at least four times a day combined Levodopa treatment and reported a minimum of 2 hours off periods/day (without early morning akinesia). The patients were evaluated to establish the opportunity of device aided therapy (DAT).
Background: DA's have a clearly defined role in relieving motor and non-motor symptoms in every stage of Parkinson's disease. Amongst young patients with mild symptoms they can delay substitution therapy, whilst in APD are quintessential in correcting the dopaminergic tonus in patients with motor complications (add-on therapy).
Methods: We retrospectively reviewed all patients with APD evaluated in our department between 1st June 2011 and 31st May 2017. We analyzed the particularities of DA's usage based on the last treatment recommendations. In some patients, if we considered that the limits of conventional therapeutical choices were not reached, we evaluated the role of DA in later treatment recommendations.
Results: During the six years, out of 311 patients considered initially 286 patients with APD were evaluated (147 men, 139 women), with a disease duration of 9.1±3.8 years (mean±SD). In this cohort the mean age was 69.1±9.0 years. The average treatment duration with Levodopa was 8.9±3.7 years with a mean daily dose of 680.9±207.4 mg divided in 4.5±0.8 doses. Most patients (215) had treatment also with DA, namely Pramipexole in 73 cases (average dose 2.1±0.6 mg), Ropinirole in 64 patients (11.3±4.9 mg) or Rotigotine patch in 84 cases (6.4±2.8 mg, in 6 cases combined with other DA). All patients had off periods with an average duration of 3.6±1.3 hours/day and 110 patients also had 2.7±0.9 hours/day dyskinesias. DAT was advised in 125 cases, out of these 107 were tested for Levodopa Carbidopa Intestinal Gel. The rest (161 patients) continued conventional treatment; in 29 cases DA introduction completed the treatment and in 41 patients DA doses were increased.
Conclusions: According to our data DA represents an efficient and often used therapeutical option in APD that enables the maximal utilization of conventional therapy before DAT.

P20.11

Construction and operation of LCIG treatment system with cooperation of medical specialists
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Introduction: There is a medication in advanced Parkinson's disease (PD) patients called "levodopa carbidopa intestinal gel (LCIG) treatment system." It requires the cooperation of various medical specialists as well as neurologists and nurses (team medicine) to provide safe and proper treatment for patients. We

have introduced LCIG treatment system since May 2017, and there have been 13 patients by November 2018. This is a report of our cooperation in constructing and operating LCIG treatment system with medical specialists.
Methods: Medical specialists included neurologists, gastroenterologists, nurses for in- and outpatients, pharmacists, nutritionists, physical therapists, occupational therapists, speech-language-hearing therapists, medical social workers and clinical engineers. LCIG treatment system consisted of the process such as arrangement of admission and discharge, patient education, dose assessment and control, medication reconciliation, physical function assessment, control of gastrostomy, medicine, and medical instruments, nutrition management, and daily-life support after discharge. Satisfaction with the treatment in 13 patients was evaluated 3 months after discharge, based on visual analog scale (VAS) of 1 to 10. We also examined the details of mentioned problems.
Results: Most patients felt anxiety at the beginning of LCIG treatment because the effect was not enough or the pump operation was difficult. Then, it was revealed that, in 12 of 13 patients, wearing-off was improved with the continuous administration of LCIG, and VAS score turned to be 7.5 on average. Patients had a good impression with the improvement of wearing-off, while they pointed out problems including the weight of a heavy pump, need of many support, pain at gastrostomy site, trouble with the tube, and lower effect than expected.
Discussion: LCIG treatment leads to a good result in many patients. At the same time, the need of care givers or troubles with gastrostomy site or with tubes was mainly indicated as a problem. Medical support by nurses, clinical engineers, and pharmacists will be required to deal with those problems. Medical specialists should start the intervention prior to providing LCIG treatment to a PD patient and fully explain the range of support for expectations, so that the treatment system can be accomplished safely and properly.

CLINICAL SCIENCE: Surgical therapy, including cell and gene therapy

P21.01

Outcomes of a prospective, multicenter, international registry of deep brain stimulation for Parkinson's disease
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Background: The effectiveness of Deep Brain Stimulation (DBS) for reducing motor complications of Parkinson's disease (PD) has been substantiated by randomized controlled trials (Schuepbach 2013). Additionally, motor improvement can be sustained for up to 10 years (Deuschl et al. 2013). Large patient data registries may facilitate insights regarding real world, clinical use of DBS. However, no registry database currently exists for a multiple-source, constant current DBS system. This report describes a large-scale registry of DBS clinical outcomes using a system capable of Multiple Independent Current Source Control (MICC) used for the management of symptoms of levodopa-responsive Parkinson's disease (PD).
Design/Methods: The Vercise DBS Registry (ClinicalTrials.gov Identifier: NCT02071134) is a prospective, on-label, multi-center, international registry sponsored by Boston Scientific Corporation. The Vercise DBS system (Boston Scientific) is a multiple-source, constant-current system. Subjects were followed out to 3 years post-implantation where their overall improvement in quality of life and PD motor symptoms was evaluated. Clinical endpoints evaluated at baseline and during study follow included Unified Parkinson's disease Rating Scale (UPDRS), MDS-UPDRS, Parkinson's disease Questionnaire (PDQ-39), and Global Impression of Change.
Results: To date, 360 patients have been enrolled in the registry and this report will provide an overview of data collected so far from implanted patients within this cohort. At 1 year post-implant, 35% improvement in MDSUPDRS III scores (stim on/meds off) compared with baseline was reported. This improvement in motor function was supported by an improvement in quality of life as assessed by PDQ-39 Summary Index (4.7-point improvement, n=193) at 1 year. Roughly 90% of patients and clinicians reported improvement as compared with Baseline. New data collected out to 2 years post-implant will be reported.
Conclusions: This DBS registry represents the first comprehensive, large scale collection of real-world outcomes and evaluation of safety and effectiveness of a multiple-source, constant-current DBS system.

P21.02

Patient engagement in the development of OUR DBS: A global patient registry addressing outcomes and unanswered questions for DBS
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Objective: To discuss the role of patient engagement in the development of a deep brain stimulation (DBS) patient registry for the purpose of improving DBS therapy and outcomes for Parkinson's disease (PD).
Background: Considerable evidence favors DBS over continued medical management when bothersome motor complications are present. However, despite more than 100,000 DBS procedures for PD worldwide, variability in outcomes remain, and best practices are not well-defined. Prospective, long-term comparisons of DBS treatment techniques are lacking. Because Parkinson's manifests with a broad range of symptoms, investigators and clinicians employ a wide variety of clinical observations and patient-reported outcomes.
Methods: Formed under the designation RAD-PD (Registry for the Advancement of DBS in PD) a planning committee consisting of neurologists, neurosurgeons, neuropsychologists, imaging specialists, data experts, and a patient advocate developed a framework for a large scale, prospective registry of DBS patients. To reflect and encourage the pivotal role of patient involvement, the patient-facing effort was renamed OUR DBS. Beginning with 20 treatment centers, OUR DBS will recruit a large and heterogeneous PD cohort undergoing DBS. Registry patients will be prospectively and comprehensively characterized using a standard clinical assessment battery and image analysis. Clinician-measured and patient-reported outcomes and imaging will be gathered from nearly

500 participants over two years, and spanning 5 years of DBS therapy.
To ensure that the registry addresses issues that are most compelling to patients, the steering committee includes a DBS patient, who in turn has solicited the input of an advisory panel of both DBS- and non-DBS-patients, including members of the Parkinson's Advocates in Research program to select patient-focused measures of outcome. In conjunction with participation, patients will access their own data and through a patient portal that will link to the clinician database and receive reports on their progress with DBS.
Discussion: RAD-PD/OUR-DBS will prospectively capture long-term clinical and patient-reported outcomes for a large cohort of PD patients undergoing DBS. Patient engagement improved the selection of outcome measures by including patient-reported outcomes most pertinent to the patient experience, and will be crucial to the retention of patients in the registry.

P21.03

The effect of long-term L-DOPA administration on hESC-derived dopaminergic grafts
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Background: Patients with moderate Parkinson's disease who are the likely recipients of future hESC-derived transplants are typically taking dopaminergic medication including L-DOPA regularly. Preclinical data indicates that exposure to dopaminergic agents during development could influence the final phenotype of the transplanted neurons. Functional recovery is improved by increased GIRK2 expression and widespread innervation of the dendrites. Thus far no studies have examined the impact of L-DOPA administration on the outgrowth or phenotype of a hESC derived dopaminergic graft and we have previously demonstrated an increase in inflammatory mediators.
Methods: Two groups of female 6-OHDA lesioned Sprague Dawley rats were given either saline or L-DOPA (6 mg/kg s.c.) administration for 4 weeks. Half of each group received intrastriatal grafts of hESC-derived dopaminergic neurons (either H9 (Lund) or RC17 (Edinburgh) (n=8–9) and then continued to receive their pre-graft treatment. Behavioural assessments for functional improvement and AIMs were performed before transplantation and at repeated intervals post-transplantation. Brains were then harvested for histological analysis for TH, GIRK2 and markers of inflammation.
Results: All transplanted groups showed improvement in amphetamine rotations at 12wk post-transplantation. AIMs scoring and L-DOPA-induced rotations were significantly reduced from 6wks post transplantation in all groups, L-DOPA treatment did not affect the outcome. Histological analysis showed good survival in the H9-derived neuron with less but still functional survival in the RC17-derived hESC group. L-DOPA administration had no significant effect on total TH+ neurons as a proportion of the total graft but did increase the ratio of GIRK2 positive neurons in both groups.
Conclusions: We show for the first time that co-administration of L-DOPA throughout transplantation may be supportive for the development of the graft into a functionally beneficial phenotype. Ongoing work will determine whether this effect is specific to L-DOPA or whether other drugs used in the treatment of Parkinson's have similar effects.

P21.04

Bilateral deep brain stimulation in Parkinson's disease by frameless stereotaxic surgery: Long-term follow-up study results
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Bilateral deep brain stimulation (DBS) of subthalamic nucleus (STN) or globus pallidus internus (GPi) are considered as effective treatment for advance Parkinson's disease (PD). While most centers perform DBS surgery by frame-based stereotaxic surgery, here we present our long-term (>5 years) follow-up results of PD patients receiving DBS surgery by frameless stereotaxy.
We report a long-term evaluation of 33 consecutive PD patients, treated by bilateral STN or GPi stimulation ranging from 5 to 11 years (average 7.5 years). Motor symptoms, activity of daily living, and motor complications were evaluated by the Unified Parkinson's disease Rating Scale (UPDRS), and cognition and mood were assessed with neuropsychological tests. Medication dosage, stimulation parameters, comorbidity and adverse events were also recorded. At last follow-up, DBS significantly improved the UPDRS motor score and there was a significant reduction in the dosage of dopaminergic drugs and improvement of L-dopa–related motor complications in these DBS patients. The neuropsychological assessment showed some cognitive decline during the follow-up period. These results indicate that DBS performed by frameless stereotaxic surgery also achieves significant motor improvement and benefits in PD patients during this long-term follow-up study.

P21.05

A novel oral and maxillo-facial technique and device for continuous and controlled delivery of small and large molecues across the blood brain barrier in Parkinson's – a proof of concept in-vivo and ex-vivo study
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James Parkinson's original description of the "Shaking Palsy" was published in 1817. Yet even after 200 years, existing treatments for Parkinson's are inadequate. This is mainly because delivery of most drugs including dopamine into the brain is prevented by the blood brain barrier. Existing non-invasive techniques do not provide controlled and continuous brain drug delivery. Invasive techniques like trans-cranial placement of catheters into the brain parenchyma make the brain prone to infection from external agents.
Dopamine neurons have a periodic phasic firing phase and a continuous tonic firing phase. The phasic firing releases dopamine in the synaptic cleft and transmits signaling to projection areas. The continuous firing phase releases extra synaptic dopamine which primes the neuron through autoreceptors for further phasic firing. Conventional anti-parkinson's drugs treat the motor symptoms. But patients are prone to develop dyskinesias after a few years of therapy because the intermittent dosing and short half-life of the drugs cause pulsatile stimulation of postsynaptic dopaminergic neurons. This results in phasic firing only without the continuous tonic phase seen in normal physiologic conditions. The resultant changes in downstream genes and proteins produce aberrant neuronal firing in the striatum. Therefore focus is on novel therapies that effect continuous firing of diseased dopamine neurons as in normal physiologic conditions.
Dopamine cannot be given orally. Levodopa has lesser efficacy than dopamine after crossing the blood brain barrier. Continuous

intravenous delivery of levodopa is not practical. As levodopa is insoluble and acidic, transdermal route is not feasible. Intra-duodenal infusion of Levodopa has associated surgical complications. Subcutaneous apo-morphine, transdermal rotigotine and prolonged release oral formulations are partially effective. Deep brain stimulation is costly, invasive and technique sensitive. Convection enhanced drug delivery of growth factors and continuous intracerebroventricular infusion of dopamine may make the brain prone to infection.
Hence a technique and device which can deliver drugs in a controlled and continuous manner across the blood brain barrier without requiring any surgical intervention in the brain holds immense potential for Parkinson's.
In-vivo and ex-vivo proof of concept animal studies for controlled and continuous brain drug delivery from the maxillofacial and oral regions are presented.

CLINICAL SCIENCE: Rehabilitation sciences (PT, OT, SLP)

P22.01

A randomized clinical trial on the evaluation of the effect of vestibular exercises on dizziness and postural control in Parkinson patients

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Introduction: Non-motor symptoms of Parkinson disease have significant effects on the quality of life in this group of patients. Among these symptoms, dizziness is associated with the changes in orthostatic hypotension (OH). About 30% of people over 65 years have dizziness; however, the exact mechanism of dizziness in these patients was not clear. Dizziness has symptoms such as fainting, light headache, vertigo and imbalance. The present study is based on the given fact that one of the reasons for dizziness in Parkinson patients is the disturbance of balance systems. In addition, the vestibular system is one of the main elements involved in normal balance. As, the role of vestibular system in Parkinson disease has been suggested in previous studies. The main aim of current study is to investigate the effects of vestibular exercises on the dizziness of Parkinson patients.
Materials and Methods: Twenty-four patients participated in this study based on the inclusion criteria and were randomly assigned into intervention and control groups. Dizziness Handicap Inventory-Persian (DHI-P was used for dizziness measurement. In addition, Berg Balance Scale (BBS), Functional Reach (FR) and 2 Minutes Walking Test (2MWT) were used for measuring the postural control before and after interventions. The intervention group performed the vestibular exercises and the control group performed the conventional exercises (3 days a week for 60 minutes and a total of 24 sessions).
Results: The total score of DHI-P showed a significant improvement in the intervention group compared to the control group (P<0.001). Also, the BBS tests (<0/001), FR (P<0/001), 2MWT (P=0.001) showed a significant improvement in the intervention group.
Conclusion: Based on the results of this study, it could be suggested that vestibular exercises, as none sophisticated, feasible, and low cost rehabilitation–protocol has beneficial effects for patients with Parkinson disease. This protocol does not need any particular equipment and can be used in all environments while it can reduce dizziness and improve motor skills and postural control in this group of patients.

P22.02

Psychometric properties of the external Housing-related Control Beliefs Questionnaire (HCQ) among people with Parkinson's disease

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Background: In research on Parkinson's disease (PD), studies focusing on perceptions of the home are rare and existing instruments capturing perceived aspects of home have not been used. Among older people in general, perceived aspects of home are associated with health. One such aspect of interest is housing-related control beliefs.
Aim: The aim was to evaluate psychometric properties of the external Housing-related Control Beliefs Questionnaire (HCQ) among people with PD.
Method: We used baseline data of the "Home and Health in People Ageing with PD" project, including 253 community-living participants (37.9% women) with PD recruited from three hospitals in Sweden. Their mean (SD) age and PD duration were 69.9 (9.2) and 9.7 (6.4) years, respectively. The external HCQ is an interview-administered questionnaire consisting of two sub-scales ("powerful others" and "chance"). It has, however, been recommended to treat the two sub-scales as one scale. The external HCQ consists of 16 items, each with five response options (strongly disagree – strongly agree). The sum score ranges from 16–80 points (the higher the better). The psychometric properties evaluated were internal consistency (Cronbach's alpha and adherent SEM), scale homogeneity (item-total correlations), data quality (percentage of missing item responses), and floor and ceiling effects.
Results: Eight persons were unable to respond to the HCQ (as well as several other instruments). The median (q1-q3) total score was 38 (32–47) points, ranging from 16 to 71. Cronbach's alpha was 0.784, and SEM was 4.926. Corrected item total correlations ranged from 0.241 to 0.563. The proportions of missing item responses were 4% for two items and 8% for one; the remaining items had none. The floor effect was 0.4% and no ceiling effect was detected.
Conclusions: The results indicate satisfying psychometric properties for the external HCQ. Albeit at the lower end, the internal consistency was satisfactory and there were no floor or ceiling effects. Still, the homogeneity of the scale is questionable because of the somewhat low corrected item total values. While these results are promising, further psychometric studies are warranted, for example, to evaluate validity for use with the PD population.

P22.03

Pushing a client with Parkinson's disease to achieve greater functional mobility: A case report

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Purpose: Deficits in balance and loss of mobility remain a major consequence of Parkinson's disease (PD). Unfortunately, dopaminergic medications have been largely ineffective in addressing such impairments. Thus, treatment strategies such as physical therapy and exercise rehabilitation should be further explored as a viable option in treating functional mobility and balance impairments in PD. This case study will evaluate a novel multi-faceted treatment approach on an individual with PD in an outpatient clinical setting.
Client Description: A 73-year-old male with a 7-year history of PD living at home with his spouse. His parkinsonian symptoms was medically managed with levodopa (0.5mg, 4 times daily). On neurological examination, the client presented with a minor right hand resting tremor, stooped posture, bradykinesia in all four limbs and trunk, rigidity in the lower extremities, and a festinating gait pattern but managed to ambulate independently.
Intervention: The client participated twice weekly in a multi-faceted exercise program incorporating high-cadence activities such as high-speed walking and cycling, high-amplitude activities such as marching with long steps or deep lunges, balance and coordination activities and a novel "forced exercise" approach which included a pushing force being applied to the client's back, in effect forcing the client to walk at a faster pace than he would ordinarily produce.
Measures and Outcome: Timed-up-and-go (TUG) outcome measure was carried out at baseline and after 4 weeks of therapy. The client's TUG time decreased from 17 seconds to 10 seconds over a 4 week period.
Implications: The client with moderately advanced PD demonstrated a clinically important improvement in functional mobility within a relatively short period of time. From a clinical standpoint, this improvement not only demonstrated a minimal detectable change in TUG time but decreased the client's risk for falls based on previous work by Nocera et al (2013). Thus, it may be beneficial to implement a multi-faceted treatment approach to address functional mobility deficits in individuals with PD in an outpatient clinical setting.

P22.04

Comparing Forward (FW) and Backward Walking (BW) speeds with age and disease severity in persons with Parkinson's disease (PwP)

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Background: Laboratory-based studies suggest kinematic measures for BW are more strongly associated with age than FW in HCs and more predictive of walking difficulties and falls in ECs (Husu et al., 2007; Fritz el al. 2013; Laufer, 2005). In PwP, BW deficits may surpass FW deficits, be correlated with disease severity, and be impacted earlier in the disease (Hackney and Earhart, 2009; Nemanich et al., 2013; Crenna et al., 2007). Considering the multidirectional nature of negotiating complex environments while walking, there is a need to have a simple clinical test of BW that may capture deficits, detect fall risk, and be sensitive to improvements. Recently, Carter et al. 2018, introduced a clinical 3 meter BW test (3MBWT) and compared its' accuracy to other common clinical measures used to identify elderly fallers, including the 10 meter FW test (10MWT).
Objective: To determine whether gait speeds during the 3MBWT and 10MFWT differed based on age and disease severity in PwP.
Methods: Retrospective chart reviews were performed at a physical therapy clinic that specializes in working with PwP. All measurements reported were part of a comprehensive evaluation performed at baseline. Demographics were summarized (mean/standard error). Differences in FW and BW gait speeds were analyzed using a one-way ANOVA (age/disease severity) This was followed up with post hoc comparisons (Bonferroni $p<.05$).
Results: Gait speed was shown not to be related to age for either BW or FW. Between group differences were significant for disease severity (H&Y stages 1–4) for BW at fast speeds and for FW at preferred and fast speeds ($p<.05$). Post hoc tests revealed that for BW, H&Y 1 and 2 were not different from one another, but were both different from H&Y 3 and 4 ($p<.05$). In contrast, for FW, there were no differences revealed across H&Y.
Conclusions: BW gait speed (3MBWT) may be able to detect declines in gait speed better than FW gait speed (10MWT), especially when comparing the early and later stages of PD. Future studies need to continue to validate 3MWT with other measures; and to determine if it can detect improvements with rehabilitation interventions that target falls and gait in PwP.

P22.05

Innovative delivery of a home-based gamified rehabilitation for early Parkinson's disease – A protocol for a usability evaluation of a digitalized healthcare approach

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Background: Emerging evidence shows that exercise has beneficial effect on both motor and non-motor symptoms, and it may potentially modify the disease course. However, people with PD (PwP) are often physically inactive and have low self-efficacy to carry out structured exercise which eventually leads to low adherence to exercise.
Methods: The objectives of this study are to develop and evaluate the feasibility of a one-stop disease portal/companion that is composed of (1) a home-based gamified exercise program and (2) a patient self-monitoring module. The first phase of the study involves the design of a smartphone application that will pair with wearable motion sensors, heart rate and activity trackers, and communicate with a web-based portal. The goal-directed exergaming module will be tailored to individual PwP specific mobility constraints with a focus on cardiovascular training; prescribed exercises will be guided by heart-rate. Gamified components of the exercises help create enjoyment and enhance compliance. Self-administered assessments including gait and functional mobility assessments and various patient-reported outcomes such as fall diary, balance confidence, quality of life questionnaires will be done via the application. The proposed digital solution will engage PwP actively with appropriately challenging, goal-orientated physical training and this habit change will be supported and sustained through continued and consistent contact with their healthcare professionals via remote monitoring. Taken together, this innovative approach will promote self-efficacy and ownership of disease management. Next, PwP in early disease stage will be recruited from community to evaluate the application and its usability. Feasibility testing will be carried out on a high-fidelity prototype and objectives are to identify existing design and functionality issues along with usability problems and to provide patients with a real look-and-feel of the mobile system. An interviewer-administered questionnaire will be

used to get feedback from participants about application's usefulness, identify problems with system features and determine the acceptance of exergaming and patient self-reported measures in PD management in the community.
Discussion: This study has the potential to determine whether home-based gamified rehabilitation for patient with early PD is feasible. This pragmatic digital healthcare approach aims to increase self-efficacy and promote disease self-management for PwP early in their disease course.

P22.06

Outcome of SPEAK OUT!® for adults with Parkinson's disease
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Interventions that focus on scaling up speech effort have been shown to effect significant improvement in communicative function for Parkinson's disease. SPEAK OUT!® therapy is a rehabilitative program developed in 2010 by Parkinson Voice Project, a nonprofit organization that conducts speech treatment of individuals with Parkinson's-related disorders. The focus of this approach is for patients to scale up their speech effort by prompting patients to speak with "intent," defined and modeled as a purposeful cognitive focus on increasing vocal loudness and intonation variability during speech. Typically administered in 40-minute sessions three times per week for 12 weeks, each session consists of a hierarchy of exercises: warm-up vocalization, sustained vowel production, pitch glides, counting, reading, and cognitive exercises. Conversational speech tasks are interwoven throughout each session to facilitate transfer of intentional speech to communication in daily life. The patient is asked to consciously and purposefully elicit that sensation every time they speak.
The present study assesses the outcome of SPEAK OUT! in adults diagnosed with idiopathic PD. This presentation focuses on data collected from the first 20 subjects of a larger study in which recruitment is ongoing. Mean SPL change and speech timing values from pre- to post-intervention and at six-week follow-up will be reported.
Patient enrollment criteria specify fluency in English, cognitive abilities sufficient to participate in all therapy activities, lack of Deep Brain Stimulation surgery, no history of speech therapy within the prior two years, and commitment to participate in the full therapy program.
Participants are assessed three times at baseline and twice post-therapy. The baseline assessments capture within-patient variability from which to compare outcomes. The two post-therapy assessments occur approximately one and six weeks after therapy completion.
Speech assessments consist of sustained vowel phonation, a one-minute monologue, and oral reading. Participants are recorded with a digital audio recorder using a 44.1 kHz sampling rate and 16-bit resolution with a built-in unidirectional voice-quality condenser microphone. The recorder is positioned at a constant distance from each patient's mouth. A 1kHz calibration tone of known intensity is recorded in parallel, corresponding to the mouth-to-microphone distance, for each speech task.

P22.07

World's largest Parkinson's chorus
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Up to 90% of individuals diagnosed with Parkinson's disease are likely to develop speech disorders during the course of their illness, and aspiration pneumonia (caused by swallowing difficulty) has been reported as the most frequent cause of death in PD patients, accounting for 70% of the mortality rate.
While these statistics can be frightening, hope may be found in singing programs for people with Parkinson's. In Richardson, Texas (USA), a group of nearly 100 singers find strength and support through their participation in the world's largest Parkinson's chorus, sponsored by Parkinson Voice Project, a nonprofit organization.
Research suggests that singing may be a viable option to improve loudness, speech clarity, respiratory support, and prosody. While the impact of singing on swallowing has not been studied, there is some evidence that therapy programs focusing on strengthening the speech musculature may also improve swallowing function. In addition, group-based approaches like singing can help reduce social isolation. In general, singing programs should be treated as one part of a larger rehabilitative program; people with Parkinson's will likely need individualized speech therapy, as well.
At Parkinson Voice Project, individuals with Parkinson's receive individual speech therapy (SPEAK OUT!®) followed by group speech therapy (The LOUD Crowd®) along with an opportunity to participate in a singing program. Each summer, this group participates in over 25 rehearsals to prepare for the annual SING OUT!® performance. Over 1,600 supporters attend the concert either in person in Richardson, Texas or online via live stream.
Parkinson Voice Project's singing program is unique in several ways. Every member of the chorus must first complete individual speech therapy (SPEAK OUT!®) before joining the singing group. In addition, this singing group is comprised entirely of people with Parkinson's. While other Parkinson's choruses invite family members and friends to join, Parkinson Voice Project's singing program adapts the music, materials, and instructional techniques to involve singers of all levels as independently as possible.
This presentation will describe this singing program and how it has been designed to maximize participation for people with Parkinson's with all levels of musical experience, cognitive function, and physical ability.

P22.08

Satisfaction and usefulness of a bootcamp educational and practical program for individuals with Parkinson's disease
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Background: Given the variety of exercise programs available, choosing a specific program can present difficulties for individuals with Parkinson disease (PD). Being able to try the different evidenced exercise programs may help guide self-selection of most beneficial exercises.
Goal: To assess the satisfaction, preferences, and usefulness regarding participation in a PD-specific educational and practical bootcamp program aiming to facilitate future exercise choices.

Methods: The bootcamp consisted of 4 days of PD-specific exercise sessions, educational workshops (strategies for disease management) and social interactions. An online questionnaire prior to the program collected demographic, clinical information and overall exercise habits and preferences. At one month follow-up, participants filled in an online questionnaire, assessing satisfaction, preferences, problems, and usefulness of the program.
Results: All 8 Participants had favorable feedback, with 100% feeling "very satisfied", "likely to attend future events" and "would recommend to another person with PD". It was the first bootcamp for all and 5/8 (62,5%) felt that much of the exercises and activities were new to them. The 2 favorite training sessions that participants enjoyed most were: dual task cognitive stepping (6/8; 75%) and warm-up with dance-like movements (6/8; 75%). The 2 less favorite sessions were: Nordic walking (2) and boxing training (2). No injuries or major problems were reported by patients except 1 patient that could not do boxing due to wound in her finger. The bootcamp was considered very helpful (7/8; 87,5%) and helpful (1/8; 12,5%) in helping participants manage their current and future exercise habits. At one month follow-up 6 participants reported making some changes in their exercise routine after the camp, namely: "more frequently I do exercise"; "Introduced power up breathing", "Taking daily commitment to exercise seriously", Joined a gym to do more exercise", "I do more walking periods and cognitive games". One participant mentioned "Not really changed anything I need more time in my day."
Conclusion: Our results suggest that the bootcamp was well-received by these 8 individuals with mild and moderate PD.

P22.09

Boxing as an alternate treatment for sleep disorders in individuals with Parkinson's disease: A feasibility study
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Over 95% of individuals with Parkinson's disease (PD) suffer from at least one sleep-related dysfunction. Sleep behavior disorder (RBD) and excessive daytime sleepiness impact mobility and increase risk of falls. Meditative and multi-modal exercise have been shown to improve sleep in individuals with PD. It is unknown if there is a relationship between the intensity of exercise and sleep quality. Boxing is a high-intensity exercise that has become a popular option with the PD community and results in improved mobility. The purpose of this feasibility study is to determine if a high-intensity exercise, i.e. boxing, has an effect on sleep and daytime sleepiness and the degree to which change in sleep impacts mobility in individuals with PD. Six community-dwellers with PD with Hoehn & Yahr scores of I-II and between the ages of 48–71 years participated in a supervised community-based, bi-weekly 6-week boxing program. Participants were fitted with a heart rate monitor during training and encouraged to exercise at 80–85% of their maximum heart rate. Training consisted of 30-minute boxing sessions one-on-one with a certified boxing coach. The training included combinations, heavy bag and focus mitt drills. Participants wore hand wraps and boxing gloves, however no sparring was involved. An occupational, physical therapist or student supervised training and led brief warm-up and cool-down exercises. Outcome measures for sleep quality, daytime sleepiness, depression, balance, mobility, and upper limb performance were taken at baseline, after 3-weeks, 6-weeks, and 12-weeks. Participants trained at 60–85% of their target heart rate. Scores improved for the Parkinson's disease Sleep Survey and Epworth Sleep Scale for daytime sleepiness within the first 3 weeks of training. Significant improvement was recorded at 12 weeks for the Hamilton Depression Scale (p=.02) and in the dual task Timed Up-and-Go from 3–12 weeks (p=.04). Participants reported improvements in symptoms and provided feedback including "…the quality of my sleep is better", "I fell asleep 1.5 hours earlier than normal" and "I can go back to sleep now; it's nice". The results of this study suggest that a community-based boxing program is feasible for adults with PD and may improve sleep and mobility.

P22.10

Acceptability of a novel trampoline intervention in rehabilitation for Parkinson's disease. Perceived barriers and facilitators
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Background: Supervised programs that challenge balance and drive motor-cognitive processes in similar ways as in real-life have recently been recommended to prevent falls in Parkinson's disease (PD). Trampoline training, where individuals can safely practice weight shifting, respond to unexpected slips/trips and train controlled falls better simulate such real-life situations.
Objective: To assess the acceptability of a supervised trampoline program (Bounce4PD) in persons with PD (PwP).
Methods: Ethical approval was obtained at the University of Lisbon (CEFMH n.11/2018). Participants received their usual physiotherapy care at the Parkinson Association plus one or two trampoline sessions at a local trampoline gym (Bounce Inc., Lisbon). Participants were included according to therapist's best clinical judgment. After 3 months, participants completed a questionnaire evaluating: (1) General demographic and clinical information; (2) participants' satisfaction; (3) perceived barriers and facilitating for participation; (4) perceived benefit of the program in managing their disease; (5) adverse events; (6) reasons of absences; (7) interest in continuing to participate; (8) if they would recommend it to another person. Trampoline sessions consisted of high-amplitude, multidirectional movements with increasing complexity and speed (fig.1). Cognitive exercises were added targeting attention, working memory and executive function.
Results: Thirteen PwP (out of 15 participating) responded to the questionnaire at follow-up. All 13 participants had a diagnosis of PD, an average mean age of 9 years, Hoehn & Yahr between I-IV. Participants were "very satisfied" (7/13) or "satisfied" (6/13) with the program. Adverse effects were mild (e.g. "feeling tired", excessive sweating). Transportation, physical disability and dependency on others were the main barriers for participation. Caregiver support, easy transportation, perceiving the benefits and flexibility in schedules were main facilitators. Reasons for absence included: unexpected medical problems (6), taxi strikes (1), medical appointments (3) and work-related issues (1). Patients had favorable perceived benefit (80% very useful; 20% moderately useful) and all referred that they were willing to continue in the program and recommend it to others.
Conclusions: Our results suggest that training on a trampoline combining balance and cognition was well received and safe for PwP. It may represent an effective alternative mode of training in a salient and safe manner in PD.

P22.11

The effect of predominately home-based physiotherapy on mobility, balance and quality of life in people with Parkinson's disease: a systematic review

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Background: It is imperative to establish an effective and sustainable model of physiotherapy to help people with Parkinson's disease (PD) live well over the course of their disease. Home-based physiotherapy is one model of care which may assist in providing long-term, sustainable physiotherapy. The aim of this systematic review was to determine: 1) the effect of predominately home-based physiotherapy on mobility, balance and quality of life and 2) if predominately home-based physiotherapy is as effective as centre-based physiotherapy for improving these activities in people with PD.
Design: Systematic review and meta-analysis of randomised and quasi randomised control trials. PROSPERO: CRD 42018107331
Method: Participants: Adults diagnosed with idiopathic PD. Intervention: Predominately home-based physiotherapy (defined as a minimum of two thirds of the intervention being completed at home). The intervention primarily involved physical practice of exercises targeting gait and/or standing balance compared with: 1) "usual care" or a placebo or 2) an equivalent predominately centre-based intervention. Outcome measures: Primary – mobility and balance; secondary – gait and quality of life.
Results: Preliminary results indicate that 15 trials met the inclusion criteria for the review. Eleven trials compared predominately home-based physiotherapy to usual care or a control group and four trials compared predominately home-based physiotherapy to centre-based physiotherapy. As different outcome measures were used for the mobility and balance, and the quality of life outcomes, data was pooled using standardised mean difference (SMD). Home-based physiotherapy improved mobility and balance (Hedge's g SMD: 0.40, 95% CI 0.07 to 0.73), and gait speed (mean difference: 0.10 m/s, 95% 0.05 to 0.15) compared to control, but did not improve quality of life (Hedge's g SMD: -0.12, 95% CI -0.25 to 0.02). There was no evidence of any difference in mobility and balance or quality of life between centre-based and home-based physiotherapy.
Conclusion: Home-based physiotherapy improves mobility and balance and gait speed in people with Parkinson's disease, and these improvements are likely to be similar to improvements following equivalent centre-based physiotherapy.

P22.12

Implementation success and challenges of post therapy LOUD for LIFE® and BIG for LIFE® exercise classes for people with Parkinson's

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The efficacy of LSVT LOUD® speech therapy and LSVT BIG® physical/occupational therapy for people with Parkinson disease (PD) has been well established over the past 25 years. LSVT LOUD is the only speech treatment for people with PD that has three randomized control trials (highest level of evidence) and long-term data of its effectiveness (Ramig et al., 2018). LSVT BIG has a growing body of literature including two RCTs (e.g., Ebersbach, 2010) and multiple smaller studies.
An important aspect of maintenance of therapy results is continued practice of exercises and skills learned in therapy. LOUD for LIFE (L4L) and BIG for LIFE (B4L) are group exercise classes that provide "graduates" of these treatments continued practice of the skills learned during therapy in a fun, motivating and social environment. Classes are led by LSVT LOUD or LSVT BIG certified clinicians who have taken an advanced training course. The classes incorporate functional, personalized activities designed to maximize maintenance of treatment effects.
We surveyed over 340 LSVT® certified clinicians in North and South America, Europe, Asia and Australia who have been trained to deliver L4L or B4L group classes, and asked them questions related to benefits and challenges to implementing these classes in their environment. Forty percent of the L4L and eighteen percent of the B4L clinicians responded to the survey. Preliminary analysis revealed that 35% of the L4L and 44% of the B4L respondents had started group classes in their environment. On a scale of 1–10 (10 being the most) those who have started classes reported on average an 8 for how effective the classes were at helping patients maintain post treatment improvements. Open-ended comments in the survey were analyzed for themes. Themes for challenges included time, cost and space requirements for classes; themes for benefits included the positive impact on maintenance, engagement and motivation of clients.
Information received from this survey provides support for the positive impact that post-therapy LOUD for LIFE and BIG for LIFE exercise classes can have on people with PD and delineates challenges to consider when developing post therapy exercise groups for people with PD.

P22.13

Global implementation of an evidence-based physical and occupational therapy (LSVT BIG®) for Parkinson's disease: Germany, France and Japan

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The goal of implementation science is translation of evidence into clinical practice to impact patient care. Implementation research examines how best to achieve this goal across diverse global settings (e.g., health systems, cultures) (Peters et al., 2013).
Lee Silverman Voice Treatment (LSVT BIG®), a physical/occupational therapy developed in the USA, improves mobility and activities of daily living in people with Parkinson disease (PD). Published studies in the USA, Germany, Switzerland and Japan (Farley 2005, Ebersbach 2010, Janssens 2014, Ueno 2017) support the short-term efficacy of LSVT BIG for people with PD. LSVT BIG provides a standardized framework for treatment and globally standardized training for therapists to support treatment fidelity.
This project evaluated implementation of LSVT BIG across diverse health care systems, languages, and culture in Germany, France and Japan. Since 2011, LSVT BIG Courses were held in Germany (25), France (3) and Japan (7) resulting in more than 790, 142, and 565 LSVT BIG Certified clinicians, respectively. A translated online survey was administered to these clinicians to assess implementation of LSVT BIG from the perception of practicing therapists.
Results revealed 94% of German, 93% of French and 73% of Japanese respondents felt they had received effective training in LSVT BIG. Since becoming certified 96% of German, 83% of French and 70% of Japanese respondents have implemented LSVT BIG in their practice. Of those, 93% of German, 90% of French and 36% of Japanese felt confident in their delivery of treatment, and 84%, 77% and 52% respectively felt they were achieving better outcomes with LSVT BIG.
Common challenges to implementation across countries were: 1) inadequate funding for intensive therapy 2) scheduling difficulties

and 3) patients unable to commit to the required dosage. A unique challenge for Japanese clinicians was how to deal with patient co-morbidities.
LSVT BIG is being successfully implemented by many therapists in these countries; however, there remain challenges. Understanding barriers may help us facilitate solutions, such as local advocacy, patient/physician education, and access to LSVT resources for certified clinicians. This knowledge may improve adoption and fidelity of evidence-based rehabilitation interventions around the world for people with PD.

P22.14

Implementation of a cognitive and motor exercise hydrotherapy community-based program for individuals with Parkinson's disease

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Background: People with Parkinson's disease (PwP) benefit from non-pharmacological interventions, such as physiotherapy, exercise, hydrotherapy and cognitive training. Combining these different interventions may be potentially beneficial given the positive evidence on multitask training emerging.
Objective: Assess the implementation of a hydrotherapy program for PwP that combined cognitive and physical exercises.
Methods: The PD-specific program was delivered as a community program provided by the Patient Association (APDPk) at a local hotel pool. Participants had to ambulate independently, be able to understand verbal instructions, and safely participate in pool sessions. The program consisted of a weekly group session (1 hour) incorporating physical exercise (e.g. walking, turning, jumping, standing, arm movements) as a response to cognitive exercises given by a physiotherapist. At 4 months participants assessed the program using a questionnaire, regarding: (1) satisfaction level; (2) adverse events; (3) reasons for absences; (4) interest in continuing to participate, and (5) perceived barriers and facilitating factors regarding ongoing participation.
Results: Five participants (60% male), with a diagnosis of PD with average duration of 3 years, mean age of 56 years, Hoehn & Yahr between I-III. Sixteen weekly group sessions were performed over 4 months (1h/week). All participants were very satisfied (100%) and referred that they were willing to continue in the program. Participants reported that what they most liked was the cognitive-physical challenges imposed and social interaction. Cramps were reported by 2 PwP as occasional adverse events. Physiotherapist reported that no major problems arose during sessions but unsafe behaviors in groups had to be continuously monitored. Reasons for absences included: disease related problems (2); work problems (2); laziness (1); and difficulty in schedules (1). Factors facilitated participation included: perceiving benefit (5), easy transportation (1), professionals' experience (3), socializing (1), and clean warm environments (2). Factors perceived as barriers included: difficulties in transportation (1), fluctuation in disease (1), restricted time (2), and work limitations (1).
Conclusions: Our results suggest that the combination of cognitive and motor interventions in a hydrotherapy group activity was well received and safe for these PwP.

P22.15

Music therapy on gait disturbance and gait analysis for Parkinson's disease using a portable gait rhythmogram

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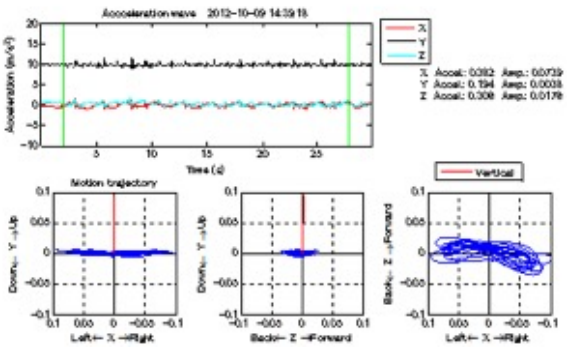
Gait disturbance is one of the most frequent and intractable motor symptoms in Parkinson's disease (PD). However, we do not have a good method to evaluate accurately daily profile of gait in the patients. The aim of this study is to develop the application of music therapy and a new method of gait analyses in PD.
The subjects of this study were 20 outpatients with Parkinson's disease (PD) with gait disturbance. We examined whether music therapy is effective as rehabilitation for gait disturbance in PD, by using a portable gait rhythmogram (PD patients' profile: H&Y: 2 or 3, duration: 6.0±5.5years, UPDRS-III: 17.3±4.7).
PD gait speed was significantly slow, the steps were small, the cadence was also slower compared as that of normal control. By the addition of 3-dimenssional acceleration measurement, the strength of PD gait was apparently weak compared as normal control (Image). The regression line indicates that gait force (acceleration) is an essential factor for gait speed. We checked a trajectory of the accelerometer, which indicates that PD patients have a large amplitude of the mediolateral direction.
The patients carried out common walking training tasks carrying a portable gait rhythmogram. The walking training tasks were walking 5m in a straight line at subjects' usual walking speeds (task 1), fast walking (task 2), walking with hand clapping (task 3), walking in step with music of 90 BPM (beat per minute) (task 4), music of 100 BPM (task 5), music of 110 BPM (task 6), and music of 120 BPM (task 7), and fast walking without music (task 8).
We recognized an effect of the music therapy by comparing walking before and after accompanied by stimulation with music. Significant improvements were observed in stride, gait speed, cadence, acceleration, and trajectory, suggesting music therapy is effective at reducing gait disturbance in PD. It is expected that music therapy will be utilized in the rehabilitation of gait disturbance in PD in the future.

PD (ID: 27)



P22.16

Respiratory responses reflecting the emotional contribution to freezing of gait in Parkinson's disease

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Purpose: Freezing of gait (FOG) in Parkinson's disease (PD) is often observed when patients are exposed to stressful situations. Changes in the heart rate and skin conductance as an emotional contribution to FOG reportedly occur just before and during FOG. Respiration is influenced by limbic factors. However, thus far, the concept of respiratory responses related to FOG has not been adequately recognized. We hypothesized that respiratory abnormality may coincide with some FOG episodes. We aimed to investigate the characteristics of respiratory responses in conjunction with FOG in actual daily living.
Methods: The subject was a 60-year-old woman with a 35-years history of PD who had L-DOPA resistant FOG. We used the Hexoskin® wearable vest. Respiratory responses (thoracic and abdominal motions) were measured using respiratory inductance plethysmography. We measured the anterior-posterior accelerations of the trunk for detecting FOG episodes. We obtained the FOG data in passing the automatic revolving door. Measurements were taken during the "on" medication cycle.
Results: While walking without FOG, the breathing pattern was regular. However, our patient presented sudden alteration in the breathing pattern not only during, but also just prior to FOG. Respiratory abnormality was characterized by a short period of apneic pause at a high lung volume. Before relief from FOG, deep expiration was observed.
Discussion: A frightened feeling may partially induce FOG. It is possible that the change in respiration that accompanied FOG was a response to the antecedent emotional stimuli because it occurred even just before the actual FOG episodes. However, this may be a different mechanism from the sympathetic response due to increased activation of the amygdale related to anxiety. Although the pathophysiology remains unclear, it appears that limbic overload leads to transiently disordered automatic control of breathing. Deep expiration before the restart of gait may be an attentional control toward breathing to release from breath holding at a high lung volume, leading to the resetting of the limbic load. Achieving an understanding of the respiratory responses may provide information to cope with emotional distress in patients with FOG. Respiratory abnormality associated with FOG may be a clinical feature of advanced PD.

P22.17

The efficacy of levodopa-carbidopa intestinal gel in patients with Parkinson's disease – a 2 year follow-up study

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Background: Levodopa-carbidopa intestinal gel (IJLC) is an efficient treatment option for Parkinson's disease (PD) patients in advanced stages of the disease. We set to evaluate the effect of ILJC on patients' perception of their own performance on meaningfull and self-chosen activities of daily living (ADL) at baseline and at 24 months post treatment.
Methods: Patients: consequtive patients with advanced PD and eligible for ILJC treatment were included in study. Assessment tool: the Canadian Occupational Performance Measure (COPM) was used to assess ADLs [1]. Perception of ADL performance was scored in terms of performance and satisfaction with performance. As such, COPM is client-centered assessment tool. Patients scored their current level of performance and satisfaction on a scale from 1 (with great difficulty or not satisfied) to 10 (with no difficulties or completely satisfied). Study design: They were assessed by the use of COPM at baseline in their best phase ON medication and at 24-month follow-up after the introduction of IJLC.
Results: Twelve patients completed the study by two years (7 females, mean age 60±15 years). The mean COPM-performance score at baseline (5.25±2.28) was not significantly different to the score at 24 months post treatment (4,77±2,09; p=0.42). Similarly, the mean COPM-satisfaction score at baseline (5.25±2.41) was also not significantly different to the score at 24 months follow-up (5.25±2.18; p=0.90).
Conclusion: Treatment with IJLC did not change the PD patients' percepation of performance as well as their satisfaction with performance as compared to baseline (best ON-medication state), suggesting that ADL functioning might be maintained stable over time as a result of treatment with IJLC.
References:
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P22.18

Group-based voice and physical therapy for persons with Parkinson's disease – an action research study

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Background: Sociographic changes and shorter hospital stays make new demands for the development of health services in the municipalities, close to where people live.
Objectives: Develop, test and evaluate a Parkinson's disease (PD) specific group-based voice and physical exercise program to strengthen persons with PD's health and function in everyday life.
Develop knowledge about PD-specific group-based voice and physical training together with users and, physical- and speech therapists within municipal health care services.
Methods: The study has a participatory action research design with three action circles: 1) collecting knowledge and evidence for the program, 2) testing and, 3) evaluation of the program together with users. The design is characterized by democratic cooperation were activities/measures and data collection and analysis are performed in parallel. Completed in 2016–18.
Inclusion criteria: Persons with PD living at home, Hoehn and Jahr 1-4. Interventions: one-hour group-based physical therapy x2/week, one-hour group-based voice therapy x1/week. Multivariate data and analysis at entry, after six- and twelve-months group-based training: Qualitative interviews, Parkinson's disease Questionnaire (PDQ-39), Mini Nutrition Assessment (MNA), Timed Up and Go (TUG), 8 meter walk test (8MWT), Step test (ST), Five Times Sit to Stand test (5xSST), Six Minute Walk test (6MWT), The Borg Scale of Perceived Exertion (Borg 6–20), Voice Handicap Index (VHI), Radbound Oral Motor Inventory for PD (ROMP), Voice Analyst (electronic assessment of pitch and volume).
Results: The voice and physical therapy program were developed with local therapists and researchers, based on recognized research, international guidelines for physical therapy, voice training, and nutrition in neurology. Becky Farley, USA, certificated

the physical therapists at Parkinson Wellness Recovery (PWR 4 life). The Voice therapist was LSTV-LOUD certificated.
39 participants, 52–91 years, 11 female, 28 men with PD were included; 3 persons had only voice training. The poster presentation with analysis includes participants who get better, the stable and, the worse.
Conclusion: Group-based voice and physical therapy strengthens exercise motivation, contributes to community and support, despite different physical and mental functions. But, the group-based therapy is demanding for the therapists who must provide individual support to those who need it.

P22.19

Design of the PERSPECTIVE study: PERsonalized SPEeCh Therapy for actIVE conversation
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Background: Speech problems in Parkinson's disease (PD) have a profound negative impact on social interaction and quality of life. Current speech treatment is, overall highly intensive and therefore not suitable for patients in all disease stages. Evidence for these highly intensive programs is growing, but still inconclusive because of small sample sizes, a lack of outcomes relevant for patients and short term follow-up. To address these challenges, we will perform a large-scale study to demonstrate the efficacy of speech therapy in PD on quality of life and speech, using personalized and home-based (remote) speech therapy, supported by a dedicated speech training app. We expect that home-based treatment will make speech therapy more available for patients in all disease stages. We also expect the personalized component and dedicated app to augment the efficacy of the treatment, and to improve the compliance of both patients and their caregivers.
Methods: We will perform a single blind, randomized controlled trial, comparing 8 weeks of speech therapy through telerehabilitation to no intervention using a waiting list design. 215 participants with idiopathic PD in all disease stages with problems in intelligibility are recruited by 12 participating specialized speech therapists. All patients will be measured at baseline and after 8 weeks. The experimental group will receive a follow-up measurement after a wash-out period of 24 weeks. The control group will receive deferred treatment after 8 weeks, but no additional follow-up assessments. The primary outcome is quality of life. Secondary outcomes are speech and voice quality, intelligibility, severity of voice and speech complaints, and caregiver burden.
Discussion: This study will be the first to investigate the efficacy of speech therapy in PD in all disease stages on a large scale, using a sufficient follow-up and outcomes that are relevant for patients.

P22.20

Case study: The effects of non-motor symptoms of Parkinson's disease patients on instrumental activities of daily living
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Background: Non-motor symptoms (NMS) in Parkinson's disease (PD) have attracted research attention, but there is little support for ADL and IADL that take NMS into account.
Object: We report on the influence of NMS, especially with respect to degree of fatigue, on the IADL of patients suffering from PD.
Method: The subject was a male in his 60s who had been diagnosed with PD six years previously. His ADL level was 'independent.' He suffered repeated falls at home and was hospitalized. He experienced physical fatigue at irregular intervals. Using the Assessment of Motor and Process Skills (AMPS), we assessed the objective levels of motor and process skills for performing ADLs on two days under different conditions. His fatigue level was mild (on 'Mild' days) and severe (on 'Severe' days). For the AMPS test, we choose two tasks on both days: vacuuming in the house ('vacuuming') and vacuuming the inside of an automobile ('vacuuming an automobile'). We also used the Assessment of Compared Qualities – Occupational Performance (ACQ-OP) to examine the extent of his awareness of the change in quality of performance due to fatigue.
Result: Mild day/Severe day: Subjective fatigue level (2/8 points), AMPS, motor skills (1.6/1.4 logit), process skills (1.2/0.6 logit), ACQ-OP (1.1/0.6). In the vacuuming task, process skills were lower than on a 'Mild' day. Predominantly decreased process skills: Sustaining Performance, Temporal Organization, Organizing Space & Objects. The patient was unaware that his process skills had decreased. Regardless of the degree of fatigue, his motor skills did not observably change.
Discussion: NMS (fatigue) affected process skills more than motor skills in the execution of IADL. The patient entered a negative spiral in which he could not devise a way to carry out his tasks in a way that compensated for his fatigue; his task performance became more inefficient; and his fatigue worsened.
Our observations suggest a need to support the provision of information that the decline in performance skill depends on the degree of fatigue and to suggest ways to adjust the task volume and the method of compensation in response to level of fatigue.

P22.21

Training Responses in Postural Rehabilitation (TRIP) using perturbations while walking
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Objective: Gait and balance disorders are a cardinal feature of Parkinson's disease (PD) that lead to increased falls risk and reduced quality of life. Poor or inadequate postural responses to external perturbation such as a slip or trip during walking are the most common reason for falls. How a person responds to an external perturbation determines if a fall will occur. There are currently no available technologies to deliver controlled perturbations in a safe and consistent way for rehabilitation of postural control during walking. The objective of this project was to extend the capabilities of the ZeroG system, a robotic body-weight support system, (Aretech, LLC; Ashburn, VA) by developing and testing a novel system (TRIP) of computer-controlled perturbations during over-ground walking in people with PD.
Methods: The ZeroG system is being assessed for feasibility in 9 people with PD and 9 healthy older adults. For this study, the ZeroG control algorithms for the support harness were modified to deliver small (150ms), medium (250ms) and large (500ms) perturbations. Subjects walked on an elliptical path over 28 meters while supported approximately 15% of body weight by the harness. Perturbation strengths were randomized over static trials (anteroposterior and mediolateral) and dynamic trials (anteroposterior and mediolateral in the direction subjects were walking or turning). Postural responses to perturbations are recorded by the number of steps to recovery.
Results: Preliminary testing has shown the perturbations applied by ZeroG to individuals with PD and neurologically intact subjects can

have a destabilizing effect, as evidenced by rapid stepping responses or in some cases a fall, which was safely arrested by ZeroG's fall detection algorithms for the support harness. Subjects tolerated the perturbations very well, stating there was no discomfort or adverse events.
Conclusions: Perturbation training is a critical aspect of rehabilitation and falls prevention. In this study, we have developed a novel tool (TRIP) for delivering safe, well-controlled, prescribed perturbations to individuals with balance disorders. We are now testing the effectiveness of successive training sessions with the ZeroG perturbations.

P22.22

Cognitively challenging exercise improved executive function in Parkinson's disease
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Introduction: Executive function, defined as a set of higher-order cognitive processes that control, integrate, organize and maintain other cognitive abilities, is often impaired in people with Parkinson's disease (PD). Executive cognitive and impairments are often associated with balance impairments. Therefore, rehabilitation interventions for PD should incorporate both physical and cognitive aspects of their disability. The purpose of this study was to investigate whether people with PD can improve executive function with cognitively challenging exercise intervention compared to a control intervention of education.
Methods: Forty-nine people with PD (mean age 69.2±6.8; Hoehn and Yahr 2.2±0.7; disease duration 7.8±5.3 years; Montreal Cognitive Assessment (MOCA) 25.69±3.49) were randomized into either a 6-week exercise or a 6-week education (n=27) intervention, followed by the alternative 6-week intervention (cross-over). The exercise intervention was a cognitively-challenging, group program based on the Agility Boot Camp-Cognition (ABC-C) for people with PD. This program includes 6 stations: (1) fast gait training (2) whole body, big movements, (3) agility course, (4) lunges, (5) boxing and (6) adapted Tai Chi. The education program taught people how to live better with PD including topics as sleep and diet. Subjects completed the Stroop Color and Word Test (Stroop) prior to the interventions (T0), before the crossover into the second intervention (T1), and at the end of the second treatment (T2). MOCA was considered as a potential covariate.
Results: Time to complete the Stroop condition improved only after exercise, irrespective of participants' cognitive status at baseline (p=0.009). The mean total time (seconds) of Stroop in the incongruous condition was 97.7±48.0 (T0), 79.4±26.3 (T1), and 78.1±78.8 (T2) for subjects in the exercise group first and 75.9±27.2 (T0), 87.5±33.1 (T1), and 32.7±38.3 (T2) for subjects in the exercise group second.
Conclusions: People with PD can improve the executive function with cognitively challenging, group balance exercise intervention. Future analysis will compare improvements of balance and gait with improvements of cognition and determine potential predictors of responsiveness, including brain imaging.

P22.23

Balance exercise increases serum brain-derived neurotrophic factor level in people with Parkinson's disease. A pilot study
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Purpose: Increasing evidence suggests that exercise may delay the progression of Parkinson's disease (PD). Their beneficial effects have been linked to increased levels of neurotrophins. In the present study, we have examined the effect of three-month moderate-intensity balance training using the Smovey Vibroswing System (SVS) on exercise-induced changes in BDNF (brain-derived neurotrophic factor) among people with PD.
Participants and methods: Volunteers were randomly divided into the Training Group (n=9, mean±SD: age 60.7±3.65 years; body mass 77.6±3.58 kg; body height 164.6±2.93 cm) and Control Group (n=9, mean±SD: age 62.8±1.61 years; body mass 79.4±2.90 kg; body height 166.2±2.55 cm). The inclusion criteria for participation in the training programme were: Hoehn and Yahr stages II–III, continuous pharmacological treatment with no change in dosage during the previous 3 months and the ability to walk independently without any aid. The Training Group performed moderate-intensity balance exercise lasting 12 weeks. Training using the SVS consisted of one-hour sessions, mainly of moderate intensity (60–70% of maximal oxygen uptake), performed three times per week. Venous blood samples were taken before and at the end of three months of balance training.
Results and Conclusion: In the Training Group, the basal serum BDNF level before the exercise programme amounted to 22.52 ±8.86 ng/mL, and after three months of training, it significantly increased (P=0.028) up to 31.51±6.53 ng/mL. No significant changes (P=0.314) in basal serum BDNF were observed in the Control Group (before training 32.64±7.30 ng/mL, and after 26.89±12.10 ng/mL). The findings of this study suggest that systematic moderate-intensity balance exercise may enhance levels of BDNF in people with PD. Including systematic exercise as a component of physiotherapy in people with PD may assist the increase in BDNF concentration, potentially leading to the enhancement of neuroplasticity and facilitating improved motor control.
Acknowledgments: We sincerely thank the volunteers for their kind cooperation in this study.
Sources of Funding: The research was carried out under a grant funded by the University of Physical Education in Krakow, Poland (Grant No. 134/BS/KRK/2017).

P22.24

A mobile application specifically designed to facilitate exercise in Parkinson's disease: Safety, feasibility, and signal of efficacy
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Objective: To test the safety, feasibility, and efficacy of a mobile application (app) that utilizes an algorithm to construct a customized exercise regimen for people with Parkinson disease (PwP).
Background: While there is considerable evidence that exercise is beneficial in Parkinson disease (PD), many PwP do not have access to exercise programs that are specifically tailored to their

needs and capabilities. The app consists of demographic questions which are fed into an algorithm that produces a tailored, video-guided exercise program using exercises designed by physical therapists.
Methods: Twenty-one PwP, who downloaded the 9zest SmartTM app, participated in this 12 week trial. Participants were encouraged to use the app to exercise 180 minutes each week. The primary endpoints were safety (adverse events and falls) and feasibility (app usage and Likert questions). The secondary endpoints were a comparison of the baseline and 8 week outcomes on the 30 second Sit-To-Stand (STS), Timed Up and Go (TUG), and the Parkinson's disease Questionnaire 8 (PDQ) with minimal detectable change (MDC) values of 3, 4.85, and 5.43, respectively.
Results: For safety, there were no bouts of dizziness, shortness of breath, or falls during the app-guided exercise. There were 4 reports of strain/sprain injuries among 3 participants, none of which necessitated medical attention. For feasibility, 9 participants averaged 150–180 minutes of app usage per week (2 averaged 120–150, 3 averaged 90–120, and 7 averaged less than 90 minutes. A majority of participants (>78.6%) felt the exercise was safe, appropriate, and enjoyable. Using the Global Rating of Change score, 78.6% felt their condition was better since starting the trial. For efficacy, there was improvement in the TUG (p=.001; 6 of 21 improved beyond the MDC) and the PDQ (p=.036; 3 improved beyond the MDC). Improvement in the STS was not statistically significant (p=.085); however, 10 of 21 improved beyond the MDC.
Conclusions: Independent, video-guided exercise using a mobile app designed for exercise in PD was safe and feasible except for some variability in app usage. Despite this, the results provide evidence of efficacy as there were improvements in 2 of the 3 outcomes. Further research is warranted.

P22.25

Changes in fear of falling: A 3-year prospective study
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Background: Fear of falling is a predictor of future falls in people with Parkinson's disease (PD) and some perceive it as their most stressful symptom. There is limited knowledge of how fear of falling changes over time in people with PD.
Aim: The aim was to investigate how fear of falling evolves over a 3-year period in people with PD.
Methods: This study is part of a larger project: "Home and Health in people ageing with PD". Participants were recruited from three Swedish hospitals; 151 participants (35% women) had complete fear of falling data at baseline as well as at the 3-year follow-up. Their mean (SD) age and PD duration at baseline was 68 (±9.0) and 9 (±6.1) years, respectively. Fear of falling data included a dichotomous (Yes/No) question and the self-administered Falls Efficacy Scale-International (FES-I), which includes 16 items (total score ranges from 16–64, higher = worse). FES-I scores were also categorized into low (16–19 points), moderate (20–27) and high (28–64) concerns about falling.
Comparisons were done between baseline values and the 3-year follow-up. McNemar's exact test was used for the dichotomous question in relation to fear of falling. Wilcoxon matched pairs signed ranks test was used for categorized and total FES-I scores.
Results: At baseline, 40% (61 out of 151) of the participants reported fear of falling, which increased (p<0.001) to 55% (n=83) three years later. The median (q1-q3) FES-I score increased (p<0.001) from 24 (18–36) to 30 (21–43). At baseline, 32% (n=49) reported low, 26% (n=39) moderate and 42% (n=63) reported high concerns about falling. Three years later, the corresponding values were 23% (n=34), 19% (n=29) and 58% (n=88), p<0.001. The three activities that were rated as the most concerning at baseline as well as at the 3-year follow-up were "walking on a slippery surface", "walking on an uneven surface" and "walking up or down a slope".
Conclusions: The study suggests that fear of falling becomes more common as well as more pronounced in people with PD after three years.

P22.26

The ParkinSong Program: Above and beyond singing
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Peer Support Groups offer social contact, practical information and mutual support for people with Parkinson's and carers. In response to demand for singing groups, Parkinson's Victoria has collaborated with The University of Melbourne, Monash Health and the Parkinson's community to develop the ParkinSong Program. Motivating, activity-based programs can provide an appealing peer support group option. Health and wellbeing benefits of singing are well documented in international literature. Research to explore therapeutic benefits of group singing for people with Parkinson's is slowly emerging. Our ParkinSong research has contributed to the body of evidence.
ParkinSong is a singing group program for people with Parkinson's, designed to support communication and wellbeing. Songs, vocal and respiratory exercises, and communication activities are selected to target Parkinson's-specific needs. Music Therapy and Speech Pathology clinicians collaborated on the design and delivery of this interdisciplinary program. ParkinSong is based on a conceptual framework and model of care that encompass factors beyond Parkinson's diagnosis and symptoms, incorporating peer support, participation, communication confidence, activity, creativity and social contact.
The program has been informed by qualitative and quantitative research into the therapeutic benefits of group singing for people with Parkinson's and their significant others. Through efforts involving members of the Parkinson's community, community volunteers, Parkinson's Victoria, and The University of Melbourne, multiple locality-based ParkinSong groups have been formed. This tested program model has provided an accessible and sustainable peer support group option for the past 5 years, offering enjoyable and engaging activities specific to supporting communication and wellbeing. Vocal warm-up and exercise, practical communication activities, group singing and social engagement are essential elements of ParkinSong. A comprehensive training package equips program leaders with the required knowledge base, skills, resources and support.
ParkinSong is a group singing and speech activity-based peer support group, offering the joy of music, social-emotional benefits and a focus on communication. Quantitative analyses indicated significant improvements in vocal loudness and voice-related quality of life at 3 months that were sustained after 12 months of ParkinSong participation. Participants' reported quality of life

benefits appear to stem from a sense of enjoyment, motivation, community, belonging, reduced isolation and social engagement.

P22.27

Power of the rhythm: A physiotherapeutic app to deliver rhythmical auditory cueing

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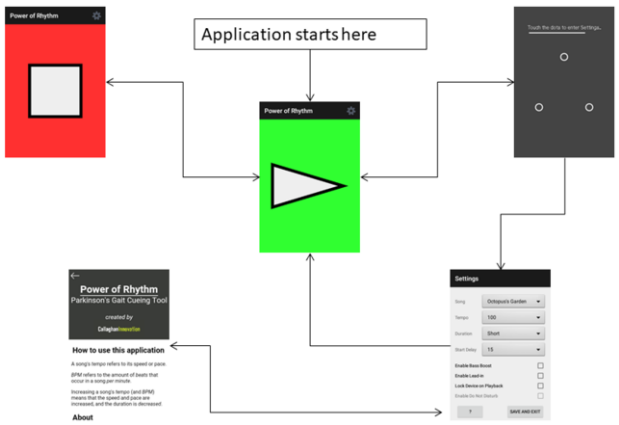
Gait impairment in Parkinson's disease is common and contributes significantly to loss of function and poor quality of life. Gait impairment is complex and resistant to medication management. Evidence supports the use of rhythmical auditory cueing (RAC) to help manage gait problems to improve stride length, gait cadence and walking velocity (Lim et al 2005, Keus et al 2004, Nieuwboer, A. et al 2009, Martin et al 2015). Delivery of RAC is traditionally provided by a metronome, however some have suggested music may be preferable to a metronome (McIntosh et al 1997, Magee et al 2017, de Dreu et al 2012). Physiotherapists may be unlikely to use music for RAC treatment due to difficulties with music selection and application, tempo modification, and copyright laws (Martin 2015). Additionally, application of RAC via a music would appear to require adequate understanding of music and rhythmic structure (Thaut et al 2015, Magee et al 2017).
Power of the Rhythm (POR) is an app developed for physiotherapists using RAC in their clinical practice. The app facilitates delivery of RAC via metronome sounds or music composed and recorded specifically using the principles of RAC and entrainment (Nombela, C. et al 2013). We tested the app with 12 physiotherapists. Participants were given sample clinical scenarios in which they might use RAC and then asked to set up the app for RAC therapy. Results demonstrated that physiotherapists initially took an average of 55 seconds to complete app set up with the first trial, but this dropped quickly with second (18 seconds) and third (25 seconds) trials. Few errors were made when using the app (average 2 for first trial and less than 1 for repeated trials) and physiotherapist satisfaction was high (average satisfaction score of 18 out of 20).
Our preliminary testing of the POR app indicate it is easy to use and could provide a useful clinical tool for physiotherapists to use RAC in their clinical practice. Further testing is required of the app in 'real world' clinical scenarios and will commence in 2019. Studies comparing RAC via a metronome versus music have not been completed and should be considered.



P22.28

Inpatient multidisciplinary rehabilitation effects on the quality of life for Parkinson's disease: A quasi-randomized controlled trial

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Objectives: To compare the effects of inpatient multidisciplinary rehabilitation and mono-disciplinary rehabilitation on the symptoms and quality of life (QOL) of patients with Parkinson's disease.
Methods: This study was a quasi-randomized controlled (alternate allocation), assessor-blinded single center study. We recruited 80 patients with idiopathic Parkinson's disease, Hoehn and Yahr (H&Y) stage 2 to 4, on stable medication. Patients were included in a multidisciplinary or mono-disciplinary rehabilitation group. Both rehabilitation programs were performed for 8 weeks (16h/week). Main outcome measures were Parkinson's disease Questionnaire-39 (PDQ-39), and Unified Parkinson's disease Rating Scale (UPDRS).
Results: Multidisciplinary intervention induced significant improvements in QOL, compared to the mono-disciplinary rehabilitation. We found that body axis symptoms (rising from a chair, posture, postural stability, falling, and walking), as well as non-motor symptoms (depression) in patients with PD, were relieved by the inpatient multidisciplinary approach.
Conclusions: Multidisciplinary rehabilitation for PD patients appears to be effective in improving the QOL. The improvement of motor and non-motor symptoms, including depression, may contribute to the improved QOL.

P22.29

Physical activity and exercise choices in people with Parkinson's disease: Preferences and barriers

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Objectives: Exercise limits disability progression in people with Parkinson's disease (PD); individuals with higher levels of physical activity have better physical function, mobility and quality of life. Most people with PD do not meet recommended physical activity levels. Preference and choice of exercise or activity are important considerations that may influence long term adherence to physical activity. Understanding factors that influence activity and exercise can provide insights into further development of interventions and health service models.

Methods: 357 community dwelling ambulant people with PD completed a cross-sectional survey focused on physical activity. Participants were 60% male, mean age 68.6 (8.8), with PD duration of 6.1 years ±7.0, with mild to moderate disability. The survey explored physical activity and factors influencing physical activity and exercise behaviour. A survey element asked participants to identify any unmet choices of exercise or physical activity, with participants invited to nominate activities they would choose or prefer to do, but were currently unable to engage in.
Results: 142 (40%) participants identified one or more activity or exercise choice that they were currently unable to engage in. The most common preferred activities were walking, running, cycling, dance, golf and tennis, in both individual and group contexts. Barriers to participation were considered according to the COM-B (Capability Opportunity Motivation Behaviour) model [1]. The most frequently identified barriers related to physical capability (e.g., balance, gait disorders, pain, joint problems), psychological capability (e.g., knowledge, confidence, anxiety), and physical opportunity (e.g., cost, time, access, transport, presence of support person).
Conclusions: Identification of preferences for exercise and activity may guide community service development to support people with PD. Some barriers identified may be considered as modifiable targets of interventions. Understanding barriers may guide the development of interventions to increase physical activity.
[1] Michie et al., The behaviour change wheel: A new method for characterising and designing behaviour change interventions. Implement Sci. 2011; 6: 42

P22.30

Association of subjective postural vertical with lateral trunk flexion in patients with Parkinson's disease
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Purpose: Subjective postural vertical (SPV) has been reported to be laterally tilted in patients with stroke hemiplegia, but it has not been reported in patients with Parkinson's disease (PD). This study examined the effect of SPV on lateral trunk flexion (LTF) of patients with PD.
Methods: The subjects comprised 41 PD patients (21 men, 74±7.4 years old, H & Y stage 2.6±0.6, and disease duration 5.6±4.9 years) capable of standing and understanding instructions. Evaluation items included LTF angle in the upright position, forward trunk flexion angle, SPV angle, UPDRS, MMSE, MocaJ, and levodopa equivalent dose (LED). Reflective markers were attached at the 7th cervical and 5th lumbar vertebra for postural evaluations. The SPV angle was measured as the angle between the vertical axis and the lateral flexion axis at the point perceived by each patient as the vertical position. The SPV evaluation was measured on both the right and left three times, and the average of the 6 measurements was used as the SPV angle. The correlation between LTF angles and the evaluation items was analyzed statistically, and the group with Pisa syndrome (PS) (PS group; LTF=15 degrees) was compared with that without (non-PS group; LTF<15 degrees).
Results: The patients' LTF angle was 5.3±6.1 degrees, and the SPV was 4.8±3.4 degrees. The SPV correlated significantly with LTF angle (r=0.51, p=0.001), forward trunk flexion angle (r=0.47, p=0.003), and disease duration (r=0.51, p=0,001). Of the 5 PS group patients (LTF 20.6±3.2 degrees), 4 were aware of LTF. The SPV was tilted to the LTF side in all 6 measurements. SPV (p<0.001), forward trunk flexion angle (p<0.001), disease duration (p=0.003), and LED (p=0.04) were all significantly different between the PS group and non-PS group.
Conclusion: SPV was associated with LTF in PD patients, and it was biased to the LTF side in the PS group. Although PS group patients were aware of LTF, their SPV was tilted, and the tilt of the SPV affected LTF of the PD patients.

P22.31

Exercise and physical activity for people with progressive supranuclear palsy: A rare form of atypical Parkinsonism
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Background: Progressive supra-nuclear palsy (PSP) is a debilitating and rapidly progressing form of atypical Parkinson's disease. PSP is associated with movement disorders, disabilities and reduced social participation. Although emerging evidence supports exercise there is a need to define optimal content, dosage and scheduling.
Aim: Our aims were to (i) critically evaluate the literature on exercise, movement rehabilitation, physiotherapy and physical activity for PSP and (ii) make PSP-specific recommendations for exercise program and trial design.
Methods: The review protocol was registered on PROSPERO (CRD42018103845). Review methods were informed by Cochrane guidelines and reporting complied with the PRISMA Statement. English language peer-reviewed exercise and physical activity studies of any design, and in any setting, were included. Interventions were excluded if they included non-invasive brain stimulation, electrotherapy or other neurological conditions. Nine electronic databases were searched until July 31, 2018. The PEDro scale or Joanna Briggs Institute instruments were used for method quality assessment. Data were extracted under headings such as study, sample and intervention characteristics. Intervention elements were extracted using the Consensus on Exercise Reporting Template. We sought missing data and calculated effectiveness where possible.
Results: From a total yield of 7415 titles 10 studies were included. Method quality appraisal indicated overall moderate to high a risk of bias. Study designs included randomised/quasi-randomised controlled trials, quasi-experimental studies, cohort and case studies. Sample sizes ranged from one to 24 participants. Interventions consisted predominantly of treadmill training, robot-assisted walking or balance training, and ranged from three to five sessions per week for four to eight weeks. Outcome measures were predominantly gait and balance. Function, disability and quality of life were inconsistently reported and adverse events were not reported. Intervention effects were typically small to moderate and statistically non-significant.
Conclusion: Exercises tailored to the specific needs of people living with PSP are needed and effects of condition-specific exercises requires evaluation with well-designed clinical trials. Complex equipment and facilities are not always accessible. Moreover there is a need for the development of a core set of outcome measures to evaluate effects of exercise for PPSP on function, disability, quality of life and wellbeing.

P22.32

The immediate effect of rehabilitation using motor image intervention in Parkinson's disease patient: A case study

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Introduction: Parkinson's disease (PD) is a progressive degeneration of the substantia nigra of the midbrain which leads to reduced motor function. A typical PD movement disorder is slow movement, and it takes long time for daily living behavior. In recent years, motor image intervention has been successfully implemented as a rehabilitation against slowness of movement. Many previous studies tried to improve long-term behavioral slowness, but few reports focused on immediate effect. The purpose of this study was to verify the immediate effect of intervention using motor images for patients with PD.
Method: Subject is a patient (Pt) with severe PD, 5 years post-diagnosis (male; sixties; Hoehn & Yahr stages Ⅴ). Pt required some assistance in almost all daily life activities. Progression of PD was such that when Pt was "OFF-state", Pt could not stand up alone. Intervention therapy was done using motor image visualization to improve Pt's slow movement, whereby Pt would imagine himself performing the movement before actually doing it. The study intervened in three kinds of actions: "getting out of the bed", "stand up", and "peg board task with upper limbs". Comparisons were done on the time required to actually perform, before and after, using the motor image intervention.
Result: Pt's movement improved after performing the motor image. Pt was able to do "getting out of the bed", "standing up" in one-third of the time and finished "peg board task with upper limbs" in one-half of the time. However, after Pt repeated the same action, all performance time extended.
Conclusion: Because supplementary motor area is suppressed, PD patients have difficulty in motor planning. In this study, it was thought that as a compensatory approach to the motor plan, by performing a smooth motor image before the actual exercise, the actual operation time was shortened. Although it is a case study, the positive results seem to indicate that there is an immediate effect on intervention using motor image for PD.

P22.33

A survey on the regional support system on dysphagia of Parkinson's disease patients

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Introduction: Eating dysphagia of Parkinson's disease (PD) is seen in 50–90%. However, eating dysphagia is often poorly aware of, and diagnosis of dysphagia is often made after pneumonia develops. Early detection is necessary for prevention of pneumonia, but the social environment is not well prepared in many cases.
Purpose: We aimed to grasp support system for dysphagia by conducting questionnaire survey on PD patients.
Methods: For 24 PD patients (11 men, age 65.0±9.5 years old, contraction of a disease period 6.3±4.4 year, Hoehn & Yahr classification median 3) who participated in "PD cafe", we performed questionary survey, "Japanese version of the 10-item Eating Scale Tool (EAT-10)", "Japanese translation of the Dysphagia Handicap Index (DHI-J)". The contents of the questionnaire were taken as "history of hospital visit, outpatient frequency, weight loss of 3 kg or more (recent 1 year), past pneumonia, histories of suffocation, hyper-salivation, swallowing video fluorography (VF) or swallowing video endoscopy (VE). Eat-10 was regarded as suspected of dysphagia with three or more points. DHI-J measured total score. The questionnaire items, EAT-10, and the correlation of DHI-J total score were measured using a coefficient of correlation of Spearman.
Results: It was 19 people (79.1%) that a questionnaire answer was obtained. We provided all the members going to hospital treatment, and the going to hospital frequency was 1.0±0.9 times a month. As for the pneumonia past, as for the one (5.2%), the suffocation past, as for two people (10.5%), the weight loss, four people (25.0%), the hyper-salivation were nine people (47.4%). Six people (37%) had dysphagia suspicion, and the enforcement history of V.F. of those and VE was alone (16.6%). The DHI-J total score was 7.1±6.9 points. "EAT-10" accepted a significant correlation in "hyper-salivation presence" (ρ=0.59, $p<0.01$), "The DHI-J total score" (ρ=0.77, $p<0.01$), "suffocation history" (ρ=0.54, $p<0.05$). Also, "The DHI-J total score" accepted a significant correlation in "hyper-salivation" (ρ=0.46, $p<0.05$).
Discussion: Even in PD patients suspected of swallowing disorder, the rate of VF and VE was low, there was a possibility that dysphagia was overlooked.

P22.34

Fall-related activity avoidance: A 3-year follow-up in people with Parkinson's disease

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Objective: This study aimed to investigate how activity avoidance due to a perceived risk of falling evolved over a 3-year period in people with Parkinson's disease (PD). A specific focus constituted those with a history of falls at baseline.
Methods: Participants with PD were recruited from three hospitals in Sweden; 151 participants (36.4% women) had data at baseline as well as at the 3-year follow-up. At baseline, their mean (SD) age and PD duration were 68.0 (±8.8) and 9.3 years (±6.3), respectively. The following assessments were included in relation to fall-related activity avoidance: A) a dichotomous (No/Yes) question: "Do you avoid activities due to a risk of falling?", B) the modified Survey of Activities and Fear of Falling in the Elderly (mSAFFE), which includes 17 activities (possible total score ranges from 17–51 points, higher scores=worse). Each activity (i.e., item) has three response categories: would never avoid/sometimes avoid/always avoid. Comparisons were done between baseline and 3-year follow-up data. McNemar's exact test was used for the dichotomous question whereas the Wilcoxon matched pairs signed rank test was used for mSAFFE scores.
Results: In the total sample (n=151), the proportion of participants that reported fall-related activity avoidance increased ($p<0.001$) from 34% to 50% three years later. Among those with a history of falls at baseline (n=64), 48% reported fall-related activity avoidance versus 64% three years later. In the total sample, the median (q1-q3) mSAFFE score increased ($p<0.001$) from 21 (18–28) to 25 (18–33). At both time points (baseline, 3-year follow-up), the two most commonly avoided activities were: "Go out when it is slippery" and "Walk half a mile". This was followed by "Reaching for something above your head" at baseline, whereas it was "Go to a place with crowds" three years later.
Conclusions: This study suggests that activity avoidance due to the perceived risk of falling increases in people with PD after three

years; fall-related activity avoidance became more common and increased in severity. Further studies are needed to identify predictive factors.

P22.35

Clinical characteristics for long-term therapeutic effects of LSVT LOUD® in Japanese patients with Parkinson's disease

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Background and Purpose: LSVT LOUD® is a 4-week vocal loudness training program for patients with Parkinson disease (PD). Although clinically efficacious short- and long-term treatment effects have been proved, clinical factors which concern them have not been fully examined. In this study, we examined the relationship between baseline demographic and clinical characteristics and therapeutic effects of LSVT LOUD®.
Methods: We enrolled consecutive PD patients who underwent LSVT LOUD® in our hospital from July 2011 to October 2016 and observed more than 12months after treatment. Associations of baseline clinical characteristics and a short- and a long-term (3, 6 and 12 months later) treatment effects were retrospectively analyzed. Main outcome measure was set as the sound pressure levels (SPLs) of sustained "Ah". We defined the patients showed =10 dB increase in SPLs at 12 months after the treatment as responders and others were non-responders. Baseline clinical characteristics of age, gender, duration of disease, disease severity, motor-symptom scale, cognitive function, and frontal lobe function were collected and compared between the groups.
Result: Thirteen patients (mean age of 66.0±7.1 years) were recruited for this study. The responder group at 12 months eight patients (61.5%) showed higher mini-mental state examination scores than the non- responder group (Mann Whitney test p=0.0051).
Conclusion: Lower baseline cognitive function affects a long-term therapeutic effect of LSVT LOUD® in patients with PD.

P22.36

Effect of virtual reality gaming and conventional rehabilitation on physical function and quality of life in patients with Parkinson's disease

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Background: Parkinson's disease (PD) poses significant health burden worldwide owing to increasing ageing population and chronic illnesses. Mobility and balance limitations are some of the most significant consequences of PD leading to functional impairments and reduced quality of life (QoL). Virtual reality gaming (VRG), an emerging rehabilitation means, seems to encourage people to exercise. There is however dearth of studies investigating the effects of VRG on gait, balance and QoL in patients with PD
Purpose: To assess and compare the effect of VRG and conventional activity based gait and balance training (CAGBT) on gait, balance and QoL in patients with PD
Methods: 43 patients (33 males, 10 females) with idiopathic PD, H&Y (2.60±0.44) purposively recruited from the Physiotherapy department of Obafemi Awolowo University Teaching Hospitals Ile-ife, Nigeria, volunteered to participate in this pretest, posttest, quasi-experimental study and were assigned to both groups. Baseline parameters of balance, gait and quality of life were assessed using Berg balance scale, BTS G-walk gait device and PDQ-39 respectively. Participants in both groups had 5–10 minutes warm-up and warm-down periods. VRG consisted of 3 kinect games: river rush, bubble game and tight rope tension for 10minutes each (30minutes) while participants in the CAGBT had treadmill training at moderate intensity for 25 minutes and balance board training for 5 to 10minutes. Both groups had two sessions per week for 8 weeks. Gait, balance and QoL were re-assessed after 4 weeks and 8 weeks of intervention.
Results: The mean age, height, weight and BMI of the participants were 68.18±8.81 years, 1.67±0.09 m, 64.13±12.50 kg and 22.85 kg/m2 respectively. Participants in VRG had significant improvements in balance (F=689.30, p=0.001), stride length (F=721.20, p=0.001) and QoL (F=107.01, p=0.001), as well as the CAGBT: balance (F=1030, p=0.001), stride length (F=546.70, p=0.001) and QoL (F=35.76, p=0.001). Comparison between the two groups showed that participants in the CAGBT had significantly higher stride length (t=-2.075, p=0.045) and gait velocity (t=-2.52, p=0.016) at the end of 8 weeks.
Conclusion(s): VRG and CAGBT were comparably effective in improving gait, balance and QoL of patients with PD. Conventional intervention led to a more considerable increase in stride length and gait velocity.

P22.37

The effectiveness of facial exercises on the facial expression and the mood in persons with Parkinson's disease

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Aim: Recent advances in neuroscience have suggested that physical exercises can improve motor symptoms and mood in persons with Parkinson's disease (PD). Persons with PD also often have a deficit of facial expression and depression. We demonstrated facial exercise improve facial expression and mood in healthy elder people, In this study, we assessed the effects of facial exercises on the facial expression and the mood in persons with PD.
Methods: Community-dwelling persons with PD (N=13, age range=33–78 years) were randomly divided into a facial exercises group and a wait-listed control group. A facial exercises program of 60 min was given once a week for 12 weeks. This program consisted of rhythmic facial movement, muscle stretching, facial yoga, and Tanden breathing. The mental health, facial expression and mood were measured.
Results: Thirteen participants completed the protocol. In the intervention group, the facial expression, and mood improved post-intervention, while the control group did not show any changes.
Conclusions: These results suggest that facial exercises are effective in improving the facial expression, and mood of persons with PD, and that the facial exercises may be useful as a therapeutic modality in this population.

P22.38

Voice quality and prosody changes of persons with Parkinson's disease undergoing "SPEAK-OUT!®" therapy during conversational and reading speech

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This study explored the efficacy of SPEAK OUT!® therapy by measuring voice quality and prosodic changes in persons with Parkinson's disease using the Acoustic Voice Quality Index (AVQI, Barsties and Maryn, 2016) and the Acoustic Multi-Dimensional Prosody Index (AMPI; Dvorak, Boutsen, & Ding, under review) during conversational and reading speech. Approximately 89% of people with PD exhibit hypokinetic dysarthria, characterized by poor voice quality (e.g., breathy, hoarse, voice tremor), reduced prosodic features (e.g., reduced loudness, mono-pitch, intermittent rapid rushed of speech), and imprecise articulation. SPEAK OUT!® is a voice-therapy program to improve functional communicative ability, stressing "speaking with intent" to increase amplitude and speech intelligibility. The acoustic voice Quality Index (AVQI) is an objective measure to quantify voice quality such as dysphonia severity with good validity across different languages (e.g., English, Dutch, German, and French). The AMPI is an acoustic metric of prosodic variation and flexibility across multiple dimensions (duration, intensity, and pitch), and is significantly predictive of dysarthria in English speakers.
Sixteen participants with PD (mean age 71.6±6.7 yrs, a mean duration of PD 7.9±8.0 yrs) took part in this study. Data included audio recordings, and demographic data such as age, gender, handedness, diagnosis, and the onset of PD. Participants were asked to (a) perform a diadochokinetic task for a duration of 10 seconds, (b) read the My Grandfather passage, (c) produce a sustained vowel sound (/a/), and (d) produce conversational speech. All data were recorded during pre-test before SEPAK OUT!® training and during post-test after the training. All recordings were made using a Zoom H1 Handy digital Recorder with a TUBEPre preamp and headset placed 8cm away from the participant's mouth. Settings were maintained for both recording sessions. Our previous research findings (Boutsen, Park, Dvorak, & Cid, 2018) show that persons with PD undergoing SPEAK OUT!® demonstrate improved prosodic features and voice quality in both passage reading and conversational speech, as measured perceptually by experienced clinicians. This research compares conversational and reading speech performance using a quantitative voice quality and prosody index methods to see if efficacy can be demonstrated objectively in these speech performance domains following SPEAK OUT!®.

P22.39

The severity of motor symptoms is the best predictor for level of functionality according to FIM in people with Parkinson's disease

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Background: The Functional Independence Measure (FIM) is a tool used to assess a patient's level of disability as well as change in patient status in response to rehabilitation or medical intervention. Although the FIM has been used for several neurological disorders, there is reduced number of study investigating its application in Parkinson's disease.
Objective: to identify among several motor, cognitive and mental measures, which of them has the higher power to predict the Level of functionality according to FIM in people with PD.
Methods: Participated this study 32 people with idiopathic PD with mean age of 69 years in I-V stages of disease evolution according to Hoehn and Yahr (H&Y) classification (6.10+4.5 years of disease evolution). The evaluations were fulfilled in two individual sessions, during the ON period of medication, using Unified Parkinson's disease Rating Scale (UPDRS) to assess general aspects of disease, the Mini-Balance Evaluation Systems Test (MiniBest), Falls Self-Efficacy Scale (FES) to assess balance and the fear of falling, respectively, Montreal Cognitive Assessment (MoCA) to assess cognition, Geriatric Depression Scale (GDS) to assess depression, Timed Up and Go test (TUG) to assess the functional mobility, Six-minute Walk Test (6MWT) and Five times sit-to-stand test (5XT) to assess physical capacity, the Nine Hole Peg Test (9HPT) to assess manual function and FIM to assess the level of functionality in tasks including bowel and bladder control, transfers, locomotion, communication, social cognition and six self-care activities.
Results: The statistical analysis showed a significant correlation between scores obtained in FIM and H&Y, UPDRS, 9HPT, FES, MiniBest, TUG, PDQ-39, 6MWT ($p<.05$). However, the multiple regression model showed that only UPDRS-section III and 6MWT were able to predict the FIM scores ($R=.88$; $R^2=.78$ Adjusted $R^2=.76$; $F(2.33)=58.56$; $p<.000001$). The analysis of predict and observed values confirmed the power of model.
Conclusion: The severity of motor symptoms associated to performance for walking long distance are the best predictor for the decrease in functionality in people with PD, in terms of Grading categories range from total independence to total assistance.

P22.40

Depression instead of the motor or cognitive alterations is the crucial factor in determining the performance perception and performance satisfaction in people with Parkinson's disease

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Background: The Canadian Occupational Performance Measure (COPM), a scale developed for use by occupational therapists (OT), is a recommended tool to enable personalized health care in people living with Parkinson's disease (PPD). COPM has as the primary purpose to identify issues of personal importance to PPD and to detect changes in a patients' self-perception of occupational performance over time. Although the vital role of OT for care of PPD has been progressively recognized, there is a reduced number of evidence about the impact of the motor, cognitive and mood alterations on performance perception and performance satisfaction.

Aim: To investigate the impact of the motor, cognitive and mood alterations on performance perception and performance satisfaction in PPD.
Methods: Participated in this study 22 people with idiopathic PD, with 68.2+8 years of age, in stage I-V of disease evolution according to Hoehn and Yahr (H&Y) classification. The participants were evaluated in two individual sessions in ON period of dopaminergic medication, using the COPM performance to measure is the performance (COPM-P) and satisfaction (COPM-S) on occupational performance; Unified Parkinson's disease Rating Scale (UPDRS)-section III to assess the severity of motor symptoms; Montreal Cognitive Assessment (MoCA) to assess cognition; and the Geriatric Depression Scale (GDS) to assess depression. The statistical analysis investigated the correlation between COPM-P and COMP-S with age, gender, schooling, disease progression, UPDRS, MoCA and GDS.
Results: The statistical analysis showed a significant correlation only between COMP-S and GDS (r=-.60, p=.01), confirmed by the multiple regression model showed that only GDS is able to predict the COPM satisfaction scores (R=.37; R^2=.34; Adjusted R^2=.29; p<.05).
Conclusion: According to COPM, despite the disease evolution, the severity of motor symptoms and cognitive decline, the only factor correlated with performance satisfaction occupational performance in all areas of life, including self-care, leisure and productivity is the level of depression.
Clinical implication: The integrative care including psychological support is crucial to improving the performance satisfaction in occupational tasks in PPD.

P22.41

Construct validity of more affected hand performance on the 9-Hole Peg Test in people with Parkinson's disease

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Objectives: Rehabilitation for people with Parkinson's disease (PD) may include evaluation and treatment of dexterity impairments that impact on performance of everyday manual tasks. The 9-Hole Peg Test (9HPT) is recommended for dexterity evaluation in PD; however, evidence to support its validity is limited to an investigation in a small sample (n=30) of people with mild to moderate PD. The current aim was to explore the convergent and known groups validity of 9HPT scores for the more affected hand (MAH) in a large sample of people with mild to severe PD.
Methods: This was a secondary analysis of baseline data from the ParkinsonNet trial. Participants were independent community dwellers with no major comorbidities, assessed when 'on'. Outcome measures included a single trial of the 9-Hole Peg Test (9HPT), the Patient Specific Index Parkinson's disease (PSI-PD), where individuals prioritise activity limitations from key domains including the upper limb (UL), and the Self-assessment Parkinson's disease Disability Scale (SPDDS). To investigate construct validity, we compared 9HPT performance of participants prioritising UL problems with that of participants prioritising other activity limitations (known groups validity). We also explored the relationship between 9HPT MAH performance and self-reported hand function scored with the 13 fine coordination items contained in the SPDDS (SPDDS-FC) (convergent validity).
Results: The 572 participants (332 men, 240 women) had mild to severe PD (HY I-IV), a mean age of 68.3±7.7 years and disease duration of 5.1±4.5 years. Participants prioritising UL problems (n=260) were significantly slower at completing the 9HPT than participants prioritising other limitations (-5.80 seconds; 95% CIs -3.46, -8.01; p<0.01). There was a moderate correlation (Spearman's rho = 0.39; p<0.001) between 9HPT MAH dexterity and self-reported hand function (SPDDS-FC).
Conclusions: Our results provide support for the known groups and convergent validity of 9HPT MAH scores in the evaluation of dexterity in people with mild to severe PD during their medication 'on' phase. Associations between MAH dexterity performance and self-reported function were moderate, therefore, incorporating 9HPT performance with self-reported function in the assessment of manual dexterity limitations in PD is recommended.

P22.42

Parkinson's Foundation Physical Therapy Faculty Program evaluation

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Objectives: In 2016, the Parkinson's Foundation partnered with clinical and research experts to implement a training program for physical therapy (PT) faculty members who want to develop skills in teaching entry-level PT students about Parkinson's disease (PD). This report describes the PT Faculty Program and its outcomes in 2018.
Methods: The PT Faculty Program provides faculty with PD-specific didactic and observational training at expert clinical and research centers. The PT Faculty Program grew from one to two expert care centers in 2017. Training focuses on (1) knowledge of PD medical management, (2) PT treatment strategies for PD, and (3) curriculum development. Twelve PT faculty participants from the two 2018 Faculty Training Programs completed surveys investigating changes in knowledge immediately following the course, and follow up changes in confidence and teaching behaviors were assessed 4 months after training (n=10).
Results: Physical Therapy Faculty Program participants reported improved confidence in their ability to teach PT students about PD (63% to 89%; p=0.0004) and improved confidence in treating people with PD (74% to 94%; p=0.0001). After training, six participants (50%) reported increased lecture time in their curriculum devoted to PD content, four of whom also increased laboratory time. Faculty had good knowledge on basic topics before the training program (neural circuits, fall risk factors, quality care indicators). Following the PT Faculty Program, participants had improved knowledge in specialized areas (DBS targets and pelvic floor health). Participant feedback included a desire for increased pedagogical content and assist with curriculum development resources.
Discussion: The Parkinson's Foundation PT Faculty Program improves PT faculty teaching confidence, treatment confidence, and specialized knowledge. Past evaluations indicate that PT faculty trainees teach an average of 60 new PT students each year;

therefore, training 12 new faculty members improves the content delivered to approximately 720 PT students each year. Planned improvements in the Faculty Program include increased curriculum development content and specialized knowledge consistency across training centers. An online educational platform is being developed by the Parkinson's Foundation to share curriculum development resources with faculty trainees.

P22.43

Physical therapy practice patterns, barriers, and facilitators at Parkinson's disease expert centers in the United States: A mixed methods study

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Background: Physical therapy (PT) is an evidence-based intervention that is often underutilized by people with Parkinson's disease (PD), particularly early in the disease. This mixed methods study blends quantitative and qualitative data to describe current practice, identify barriers to evidence-based practice, and to elicit implementation strategies for improved care.
Materials/Methods: Online surveys were sent to 251 physical therapists (PTs) and 268 doctors (MDs) at 32 academic medical centers with PD expertise in the United States. Surveys addressed PT referral practices, exercise prescription, and use of evidence-based PT measures and interventions. Based on survey results, explanatory focus groups and interviews were conducted with MD, PT, and consumer stakeholders at 6 centers selected for regional variability (urban/rural), proactive PT practice, and use of routine long-term PT monitoring. Discussion topics included PT referral processes, barriers, and improvement strategies.
Results: Survey response rates were 43% for PTs (n=108) and 29% for MDs (n=78). Over 80% of MD respondents reported referring more than 60% of their patients in Hoehn and Yahr (HY) 3–4 PD to PT, while less than 25% reported frequent referrals in HY 1, 2, and 5. 70% of MD and PT respondents would recommend that an infrequent exerciser with HY 1 PD should attend PT at least every 6–12 months in the absence of personal or environmental barriers. Intervals decreased to 1–2 months in HY 4, but only 40% of PTs reported using routine follow-ups. Two delivery patterns emerged from the explanatory interviews: (1) centralized expert model of PT and (2) dispersed knowledge model linking centers of excellence with community PTs. Centers with high PT utilization used both models. People living in rural and suburban areas, particularly those with additional transportation barriers preferred the dispersed knowledge model. Modifiable barriers for both models include: communication and scheduling logistics, patient and clinician knowledge of insurance, routine follow-ups to assess function and provide motivation to exercise, and disseminating research on PT and exercise to patients and clinicians.
Discussion: Identifying two distinct models of care could improve our ability to target future implementation strategies for quality improvement. Future quality improvement efforts should target physical therapists, physicians, and consumers of PT.

P22.44

Global implementation of efficacious voice treatment for Parkinson's disease: LSVT LOUD Germany, France and Japan

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Abstract: This project was designed to evaluate the implementation of an efficacious voice treatment, Lee Silverman Voice Treatment (LSVT LOUD), into scope of clinical speech practice in Germany, France and Japan. 404 clinicians trained in LSVT LOUD were surveyed on a range of variables including training effectiveness and treatment outcomes.
Rationale: Evidence-based rehabilitation without successful implementation has limited impact on patient care (Center for Research in Implementation Science and Prevention (CRISP), 2015).This presentation will describe the implementation of LSVT LOUD, an efficacious voice treatment for Parkinson Disease (PD), with three published Randomized Control Trials (RCTs) documenting the short and long-term efficacy in the USA (Ramig et al., 2001a,b; Ramig et al., 2018), into the clinical speech practice in Germany, France and Japan.
Method: The translation pathway recommended by CRISP was followed, with emphasis on treatment fidelity. Thus a key element in the implementation process was standardized training of speech clinicians. A fundamental goal was maintaining the fidelity of the training while respecting the culture of the country.
Thirty-five LSVT LOUD Training and Certification Courses were held throughout Germany, France and Japan since 2000 resulting in more than 3,000 LSVT LOUD Certified clinicians. All training materials were translated into German, French and Japanese by native speakers and all training courses were delivered live with either simultaneous or subsequent translation.
To assess implementation and treatment fidelity of LSVT LOUD, an online survey (translated into German, French and Japanese) was administered (Survey Monkey) to these LSVT LOUD Certified clinicians.
Results: Preliminary results revealed 72–90% of clinicians surveyed felt they had received effective training in LSVT LOUD and 62–72% felt they were achieving better outcomes with LSVT LOUD than previous approaches. These findings were consistent with a pilot surveys of groups of German and French clinicians (Brauer et al., 2016; 2018).
Conclusion: LSVT LOUD is being implemented successfully into scope of clinical speech practice in Germany, France and Japan. This successful implementation of science into clinical practice model provides a road map for other countries where LSVT LOUD clinicians are trained (over 20,500 LSVT LOUD clinicians in 75 countries).

P22.45

Classifying Parkinson's disease by movement subtypes: Findings from a multimodal exercise program

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Individuals with Parkinson's disease (PD) experience numerous functional deficits, most notably in postural control (PC). The Sensory Organization Test (SOT) offers a quantitative measure of postural control assessing the somatosensory, vestibular and visual systems. Currently, there is a move to clarify the subtyping of PD by categorizing individuals by movement subtypes of tremor, gait/posture (GP), and symmetrical disease. (Lawton et al., 2018) Therefore, this retrospective analysis will compare SOT scores between the Hoehn and Yahr (HY) scale and the movement subtypes in individuals undergoing a 5 week exercise program.
Methods: Participant recruitment was from the local Parkinson's Support Group. Protocol for testing followed the protocol for the SOT using a Computerized Dynamic Postural device. Participants: n=12, mean age=66.6±8.2, 6 males, 6 females, HY1=2; HY2=7; HY3=3 with the following movement subtypes, T=2, GP=7, and S=3. Individuals participated in a five week program of agility, dual tasking emphasizing gait and PC. Intervention provided the program 2 times per week with an additional one hour Yoga session. Statistical analysis was performed by SPSS 25, analyzing SOT conditions and sensory scores using pair t-tests. Between group analysis of HY and movement subtypes were performed using two way ANOVA. P value set at <.05.
Results: There were positive pre and post-test changes in SOT 4–6, composite, vestibular and vision sensory scores, although there was no statistical difference within this analysis. In analysis of the movement subset, the tremor group appeared to have greater change throughout SOT scores while the symmetrical group showed limited pre post changes. Between groups effects using two way ANOVA found statistical differences in composite scores for both HY and movement subsets with significant differences in vision and SOT6 between the HY groups
Discussion: A shift has begun in subtyping PD based upon clinical motor presentation. (Marras & Lang, 2013). From this analysis, activity intervention shows sensory score increases in the tremor group with less robust changes in individuals with symmetrical findings. Further studies need to be performed to ascertain these findings in order to direct therapeutic programs.

P22.46

Elderly with Parkinson's disease evaluated in the neurological center: CENPAR, Chile

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Objective: To analyze specific characteristics of the elderly Chilean with Parkinson's disease (PPD) to know the correlations and trends of their disease in terms of physical, cognitive and functional alterations, their age and years of diagnosis to meet their needs early avoiding the dependence and prostration.
Method: Random retrospective descriptive study. 110 older PPD adults aged between 61 and over are evaluated, they went to CENPAR rehabilitation between 2017–2018. Those who fail to complete the tests are excluded. Standard deviation (STD) is measured for static equilibrium with open and closed eyes, Moca cognitive test, and Barthel independence test. The average, minimum and maximum ranges, correlation and trend are calculated.
Result: PPD 44% are women and 56% men. The average age is 73 years. Average diagnosis age is 6 years, 65% <6 years; 15% 6 to 10 years; 20% 11 years. Static balance open eyes (OA) STD average 4.23 mm/sec, 60% 10 mm/sec Eyes closed (OC) STD average 8.45 mm/sec, 20% 10 mm/sec. MOCA cognitive test average of 22 points, 12% without cognitive impairment (26 and 29 points); and 88% cognitive impairment (5 and 25 points); Nobody 30 points. Barthel independence test the average is 90 points, 7% moderate dependence; 71% mild dependence; 22% independence.
Conclusion: The sample has variables related to age, PD and rehabilitation, 65% are PPD between 0 and 5 years of diagnosis; 88% have dependency on daily activities; 88% cognitive impairment; 80% visual dependence on static equilibrium. Correlation between age and Barthel is low reverse (-0.26), the others (years PD, Moca, equilibrium) are very low inverse. Between years EP and Barthel (-0.28) is low reverse; OA (0.32) and OC (0.25) direct low; Reverse mocha very low. Between Moca and Barthel (0.28) direct low. Trend to horizontality, except in the correlation between OA and very high direct OC (0.85).

P22.47

Health in Chile and Parkinson's disease, case study: CENPAR, Chile

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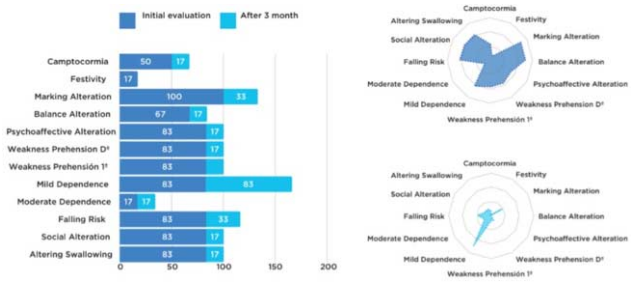
Objective: To determine the level of impact and biopsychosocial benefits obtained by people with Parkinson's disease(PPD) with low level of wealth by receiving free interdisciplinary rehabilitation for 3 months in a first study.
Method: 12 sessions (3 months) of free interdisciplinary rehabilitation with kinesiologist, occupational therapist, voice therapist of 60 minutes once a week at 6 PPD with low level of wealth. Initial evaluation of dimensions was presence of camptocormia, off-course, biomechanical change in gait, alteration of static equilibrium, risk of falling, alteration of swallowing, weakness of prehension of hands, psycho-affective alteration (signs of depression), social disturbance(isolation), dependence on third parties when carrying out activities of daily life. At the end they are re-evaluated, compared, the impact and possible benefits are measured.
Result: Initially the dimensions presented a high incidence of PPD due to alterations in mobility, functionality and independence, affecting their emotional and social state, generating isolation. At the end of the period it is reevaluated, finding a noticeable improvement in its neuromotor conditions (balance, gait, posture) leaving almost no risk of falling and decreasing swallowing disorders. Recovers some variables of independence in daily life, signs of depression disappear, and dare to interact with their environment, being a great

impact to increase the quality of life of PPD, managing to experience lost roles, decreasing expenses associated with injuries and hip fractures, absenteeism, avoiding the collapse of waiting lists presented by the country's health service.
Conclusion: Granting interdisciplinary care in PPD with less wealth generates positive impact on their lives and quality of life, benefiting their biopsychosocial context, being a benefit because it improves their neuromotor condition, decreases depression and social isolation, returns to work, decreases the risk of falls and possible injuries; it is a benefit for your family because it decreases the dependency avoiding the caregiver syndrome and the associated debts; and it is a benefit for the country because it reduces expenses for surgeries, hospitalizations and disability. It is a challenge for the authors of this study to carry out a larger study that achieves changes in national Parkinson's programs for the benefit of people.



P22.48

The effect of nordic walking in Parkinson's disease – Successive three-dimensional gait analysis of a patient for three years
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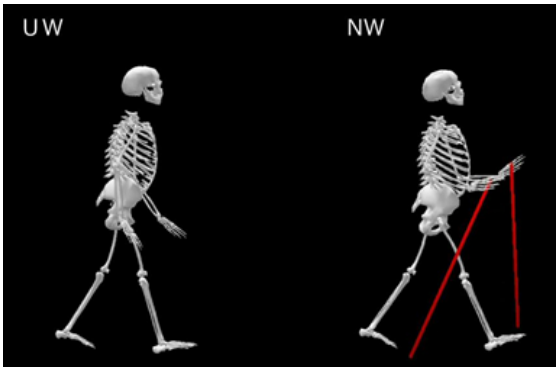
Background and Purpose: Nordic walking (NW) is reported to ameliorate the motor (gait speed, postural stability, and exercise capacity) and non-motor symptoms (pain, apathy, attention, and concentration) in patients with Parkinson's disease (PD). We focused on the gait pattern and analyzed the gait parameters in usual walking (UW) and NW in one case for three years.
Subjects and Method: The subject was a 72-year-old man, with a 10-year history of PD and whose condition was at Hoehn-Yahr stage 3 (bradykinesia (-); rigidity (+: right < left, upper extremity = lower extremity, resting tremor (-); postural instability (-); trunk bending mildly to the left side). We performed a three dimensional gait analysis of his UW and NW, once in six months for three years.
Results: The NW resulted in increased gait speed and stride length, when compared to those observed for UW. The hip joint of the stance leg was extended widely (due to decreased pelvic nutation) in the terminal stance phase because postural balance was stabilized by the use of the two sticks in NW. This contributed to gait improvement. We compared the UW before and after NW to confirm the immediate effects of NW. We found that the extended hip joint at the terminal stance phase induced by NW, was carried over in UW after NW.
Conclusion: We concluded that NW is not only a support tool, but also an effective exercise therapy by itself.



P22.49

Effect of nordic pole walking with Visual Analog Scale for time course in Parkinson's disease
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Objective: Physical activity has positive effects in general and also in patients with Parkinson's disease (PD). The impact of Nordic walking (NW) in PD has been investigated in several studies but results are inconsistent. This purpose of this study was to aim at evaluating predictive factors by visual analog scale daily complaint for effect of NW on PD.
Methods: One participants (age:60 years, high:172cm, body weight: 80 Kg) with PD (diagnosis: 12 years; Hoehn and Yahr stages 3) recruited from near relative. It was applied to custom-build light weight Nordic pole with exterior kurtosis for this experiment. Measurement item were steps and chief complaints of daily activity as visual analog scale for time course during over 20 weeks on NW trainings. In addition, we performed quantitative calculating 10 m walking test in each month.
Results: This study focused on the determination of predictive factors associated with an improvement of the QOL as motor part in PD patients who performed a daily working trip on NW training program. There was disappeared parkinsonian tremor during NW. xcvOur finding was expected to increase the length of stride during NW, to keep the postural stability and to improve the enhanced mood in QOL. However, it was observed muscle soreness around upper part of the thigh and hip joint muscles beginning of 4 weeks. Thus, it was not demonstrated to improve immediately the chief complaints in VAS by Nordic walking.

P22.50

The consideration of personality in patients with Parkinson's disease and freezing of gait

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Background/Objective: Freezing of gait (FOG) in patients with Parkinson's disease (PD) is the main cause of falls, and it strongly affects the patients' activities of daily living and quality of life. The cause of FOG has been reported to involve motor symptoms, cognitive dysfunction and mood dysfunction. We investigated personality in Japanese PD patients with FOG.
Method: The study included 39 idiopathic PD patients. To evaluate FOG, we administered the Japanese version of the New Freezing of Gait Questionnaire (NFOG-Q), which has a cutoff for FOG at ?1 point. We evaluated the personalities of PD patients using the Japanese version of the Temperament and Character Inventory-Revised (TCI-R), the Movement Disorder Society-Unified Parkinson's disease Rating Scale (MDS-UPDRS), levodopa-equivalent daily dose (LEDD), cognitive dysfunction including the Mini-Mental State Examination (MMSE), the Japanese version of the Montreal Cognitive Assessment (MoCA-J) and the Frontal Assessment Battery (FAB). Non-motor symptoms including depression, apathy, sleep disorders and fatigue, were also assessed.
Result: Nineteen patients were FOG positive. Scores on the MDS-UPDRS and LEDD were significantly higher in the FOG-positive group than in the FOG-negative group. There were no significant differences in cognitive function between the groups. Scores for sleep dysfunction, daytime sleepiness, REM sleep behavior disorder and fatigue were significantly higher in the FOG-positive group than in the FOG-negative group. On the TCI-R, the novelty-seeking score was significantly higher and the self-directedness score was significantly lower in the FOG-positive group than in the FOG-negative group. There was a significant positive correlation between the NFOG-Q score and the persistence score (r=0.41).
Conclusion: The FOG-positive patients were shown to have strong impulsivity and decreased decision-making ability. The maladaptive behavior strategy correlated with the severity of FOG. Personality changes might be associated with the onset or severity of FOG in PD patients.

P22.51

Speech intelligibility of individuals with Parkinson's disease in noise following voice or articulation treatment

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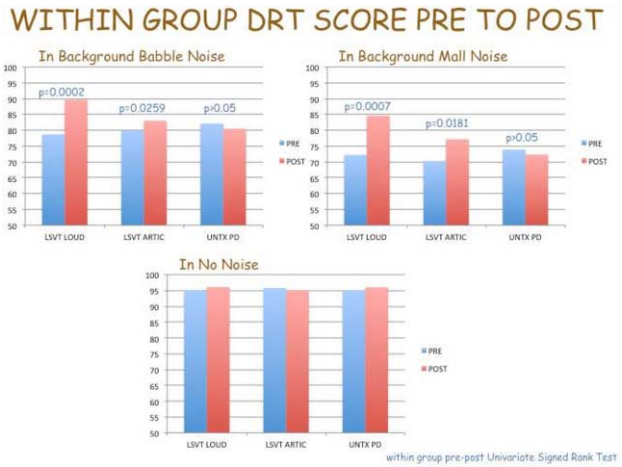
Speech intelligibility is significantly reduced in PD and can be a main concern for people with PD especially in the presence of background noise. Reduced intelligibility may lead to significant declines in functional communication, communicative participation, and quality of life. We studied speech and consonant intelligibility in Parkinson disease (PD) using the Diagnostic Rhyme Test (DRT) in noise and non-noise conditions following two different intensive speech treatments, LSVT LOUD(®) and LSVT ARTIC(TM). Our aim was to determine whether increased loudness or enhanced articulation had the larger impact on improving the perception of speech and consonants in individuals with PD. 58 individuals with PD were randomly assigned to participate in LSVT LOUD (20), a contrastive, parallel treatment LSVT ARTIC (20), or an untreated group (18, UNTX) and were recorded while reading half of the DRT word list pre and post treatment. Noise was then added to the DRT sound files, and they were analyzed according to standardized protocols by trained listeners at Dynastat, Inc. in three noise conditions: No noise, Mall and Babble. Mall and Babble noise were presented at a 0 dB SNR pre-treatment. The dB SPL of the noise file was the same both pre and post. The dependent variables were DRT score and SPL.
Pre to post therapy changes in DRT scores in Babble noise for the LSVT LOUD group were significantly greater than those for the LSVT-ARTIC and UNTX groups. Pre to post therapy changes in DRT scores in Mall noise for the LSVT LOUD group were significantly greater than those for the UNTX group. Changes from pre to post SPL for LSVT LOUD group were significantly greater than those for both the UTX and the LSVT ARTIC groups. In general, the perception of consonants post therapy of the LSVT LOUD group was better than the LSVT ARTIC group in both background noise conditions.
These results reinforce the need to assess intelligibility of individuals with PD in the presence of background noise. Intensive therapy that focuses on increased loudness (LSVT LOUD) had the larger impact on improving speech and consonant intelligibility than intensive therapy that focuses on enhanced articulation (LSVT ARTIC).



P22.52

Measurement and correction of stooped posture during gait using wearable sensors in patients with Parkinsonism

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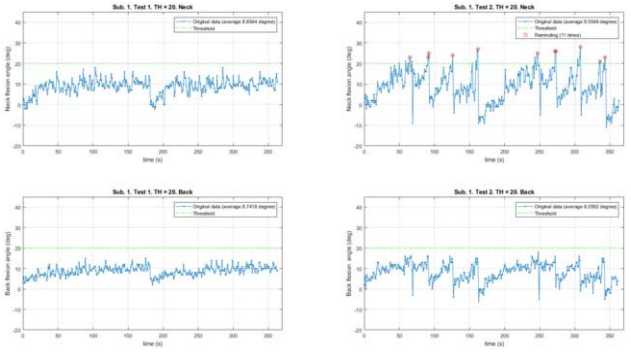
Background/Objectives: The stooped or bent posture is one of the typical postural deformities in patients with Parkinsonism. This deformity usually aggravated during walking. The study objectives were to measure the degree of stooped posture using wearable sensors during walking in patients with Parkinsonism and to investigate whether sensory feedback using vibration of the sensors improve their posture.
Methods: Patients with Parkinsonism and stooped posture were recruited in this study. Two wearable sensors containing 3-axis accelerometers were attached at the upper neck, and just below the C7 spinous process, respectively. After calibration of the sensors in most upright posture (defined as 0 degree), the sensors continuously recording the sagittal angles at 1 kHz and averaged the data at every seconds during 6-min walking test. In the control session, the patients walked with the sensors as usual. In the vibration session, sensory feedback was provided by vibration of the neck sensor when the sagittal angle was lower than the threshold angle. The sequence of the sessions was quasi-randomized according to the order of participation. The absolute sagittal angles in most upright posture before walking and mean changes of the sagittal angles during walking were measured in each patient.
Results: Ten patients with Parkinsonism participated in the study. Because 2 patients were excluded due to measurement errors, data of 8 patients (7 females and 70.25±6.11 years old) were analyzed. The neck and back flexion somewhat aggravated during gait, but the changes were less than average 10 degree in most patients in both measurement sessions. Therefore, it was difficult to evaluate the effect of sensory feedback by vibration. However, some patients showed immediate response to the feedback and corrected their posture during gait (Figure).
Conclusion: This study suggests that stooped posture could be measured quantitatively during gait using the wearable sensors in patients with Parkinsonism. Sensory feedback by vibration of the sensors may be helpful to correct the posture during gait in selected patients.
Acknowledgement: This research was supported by the Bio & Medical Technology Development Program of the National Research Foundation (NRF) funded by the Korean government (MSIT) (No. NRF-2016M3A9F1941984).



P22.53

Staying UpRight in Parkinson's disease: A novel postural intervention

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Postural changes are common in Parkinson's disease (PD), from the classic flexed posture to Pisa syndrome (lateral lean). Poor posture in PD has a negative effect on pain, balance, and mobility, with links to increased falls risk. Currently few interventions for postural misalignment exist. Recently, cueing, in the form of tactile stimulation, has shown promise in improving postural alignment in PD. Therefore, this study aimed to determine the feasibility and efficacy of an off-the-shelf tactile feedback wearable device (UpRight) for improving postural alignment in PD.
Postural angles were measured for two minutes in sitting, standing and during walking in 11 people with PD (Disease duration; 11.4±6.6years, UPDRS-III; 41.9±11.5, On meds, n=6 Pisa syndrome) using inertial measurement units (Moveo, Opals, APDM) under single and dual-task (forward digit span) conditions. Standardized clinical tests (distance of tragus, occipital, C7 to wall while standing) also measured posture. Testing was conducted without and with an UpRight device on the upper back, which was paired to a smartphone application. The device was calibrated after participants were positioned in an upright posture by a clinician; it then vibrated when posture became flexed (~5°). Primary outcomes included maximal neck and low back flexion angles.
Results showed that postural alignment improved with the UpRight device in PD. A significant improvement in neck posture was found in all clinical measures (Tragus; p=.012, Occiput; p=.008, and C7; p=.008). There was also reduction in maximal neck flexion angles during sitting (Average; 8.8° to 5.4°), standing (7.3° to 6.4°) and walking (4.6° to 3.7°) under single-task, particularly for those with Pisa syndrome. However, maximal low back flexion angles did not change, and flexed posture worsened with feedback while using the UpRight under dual-task.
Our preliminary findings suggest that an off-the-shelf, novel, wearable tactile feedback system can improve postural alignment in PD, particularly neck flexion. However, this kind of tactile feedback may distract attention and is possibly not effective for low back postural issues. In addition, long-term effects and ability of the patient to use the application need to be further investigated on a larger cohort.

P22.54

Relationship between speech, voice and swallowing disorders with non-motor symptoms in Parkinson's disease: A study conducted in a group of people with Parkinson in Venezuela

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Introduction: People with Parkinson's disease (PD) in addition to motor symptoms, manifest non-motor symptoms (NMS), that limit vocal, breathing and swallowing functions, which cause symptoms in their speech, voice, and feeding areas that will be named as phonoaudiological symptoms (PS).
Objectives: to study the general symptomatology of a group of 34 people with PD and to analyze the possible relationship between

phonoaudiological symptoms (PS) such as hypophonia, dysprosody, dysarthria and dysphagia, with NMS as: gastrointestinal disorders, depression, sleep disorders and cognitive impairment.

Method: from the results obtained by applying a speech and language assessment protocol, a descriptive study was conducted in 34 people (28 men and 6 women) diagnosed with PD (stages I to V), with ages between 25 and 83 years. After completing the data record, a qualitative analysis was carried out using a Chi-Square analysis together with the C statistics of Crammer and the Contingency Coefficient, relating some NMS with the PS.

Results: The data show that the most frequent NMS were sleep disorders in 23 subjects (67.6%), followed by depression in 20 (58.8%), gastrointestinal disorders in 10 (29.4%) and cognitive impairment in 5 patients (15%). When the NMS was related to the PS, depression was positively related to: hypophony 47%, dysprosody 53%, dysarthria 35% and dysphagia 18%. Sleep disorders did so in the following relationship: hypophonia 56%, dysprosody 62%, dysarthria 32%, dysphagia 24%. Gastrointestinal disorders: hypophonia 26%, dysprosody 24%, dysarthria 12%, dysphagia 9%. Cognitive impairment was related to: 12% hypophony, dysprosody 15%, dysarthria 6% and dysphagia 3%. These data indicate that sleep disorders and depression have the most negative impact on the phonoaudiological performance of the person with PD. On the other hand, 73% of the patients with high educational level did not present cognitive impairment, while 100% with low educational level had their cognitive performance affected.

Conclusions: people with PD have a variety of PS that can become more complex due to the presence of NMS, such as sleep disorders, depression, gastrointestinal disorders, and cognitive impairment. This impacts patient's quality of life and determines a comprehensive intervention approach.

Table 1. Relationship between NMS vs PS in PD

NMS	PS	Subjects	Percentage
Depression	Hypophony	16	47,1%
	Dysprosody	18	52,9%
	Dysarthria	12	35,3%
	Dysphagia	7	20,6%
Sleep disorders	Hypophony	18	52,9%
	Dysprosody	21	61,8%
	Dysarthria	11	32,4%
	Dysphagia	9	26,5%
Gastrointestinal disorders	Hypophony	9	26,5%
	Dysprosody	8	23,5%
	Dysarthria	4	11,8%
	Dysphagia	3	8,8%
Cognitive impairment	Hypophony	4	11,8%
	Dysprosody	5	14,7%
	Dysarthria	2	5,9%
	Dysphagia	2	5,9%

Table 1 shows the results of the relationships between NMS and PS, where the number of subjects who have both pathologies and the corresponding total percentage for each of the related symptoms is observed. In depression disorders and sleep disorders a greater number of subjects is obtained, as well as a higher percentage of affectation, since, in the first place, in depression disorders it is shown: hypophony in 16 subjects (47.1%), dysprosody in 18 (52.9%), dysarthria in 12 (35.3%) and dysphagia in 7 (20.6%). Secondly, in sleep disorders, hypophony was obtained in 18 subjects (52.9%), dysprosody in 21 (61.8%), dysarthria 11 (32.4%) and, finally, dysphagia in 9 (26.5%). On the other hand, gastrointestinal disorders and cognitive impairment showed a lower number of affected subjects, with a lower percentage of the aforementioned symptoms. First, the following was obtained in relation to gastrointestinal disorders: hypophony in 9 subjects (26.5%), dysprosody in 8 (23.5%), dysarthria in 4 (11.8%) and dysphagia in 3 (8.8%). And second, regarding cognitive impairment: hypophony in 4 subjects (11.8%), dysprosody in 5 (14.7%), dysarthria in 2 (5.9%) and, finally, dysphagia in 2 (5.9%). In conclusion, it can be observed that in patients with PD that present depression or sleep disorders may show a greater impact in PS.

P22.55

Hand tapping for screening dysfunctional rhythmic coordination in patients with Parkinson's disease

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Patients with Parkinson's disease (PD) are known to have motor control difficulties that lead to hastening phenomenon. In this study, a hand tapping of a PC-connected switch was used to screen PD patients with rhythm deficits. Fifty-eight PD patients and age-matched thirty-three healthy controls performed two tasks of 120-sec repetitive 90 bpm cyclic right-hand tapping; a task with metronome tone (TONE), and a task with no tone except for the initial 10-sec guide period (NO-TONE). The mean inter-tap-interval (ITI) for every 10-sec period was computed for the evaluation of tapping rhythm. The patients could perform the TONE task relatively well except for few whose ITIs dropped more than 10% after 60 sec. During the NO-TONE task, the PD group's mean ITI was dropped by 14% at the 120-sec execution period whereas that for the control group was 2%. The patients' ITI data for the NO-TONE task also exhibited a large inter-individual variation. Based on the mean minus 2 standard deviation NO-TONE data of the control group, individuals tapping with apparently shortened ITI were determined. The 3rd, 6th, 9th, and 12th mean ITIs showed that 20, 27, 29, and 29 individuals, respectively, were below the range, suggesting about a half of the patients are having deficient internal rhythm formation. A simple correlation analysis with the 12th data revealed that while the 3rd data had the r2 value of 0.71, the 6th and 9th data were 0.92 and 0.95, respectively, suggesting that a tapping period of 60 sec can give a relevant duration for estimating PD-related rhythm dysfunctions. Whether hastening hand tapping is related to festinating walk and/or speech acceleration is under the investigation.

P22.56

A home-based app aimed at home-based movement rehabilitation in Parkinson's disease

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Effective non-medical approaches to improve movement and everyday functioning in Parkinson's are needed, with consideration of individual rehabilitation needs. Action observation (AO) and imagination of actions (motor imagery; MI) engage the motor system and facilitate movement, particularly when used in combination. This project aims to develop a personalised, flexible, home-based therapy for people with Parkinson's, using observation and imagery of everyday actions.

A Parkinson's-specific AO+MI intervention was designed in consultation with people with Parkinson's1, using a tablet-based app modified from a program used with stroke patients2. A focus group explored intervention delivery and obtained feedback on a prototype app. Preliminary testing was then conducted with 4 individuals with mild to moderate Parkinson's. The 6-week intervention involved

using the app to observe videos of personally-selected everyday actions with simultaneous MI, followed by physical practice.
Training diaries and post-training interviews indicated that the app was acceptable and usable, but the training schedule may have been too intensive, and a greater range of actions was desired. Participants perceived improvements in the trained actions and some transfer to other daily tasks; changes in MI ability and psychological benefits were also noted. Examination of the data indicated quantitative improvements in dexterity and MI ability.
In conclusion, a home-based therapy using action observation and motor imagery is feasible in mild to moderate PD, and may offer both physical and psychosocial benefits.

P22.57

Efficacy of a mobile technology-based brisk walking program in improving dynamic balance and motor performance in people with Parkinson's disease – a randomized controlled trial
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Background: Brisk walking is a form of moderate-intensity aerobic exercise involving whole body coordination with large steps and big arm swing. Our previous pilot study indicated that a 6-week brisk walking program increased walking capacity up to 6 weeks post-training in people with early Parkinson's disease (PD). However, the effects of brisk walking in balance and motor performance among people with PD have not been investigated.
Objectives: To examine whether the brisk walking program using mobile technology would be effective in improving balance and motor performance, and aerobic capacity in people with PD at 6-week post-training.
Methods: Eligible participants were randomized into either experimental group (EXP) or upper limb group (CON). The EXP group received aerobic walking training using an activity tracker with heart rate monitoring (at 40–60% heart rate reserve). The CON group practiced stretching, strengthening, timed fine motor control exercise and craftwork in sitting. All participants attended six 90-minute training sessions under supervision of physiotherapists, and performed home exercise twice weekly for 6 weeks in the short-term. They will continue to receive monthly training and practice up to 6 months in the long-term. The data collected by activity trackers was accessible by trainers via on-line portal. The communications between trainers and EXP group about training targets, progression and feedback were facilitated using mobile message apps. Outcome measures included Mini-BESTest % total scores, MDS-UPDRS motor scores and 6-minute walking distance (6MWD).
Results: Forty-two participants (23 EXP, 19 CON) completed 6 training sessions in the first 6 weeks of the 6-month programs. Significant group*time interactions were found for all outcomes using 2-way ANOVA. Immediately post 6-week training, only the EXP group significantly increased the Mini-BESTest total scores (mean change=+8.4%, $p<0.001$*), decreased MDS-UPDRS motor scores (mean change=-6.8, $p<0.001$*), and increased 6MWD (+56.8m, $p<0.001$*). The 6-week attendance was 97.7% and no adverse effects were reported during the training period.
Conclusion: The mobile technology-based brisk walking program enhanced dynamic balance and motor performance, and aerobic capacity in people with PD at 6-week post-training. Further study is important to investigate the long-term effects of this program and the participants' exercise compliance.

CLINICAL SCIENCE: Clinical trials: Design, outcomes, recruiting, PwP involvement, communications

P23.01

Intrinsic auricular muscle zone stimulation improves walking parameters faster than the medications in motion capture analysis of Parkinson's disease patients
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Background: We recently demonstrated a novel approach of intrinsic auricular muscle zone stimulation (IAMZS) that can improve the motor symptoms of PD patients. In the present study, we aimed to validate IAMZS efficacy as a sole intervention in comparison to medication as well as in combination with medication using motion capture technology as an objective measurement.
Method: 10 participants(mean age: 54.8±10.1) were enrolled in the study. Each participant in three different days (separate day for each session: Sole medication(n=9), 20 minutes of IAMZS-Sole stimulation(n=10), and Combined IAMZS&medication(n=10). The sequence of sessions was randomized for each patient.
Each participant underwent 4 different motion capture recording sessions (baseline, 20th-minute, 40th-minute, 60th-minute) on each day they attended the study. The recordings were taken while the patients were "ON" medication except for the Sole stimulation session where they skipped one-dose medication and received an IAMZS instead of a medication.
Statistical analysis was conducted with one-way repeated measures ANOVA. Bonferroni analysis was used as a post-hoc test for pairwise comparisons.
Results: The motion capture analysis demonstrated that Sole medication was ineffective to improve stride velocity in the first hour following the drug intake (p-values=0.999, 0.542, and 0.151 for 20th-minute, 40th-minute, and 60th-minute, respectively).
In the sole stimulation group, the stride velocities were found to be significantly increased ($p=0.021$, baseline: 0.69±0.09 m/s·stature versus 40th-minute: 0.74±0.08 m/s·stature) at 40th-minute (20 minutes after the 20 minutes long stimulation). There was also a tendency to be significant ($p=0.069$) at 20thminute and the significant effect that was obtained at 40th-minute (20 minutes after the termination of 20 minutes long stimulation) was disappeared at the 60th-minute ($p=0.205$).
The combined IAMZS&medication session demonstrated significant improvements in all time segments. $p=0.010$ (20th-minute), $p=0.017$ (40th-minute), $p=0.002$ (60th-minute).
Conclusion: These findings indicated a slow onset of medication effects and fast onset of IAMZS on PD motor symptoms. In addition, following the termination of the 20 minutes long of IAMZS, a prolonged improvement of symptoms was observed at 40th-minute. The results of the present study validated IAMZS' efficacy as a sole

treatment to alleviate PD motor symptoms as well as a potential beneficial effect of combined use with the PD medications.

P23.02

Multimodal balance training with rhythmical cues in Parkinson's disease: A randomized clinical trial

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Balance impairment in Parkinson's disease (PD) improves only partially with dopaminergic medication. Therefore, non-pharmacological interventions such as physiotherapy are important elements in clinical management. External cues are often applied to improve gait, but their effects on balance control are unclear. **Objectives:** To study the effectiveness of balance training with and without rhythmical auditory cues to improve balance in PD. We also studied the effects of auditory cues on gait.
Methods: We performed a prospective, single-blind, randomized clinical trial. Between July 2015 and May 2017, we enrolled PD patients in Hoehn and Yahr stage 1–3, with a history of falls and on stable dopaminergic medication. We screened 201 volunteers by telephone; 154 were assigned randomly into three groups: (1) balance training with rhythmical auditory cues delivered by a metronome (multimodal balance training); (2) standard balance training without rhythmical auditory cues; and (3) no intervention (control group).
Interventions: Training was performed for 5 weeks, two times/week. Primary outcome was the Mini-BESTest (MBEST) score directly after the training period. Assessments were performed by a single, blinded assessor at baseline, directly post intervention, and after one and 6-months follow-up. Treatment effects were estimated with a linear mixed model, adjusted for MBEST scores and UPDRS at baseline and levodopa equivalent daily dose.
Results: 154 patients were included: multimodal training (n=52); standard training (n=44); controls (n=37). Groups were comparable at baseline. Directly post intervention, multimodal training was more effective than standard training (difference 3.6 (95% Confidence Interval (CI) 2.3; 4.9)), p<0.001). Patients allocated to both active interventions improved compared to controls (MBEST estimated mean difference versus controls 6.7 (CI 5.3; 8.1), p<0.001 for multimodal training; and 3.1 (CI 1.7; 4.5), p<0.001 for standard training). Improvements were retained at one-month follow-up for both active interventions, but only the multimodal training group maintained its improvement at 6 months. In conclusion, both multimodal training and standard training improve balance, but multimodal training – adding rhythmical auditory cues to routine physiotherapy – has greater and more sustained effects. Trial Registration clinicaltrials.gov: Identifier NCT0248826

P23.03

Targeted digital marketing campaigns successfully recruit diverse cohorts of people with Parkinson's disease and healthy controls to the Fox Insight Longitudinal Study

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The Michael J. Fox Foundation for Parkinson's Research (MJFF) recently launched Fox Insight, an online longitudinal study that collects participant-reported outcome data about health experiences from people with and without PD, in order to accelerate future research. To date, Fox Insight has collected survey data from >30,000 volunteers and seeks to prospectively follow a 125,000-person cohort over 5- years. The online data collection platform of Fox Insight affords a unique opportunity to evaluate the impact of novel and innovative recruitment techniques, including the impact of digital marketing campaigns aimed at attracting diverse cohorts of study participants. The three studies presented here {Early Stage PD, Late Stage PD, and Geotargeting Recruitment Campaigns} serve as proof of concept that digital marketing is an effective means of study recruitment and one that can be tailored to target specific cohort characteristics, for both PWP and healthy controls. Unique Facebook and google campaigns targeting the sub-group of interest were each run for 4–6 weeks, during distinct periods of time, between 2017 and 2018. The effectiveness of these targeted campaigns was compared to broad online recruitment efforts and periods of time in which there were no special promotions (e.g., organic recruitment). Each targeted recruitment campaign successfully enrolled more individuals in the specified participant cohort, compared to organic recruitment [Early Stage: 134 vs. 38, p<.0001; Late Stage: 190 vs. 35, p<.0001; Geotargeting: 65 vs.4, p<.0001]. Of note, there were significant differences on several demographic and clinical variables, such as age, gender, SES, employment status, ethnicity, medical comorbidities, education, PD family history, and prior clinical trial participation (which were not the focus of the particular campaign) between PWP and healthy controls recruited via targeted vs. non-specific methods. For example, healthy controls recruited via targeted methods were more likely to be older (e.g., mean age of 65 vs. 44, p<.0001) and female, and PWP enrolled in response to tailored campaigns were more likely to be research naïve, have less formal education, and report lower annual income. The potential for novel digital recruitment methods to fill the white space in PD research at large will be addressed.

P23.04

Expedited access to therapies: How measuring and incorporating patient preferences can make clinical trials more efficient and more effective

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Medical innovators and regulators have increasingly recognized the importance of working with patients to design medical therapies and clinical trials that meet the needs of specific patient populations. For

diseases such as Parkinson's disease (PD), a progressive, degenerative disease with few effective treatment options, traditional randomized clinical trials with a fixed statistical threshold may not reflect patients' perspectives on the trade-off between the risk of endorsing an ineffective therapy (false positive) and the risk of rejecting an effective therapy (false negative). This collaborative project, which involved academia, industry, FDA, patient-scientists and MJFF, developed and tested methods for incorporating patient preference information as explicit means to set significance levels in clinical trial design.
Methods: With direct input from patients with PD, we developed a patient preference survey and deployed it online through Fox Insight for 6-weeks and received 2,752 complete responses (24.4%), allowing us to analyze differences in outcome priorities among various demographic groups. We then assigned weights to the consequences of errors based on identified patient preferences, and proposed a hypothetical clinical trial design optimized to maximize the values identified by patients.
Results: Movement symptoms, which are common endpoints in PD clinical trials, were ranked as most important, and psychological and cognitive symptoms, which are less commonly studied, were ranked as the next most important. Differences emerged from different groups within the patient population, depending upon how the disease manifested itself. Preferences from respondents with mild PD symptoms and no prior experience with deep brains stimulation (DBS) resulted in larger, more conservative trials, with acceptable significance level less than 5%. Preferences from respondents with severe PD symptoms and history of DBS resulted in smaller, less conservative trials, with acceptable significance level greater than 5%.
Conclusions: This method has the potential to remove barriers to access to innovative technologies by giving patients a pathway to breakthrough, lifesaving technologies based on their treatment priorities and risk tolerance and the resulting potential for reduced clinical trial size. Though this test case was in Parkinson's disease, we envision that this method may have dramatic implications for the design of clinical trials for many diseases.

P23.05

Use of digital techniques to recruit Parkinson's clinical trials
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Objective: To describe digital approaches used to support patient recruitment into clinical trials in Parkinson's disease (PD) targeting disease modifying therapies.
Background: Reliance on the traditional techniques of physician directed enrolment or hard copy advertising no longer suffices to recruit the number of subjects required for the increasing number of PD clinical trials. In addition, disease modifying approaches typically look for early PD subjects whom may still be educating themselves regarding their diagnosis through online research.
Methods: For the purposes of recruitment planning in case study NCT03318523 and in order to promote trial opportunities to relevant audiences we launched a targeted digital outreach campaign to both patients and physicians that included an array of strategies that could be optimized throughout the lifecycle of the study recruitment period. It included the provision of PD patient-centric content via search engine marketing, social media advertising, programmatic display, and patient advocacy referrals (i.e., Fox Trial Finder, Take Part Hub). These approaches were selected as they allow for specialized targeting of the trial population audience including geo-location, eligibility criteria and interests. Throughout the campaign, our real-time performance metrics and analysis allow for a high level of control to increase and optimize relevant traffic and awareness.
Results: Evaluation of digital techniques implemented in NCT03318523 remains ongoing through 2019. The data obtained through 2018-Q1 2019 will be presented.
Conclusions: Search engine marketing is proving the most successful technique to date for generating qualified patient referrals for study screening. It is hoped that results of this analysis will enable the use of more targeted digital techniques with improved patient centric approaches to enable optimized engagement between the PD community and available research opportunities in the future.

P23.06

Safety, tolerability and pharmacokinetics of oral venglustat in Parkinson's disease patients with a GBA mutation
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Objective: Assess the safety, tolerability, pharmacokinetics (PK), and pharmacodynamics of oral venglustat, a CNS-penetrating glucosylceramide (GL-1) synthase inhibitor, in Parkinson's disease (PD) patients with a GBA mutation.
Background: Mutations in GBA, which encodes glucocerebrosidase, are associated with increased risk of developing PD, characterized by a younger onset, higher prevalence of cognitive impairment, and more rapid disease progression.
Design/Methods: Part 1 of MOVES-PD (NCT02906020) was an up-to 36-week randomized, placebo-controlled, double-blind, sequential-cohort study of the safety/tolerability of venglustat at 3 escalating doses. PD patients age 18–80 years with symptoms =2 years at baseline who were heterozygous carriers of a GBA mutation were eligible. The primary endpoint was the safety/tolerability of venglustat. Secondary endpoints included plasma and cerebrospinal fluid (CSF) PK. Exploratory endpoints included pharmacodynamics.
Results: Seventeen patients were randomized to placebo (n=4) or venglustat (n=13). Mean age at enrollment was 58.4 years. Mean years since symptom onset was 6.7, and since diagnosis was 5.2. GBA mutations included N370S, 84GG, L444P, and E326K. Twelve venglustat-treated and 4 placebo-treated patients reported at least 1 treatment-emergent adverse event; most were mild or moderate and

resolved without corrective treatment during the study, and the most common were psychiatric, neurological, and gastrointestinal events. No serious AEs or deaths occurred. Two patients on venglustat discontinued due to TEAEs (confusional state [n=1], panic attack [n=1]) after the primary analysis period (Week 4). Venglustat exposure in plasma and CSF increased in a close to dose proportional manner, and GL-1 levels decreased in a dose-dependent manner over 4 weeks. CSF GL-1 decreased 74.3% (high-dose).
Conclusions: The data demonstrate a favorable safety and tolerability profile of venglustat at all doses investigated for up to 36 weeks of treatment. Dose-dependent plasma and CSF exposure and reduction of plasma and CSF GL-1 were observed. Part 2 of MOVES-PD, a 52-week randomized, double-blind, placebo-controlled 2-arm study, is currently ongoing to assess the efficacy, safety, PK, and pharmacodynamics of venglustat in PD patients carrying a GBA mutation.
Funding: Sanofi Genzyme.

P23.07

Infus|On, a Phase 3, open-label study of the safety and efficacy of continuous apomorphine infusion in patients with Parkinson's disease: Design and baseline characteristics
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Background: The recent TOLEDO study (Katzenschlager et al, Lancet Neurology 2018), conducted in Europe, provided Level I evidence for the efficacy and safety of apomorphine infusion in patients with fluctuating Parkinson's disease (PD). The study found that apomorphine infusion significantly reduced OFF time by a mean 1.89 hours versus placebo, with most (68%) patients achieving =2 hours OFF time reduction. However, there is lack of data from US regarding this therapy and there remains a need for prospective analysis of apomorphine infusion outcomes.
Objective: To investigate the safety and efficacy of apomorphine subcutaneous infusion in PD patients not well controlled on available therapy.
Methods: Infus|On (NCT02339064) is an ongoing Phase 3, open-label, outpatient study designed to evaluate the safety, tolerability and efficacy of apomorphine subcutaneous infusion. PD patients with =3 hours of daily OFF time who were unable to achieve adequate motor control despite optimized treatment with levodopa and additional PD therapy (including levodopa intestinal infusion or deep brain stimulation) were eligible for the study. Patients were titrated in the outpatient setting to an apomorphine dose delivered continuously over 16 hours/day, optimized for best waking-day efficacy without intolerable adverse effects (AEs), to a maximum dose of 150 mg/day (infusion rate, 8 mg/h). Once the optimal infusion dose was reached, patients entered a 52-week, open-label maintenance period. The primary efficacy endpoint was change from baseline to maintenance Week-12 in daily OFF time, as assessed by patient home diary. Safety and tolerability were assessed through AE reporting.
Results: Ninety-nine patients were enrolled at 18 PD centers across the USA. Overall, the mean (SD) age was 61.6 (9.41) years, with males composing 69.7% of the cohort. Patients had a mean PD duration of 9.9 (6.18) years and had motor fluctuations for 7.5 (6.76) years. The mean levodopa dose was 1261 mg and the levodopa equivalent dose 1343 mg.
Conclusions: This Phase 3 study provides prospective, long-term safety and efficacy data for apomorphine subcutaneous infusion for the use of this therapy in US patients.
Funding: US WorldMeds LLC.

P23.08

INTREPID: A 2-year follow-up of a prospective, double blinded, multi-center randomized controlled trial evaluating deep brain stimulation with a new multiple source, constant-current rechargeable system for treatment of Parkinson's disease
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Background: Deep Brain Stimulation (DBS) is a surgical therapy used for treatment of the motor signs and fluctuations associated with Parkinson's disease (PD). Its efficacy has been substantiated by several randomized controlled trials. Moreover, motor improvement following DBS may be sustained for up to 10 years (Castrioto et al. 2011). The objective of the INTREPID clinical trial assessed improvement in motor function and quality of life in patients with advanced, levodopa responsive Parkinson's disease (PD) following bilateral subthalamic nucleus (STN) DBS using a new device equipped with multiple current sources. In this analysis, 2-year follow-up data will be reported.
Design/Methods: INTREPID (ClinicalTrials.gov Identifier: NCT01839396) is a multi-center, prospective, double blinded, randomized controlled trial (RCT) sponsored by Boston Scientific. Subjects with advanced PD were implanted bilaterally in the STN with a multiple-source, constant current DBS System (Vercise, Boston Scientific). Subjects were randomized to either receive active vs. control settings for 12-week blinded period. Subjects were blinded to treatment assignment and study assessments were administered by a clinician blinded to treatment condition. Motor improvement was evaluated using several assessments including subject motor diaries, UPDRS scores, etc. Assessments for quality of life (e.g. PDQ39) were also administered.
Results: The study met the primary endpoint demonstrated by mean difference of 3.03±4.52 hrs. ($p<0.001$) between active and control groups in ON time w/o troublesome dyskinesia, with no increase in antiparkinsonian medication, from post-implant baseline to 12-weeks post-randomization. At 1-year compared to pre-surgery screening, a 49.2% improvement in UPDRS III scores was reported, and overall improvement in quality of life was maintained. Reporting of 2-year follow-up data is planned.
Conclusions: Results of the INTREPID RCT demonstrate that use of a multiple-source, constant-current DBS system is safe and effective for treatment of Parkinson's disease symptoms. This analysis will describe outcomes derived from subjects assessed out to 2-years follow-up.

P23.09

The effectiveness of boxing exercise in elderly people including people with Parkinson's disease

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Objective: To clarify the effect of boxing exercise in elderly people with chronic disease including Parkinson's disease (PD).
Background: Boxing training might improve balance and mobility, and help prevent falls in elderly people with PD. Fasano A. recommended group or minimally to moderately supervised exercise including boxing in people with early stage PD. However, there are few reports investigating the effect of boxing exercise in elderly people.
Methods: This study was a pilot study at a single site and open label case series. Inclusion criteria for people were being able to walk independently with or without an assistive device and having support level 1 or 2 or care level 1 or 2 under the Japanese care insurance system. The exclusion criteria were severe dementia (Mini-mental state examination: MMSE<15) and recent cardiovascular disease. The participants chose between the weekly boxing exercise group (group B) and the weekly ordinary exercise group (group O) under the outpatient day service. Physical or occupational therapists supervised these exercises moderately. The primary outcome measured was the functional reach test. We also evaluated times for 5 meters walking and standing on one leg, as well as grip power. We assessed those at the pre-intervention (T0) and after 3 (T1), 6 (T2), and 9 months (T3) of exercise.
Results: 18 people (mean age 80.9 y., male 8, MMSE 26.4) were included. 4 people had PD (HY 2.3) and 4 people had mild dementia. 9 people who chose group B had stronger grip power (kg. rt. 25.9, lt. 25.9) than those in group O (rt. 16.6, lt. 15.3) at T0. The mean functional reach distance (cm) in group B increased significantly from 24.5 at T0 to 28.8 at T3 (95% confidence interval, -8.00 to -0.54; p=0.030). The functional reach distance showed a significant difference between group B and group O at T2 (p=0.022) and T3 (p=0.013) but not at T0. We didn't find significant improvement in the other measured values in the two groups.
Conclusions: Nine months boxing exercise increased the distance at functional reach test. More frequent training for longer period of time might produce good results.

P23.10

Inhaled levodopa (CVT-301) for treatment of off periods in Parkinson's disease: efficacy as assessed by 39-item Parkinson's disease quality of life (QoL) questionnaire

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Background: CVT-301 is a levodopa inhalation powder under development for the treatment of OFF period symptoms in Parkinson's disease (PD). In a phase 3, placebo-controlled study (SPAN-PD[SM]) of PD patients experiencing OFF periods, CVT-301 84 mg significantly improved motor function, as measured by lower Unified Parkinson's disease Rating Scale Part III (motor) scores 30 minutes post-dose, evaluated at 12 weeks.
Objective: Pre-specified and post-hoc analyses investigated QoL changes as assessed by the 39-item Parkinson's disease Questionnaire (PDQ-39) subscores over the 12-week period of SPAN-PD[SM] and its correlation with changes in the Patient Global Impression of Change (PGIC).
Methods: This was a 12-week study of PD patients experiencing motor fluctuations on a standard oral carbidopa/levodopa regimen. Patients were randomized to placebo, CVT-301 60 mg or 84 mg (1:1:1) for the treatment of OFF period symptoms as needed up to 5 times daily. PDQ-39 and PGIC were completed at baseline, 4, 8, and 12 weeks. A post-hoc analysis using an anchor-based approach examined the change in PDQ-39 domains (mobility and activities of daily living [ADL]). The PGIC (score from 1 for "much improved" to 7 for "much worse") was used as the anchor for the 12-week study period.
Results: Improvement in PGIC showed a high correlation with improvement in PDQ-39 ADL and mobility scores with estimated changes of –1.979 for ADL and –1.335 for items linked to overall mobility for the minimum improvement in PGIC ("a little improved") when the 3 treatment arms were pooled. Estimated treatment differences vs placebo for the CVT-301 84-mg dose were –2.08, for ADL, and –2.19 for mobility. For both doses, treatment differences in ADL and mobility were above the estimates correlating with minimum improvement in PGIC.
Conclusions: Patients who showed improvement in PGIC and who were also treated with CVT-301 reported improved ADL and mobility as assessed by the PDQ-39, as compared with placebo-treated patients at 12 weeks. Maintaining independence in ADL is important for optimizing QoL for chronically-treated PD patients.

P23.11

A Promotores model to increase Parkinson's disease (PD) research awareness and participation in the Hispanic community in Phoenix, Arizona

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Objective: Explore the role of promotores in providing education about clinical trials and exploring research perceptions in the Hispanic PD community in Phoenix, AZ.
Methods: Promotores: trained lay people from the target population, share the culture and the language, and are recognized as valuable members of their community. These characteristics allow promotores to build trust and become effective patient navigators among hard to reach populations.
The Muhammad Ali Parkinson Center (MAPC) included promotores as collaborators in our research outreach efforts in the Hispanic community as part of PD- TRI (Parkinson's disease Trial Recruitment Innovation) program – an initiative funded by The Michael J Fox Foundation to increase clinical trial awareness, research diversity and accessibility.
A group of five MAPC promotores received formal training about clinical trials and participated in 2 focus groups with Hispanic PD patients and care partners about the topic of research. The promotores and the MAPC Hispanic outreach coordinator created a presentation in Spanish about clinical trials. The presentation included an interactive icebreaker and a comedy role play to explain some of the research terminology. The MAPC survey about research perceptions was translated to Spanish and Hispanics with PD took the survey during educational events and community programs delivered by the MAPC.
Results: Four presentations were delivered by the promotores with active participation from an audience of Hispanic PD patients and

caregivers. Attendees reported better understanding of terminology such as placebo, protocol, randomization and double blind studies.
The promotores identified the following topics as important in establishing trust and willingness to participate in research:

- Being able to communicate in Spanish with a member of the research team who has an understanding of the Hispanic culture
- Having materials available in Spanish explained at a literacy level they can understand
- Avoid creating false expectations, such as providing information in Spanish about a study but not having consent forms in Spanish and/or Spanish speaking research team members
- Making research a topic easier to understand and less intimidating

With the help of the promotores, a total of 63 Spanish surveys about research perceptions were completed by Hispanics with PD. Analysis of surveys is currently in progress.

P23.12

Meta-analysis of mortality following subthalamic and pallidal deep brain stimulation for patients with Parkinson's disease

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Objective: The aim of this meta-analysis is to compare mortality after subthalamic (STN) and pallidal (GPi) deep brain stimulation (DBS) for patients with Parkinson's disease (PD).
Background: DBS is a surgical treatment for advanced PD. STN and GPi are two common targets for DBS in patients with PD.
Design/Methods: We searched PubMed through September 2018 for prospective controlled studies comparing STN DBS and GPi DBS for PD patients. Records were screened for prospective controlled trials comparing STN DBS and GPi DBS for PD patients. The frequency of mortality in both groups was pooled as risk ration between the two groups in a fixed effect model meta-analysis. In the case of multiple reports, we analyzed data from the most recent data set. We introduced subgroup analysis according to the follow-up duration to investigate whether the effect size differed from different time periods. Heterogeneity was assessed by visual inspection of the forest plots and measured by I-square and Chi-Square tests. We used RevMan 5.3 for windows.
Results: Four trials (7 full-text articles) were included in the final analysis with a total of 479 patients (STN 253 patients, and GPi 226 patients). Follow up duration ranged from 6 months in the COMPARE trial to 6 years in the study of DBS group 2001. The overall risk ratio favored GPi DBS than STN DBS with RR 3.64, 95% CI (1.68 to 7.87). This result suggests more than 3-fold increase in mortality following STN DBS than GPi DBS.
Conclusions: Death was more common after STN DBS than GPi DBS in PD patients. But most of the death cases were due to postoperative complications and were not related directly to stimulation. Our results highlight the importance of considering postoperative complication while choosing the surgical target for PD patients.

P23.13

Long-term efficacy of zonisamide on parkinsonism in dementia with Lewy bodies: A post-hoc analysis of phase III trial

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Objective: Zonisamide is available as an agent for parkinsonism in both Parkinson's disease and dementia with Lewy bodies (DLB) in Japan. The objective of this presentation is to characterize the long-term efficacy of zonisamide on motor symptoms in DLB.
Methods: Of the patients participated in the phase III trial consisting of 12-week, randomized double-blind and subsequent 40-week, open-label phases, those who were assigned to zonisamide groups (25 or 50 mg/day) in the double-blind phase and received zonisamide at least once were included in this analysis. Because the flexible dose (25 or 50 mg/day) of zonisamide was allowed in the open-label phase, both zonisamide groups were summed as an analysis population. UPDRS part III was employed for the evaluation of motor dysfunction. Focusing on the individual motor symptoms such as tremor (UPDRS part III item number; #20, #21), rigidity (#22), bradykinesia (#23 to #26, #31) and gait disturbance/postural instability (#29, #30), the respective summed scores were analyzed.
Results: Summary statistics showed that tremor, rigidity and bradykinesia were improved with time. At around Week 28–32, the maximal effect on rigidity and bradykinesia were observed (Change [%change] from baseline: rigidity, -1.4 [-20.6%]; bradykinesia, -2.5 [-18.2%]). In addition, Tremor known as the symptom which is non-notable one in DLB was remarkably improved at around the final evaluation time point (-1.6 [-51.8%]).
Conclusion: Long-term use of zonisamide was found to improve individual symptoms such as tremor, rigidity and bradykinesia besides overall parkinsonism in DLB patients. Other data will be shown on the day.

P23.14

Use of pimavanserin in combination with selective serotonin reuptake inhibitors (SSRIs)

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Objective: This post-hoc analysis evaluated a subgroup of Parkinson's disease psychosis (PDP) participants from the pimavanserin clinical program to determine if there was any difference in response between the subjects receiving pimavanserin in combination with an SSRI versus those receiving pimavanserin alone.
Background: PD patients have significant neuropsychiatric comorbidities including depression, which affects up to 60% of patients. PDP is common and is associated with increased morbidity/mortality, complicates management of motor symptoms, and often leads to long-term care placement. Pimavanserin, a selective 5-HT2A inverse agonist/antagonist, is the only treatment approved in the U.S. for hallucinations and delusions associated with PDP.
Methods: A pooled analysis of two 6-week Phase 3 studies of pimavanserin 34 mg (PIM) versus placebo, consisting of the ACP-103-020 and ACP-103-012 study data from North American sites, was conducted to assess the overall treatment effect of PIM on psychotic symptoms, as measured by the SAPS-PD in patients receiving concomitant SSRIs compared with those without. The mITT population included 268 participants (PIM=135, PBO=133). The full safety dataset included 433 participants (PIM=202, PBO=231). Of the 268 participants, 77 took concomitant SSRIs, while 189 did not; 2 subjects with prior but non-concomitant SSRI use were excluded from the SSRI subgroups.
Results: Overall, PIM demonstrated a 6.21-point improvement in SAPS-PD scores from baseline to Week 6. The treatment difference

was 2.87 points over PBO (p<0.001). Among patients taking concomitant SSRIs, the decrease in psychosis symptoms as measured by SAPS-PD was more prominent for both PIM and PBO subjects (8.33 vs. 4.01; p=0.010) compared with the 189 subjects not taking SSRIs (5.36 vs. 3.01; p=0.003); the treatment difference was of greater magnitude in the concomitant SSRI treated group (4.32 vs. 2.34). A total of 10% (4/40) and 7.4% (12/162) of PIM treated patients reporting AEs, with and without SSRIs, respectively, discontinued because of adverse reactions.
Conclusions: The results of this analysis suggest that the combination of selective 5-HT2A agonist/antagonists and SSRIs may lead to an enhanced antipsychotic effect.
References:
Previously accepted to American Association for Geriatric Psychiatry 2017

P23.15

Can non-invasive brain stimulation enhance dual-task performance in Parkinson's disease?
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Parkinson's disease (PD) is a degenerative disease of the central nervous system. Motor dysfunction is a primary feature of PD, with postural instability, one of the key features that leads to an increased likelihood of falls. When asked to perform concurrent motor and cognitive tasks, (e.g. standing while counting numbers), postural control can deteriorate further. Transcranial Direct Current Stimulation (tDCS) can be used to safely modulate cortical excitability without serious adverse effects. It has been employed to promote executive function, attention and working memory in healthy older people and has shown potential benefits to people with PD.
The purpose of this study is to investigate the effects of tDCS on dual task performance in people with PD.
Three groups of participants (healthy young, healthy older people and people with PD) will complete the following tasks in a randomised order. Under both real and sham stimulation conditions participants will stand on stable and unstable surfaces on a force plate. Performance under the single task (quiet stance only) and dual task (quiet stance + serial subtraction task) conditions will be assessed on both surfaces prior, during and after stimulation. Sham condition will consist of 15s of stimulation at the beginning and the end of intervention period only.
It is anticipated that when compared with sham tDCS, real tDCS will reduce the cost of secondary cognitive task on postural control. Participants will have greater enhancement of postural control on unstable surface (foam) when compared to the stable surface (firm). Furthermore, it is expected that when compared with healthy participants, people with PD will have greater benefits from non-invasive brain stimulation, and show greater improvements on both postural and cognitive performance after real tDCS.
The efficacy of tDCS for improving cognitive performance and promoting balance in people with PD will be determined. The effects of current stimulation over left DLPFC on dual task in different populations will be ascertained.
Use of tDCS may provide an effective and safe strategy for treatment of motor and cognitive dysfunction of people with PD. It will also provide better understanding of the relationship between cognition and balance in PD.

P23.16

Understanding trial specific recruitment challenges – A dynamic approach to identifying and overcoming obstacles: PD patient's perspective
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Objective: Analyze the trial specific obstacles to recruitment efforts in NILO-PD, a multi-center clinical trial.
Background: In 2015, a press release from Georgetown University announced the results of a small, open-label Phase1 clinical trial of Nilotinib (a drug approved to treat leukemia) as a potential treatment for PD. This resulted in a whirlwind of over-hyped media reports and extreme excitement in the PD community. Headlines included:
- Parkinson's victims 'brought back to life' by cancer drug nilotinib (Daily Mail, 10/19/2015).
- Cancer drug nilotinib promises to reverse Parkinson's disease (Next Digit, Oct. 18, 2015).

The news and excitement eventually led to the funding and implementation of the NILO-PD trial (ClinicalTrials.gov Identifier: NCT03205488).
Recruitment Challenges: Most PD research Steering Committees (SC) are aware of the inherent difficulties of patient recruitment and attempt to design the trial protocol to overcome them. However, some trials, like NILO-PD, have numerous obstacles that are more specific to the actual trial that make for additional challenges. This requires an iterative process of constantly reviewing recruitment techniques and the dynamic aspect of adjusting procedures during the trial to overcome the obstacles.
Some of the Trial Specific Obstacles in NILO-PD were:
- Restrictive inclusion/exclusion criteria.
- Patient confusion and disappointment regarding the initial drug "hype."
- IRB restrictions on Patient Representative's (PR) communication to PD community.
- Use of the drug off-label.

Solutions Utilized during the Recruitment Process:
- PR sent a personal letter to 721 PD advocates describing the trial and requesting their assistance to recruit volunteers.
- PR and PI presented NILO-PD to PD advocate groups.
- MJFF and The Cure Parkinson's Trust utilized social media to notify their bases about the trial and the need to volunteer.

Considerations for future trials:
- Early involvement of patient Ambassadors in the development of the Protocol and Consent Form. Clarify trial goals, Inclusion/Exclusion criteria and potential risks. Discuss possible patient objections to the trial.

- Organize, educate and motivate Ambassadors prior to trial start-up. Provide marketing material. Assign recruitment territories and maintain continuous interaction throughout trial.
- Conduct formal exit surveys with patients, including enrolled volunteers, those screened but excluded, and those screened who elect not to enroll.

P23.17

A model of patient engagement in research: Takeda and Parkinson's Foundation co-creating clinical trials

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Objective: To create a structured, collaborative approach to patient engagement in research between the Parkinson's Foundation, a United States-based nonprofit with global impact, and Takeda, a worldwide pharmaceutical company, to optimize clinical trials.
Methods: Takeda and the Parkinson's Foundation, both leaders in patient engagement in research, entered into a formal collaboration to optimize clinical trials at Takeda. A contractual agreement was created, detailing the scope of work and roles and responsibilities of each stakeholder. A person with Parkinson's was identified as a patient advisor to Takeda-Parkinson's Foundation partnerships. The Patient Focused Medicines Development Patient Engagement Quality Guidance, a tool co-created through multi-stakeholder workshops to provide actionable guidance and best-practice examples of patient engagement in medicines development, was piloted to plan patient engagement in research activities. This included defining shared purpose, a strategy for engaging diverse and underserved populations, and methods for maintaining transparent, bidirectional communication and an ongoing working relationship. Activities such as patient journey mapping, selection of therapeutic targets, optimization of patient reported outcomes tools, determination of study endpoints, protocol review and improvement of recruitment and retention were reviewed and prioritized as potential co-creation projects. Metrics were defined to track the quality of patient engagement and how patient engagement impacted research at Takeda.
Results: A successful model of collaboration between Takeda and the Parkinson's Foundation was created. This model was utilized to conduct a patient panel and patient advisory board to discuss Parkinson's clinical trials and integrate the patient perspective into research and development of new therapies. Patient engagement impacted Takeda's approach to clinical development, and the creation of a refined model of patient engagement, supported by the Patient Engagement Quality Guidance, influenced both organizations' approach to this work.
Conclusions: Structured, collaborative models are critical to advancing patient engagement in research and co-creating clinical trials. Bringing their shared expertise to the table, pharmaceutical companies and patient advocacy organizations can optimize clinical trials through patient engagement in research.

P23.18

Improving clinical trials through the science of patient engagement

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Background: Patient engagement in research is the meaningful inclusion of patients as equal partners in research decision making, from determining therapeutic targets to disseminating study results and at each point in between. Although patient engagement is a rapidly expanding field, rigorous methodology and metrics are not yet well established. To fill this gap, the Parkinson's Foundation is leading the development of an evidenced-based, standardized approach to patient engagement in research.
Objective: To make Parkinson's disease clinical trials more efficient and effective by leading the development and implementation of the science of patient engagement in research.
Methods: A landscape review of patient engagement was conducted. Gaps in methodologies, metrics, tools and best practice models were identified. The Parkinson's Foundation determined four key gaps as priorities to address:

- A lack of clarity of the role of patient advocacy groups in patient engagement.
- Poorly-defined metrics for the quality and quantity of patient engagement and the impact of patient engagement on the research process.
- Few standardizes tools to conduct patient engagement.
- No models for partnerships between international Parkinson's patient organizations conducting patient engagement.

A strategic plan was created to address these gaps and establish a basis for the science of patient engagement.
Results: The Parkinson's Foundation successfully launched one project to address the lack of clarity of the role of patient advocacy groups. Another project to better define metrics in patient engagement was also successfully launched. A standardized tool for patient engagement which the Foundation took a leadership role in developing is in beta testing. A collaboration with Parkinson's UK on patient engagement in research established a successful model for partnerships between international patient organizations. Evaluation of these initiatives is ongoing. Based on impact, initiatives maybe replicated and scaled.
Conclusions: The Parkinson's Foundation has built on its track record of 15 years leading the field in developing the science of patient engagement in research. New methodologies, metrics and tools are emerging that can serve to standardize the field of patient engagement.

P23.19

Examining Parkinson's disease psychosis treatment and outcomes in the real world: Interim year 1 findings from the INSYTE observational study

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Introduction: Parkinson's disease is the second most common neurodegenerative disease, and over 50% will experience symptoms of psychosis at some point during the course of the disease. Despite the prevalence of Parkinson's disease psychosis (PDP), longitudinal studies have not evaluated treatments and outcomes in clinical practice, and a considerable gap exists in our understanding of them. The goal of the study is to examine real-world management of PDP and its treatment outcomes.
Methods: The INSYTE Study is enrolling up to 750 PDP patients and their caregivers, from up to 100 sites in the United States, with a prospective, non-interventional, observational design. The study will collect clinical, humanistic, and economic data at follow-up visits for up to three years from enrollment.

Results: Preliminary baseline findings from 55 enrolling sites indicate that investigators at the majority (75%) of enrolling sites are neurologists, of whom 44% are in private practices, as opposed to academic or hospital-based centers. Baseline findings from 334 enrolled patients indicate that most are Caucasian (95%), male (63%), retired (76%), married (75%), and live in a private residence (92%). Most patients (86%) are participating in INSYTE with a caregiver. Average patient age is 74.7 years. Mean duration since PD and PDP diagnosis were 8.8 and 2.6 years, respectively. At baseline, 12% had no cognitive impairment, 50% had slight or mild impairment, and 38% had moderate or severe impairment. At enrollment, 33% of patients were utilizing an antipsychotic: of those, 82% were utilizing an antipsychotic as monotherapy (primarily pimavanserin [50%] and quetiapine [25%]). Pimavanserin+quetiapine was the most frequently employed combination antipsychotic therapy (15%).
Conclusion: The INSYTE Study is the largest observational study to date to explore PDP treatments and patient outcomes in a real-world setting. Results from this study will better inform the scientific community on current practices and potentially support updates to treatment guidelines and standards of care for the management of PDP. These data represent baseline characteristics of the enrolled patients (and caregivers, when present). Initial follow-up data with clinical, economic, and humanistic findings will be presented, reflecting the year 1 interim analyses.
Funding: The INSYTE Observational Study is funded by ACADIA Pharmaceuticals, Inc.

P23.20

NILO-PD: A phase 2A study of nilotinib in patients with advance Parkinson's disease: Recruitment initiatives
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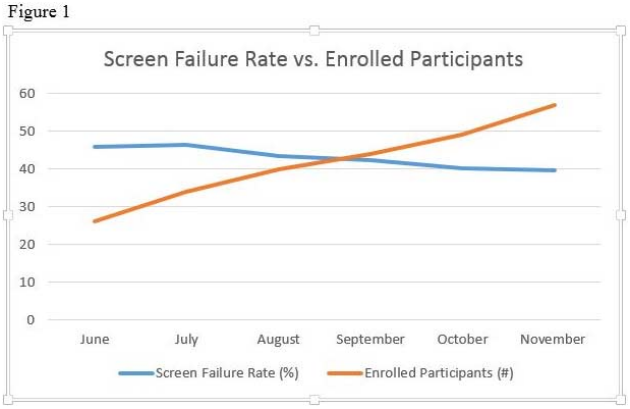
Objective: To review a multi-modal recruitment strategy used in a Phase 2 clinical trial of moderate/advanced Parkinson disease (PD).
Background: NILO-PD is a multicenter, Phase 2 trial assessesing safety and tolerability of daily nilotinib compared to placebo in 75 moderate/advanced PD participants. The study is conducted at 25 Parkinson Study Group (PSG) sites in the US. Recruitment began in November 2017, expected completion in late 2018. A higher than anticipated screen failure (SF) rate required implementation of additional recruitment strategies to meet study timelines.
Methods: A Recruitment Committee (RC) comprised of the study principal investigator, several members of the study team, and a patient representative formed to create a multi-modal recruitment strategy to increase awareness among the PD community about NILO-PD.

- Recruitment tools: toll-free number, study specific email address and study website were created to connect interested participants with participating sites. Recruitment brochures, posters, and healthcare provider outreach letters.
- Involvement and support from advocacy organizations in recruitment efforts. The study was highlighted on PD focused social media pages and websites including Fox Trial Finder and PSG. The study was presented to patient advocates and updates provided as the study progressed.
- Monthly coordinator and investigator teleconferences to discuss current recruitment barriers, strategies to overcome and new initiatives.

Results: As of November 27, 2018, 120 subjects have been screened, 38 screen failed, 6 declined, and 64/75 have been randomized. Our SF rate has been consistently decreasing (see figure 1). A qualitative analysis revealed the most effective recruitment strategies included engaging PD advocates and open diucssion between sites about recruitment barriers and successes. A number of recent social media posts and communications with advocates helped potential participants connect with local study sites.
Conclusion: Future studies of nilotinib in PD should be aware of the high screen failure rate related to the intrinsic safety profile of the drug triggering strict inclusion/exclusion criteria. Realistic planning of study timelines and implementation of comprehensive recruitment plans are essential for success of future nilotinib studies or any other agents with a similar risk profile in PD. RC efforts have been essential in supporting the trial.

Figure 1



P23.21

A Phase 3 study of isradipine as a disease modifying agent in participants with early Parkinson's disease (STEADY-PD III): Final study results
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Objective: To assess the efficacy of isradipine, a dihydropyridine calcium channel antagonist to slow the progression of Parkinson's disease (PD).
Background: Isradipine, a dihydropyridine calcium channel antagonist has been shown to be neuroprotective in animal models of parkinsonism. Epidemiological data also points to a reduced risk

of PD with chronic use of dihydropyridines. Previously completed Phase 2 study shown that isradipine was safe and tolerable at doses that were neuroprotective in animal models.
Methods: STEADY-PD III is an NINDS funded Phase 3, parallel group, placebo-controlled 36 months study evaluating the efficacy of isradipine 10mg daily as a disease-modifying agent in early PD. The study is being conducted at 54 Parkinson Study Group sites in US and Canada. The study recruited 336 participants with de novo PD not requiring symptomatic therapy and followed them prospectively for 36 months. The primary outcome is the change from baseline in the Unified Parkinson Disease Rating Scale (UPDRS) Part I-III score as measured in the ON state at month 36, in the active arm compared to the placebo arm. Secondary outcome measures include: 1) Time to initiation and utilization of dopaminergic therapy; 2) Time to onset of motor complications; 3) Change in non-motor disability and other PD motor and non-motor outcome measures.
Results: Enrollment was started in November 2014 and was completed in 12 months, 6 months ahead of schedule including 10% minority recruitment. At baseline the cohort was age 62 (SD=9), 68% male, and 0.9 (SD=0.7) years from PD diagnosis. As of November 16, 2018, 317 subjects have completed the study, 17 have prematurely withdrawn (96% retention) and 297 have initated PD symptomatic therapy. Final data analysis will be available early February 2019 and presented at the meeitng.
Conclusion: The study has a number of unique design features, including a 3-year duration of intervention, and assessment of the primary outcome in the medications ON state. Retention and completion rates have been remarkably high for this type of trial due to the joint effort of multiple stake holders (the study team, sponsors, advocacy organizations and people with PD).
Study supported by the NINDS U01NS080818 and U01NS080840

P23.22

Long-term efficacy for parkinsonism and safety of zonisamide in patients with dementia with Lewy bodies: A phase III trial
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Objective: To evaluate the long-term efficacy for parkinsonism and tolerability of zonisamide in patients with dementia with Lewy bodies (DLB)
Methods: Outpatients diagnosed with probable DLB were randomized into 3 groups (placebo, zonisamide 25 and 50 mg/day) and then treated with fixed dose of test drugs for 12 weeks in a double-blind (DB) manner. Subsequently, all patients received 25-mg/day zonisamide over 2 weeks and then the flexible dose (25 or 50 mg/day) was allowed according to patients' conditions in a 40-week, open-label (OL) extension phase. The efficacy (UPDRS part III, MMSE and NPI-10) and safety were evaluated.
Results: After randomization, 346 patients who took zonisamide at least once after the DB phase were included in the analyses (At baseline; mean age, 77.2 years; mean durations of dementia and movement dysfunction, 3.6 and 2.7 years; mean levodopa dose, 251 mg/day). Approximately 60% of patients took zonisamide 50 mg more frequently than 25 mg in the final 4-week period. The score reduction in UPDRS part III continued until 24–28 weeks around, and then the score maintained until the final evaluation time point (31.9 to 25.6 in the 25-mg/day group; 31.2 to 25.1 in the 50-mg/day group). No remarkable score change in MMSE or NPI-10 showed throughout the trial. Adverse events newly developed in the OL phase or largely increased compared with those developed in the DB phase were not found.
Conclusions: Zonisamide shows the long-term efficacy for DLB parkinsonism without deterioration of cognitive function, BPSD and safety in DLB patients.

P23.23

The protocol for a combined upper limb exercise and Do-It-Yourself community program for people with Parkinson's disease
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Background: Most people with Parkinson's disease (PD) focus on mobility training in the community, but may neglect the importance of regaining hand dexterity and upper limb daily functions. Besides, social isolation, without any involvement in meaningful and sustainable leisure activities, may affect mood and participation. This 6-month upper limb program serves as the active control arm of an aerobic walking study.
Objectives: The aim of the present study is to promote the participants' long-term exercise compliance on upper limb training combined with Do-it-yourself (DIY) projects. Their feedback and satisfaction with the exercise program will be explored.
Methods. Eighty participants will be randomized into either the upper limb or aerobic walking group. A 6-month upper limb program consisted of stretching, strengthening, timed fine motor control exercise and DIY practice (including patchwork, Origami, knot and upcycling craftwork) will be provided under the supervision of a physiotherapist. Participants will receive ten 90-minute sessions, (i.e. once/week in the first 6 weeks, followed by once/month for the next 20 weeks). Participants will perform home exercise for 2 sessions per week for 26 weeks (30 to 45 minutes per session). Using mobile message apps, the trainers will communicate with participants by uploading the training schedule and materials, monitoring progression and providing instant feedback. The 6-week exercise attendance will be documented and the participants will report 6-month exercise compliance and adverse effects using exercise diary. A satisfaction feedback survey will be conducted after treatment completion.
Results: Seven participants completed the 6-month program. The 6-week attendance was 97.6% and the 6-month exercise compliance was indicated by 72% of all participants completing at least twice a week of 30-minute home exercise. No adverse effects were reported. The majority of participants agreed the combined program was appropriate and enjoyable, as well as beneficial to their hand dexterity and daily functions.
Conclusion: This combined upper limb exercise and DIY community program is safe and feasible for people with PD, and could promote their long-term exercise adherence and sense of achievement. Further study is important to investigate the effects of this program on hand dexterity and upper limb daily functions in PD management.

P23.24

Levodopa carbidopa prodrug (ABBV-951) 24 hour continuous subcutaneous infusion shows similar pharmacokinetics in Caucasian and Japanese healthy volunteers

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Objective: Characterize levodopa pharmacokinetics (PK) and safety/tolerability of ABBV-951 in healthy Caucasian and Japanese subjects.
Background: Parkinson's disease is the second most common neurodegenerative disease and is characterized by progressive degeneration of the dopaminergic system resulting in bradykinesia, rigidity, tremor and postural instability. Early stage symptoms are managed with oral treatment; however, as Parkinson's disease progresses, symptoms are no longer well controlled by oral medication due to the short half-life of levodopa and a narrowing therapeutic window. ABBV-951 is a novel levodopa/carbidopa prodrug which has the potential to be delivered through a minimally invasive subcutaneous (SC) infusion and provide therapeutic levels of levodopa over 24 hours.
Methods: In this Phase 1 open-label study, ABBV-951 was administered as a single continuous SC infusion to the abdomen to Caucasian and Japanese healthy volunteers (45–75 years old) over a 24 hour period. Serial plasma PK samples were collected to assay for levodopa concentrations. Safety and tolerability were assessed throughout the study.
Results: Following ABBV-951 administration, levodopa PK profiles were similar between Caucasian and Japanese healthy volunteers. No clinically meaningful differences in mean levodopa exposures as assessed by Cmax, AUCt and AUCinf were observed between ethnicities (<15% difference). The median levodopa half-life was also comparable between Caucasian and Japanese subjects (1.5 vs. 1.6 hours, respectively). Stable levodopa exposures were achieved for the majority of the treatment period in both ethnic groups. There were a total of 2 adverse events reported in the completed group (8 Caucasian and 8 Japanese) by different subjects: one headache and one report of erythema at the infusion site. Both adverse events were mild in severity.
Conclusions: Following 24 hour ABBV-951 SC infusion, levodopa PK was similar between Caucasian and Japanese subjects. The infusion was well tolerated in both ethnic groups.

CLINICAL SCIENCE: Rating scales

P24.01

Validating a new dependency measure for Parkinson's disease

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Background: Functional dependency (i.e. requiring help from others with basic activities of daily living) is an important patient-centred outcome in Parkinson's disease (PD). We aimed to create a simple tool to dichotomously assess dependency in PD patients, based on the Unified Parkinson's disease rating scale (UPDRS) part 2 scale, which is widely collected in PD research studies.
Methods: We used data from the Parkinson's Incidence Cohorts Collaboration, an international collaboration of incidence cohorts in Northern Europe with about 1100 participants. Each patient had serial measurements with the original or MDS Unified Parkinson's disease Rating Scale (UPDRS). We defined dependency from only the specific items of these scales relating to activity limitation (hygiene, dressing, feeding, and walking [and getting out of a chair in the MDS version]). We validated this new measure against cut-offs from other activity limitation scales (Schwab & England score <80% and Barthel Index <19) by testing sensitivity and specificity. We assessed construct validity by comparing motor impairment (UPDRS part 3), cognition (MMSE) and quality of life (PDQ-39) between those defined as dependent and independent on the new scale.
Results: Our dependency tool showed high specificity and good sensitivity versus Schwab & England (specificity and sensitivity 94% and 70% respectively at baseline; 90% and 84% respectively at 5 years) and similar results versus the Barthel Index. We also found evidence for construct validity with lower MMSE and poorer quality of life in those dependent.
Conclusion: We have validated a simple tool to dichotomously assess dependency in PD patients, which can be widely used in research studies which have collected UPDRS data but not specific data on dependency.

P24.02

The new Parkinson's disease Composite Scale: A proven instrument for the quick and holistic assessment of Parkinson's patients

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Background: An instrument that can quickly assess the most relevant symptoms experienced by people with Parkinson's disease (PD) in general, and overloaded clinical settings, is needed. The recently validated Parkinson's disease Composite Scale (PDCS) was designed to fulfill this gap as a quick, comprehensive instrument for PD evaluation.
Objective: Extensive evaluation of the clinimetric properties of the PDCS using a large international sample.
Methods: International, cross-sectional study. In addition to the PDCS, the Movement Disorder Society-Unified Parkinson's disease Rating Scale and the Clinical Impression of Severity Index for PD were applied. Basic clinimetric attributes of the PDCS were analyzed.
Results: 776 PD patients were included. Missing data percentage was low (3.2%). The PDCS total score showed negligible floor and ceiling effect. Three factors (54.5% of the variance) were identified: Factor 1 including motor impairment, fluctuations, and disability; Factor 2, non-motor symptoms; and Factor 3, tremor and complications of therapy. Cronbach's alpha was 0.66 to 0.79 for the multi-item domains. Inter-rater reliability of 209 cases showed weighted kappa values 0.79–0.98 for items and intraclass correlation coefficient values 0.95 (Disability) to 0.99 (Motor and Total score). The Bland-Altmann method, however, did show irregular concordance. PDCS precision, on standard error of

measurement from inter-rater assessments, and convergent validity with equivalent constructs of other measures (=0.70) was acceptable. PDCS scores were significantly different by HY stage (Kruskal-Wallis test, all p<0.001).
Conclusion: Overall, in line with previous findings, the PDCS is a feasible, acceptable, valid, reliable, and precise instrument for quick assessment of PD patients.

P24.03

Rasch analysis of the clinimetric properties of the Korean dizziness handicap inventory in patients with Parkinson's disease
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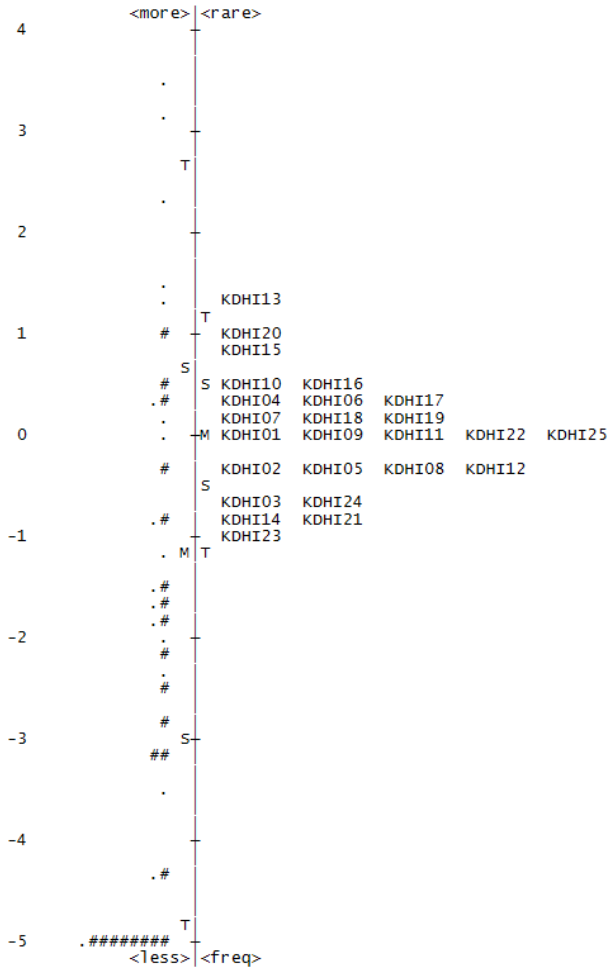
The Korean Dizziness Handicap Inventory (KDHI), which includes 25 patient-reported items, has been used to assess self-reported dizziness in Korean patients with Parkinson's disease (PD). Nevertheless, few studies have examined the KDHI based on item-response theory within this population. The aim of the present study was to assess the feasibility and clinimetric properties of the KDHI instrument using polytomous Rasch measurement analysis. he unidimensionality, local independence, scale precision, item difficulty (severity), and response category utility of the KDHI were statistically assessed using Rasch measurement analysis with the Andrich rating scale model. The utilities of the ordered response categories of the three-point Likert scale were analyzed with reference to the probability curves of the response categories. The separation reliability of the KDHI was assessed based on person separation reliability, which is used to measure the capacity to discriminate among groups of patients with different levels of balance deficits.Principal component analyses of residuals revealed that the KDHI had unidimensionality. The KHDI had satisfactory PSR and there were no disordered thresholds in the three-point rating scale. However, the KDHI showed several issues for inappropriate scale targeting and misfit items (item 1 and 2) for Rasch model. The KDHI provide unidimensional measures of imbalance symptoms in patients with PD with adequate separation reliability. There was no statistical evidence of disorder in polytomous rating scales. The Rasch analysis results suggest that the KDHI is a reliable scale for measuring the imbalance symptoms in PD patients, and identified parts for possible amendments in order to further improve the linear metric scale.



CLINICAL SCIENCE: E-health and technology

P25.01

Telehealth – Current trends and future potential
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Introduction: Parkinson's disease (PD) is a chronic and complex neurodegenerative disorder characterized by disabling motor and nonmotor symptoms. Geographical barriers, financial obstacles, and progressive physical disability limit safe, high quality, patient-centered care. With readily available access to personal health information through cloud computing, innovative software applications, and collaborative networks, telehealth is overcoming barriers to deliver health care to the home. The utilization of telecommunication technologies to enhance access to care with a patient-centered approach can assist to overcome these barriers. The purpose of this review is to discuss the current trends and future potential for telehealth in adults with PD.
Method: A literature search was conducted without time restriction on the publication year using MEDLINE, Academic Search Premier, CINAHL, PsycINFO, Health Source: Nursing/Academic Edition, Computers & Applied Sciences Complete, Regional Business News, Business Source Elite, Library, Information Science & Technology Abstracts, Newspaper Source, Education Research Complete, SPORTDiscus, Communication & Mass Media Complete, SocINDEX, Humanities International Complete, and PsychTESTS using the keywords telehealth, telemedicine, telemonitoring, telepreactice, telenursing, telecare, Parkinson's disease, Parkinson disease, Parkinson's disease, pd, parkinsons, and parkinsonism.
Results: Based on the 80 eligible studies, an analysis of current trends of interdisciplinary trends of telehealth and possibilities for future research in the care of patients with Parkinson's disease is discussed.

P25.02

The facilitators and barriers of telemedicine: How it can affect patients with Parkinson's disease

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Introduction: Telehealth first began in 19681, and now with the advancement in technology, the increasing number of individuals with chronic illness, and the need to increase accessibility of treatment, finding a successful telehealth system is more important than ever. This review focuses on the barriers and facilitators of telehealth and theories as to how to implement a successful system. Additionally, it will focus on how telehealth can be successfully implemented and benefit persons with Parkinson's disease.
Methods: Two literature searches were completed, each using PubMed, CINAHL, and MEDLINE. The first search was conducted to find any potential barriers or facilitators for telehealth. A total of 2,224 articles were found, and after implementing the exclusion and inclusion criteria a total of 13 studies were reviewed. The second search was conducted to see how telehealth is being implemented for persons with Parkinson's. A total of 203 articles were found initially, however only 8 pertained to the inclusion/exclusion criteria.
Results: Five main barriers were found for telehealth along with three main facilitators. With respect to telehealth and its beneficial implementation to patients with Parkinson's, there seems to be two popular barriers and one main facilitator. Each search yielded more than what was stated above and were summarized and quantified.
Discussion and Conclusion: Working to create a well-functioning telehealth system would be highly beneficial to our healthcare system, and therefore any limiting factors should be diminished. Such systematic shortcomings can be hard to address, and any changes may not be readily adopted by patients, care givers, and health professionals. Focus is needed on why these barriers exist and further research is needed with the goal of reducing them.
Keywords: Telehealth, Barriers and Facilitators, Parkinson's disease

P25.03

Technology serving elderly couples living with Parkinson's: Key steps and components of a web-based intervention

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Background: Technology appears to be promising for meeting the support needs of elderly couples living with Parkinson's in urban and rural areas.
Aims: A study was undertaken in Montreal (Canada) with eight elderly couples to develop and evaluate a Web-based intervention that is accessible, functional and complementary to existing health and community services.
Method: Based on the Intervention Mapping framework, the action research consists of four steps: 1) the development of messages algorithms oriented towards couples; 2) the validation of the intervention contents with the couples participating in the study and expert clinicians; 3) the transposition of the intervention contents into a Web application; and 4) qualitative assessment of the acceptability, functionality and utility of the intervention with the couples.
Results: The Web-based intervention consists of seven sessions (15–30 min./session), 112 support videos from a virtual nurse, 60 animations featuring couples who have successfully solved Parkinson's related difficulties, 40 different coping strategies and 20 printable reminders in the Web platform. Action research and ongoing feedback with the participating couples and the multimedia team has helped to create an innovative intervention that improves their ability to self-manage Parkinson's disease, by mobilizing their ability to work together to meet their support needs and by helping them to plan their future. The validation loops, the relational approach favored to carry out this intervention and the various role models proposed throughout the Web-based intervention seem to be the key components to promote the couples' empowerment, self-efficacy and quality of life.

P25.05

A wearable sensor device with internet connectivity for accurate movement assessment in Parkinson's patients

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The objective of this study was to design a wearable sensor device with internet connectivity to quantify the movement assessments associated with Parkinson's disease, which is commonly performed during regular clinic visits. Having an objective assessment of disease prognosis will support treatment modification for accurate and timely intervention. Although several studies have successfully explored the feasibility of motor symptom measurements, common clinical practice still relies upon a subjective assessment performed every 3–6 months, which encompasses finger tapping, pronation and supination, hand opening and closing, and the evaluation of resting, and postural tremors. The proposed wearable system has the potential of decreasing the burden associated with the snapshot effect of clinic visits while tracking interventional outcomes.
In this study, ten persons with Parkinson's disease were recruited, from a cross-sectional group of patients ranging from no motor symptoms to level 2 in the MDS UPDRS. Data was collected using an angle sensor located along the purlicue and an inertial measurement unit at the distal part of the index finger. A total of 20 samples were recorded for the motor assessments at a sampling rate of 125 Hz. Metrics for classification included a measure of bradykinesia, calculated as the decrease in opposition of index flexion amplitude from consecutive iterations, as well as, the

slowness and irregularity of finger tapping. Machine learning algorithms were trained using data scored by a movement disorder expert. Preliminary results show a predictive accuracy of 83.3%, signifying the potential for use of the designed tool to quantify movements objectively and accurately. The developed wearable device for objective motor symptom monitoring may be used as a clinical tool to support movement disorder specialist's motor diagnosis. Future work will focus on gathering motor data from different levels of disease prognosis to prevent biased predictive models. Moreover, motor symptoms will be blindly scored by a second movement disorder specialist, to explore the effects of interobserver error.

P25.06

Feasibility analysis of hand rotation test for quantifying Parkinson's disease motor states: Smartphone vs wristband motion sensor

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Aim: To investigate the feasibility of using smartphone inertial measurement unit (IMU) sensors for quantifying motor states of Parkinson's disease (PD) patients. More specifically, the aim is to compare results from IMUs and wristband motion sensors during hand rotation (Hr) tasks.
Background: Motion sensors are common for evaluating the motor states in PD. They are potentially improving the management of PD. Previous research has shown objective measures derived from wristband motion sensors are valid, reliable and responsive to PD treatment [1]. Smartphones are available, and customizable with sending notifications. Assessment of Hr task with smartphones can facilitate remote monitoring of PD.
Method: A healthy subject performed repeated Hr tests during a week while wearing a wristband sensor (Shimmer3) and holding a smartphone (iPhone 7). Tests lasted for about 10 to 20 seconds and were performed with dominant hand. Data consisted of 3D accelerometer recordings of both instruments. Similarity score for smartphone IMUs and wristband sensor signals were measured by cross-correlation coefficients between their corresponding magnitude acceleration signals. Features were extracted according to previous study (P_Std) [1] and Treatment response index score (TRIS) was estimated to predict the symptom states. Similarity of important features calculated for both instruments in this study and P_Std were estimated. The pre_developed machine learning algorithm [1] was trained using features of healthy subjects and PD patients in P_Std. IMU feature set in this study was used as testing set. TRIS for subject in this study was estimated. Mean of TRIS was calculated.
Results: Mean similarity score between IMUs and wristband sensor was 0.84 indicating good similarity. More than 50% of important features from both instruments were similarly important as in P_Std. Mean TRIS using IMUs data as testing set was 0.01 (SD=±0.03) indicating IMU data is sufficient for estimating the status of the subject.
Conclusions: It is feasible to use IMUs integrated in smartphones for collecting Hr test data. Results need to be further investigated in larger scale study.
[1] I. Thomas, et al., "A Treatment-Response Index From Wearable Sensors for Quantifying Parkinson's disease Motor States," IEEE Journal of Biomedical and Health Informatics, vol. 22, pp. 1341–1349, Sep 2018.

P25.07

An Internet of Things system for patient empowerment: a case study on measuring patients' understanding of causal relationships between symptoms and behaviour

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Background: People with Parkinson's disease (PD) must adhere to medication schedules and some need to adjust their medication to the rapid fluctuations of their motor function. Consequently, disease self-management is essential in PD and this requires high level of patient health literacy and empowerment. The research project EMPARK aims to achieve this goal by home monitoring using Internet of Things-based system complemented with self-registration of exercise, meal times and quality of life assessment. The registered data are presented in a comprehensive summary view in a tablet app. Preliminary results from previous evaluations indicate high level of technology acceptance and identified improved anticipated health literacy and empowerment among the patients. Before deployment and field tests, further studies are required to understand how patients interpret data presented by the system.
Aims: To evaluate the ability of patients to understand causal relationships between disease symptoms and behaviour presented from synthetic representative cases using the system. Secondary and tertiary aims are to assess usability and identify requirements for improvement of the application before deployment.
Methods: Based on previous work in the patient empowerment domain where empowerment factors such as health literacy is positively associated with use of health information technology, we measure patient understanding of possible causal associations between symptoms and management of the disease. Patients are recruited through the Swedish Parkinson Association during spring, 2019. Patients will be represented with synthetic realistic, clinically derived cases of PD scenarios including symptoms and related self-management data. Each case is developed and validated by clinical experts. The understanding of the possible causal associations is qualitatively assessed by semi-structured interviews. In addition, quantitative, questionnaire-based assessment of patient comprehension is performed based on an online video representation of the clinical scenarios. Results of the analyses will be triangulated.
Expected results: By using simulation of the system, patients will be able to identify causal relationships between symptoms and self-management. This pre-implementation study will help in understanding the abilities and assumptions of the PD patients when applying the system, and therefore can become a useful method for assessment of the usability and further development of systems for PD patient empowerment.

P25.08

Parkinson's Kinetigraph (PKG) in clinical management of Parkinson's disease

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Aims: To assess role of PKG in management of Parkinson's disease (IPD) and its effect on drug treatment as well as decision for advanced treatment.

Methods: 45 PKG reports between February '16 and May '18 from IPD patients in the Movement Disorder Clinic were studied. 37 had a valid reason documented for PKG. 17 male, 20 female. Mean age 71.6 years. Mean duration of IPD 6.37 years, range 1 to 26 years.
Results: There were multiple indications for PKG for most patients. These included dose failure (14 patients), off periods and wearing off (11), possible off dystonia or dyskinesia (5), freezing, falls and relationship with medication (6), bradykinesia and pain (7) and to quantify dyskinesia (3).
On clinical grounds, we felt that 10 of the 36 patients are likely to need complex treatment before PKG. One was already on Apomorphine (Apo-go pen).
After PKG, 4 patients started complex treatment (all had Apo-Go pen). One patient is being assessed for DBS. 5 patients did not need complex treatment but changed their medication with increase in dosage of L-dopa in 4 patients and a reduction in dosage in one patient. We envisage that 2 of these 5 patients are likely to need a form of complex treatment in the near future.
Cost of postponing advanced treatment for 5 patients: Apo-go pump (average cost of £5400/pump/year) led to a saving of £27,000/year. Postponement of Apomorphine (Apo-go) pen treatment (average cost of £3,200/year) led to a saving of approx. £16,000/year.
35 patients changed their PD medication after PKG.
Furthermore, 13 were found to have mild to significant dyskinesia with 6 needing a reduction in drug doses. 26 patients were under treated, mostly with off-periods, with 23 needing an increase in drug dosage.
Conclusion: PKG is useful for patients with Complex Parkinson's disease to delineate symptoms of dyskinesia, dystonia and wearing off periods.
PKG often assists in a change in the patient's medication leading to better symptom control.
PKG can be useful in postponing complex treatments in IPD, resulting in significant financial saving.

P25.09

A Swedish self-tracking app for improving neurology visits for Parkinson's disease

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Introduction: The Swedish national guidelines for Parkinson's disease (PD) were launched in 2016. The guidelines comprise recommendations for diagnostics, treatment and rehabilitation. However, it could be difficult to conclude what treatment and rehabilitation people with PD (PwP) should have without objective data; e.g. perceived health, sleeping patterns, motor skills and medication intake. Such data could be a learning possibility for PwP and supportive in the dialogue with healthcare providers, especially when considering advanced treatments. The aim here is to 1) examine the needs of PwP for better learning possibilities and dialogue with their healthcare team, and 2) to pilot test a smartphone app for self-tracking; ParkWell.
Method: As a needs assessment, we used the result of a survey (from early 2018), conducted by The Swedish Parkinson's disease Association (SPDA) which aimed to follow up the Swedish guidelines and targeted all members – 5 200 persons. Pilot usability tests of ParkWell were also conducted with five PwP.
Result: The results from the survey (response rate 69%, n=3588) showed that 74% considered knowledge about PD to be very important. However, only 8% experienced they had very good knowledge, and 54% said they had good knowledge about their PD. According to the guidelines a person with ineffective treatment should be assessed by PD specialists, for potential advanced treatment. Only 30% reported such an assessment. However, when not given advanced treatment, only 19% of the participants received an explanation. The five pilot usability tests done with PwP, shows that they are all positive towards a self-tracking tool. The participants expressed the need for learning more about how they feel in connection to different situations.
Conclusion: PwP in Sweden feel the need to have knowledge about their PD, and pilot tests indicate that they are positive towards ParkWell. With objective data there is a learning possibility, and it could be supportive in the dialogue regarding decision of advanced treatment.
Acknowledgements: The authors wish to thank Birgitta Björnek, AbbVie AB, for valuable input regarding ParkWell.

P25.10

Assessing tele-health outcomes in multiyear extensions of Parkinson's disease trials (AT-HOME PD): Initiation of a long-term observational study

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Objective: To develop, implement, and evaluate a model for the remote, long-term observation of Parkinson's disease (PD) clinical trial cohorts. We will 1) establish the infrastructure for a new research model, 2) compare patient-driven and clinician-driven outcomes, and 3) explore novel biomarkers of PD disability and progression.
Background: Mobile and remote technologies permit frequent data collection and objective assessment in the home setting, may reduce barriers to participation, and may enable the development of digital biomarkers of disease progression, potentially improving clinical trial efficiency.
Methods: An estimated 420 participants from two active NINDS-funded phase 3 interventional studies of potential disease-modifying therapeutics for PD (STEADY-PDIII and SURE-PD3) will enroll into AT-HOME PD. This 24-month observational study will remotely characterize long-term clinical outcomes using three platforms: virtual research visits (tele-visits), smartphone-based assessments, and web-based surveys. Centralized movement disorders specialists conduct tele-visits annually. Participants complete two-week sessions of smartphone-based motor tasks using mPower on a quarterly basis. For consented participants, mPower passively collects GPS- and accelerometer-based movement and activity data. Participants are also asked to enroll in an online companion study (Fox Insight) and to complete surveys quarterly. Data from the three platforms will be integrated with data from the parent studies, and the complete dataset will be transferred to the Parkinson's disease Biomarkers Program's Data Management Resource for use by the broader research community.
Results: To date, 264 of 336 STEADY-PDIII participants and 139 of 298 SURE-PD3 participants have consented to contact by the University of Rochester. The first participant enrolled in AT-HOME PD on October 8, 2018. There are currently 26 participants enrolled and 9 have completed the baseline tele-visit. Of the enrolled participants, 89% have consented to the smartphone-based assessments and 73% have enrolled in Fox Insight.
Conclusions: Enrollment in AT-HOME PD has successfully been initiated. The study is poised to investigate novel tele-health metrics of PD progression and to assess the feasibility of utilizing them in future clinical trials.

P25.11

Collaborative framework for delivering on ways that digital technologies can help to optimize new Parkinson's treatment trials

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Background: Development of effective therapies for Parkinson's is a high risk and costly endeavor. Recently, a focus on data collected using new digital technologies has been introduced to improve the assessment of day-to-day experience of people living with Parkinson's. Worldwide collaborative initiatives are in place to take advantage of mobile sensors and devices as new tools to inform drug development decision-making. The Critical Path for Parkinson's (CPP) consortium, a public private partnership sponsored by Critical Path Institute, Parkinson's UK and industry aims to advance innovative new tools to optimize clinical trials.
Objectives: To present CPP's pre-competitive collaborative worldwide network and describe how all stakeholders are working together to advance the utility of digital technologies for use in Parkinson's trials.
Methods: Five nonprofit (NPO)/research charity organizations from around the world have convened under the CPP consortium in partnership with industry and academic experts to participate in a working group with the goal of defining ways to optimize the use of digital technologies in Parkinson's clinical trials. The strategy includes near term focus on the following goals 1) to identify what symptoms and measurements are important to people living with Parkinson's and 2) to assess the landscape of digital measurement of signs/symptoms by carrying out a comprehensive data inventory of studies being carried out around the world.
Results: The CPP initiative recognizes the need to catalogue and inventory relevant Parkinson's studies where data collection by digital technologies have been implemented to date. The findings will inform best practice for data collection using digital technologies in future studies.
Conclusions: The information gathered from CPP's assessment of the use of digital technology in Parkinson's studies will apply learnings from other consortium initiatives to develop novel tools to improve Parkinson's clinical trials. A robust collaboration between all stakeholders around the world centered on data standards and data sharing is key for success in the future.

CLINICAL SCIENCE: Neuroimaging

P26.01

MIBG scintigraphy in the differential diagnosis of Parkinsonism

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Introduction: The differential diagnosis in patients with parkinsonism can be challenging. A 123I- metaiodobenzylguanidine (MIBG)-scintigraphy gives valuable information about the (dys)fuction of the postganglionic neurons of the cardiac sympathetic nervous system. It is known that there is a reduced cardiac uptake and enhanced washout of 123I-MIBG in patients with idiopathic Parkinson's disease (IPD) and Lewy body dementia (LBD), but not in other parkinsonian syndromes.
Materials and Methods: In this study, 20 patients with a parkinsonian syndrome who were referred to our department for a MIBG-scintigraphy between 2012 and 2018, were retrospectively evaluated. Descriptive statistics were calculated and correlation between scintigraphic diagnosis (according to the heart tot mediastinum ratio (HMR), a cut-off value of 1.6 was used) and clinical diagnosis after follow-up was examined.
Results: In this patient group, there was a concordance between clinical diagnosis and scintigraphy diagnosis only in half of the patients. It has to be noted that age can be a confounding factor, with a lower heart/mediastinum ratio with increasing age. There were no significant differences between men and women. No clear effect of medication was found.
Discussion: In this studied patient population, there was no significant accordance between a decreased HMR and the diagnosis of IPD or LBD. Only in half of the cases, the scintigraphic diagnosis concorded with the clinical diagnosis. A new cut-off value could be proposed.

P26.02

Impact of white matter lesions on cognition and gait in Parkinson's disease

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White matter lesions (WMLs) are known to affect gait and motor functions in Parkinson's disease (PD) patients, and are associated cognitive impairment in healthy elderly subjects. WMLs may contribute to these symptoms due to disruption in neuronal connectivity, specifically projection axons. WMLs are traditionally evaluated using visual scales on magnetic resonance imaging (MRI), which can be time-consuming. We aim to use semi-automated segmentation to evaluate the correlation between location of WML volumes and functional decline in PD and healthy subjects.
Whole brain MRI was performed at 1.5- and 3-Tesla on a case-control cohort of 55 (20 PD and 35 controls). Global cognitive ability and executive function were assessed using the Montreal Cognitive Assessment (MoCA) and Frontal Assessment Battery (FAB). Motor symptoms were evaluated using the Unified Parkinson's disease Rating Scale (UPDRS) Motor Scale. WMLs segmentations were assessed using an automated method based on a supervised approach and refined by a partial volume estimation.
Periventricular, frontal and prefrontal WML were positively correlated with UPDRS ($r=0.51$ to 0.57, $p<0.01$). Stepwise regression showed that periventricular WML alone significantly predicted UPDRS ($b=4824$, $F(1,50)=23.88$, $p<0.01$) and TBS ($b=-1498$, $F(1,50)=9.581$, $p<0.01$) scores, while frontal WML alone significantly predicted MoCA ($b=-907$, $F(1,50)=34.15$, $p<0.01$) and FAB scores ($b=-376$, $F(1,50)=19.22$, $p<0.01$).
WML volumes segmented using a fully automated multi-modal segmentation algorithm strongly correlated with overall motor and gait impairments, as well as deficits in executive functioning. Frontal lobe functions are more severely affected by WMLs in PD. Future

studies should aim at evaluating impact of periventricular WMLs on other PD motor subtypes and in other specific cognitive domains.

P26.03

Selective parafoveal inner retina thinning predicts visual outcomes in Lewy body diseases

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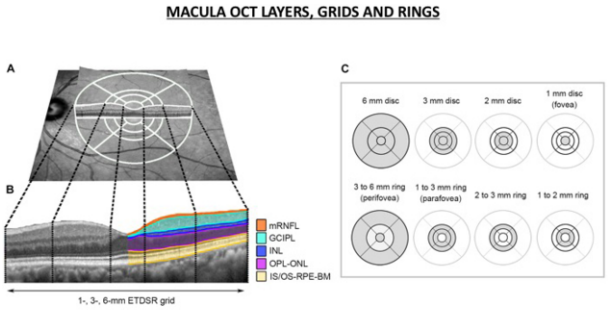
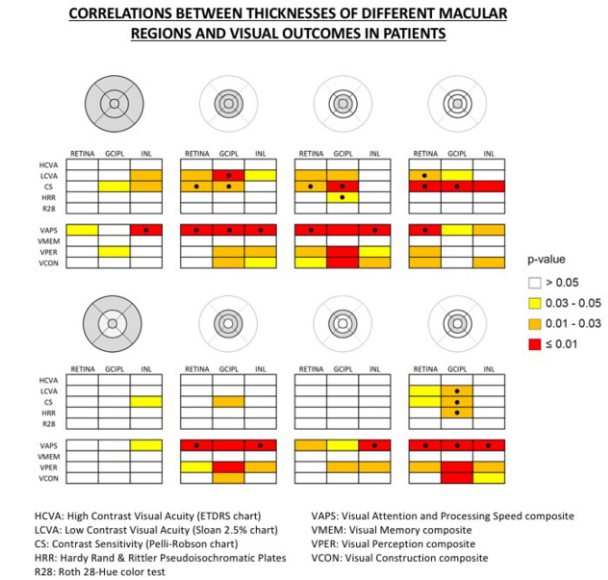
Objective: To evaluate whether a region-specific thickness analysis of retina OCT measurements could improve macular atrophy detection and prediction of visual disability in patients with Lewy Body Diseases.
Methods: Sixty-two patients with Lewy Body Diseases (LBD), including patients with idiopathic Parkinson's disease (iPD, n=50), dementia with Lewy bodies (DLB, n=8) and E46K-SNCA mutation carriers (E46K-SNCA, n=4), and healthy controls (HC, n=26) were included. All participants underwent Spectralis optical coherence tomography (OCT) macular acquisitions and a comprehensive battery of primary and visual cognitive function tests. We computed bilateral average retinal layer thicknesses within 1-, 2-, 3-, and 6-mm diameter macular discs and in concentric parafoveal (1 to 2-mm, 2 to 3-mm, 1 to 3-mm) and perifoveal (3 to 6-mm) rings. Group differences in OCT parameters and the relationship between inner retinal layer thicknesses and clinical measures were analyzed.
Results: compared to controls, most aggressive LBD (DBL and E46K-SNCA) had a significant selective macular thinning of ganglion cell-inner plexiform layer complex (GCIPL) and inner nuclear layer (INL) within central 3-mm disc. There was a positive correlation between inner retinal layer thickness and visual outcomes in patients, but not in controls. Remarkably, macular GCIPL atrophy in the parafoveal ring (1 to 2-mm ring) was significantly associated to worse low contrast visual acuity, contrast sensitivity, color vision and visual attention processing and speed (Bonferroni adjusted p<0.05).
Conclusion: Our findings support parafoveal thinning of inner retinal layers as a sensitive and clinically relevant OCT biomarker in Lewy body diseases.





P26.04

Asymmetric dopaminergic depletion is related with cardiovascular non-motor symptom in drug-naïve patients with Parkinson's disease

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Background: Even though dopamine transporter (DAT) imaging is helpful for diagnosis of Parkinson's disease (PD), the relationship between clinical symptoms and DAT imaging data has not been clearly elucidated yet.
Methods: We performed [18F] N-(3-fluoropropyl)-2β-carbon ethoxy-3β-(4-iodophenyl) nortropane positron emission tomography (FP-CIT PET) in drug-naïve patients with PD. Parkinsonian motor symptom was evaluated by the Unified Parkinson's disease rating scale (UPDRS) part 3 and non-motor symptoms with non-motor symptom scale for PD (NMSS). We analyzed correlation between motor and non-motor symptoms, and FP-CIT PET data.
Results: We recruited 42 drug-naïve PD patients in this study. In terms of motor symptoms, only bradykinesia score was correlated with dopamine transporter uptake in striatum and putamen when age and sex were controlled. For non-motor symptoms, we controlled age, sex, and UPDRS part 3 sub-scores (tremor, bradykinesia, rigidity, axial scores), and cardiovascular symptom was the only non-motor symptom that had a significant relationship with asymmetric index of striatum.
Conclusion: Based on our results, among the motor symptoms, bradykinesia was associated with FP-CIT uptake in putamen and striatum. In non-motor symptoms, cardiovascular symptom was correlated with asymmetric DAT uptake in striatum regardless of age, sex and motor symptoms.

P26.05

Abnormal verticality perception in Parkinson's disease patients with lateral trunk flexion is associared with hypoperfusion in the right temporoparietal junction

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Background: Lateral trunk flexion (LTF) is often observed in Parkinson's disease (PD). Abnormal verticality perception has been suggested in PD. We expected that altered verticality perception would be one of the principal causes of LTF. The purpose of this study was to investigate the association of verticality perception to LTF, and to clarify the associated brain regions with functional impairment.
Methods: Subject visual vertical (SVV) deviation angles which represented verticality perception were examined in 81 PD patients and 14 healthy controls (HC), and their LTF angles were measured. Abnormal LTF was defined by the maximum LTF in HC. SVV deviation angles were compared between the groups of PD with LTF, PD without LTF, and HC. We further evaluated 50 patients who performed [123I]iodoamphetamine-SPECT images. Two sample t-test was used for the voxel-wise group comparison of the SPECT images between PD with LTF and PD without LTF. We examined the relationship between SVV deviation angles and regional perfusion showing a significant change in group analysis.
Results: The SVV deviation angles significantly differed in PD. Abnormal SVV deviation was detected not only in PD with LTF but also in PD without LTF. SPECT images showed a significant decreased perfusion in the superior parietal lobule, the inferior parietal lobule, the postcentral gyrus, the dorsal posterior cingulate cortex, and the superior temporal gyrus in the right hemisphere. And there was a significant negative correlation between SVV deviation angles and each brain regions.
Conclusions: These results suggest that LTF in PD could be caused by abnormal verticality perception, which was related to functional abnormalities in the cortex around the right temporoparietal junction.

P26.06

Iodine-123-metaiodobenzylguanidine scintigraphy (MIBG) in routine clinical practice – a local experience in movement disorder clinic

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Introduction: MIBG scan is a helpful diagnostic tool to differentiate atypical Parkinsonism Multi system atrophy (MSA) from Lewy Body disease (LBD) including Parkinson's disease (PD), Dementia of Lewy Body (DLB), Primary autonomic failure and REM sleep behaviour disorder (RBD). it has specificity of 77% and sensitivity of 89%.
Clinical diagnosis of MSA can be difficult in early stages in spite of postural hypotension, persistent low BP, coat hanger symptoms and bladder issues.
It is important to differentiate these conditions for better prognostic and treatment options.
Methods: Our Movement disorder service has 700 patients with approximately 550 with LBD (PD and DLB, few RBD, one Pure autonomic failure). Over last two years we analysed approximately 10 patients who have suggestive clinical features of Multisystem Atrophy Parkinson (MSA-p) type. Locally MIBG cardiac scans became available in 2017 and 9 patients underwent this investigation over 22 months. We reviewed clinically effect of scan results on diagnosis and management. All nine patients had MIBG scans analysing early (15mins) and delayed (4hr) acquisition and mediastinal/heart ratio calculated as well as washout recorded.
All results were matched against case history, clinical features and initial diagnosis of each patient as well as follow up diagnosis after the scan. Diagnosis of MSA was recorded as probable/possible/ most likely.
Results: Mean age was 73.4, six male, none had history of cardiac disease. Mean follow up before suspected diagnosis of Atypical PD was 26 months.
See table.
One MIBG scan was normal and subsequently matched with clinical feature of MSA on follow up suggesting diagnosis most likely. Eight abnormal scans when reviewed with subsequent clinical follow up showed probable MSA 1, possible MSA in 2, PD in 4 and DLB in 2.
Conclusion: In this small clinical study, 7 of 9 scan results, matched subsequent clinical manifestations of revised diagnosis 78%.
2 scan results were not in concordance with clinical picture (22%) but follow up data is less than 12 months at present.
This clinical study shows role of MIBG scan in helping diagnosis of patients with complex symptomatology overlapping many facets of Parkinsonism in day to day practice.

Orthostatic Hypotension / Low BP	9
Poor L-dopa response	3
Falls backwards	2
Light headed	2
Early speech / swallow problem	3
Bladder symptoms	1
Stridor	1
Blue fingers	1
Escalation of Treatment	1
Myoclonus	1
Dementia	2
Normal cognition	9

Table of atypical symptoms and clinical features

CLINICAL SCIENCE: Prodromal

P27.01

Clinical characteristics of patients with idiopathic REM sleep behavior disorder (RBD): Comparing groups with short-term, intermediate-term, and long-term disease duration

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Idiopathic rapid Eye Movement (REM) Sleep Behavior Disorder (IRBD) is well known as preclinical marker of neurodegenerative disease, especially α-synucleinopathy. However, natural course of RBD is not represented obviously, because the lacking of large cohort study. The aim of this study is to assess clinical characteristics among RBD patients with short, medium, and long disease duration and to identify effects of disease duration among these patients.

Seventy-one patients with a polysomnography (PSG) confirmed idiopathic RBD were enrolled to participate in this cross-sectional study. The patient inclusion criteria were that disease duration should be less than 2 years (short-duration group), 2 to 5 years (intermediate-duration group), and more than 5 years (long-duration group), and they should have no other neurodegenerative diseases, and be able to fill out sleep questionnaires. The study population was divided in short-duration group with 19 patients, intermediate-duration group with 28 patients and long-duration group with 24 patients. Various questionnaires (RBDQ-KR, PSQI, ESS, HDS, HAS, BDI, MMSE-K and SF-36) were fulfilled by patients. Also, quantitative data of REM sleep without atonia (RWA) was obtained by reviewing of PSG records. We compared the groups on several clinical characteristics using one-way ANOVA.
Among three groups, statistical differences were found in the age of onset, RBD-KR scores, and RWA (%). Post hoc t-tests showed that the long-duration group is significantly older age of onset than the short duration group. Long-duration group had higher total score of RBDQ-KR (P=0.017), higher percentage of RWA (P=0.010), and lower age of onset (P=0.016) than short-duration group.
This result suggests that longer disease duration make worse effect on patients with RBD and earlier age of onset is associated with long disease duration without transition to neurodegenerative disease. Our study has some limitations. The patient number is small and onset of RBD is indefinite. Also, more accurate quantitative analysis of RWA is needed. Additional larger and longitudinal studies are needed to confirm the significance of our findings.

COMPREHENSIVE CARE: Caregiving, relationships, respite care, families

P28.01

Debriefing the caregiver role: A workshop for those who have lost someone with PD

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Rational: It has been said that Parkinson's disease (PD) is a family affair. Many caregivers are involved from diagnosis and throughout the disease continuum until death. Unfortunately, once a person with Parkinson's dies, the formal support network of health professionals ceases and the informal supports (groups, home support workers) once available to the caregiver no longer exists. To complete the circle of care, the workshop was developed to support the often unaddressed needs of those who have lost someone with PD.
Method: The "Debriefing the Caregiver Role" program was developed by Pacific Parkinson's Research Centre and Parkinson Society British Columbia as a 2–3 hour in-person one time workshop for caregivers who have lost someone with PD in the past 12 months. The workshop begins with caregivers being invited to "share their story" and the facilitators then address topics including the grief process, managing difficult emotions, making adjustments, self-care and handling special occasions.
Results: Participant evaluations reveal an appreciation of the opportunity to share feeling with others who can relate to and understand the unique PD caregiving and grief experience in a non-judgmental way. Many valued the support that continued to be available to them.
Conclusions: The workshop highlights the importance of social connections during the grieving process as well as the benefits and value of helping others while receiving support at the same time. Providing caregivers with an understanding of grief and strategies to cope in a safe and supportive environment was deemed invaluable by the participants.

P28.02

Neuropsychiatric symptoms and caregiver burdens in Parkinson's disease and Alzheimer's disease – differences between spouse and offspring

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Neuropsychiatric symptoms (NPS) are common and increase burden of care in neurodegenerative disorders. Burden of care could be different according to relationship with patient. This study investigated neuropsychiatric symptoms and caregiver burdens in Parkinson's disease (PD) and Alzheimer's disease (AD), and differences in their report and relationship with burden of care between spouse and offspring.
Patients and caregivers of PD and AD were recruited from outpatient clinic of referral hospital. Semi-structured interview were done with caregivers comprehensively, and reports of spouses and offsprings were compared.
Patients with AD showed poor cognition, more NPS, and higher caregiver burden than PD. Spouse group were older, more depressed, and cared longer period than offspring group, but there was no difference in burden of care. Most common NPS reported by spouse was depression (64.8%), followed by anger (49.3%) and anxiety (49.3%). Offspring group frequently reported depression (53.3%), change of eating habit (37.8%), and apathy (35.6%). Hallucination, anxiety, and anger were significantly more common reports of spouse group, and abnormal repetitive behavior and change of eating habit were more common in offspring group. NPS showed significant correlation with burden of care. Apathy and impulse control disorder in spouse group and poor cooperation and abnormal repetitive behavior in offspring group showed highest correlation with burden of care in each group.
Neuropsychiatric symptoms in PD and AD were common and showed significant correlation with burden of care. Spouse group reported NPS more frequently than offspring group, and distribution and their impact on burden of care of spouse group were different from those of offspring group.

P28.03

Parkinson's disease care partner psychological health and well-being: A proposed assessment and treatment paradigm

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Persons with Parkinson's disease (PWP) are often cared for informally by family members, and these care partners play a vital role in the PWP's life. The complex and disabling PD symptomatology, including motor and non-motor manifestations of the disease, as well as complications from PD therapy, such as wearing off medication, dyskinesias and impulse control disorders, result in higher daily demands for care partners. Addressing carer psychological health and well-being is critical to the delivery of high quality care for PWP, as well as for the reduction of carer burnout and burden. Depression and anxiety are frequently experienced by

PD carers in the context of their helping role. In addition to the detrimental personal consequences of mood symptoms for caregivers, carers experiencing high levels of emotional distress are unlikely to accurately recognize the mental health needs of PWP, further complicating all aspects of PD care. Here we propose a model for the evaluation and treatment of carer psychological well-being. Evaluations may include validated rating scales and questionnaires for depression and anxiety, direct assessment of carer burden, and indices of caregiver quality of life, as well as perceived positive aspects of caregiving. Involving care partners at neurology consultations for PWP when possible (from initial consultation to follow-ups) can be the first step towards evaluating carer psychological health and identifying potential treatment targets. Strategies to improve carer psychological health may incorporate multiple approaches. First, effectively treating PWP for both motor and non-motor symptoms, is likely to reduce amount of care required. Second, individual treatment of anxiety and depression in carers to improve their psychological health and quality of life may prove beneficial. Lastly, patient-carer dyadic interventions for depression and anxiety, as well as relationship counseling, may increase the quality of the PWP-carer relationship. For optimal results, approaches to treatment must be flexibly tailored to meet the unique needs of each PWP/caregiver dyad, and consider specific contributors to carer burden in each individual case. Caregiver interventions may enhance PD treatment response for motor and non-motor symptoms, improve relationship health, and decrease morbidity and mortality rates for both PWP and family members.

P28.04

Share the care: Supporting Parkinson's disease caregivers through peer mentoring

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Background: Patients with advanced Parkinson's disease (PD) are frequently homebound and require intensive caregiving at home to avoid institutionalization. Caregivers shoulder a heavy emotional, physical, and financial burden, and escalating caregiver strain increases the risk that PD patients will be institutionalized. Institutionalized PD patients, in turn, have higher mortality rates relative to their age- and duration-matched counterparts in the community. As the PD population continues to grow, mitigating caregiver burden in PD also grows in importance.
Preliminary studies with dementia patients suggest that pairing current caregivers with an experienced past caregiver who is trained as a peer mentor yields subjective benefits to both mentors and mentees, and can improve caregiver strain and confidence. Peer mentoring programs have not been studied among PD populations. Share the Care was designed to offer one-on-one mentoring support to current caregivers (mentees) of homebound patients with advanced PD.
Methods: Share the Care is part of a larger year-long study, IN-HOME PD, which provides quarterly interdisciplinary hybrid in-home/telehealth visits to homebound patients with advanced PD. Share the Care mentees are part of a caregiver-patient dyad currently enrolled in the IN-HOME PD study. Share the Care mentors are volunteers that either have cared for or are currently caring for a loved one with a movement disorder. Mentors receive a five hour training prior to meeting with their mentees, which includes review of the Share the Care Mentoring Handbook, a structured curriculum of weekly topics mentors discuss with caregivers. Anxiety and depression of mentees are tracked as primary outcomes of Share the Care. Additionally, caregiver strain among mentees, and caregiver self-efficacy among mentees and mentors, is assessed alongside time spent, topics covered, and mentee satisfaction.
Results/Findings: The Share the Care program is currently underway, with 20 mentors trained. Program design, curriculum, implementation, and interim data analysis will be presented.
Conclusion: The findings will contribute to the dearth of knowledge regarding effective peer-mentoring approaches to improving quality of life and caregiver strain among advanced PD patients.

P28.05

Utilizing community partnerships to provide a respite care program for people with Parkinson's disease

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Parkinson's disease research has increasingly identified the impact of both motor and non-motor challenges on one's ability to perform daily activities. Caregiving for people with PD (PwP) can become an intensive long-term commitment, lead to significant emotional and physical stress, and reduce quality of life.
This poster will illustrate the process and practical considerations used by a regional non-profit organization to create a PD respite care 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. We understood respite services were missing from our community's continuum of care and realized collaboration with partners was necessary for development, implementation, and sustainability of a respite care program. A variety of outreach services and survey methods were used to better understand the day to day caregiving of PwP and the impact on their care partners and family.
For the last 10 years, Parkinson Partners has navigated changes in funding, respite care agencies, and quality assurance to offer an annual respite care benefit within our community.
This presentation will include:

- Examples of why respite care was needed in our community
- How evidence regarding experiences from other communities was used to support decision-making throughout the history and development of our program
- The importance of educating respite care providers about the unique motor and non-motor challenges of PD
- A discussion of barriers to accessing respite care for people with PD and their families such as finances, pride, fear, and geographic location
- Considerations for implementation including funding directives and availability of disease-specific trained respite providers
- Understanding what is valued and important to a funder can create a successful relationship for sustainability

In summary, non-profit organizations must make every effort to advocate for programs focused on benefitting people with PD and their families. Working collaboratively with community partners can provide needed resources to achieve a common goal of improved quality of life.

P28.06

Alexander technique group classes are a feasible and promising intervention for care partners of people living with Parkinson's disease

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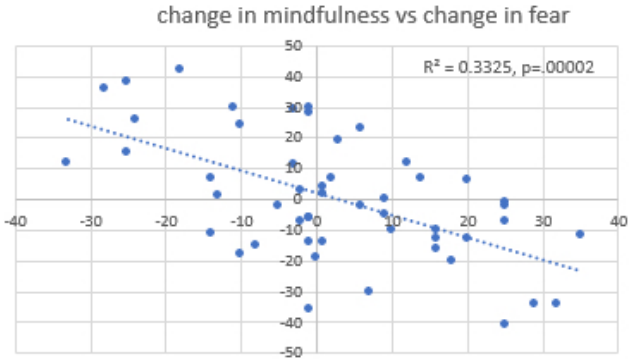
Objective: To test an adapted Alexander technique (AT) group course to improve quality of life for care partners of people living with Parkinson's disease (PlwPD).
Background: Alexander technique is an embodied mindfulness approach that aims to transform disruptive reactions to stress into adaptive responses, enhancing performance of daily activities while improving confidence and reducing anxiety. Studies show that private AT sessions can reduce neck and back pain.
Design/Setting: We delivered "Partnering with Poise", an adapted AT program, in seven cities in North Carolina (USA). Groups met 90 minutes weekly for 10 weeks. Outcomes were assessed before and after the intervention.
Intervention: Coursework included functional anatomy and self-management strategies taught through verbal instructions, hands-on guidance, partnering activities, and interactive games. A unique feature of our program is that all activities are prefaced with strategic thoughts and verbal prompts to interrupt automatic reactions. These self-regulatory strategies are presented simply enough to be remembered and used independently outside of class. Another unique aspect an AT approach is that highly time-pressured care partners do not need to set time aside to practice Alexander skills, but rather can continuously incorporate them moment-to-moment during their daily real-life activities while meeting the ongoing challenges of caregiving.
Outcome measures: Anonymous course evaluations, executive function (Stroop and Digit Span), balance (Mini BESTest), and self-report measures (mindfulness, fatigue, pain, stress, self-efficacy, and mood).
Results: Course attendance was 83%. Retention was high (83%). On a 0–10 scale, the mean rating was 9.5 for "enjoyed the interaction with other participants," 9.2 for "encountered new ideas," 8.4 for "learned skills to take care of myself emotionally," 8.3 for "likely to use the new skills in my daily life", and 8.0 on "I feel better prepared for the daily demands of caregiving." Executive function improved ($p<.05$). Neither balance nor any self-report measures showed significant improvement. However, there was strong correlation between improved self-reported mindfulness and increased self-efficacy and reduced fear and fatigue ($p<.00005$).
Conclusion: AT shows promise as a long-term self-management approach to ease care partner burden. Group classes have the potential to provide cost-effective delivery with additional social benefits.
Funding: Parkinson's Foundation, American Society for the Alexander Technique.



P28.07

A view from the corner: The experience of caregiving during the Rock Steady Boxing program

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Introduction: The Rock Steady Boxing program, designed as an intense exercise program specifically for individuals with Parkinson's disease (PD), aims to improve strength, coordination, and balance. Care partners are an important component of Rock Steady in the role of corner person. The limited research published on this program has focused on changes in the individual with PD as a participant in the Rock Steady program. No studies have been identified that specifically relate to the role of the care partner during the Rock Steady Boxing program or their perception of the impact of the program on their lives. The purpose of this qualitative study was to understand what it means to be a caregiver as corner person for a significant other with PD participating in the Rock Steady Boxing program.
Method: Face-to-face interviews were conducted with nine care partners who participated with their significant other with PD in a Rock Steady Boxing program for a minimum of six months. The interviews were transcribed and analyzed by two researchers using the phenomenological approach of van Manen.
Results: Four themes were identified that described the life experience of care partners engaged in the Rock Steady Boxing program: 1) Facing uncertainty; 2) Searching for hope; 3) Motivated to action; and 4) Fighting it together. Through a better understanding of the everyday lived experience of couples actively engaged in the journey of PD from the lens of the care partner, the health care team can more effectively join in the journey and provide meaningful support.

P28.08

Engaging the family: Adult children of people with PD private Facebook group

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Almost every person with PD has a care partner who is integral to their everyday lives and decision making. In addition to the care partner, living optimally despite the complex and progressive symptoms of Parkinson disease requires a team effort with caregivers and family members playing both offense and defense positions. They alternate planning and preparing for the future with responding and adjusting to the constant demands and problems encountered every day.
In nearly all aging populations, adult children at some point become heavily involved in screening treatments, interventions and support. This is particularly true with PD due to the length and degenerative nature of the disease.
An outgrowth of our Adult Children of People with PD conferences, the Adult Children of People with PD private Facebook group now grows at an average rate of 20 new members per week, engaging people from across the US, Canada and Europe. Using an UX model of design and the value proposition canvas, we created the page to address this particular population's pain points as based on information surfaced from conversations with more than 100 adult children of people with PD. It is a very active group!
The private group addresses the needs of adult children, helping to educate them about the disease, treatments and interventions. The group also offers them an opportunity to build skill sets based on a better understanding of PD as well as how they can support their family member with Parkinson disease and the primary care partner. The group offers an important forum for discussion, learning, and building support. In addition to conversations among the adult children, PMDAlliance posts regular information about treatments, tools and assistive devices, medical professions that assist in navigating PD, and more.

P28.09

The relationship between depression and emotional support by patients' attending physicians among primary caregivers of patients with Parkinson's disease: Focusing on cognitive evaluation of family function

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Purpose: The purpose of this study was to investigate the relationship between depression and emotional support by patients' attending physicians among primary caregivers of patients with Parkinson's disease: focusing on cognitive evaluation of family function. This was expected to shed light on the existence of formal support among medical professionals that contributes to reducing caregiving-related stress among primary caregivers of patients with Parkinson's disease.
Methods: The subjects of this study were 381 primary caregivers of Parkinson's disease patients using the outpatient clinics of four medical institutions and one adult day care center located in Prefectures A and B. Subjects answered an anonymous, self-administered questionnaire, which included questions about depression(K6), emotional support by the patient's attending physician as well as the basic attributes of the primary caregivers. The data of 122 subjects was subject to an analysis of the relationship between depression and emotional support by patients' attending physicians among primary caregivers of patients with Parkinson's disease: focusing on cognitive evaluation of family function. Data was analyzed using descriptive statistics and multiple regression analysis.
Results: Depression among primary caregivers was poorer in the group with bad cognitive evaluation of family function than in the group with good cognitive evaluation of familial function. In the group with good family function, only the patient's ADL was related to caregiver's depression. However, in the group with poor family function, emotional support by patients' attending physicians in addition to the ADL of the patient was related to depression among primary caregivers.
Conclusion: For primary caregivers with poor cognitive evaluation of family function, it was suggested that emotional support by patients' attending physicians was significantly effective for primary caregiver's depression. In the future, it is necessary to elucidate the relationship between medical professionals and primary caregivers and consider how to provide concrete support.

P28.10

The psychological impact of Parkinson's disease patients' delusions on spouses: A qualitative analysis

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The psychological impact of Parkinson's disease patients' delusions on spouses: A thematic analysis.
Introduction: Whilst there is a growing cadre of research reporting on carers' experiences of living with those with PD, to date there has been little systematic exploration of how carers are affected by bizarre and illogical thoughts expressed in PD delusions. This study sought to explore how caregiver spouses are affected by their delusional partners, in both private and public domains.
Method: Semi-structured, qualitative interviews were undertaken with spouses whose partners were being seen at a Movement Disorders clinic in Western Canada, and had reported PD related delusions. Interviews sought to establish how spouses experienced and managed the delusions and their impact on them. The data was subject to thematic analysis.
Results: Twelve spousal carers were interviewed, with analysis of data eliciting four themes – Managing incredulity: experiencing shock and trying to make sense of delusions' content; Hyper-vigilance: constant alertness to bizarre and threatening discourse; Defensive strategizing: anticipating delusions and addressing potential consequences; Concealing and Exposing: ambivalence about disclosing impact of delusions yet wishing support.
Conclusion: Spouses reported significant impacts to their emotional well-being and marital relationship. They described reactive coping strategies and challenges to an orderly, predictable life, constantly monitoring potential threat, and re-evaluating marital bonds. Spouses reported reluctance to share their experiences to mitigate a sense of emotional betrayal of their spouses and to avoid feelings of shame. Findings suggest services should be more attuned to the impact of delusions on spousal carers and strategies to facilitate disclosure to enable delivery of appropriate support.

P28.11

Caregivers burden in Parkinson's disease in Singapore

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Background: Caregiving for Parkinson's disease (PD) patients can be highly demanding. Our study aims to investigate the impact of motor and non-motor symptoms on caregiver burden among PD patients.
Methods: PD patient-caregiver pairs were recruited. Patients were evaluated on motor, non-motor symptoms and quality of life (QoL). Caregivers' burden was stratified into 3 subgroups. Statistical analysis was performed to identify differences in the no-or little, mild-moderate and high caregiver burden subgroups.
Results: Compared to mild-moderate, the high caregiver burden subgroup consisted of patients with more progressive disease (mean duration 9.63 versus 6.12 years; p=0.004), 56.3% were Hoehn & Yahr Stage =3, with mean LEDD of 556mg and more frequent and severe mood symptoms (NMSS-Mood Domain median score 8.0 versus 1.0; p=0.009 and PDQ39-Emotional Wellbeing Domain 35.4 versus 16.7; p=0.014). The mild-moderate versus no-or little subgroups showed a marked increase in PDQ39 self-reported mobility issues (40.0 versus 22.5; p=0.015), ADL dependency (25.0 versus 8.3; p=0.005) and higher NMSS Sleep/fatigue scores (8.0 versus 5.0; p=0.044).
Conclusion: Greater caregiver burden was more likely in patients with more progressed disease, poorer therapeutic control of motor symptoms, and more frequent and severe mood symptoms.

P28.12

To develop a training program with accompanying workbook for care partners

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"YOU HAVE PARKINSON'S TOO," the diagnosing Neurologist should have pronounced turning to me.
Since my husband's recent passing, my goal is to be an advocate for Care-partners of those living well with Parkinson's. After 25 years of caregiving, I have some idea of our needs and what advice would have greatly eased our lives.
Abstract: create a sustainable and practical training program model with accompanying workbook for care-partners facilitated by local professionals in the field, agencies, PD support groups, government departments and all involved with those living with disabilities.
Need: Care-partners hands-on training. Certification of Agency and Government Home Help Aides is a legal requirement. Courses typically last approximately 6 weeks.
Training Requirement for care-partners? Zero. Notwithstanding age, physical ability and temperament, overnight, ill equipped, and often alone, for 24 hours a day, Care-partners must oversee their disabled partner's daily tasks.
Project Outline: make available weekend courses. Although helpful information and gadgets are available, because they are offered by many separate organizations, it's difficult for us care-partners to discover who has what. Too late…If only the information was available earlier… is a frequent complaint.
Suggested Syllabus: Safe handling. Mobility. Dressing. Lifting. Toileting. Personal care. Aides. Therapies: Diet. Medications. Testing. Social, emotional, and financial support. The dangers of Free-range caregiving. The list: overwhelming. Confusing.

P28.13

Assessment of the long term impact of a care-partners' course: Plan of action

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Background: In August 2017, Tikvah for Parkinson held an intensive three-day fifteen-hour course for family members of people with Parkinson (PWP), consisting of
A) 9 hours with a geriatric exercise specialist
B) 3 hours with a speech pathologist
C) 3 hours with a geriatric social worker
With the goal of
1) Training family members as personal trainers in a Parkinson specific exercise program, including exercises to strengthen facial and oral muscles with the aim of a) preventing food or liquid aspiration and b) improving voice quality
2) Providing information on community resources and teaching the caregivers self-care techniques
At the conclusion of the course, the twenty-two participants were asked to fill out an anonymous program evaluation questionnaire. There was a 62% response rate. All responded positively to the question, "Would you recommend this course to others," and, out of a 1 to 5 rating, with 1 being "strongly disagree," and 5 "strongly agree," all responded with either a 4 or a 5 to the statements "I learned new things," "The instructors were experts in what they taught," and "The material was conveyed in a clear and interesting manner." Six weeks following the course, Tikvah for Parkinson contacted all participants to ask if they were using the skills learned in the course. All responded positively, and several responded that they had implemented a daily exercise program.
Aim: To see the impact of the course after one year.
Method: We will contact all participants to find out if they are still using the skills learned in the course, and ask what we could have done to help them use those skills. Based on responses, we will decide if we should conduct a second course, and what changes, if any, should be made to that course and to the follow-up.

P28.14

Availability for home-based care program concerning Parkinson's disease patients and their families

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Background: A heavy burden is placed especially on family members who care for Parkinson disease (PD) patients. We have previously provided PD patients and their families a home-based care program based on a balance ball activity. The aim of the present study was to evaluate the effectiveness of the home-based care program for PD elderly patients and their family caregivers using a self-management skills scale.
Method: 1) Study design: A single-group, pre- and post-test study design; 2) Subjects: Fourteen family caregivers who participated in a training workshop hosted by a patient advocacy group and had given consent to participate in the study; 3) Method of data collection: The home-based care program was explained by a nurse at a training workshop in 2014. The program consisted of four weeks of the following home exercises: core rotation exercises (5 minutes) right after waking up and marching in place (3 minutes) at a time of day when the body is mobile. The patients and family members were asked to keep a symptom journal. A questionnaire survey was conducted at the event venue before and after the implementation of the program. During the program period, the

investigators conducted a telephone interview once a week, and after the program finished separate group interviews for PD patients and family members were conducted.
Results: After excluding those who dropped out, nine participated in the present study. The mean age of the spouses was 65.4 years and the mean age of the children was 41.0 years. The mean age of the nine PD patients was 66.24 years, and the majority of PD patients had mobility impairment issues related to daily living. The mean State Mindfulness Scale (SMS) score was 27.4 before the program and 30.7 after the program. After confirming the variance, the results revealed that the SMS score after the intervention was significantly higher. Due to thought manipulation, the SMS score of questions related to emotional self-encouragement skills after the intervention was significantly higher.
Discussion: These results demonstrated promising effects of our home-based care program in maintaining the health of family caregivers facing emotional challenges.

P28.15

What I learnt from taking care of my mother who has Parkinson's disease
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Objectives: My mother was diagnosed with Parkinson's disease 6 years ago and as a result, the family is looking for ways and means to slow down the progression of the disease and let her live a dignified and fulfilling life. The family faced many challenges and did what we felt was the best for her.
Methods: In response to Prof. Lim's call to help Mr Samuel Ng who is suffering from Parkinson's disease to set up a Parkinson's support group in Ipoh, Perak, Malaysia, I became a committee member of Perak Parkinson's Association to help run the activities. Hence my mother spends 4 days a week at the Perak Parkinson's Association (PPA) Centre in Ipoh. The daily exercises which she did together with support people there helped her to remain active and quite mobile still she had a fall and broke her hip which significantly reduced her mobility. However she still attended the exercise sessions in the centre and also the awareness programs. A maid was also employed to take care especially of her toiletrie needs. She also does whatever exercises she can do and even consume foods which are known to be good for Parkinson's and also helps in her constipation problems. By taking care of her daily needs, I learnt a lot more about patience, tolerance, emphaty and also abou Parkinson's disease and it's management.

COMPREHENSIVE CARE: Fitness, wellness, nutrition

P29.01

A wearable ankle exoskeleton improves walking economy and balance in an individual with Parkinson's disease: A feasibility case study
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Introduction: Persons with Parkinson's (PWP) have significantly reduced ankle joint function and increased energy requirements of walking which likely plays a role in the general fatigue that is characteristic in this patient population. Robot assisted gait training (RAGts) seem to be well-tolerated by individuals with PD, however, access to commercial RAGT devices are extremely limited due to size and cost. Recent advances in electromechanical actuation offers the potential for implementing similar task-specific training via light-weight robotic devices that can be used daily by patients at home.
Purpose: The purpose of this novel case study was to determine the feasibility of using battery-powered wearable ankle assistance to improve (1) walking economy and (2) standing balance in an individual with Parkinson's.
Case description: The patient was an 85-year old female with a 5 year history of Parkinson's (Hoehn & Yahr stage 2.5). She completed metabolic analysis during baseline walking and walking with subject-specific plantar-flexor assistance following 3 powered gait training sessions (Fig, 1). On a separate visit, the participant completed a treadmill-based balance test with and without ankle assistance controlled to maximize whole-body stability.
Results: Following this brief intervention, the participant exhibited a 26% reduction in metabolic cost during walking with untethered ankle plantar-flexor assistance compared to baseline. She also experienced a 1.4 cm reduction in peak anterior-posterior center of pressure displacement during the treadmill balance perturbation with assistance as compared to without. This equated to a 10% improvement in maintaining her base of support.
Conclusion: These preliminary findings suggest that appropriately timed powered ankle assistance that can be worn outside of the clinic has the potential to improve walking economy and balance in PWP.

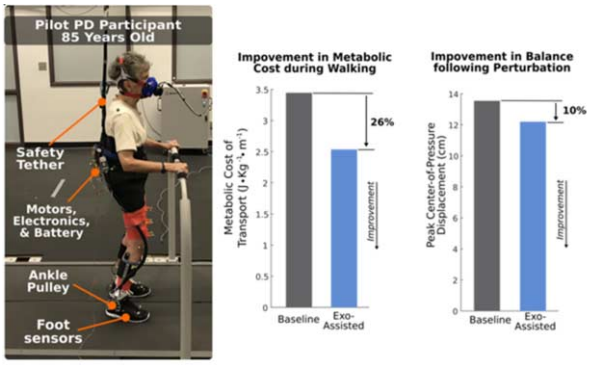

Fig. 1. *(Left) Picture of our experimental setup with the patient. (Right) Improvement in walking economy and balance as our subject used the ankle exoskeleton compared to without.*

P29.02

The success of disease specific exercise approach in persons with Parkinson's disease: An observational study
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Purpose/Hypothesis: Exercise has been shown to have a neuroprotective effect against developing Parkinson and attenuate symptoms in persons with Parkinson's (PWP). Despite affirming the benefits of exercise, there is little consensus on the most efficacious strategies to maximize functional ability and minimize secondary complications through movement rehabilitation in PWP. Therefore, this study aimed to determine which tasks in an exercise are most beneficial for improving mobility and decreasing fall risk in PWP.
Materials/Methods: Forty-two PWP (20F/22M), independent community dwellers with a mean age of 73.7 (±8.4) years from four different sites in Arizona were surveyed regarding their demographics, medication usage, and specific type and amount of exercise completed on a weekly basis. The PWP ranged from 1 to 31 years since the first diagnosis (mean: 7.6 ±6.1) and were all

within stages 1–3 on the Hoehn & Yahr scale. The data was collected on the mobility, and self-confidence and outcomes measures included the Timed Up and GO (TUG), TUG cognitive (TUG-C), and 3 meter backwards walk (3MBWT). One-way ANOVA was conducted to analyze the effect of exercise intensity, exercise duration, movement amplitude, multidirectional tasks, position, rotation, and guidance on PWP divided into two groups: (1) PWP who reported participating in disease-specific exercise approach, and (2) PWP who reported participating in limited number of tasks during exercise.
Results: Outliers were identified using the boxplot and after removing the outliers, all variables were normally distributed. Exercises that included multidirectional tasks, done for at least 30–60 minutes, and performed in different positions showed significant difference between the two groups (p.05). In addition, those participated in a disease-specific exercise approach reported more satisfaction when compared to PWP who reported participating in limited number of tasks during exercise. Conclusions: PWP should perform exercises for at least 30–60 minutes in multiple different positions and should include multidirectional tasks to increase mobility and decrease fall risk. Larger randomized controlled study with longer duration, high supervision, and facility-based interventions is needed. Clinical Relevance: Physical therapists should incorporate multiple tasks and demand exercises done for 30–60 minutes in different positions to see the positive effects on mobility and decreased fall risk in PWP.

P29.03

Impact of Rock Steady Boxing in patients with Parkinson's disease

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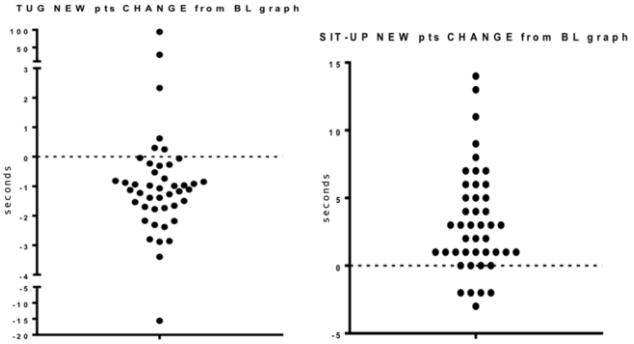
Several studies suggest that physical exercise is beneficial in individuals with Parkinson's disease (PD). Rock Steady Boxing (RSB) is a non-contact boxing exercise program specifically designed for persons with PD that targets endurance, coordination, and balance. Only one published study to date has reported the impact of RSB on six PD patients. The current study aimed to assess the impact of RSB on several clinically relevant outcome measures in a larger PD population participating in RSB sessions in the greater Boston area of Massachusetts. Data were collected on 47 adults with PD enrolled in weekly 1.5-hour RSB classes for 16 weeks. The classes included aerobic exercises and resistance training, ultimately promoting whole-body fitness. Participants were administered a timed up-and-go (TUG) test and a 30-second sit-and-stand (SaS) test before and after program completion. At the end of the 16-week course, a quality of life scale was administered, as well as a post-class satisfaction survey. Some participants (n=23) enrolled in a second 16-week RSB course, and those data are labeled as "returning" participants. Significant improvement was observed from baseline to program completion in the mean number of sit-and stand repetitions for both participants new to RSB ($p<0.0001$) and returning participants ($p=0.0004$). A significant improvement from baseline also was observed in the TUG test for both new ($p<0.0001$) and returning ($p<0.0001$) participants. On the post-class survey, participants new to RSB, but not returning participants, reported a slight increase in pain ($p=0.0437$). After their first RSB program, 76% of participants reported improvement in mood, 76% in body stiffness, 57% in fatigue, and 56% in gait or balance. Most participants (69%) reported no change in tremors. All or nearly all participants agreed or strongly agreed with the following satisfaction survey statements: enjoyed the program (100%), would recommend the class to others (97%), and would take the class again (97%). Participation in RSB can be an enjoyable and beneficial experience for patients with PD. However, due to the open-label nature of this study, motivational factors may have influenced the results. Additional research is needed to elucidate the mechanisms underlying the impact of RSB in PD.



P29.04

Kick Out PD: Mobility, quality of life, and feasibility outcomes in a pilot study of a PD-specific karate intervention

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Objective: To evaluate feasibility of a community-based karate class tailored for individuals with early- to middle-stage Parkinson's disease (PD); to assess effect of karate on objective and patient-reported outcomes.
Background: Different exercise modalities benefit PD patients. The karate program evaluated here incorporates vigorous resistance and aerobic activity with mindfulness in a community-based class of mild to moderate PD subjects.
Design/Methods: Open label, 10-week study of twice weekly, PD-specific, non-contact karate classes for patients with Hoehn & Yahr (HY) stage 1–3. Feasibility was assessed by overall dropout rate and adherence via attendance records. Participants completed pre- and post-intervention assessments of mobility (Timed up and Go), gait (Tinetti mobility test), quality of life (PDQ-8), and global impression of change (PGIC).
Results: We enrolled 19 participants; 15 completed all ten weeks of classes (79%), with mean adherence of 87% among completers. Reasons for withdrawal: scheduling conflicts, no given reason, pre-existing sciatica, and appendicitis. Among those completing the study, 53% were women, median age 68 (range 39–80), PD duration of 6 years (range 2–20), and 93% were HY 2. We found significant improvements in quality of life (PDQ-8: 25.3 vs. 19.3, $p=0.01$), and gait (Tinetti Mobility Test: 27.1 vs. 27.9 points, $p=0.01$), and a trend toward improvement in mobility (Timed Up and Go: 9.6 vs. 9.0 seconds, $p=0.1$). On the PGIC, 87% endorsed feeling moderately or considerably better. All met their self-defined pre-intervention goal, planned to continue karate, and would recommend it to a friend, respectively.
Conclusions: A twice-weekly karate class was met with high adherence and enthusiasm among people with early- to middle-stage PD. After ten weeks of participation, significant improvements were noted in gait, quality of life, and self-reported impression of change. Karate for PD is a promising intervention with potential to impact quality of life and mobility.

P29.05

Kick-out PD: Qualitative analysis of expectations and outcomes in a pilot study of a Parkinson's disease karate intervention

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Objective: To investigate expectations regarding exercise, karate, and mindfulness in individuals with early- to middle-stage Parkinson's (PD) prior to a community-based karate class, and post-intervention perceptions of change in mobility, wellbeing, and quality of life.
Background: Different exercise modalities benefit PD patients, including aerobic, resistance, and mindfulness-based activities. Karate incorporates these in a community-based class. The combination of exercise modalities and the class setting may lead to improved mobility and wellbeing.
Design/Methods: PD patients participating in a 10-week, open label feasibility study of karate were invited to participate in a focus group prior to and following the karate course. The classes were twice weekly for one hour. Patients were included in a one-hour, pre-intervention focus group led by the PI (JF) exploring prior experience with exercise and expectations for the intervention. Post-intervention focus groups explored patient perceptions of changes in their balance, mobility, and overall wellbeing, whether the intervention met expectations, and opportunities for program improvement. Qualitative data were analyzed using a grounded theory approach.
Results: Fifteen participants (8 women), 93% at Hoehn & Yahr stage 2, with median age 68 years (range: 39–80) and PD duration 6 years (2–20), completed the pre- and post-intervention focus groups. Each group comprised 6–9 individuals, the majority endorsing prior experience with and positive attitude towards exercise. Participants expressed goals of improving balance and mindfulness. Following the intervention, participants felt karate had been beneficial for movement, breathing, and wellbeing. Additional themes were camaraderie and encouragement from the instructors and each other. All participants planned to continue their karate practice and recommend it to others.
Conclusions: A twice weekly karate class tailored to individuals with PD yielded subjective improvements in balance, mobility, and general wellbeing, as well as unexpected camaraderie. There was enthusiasm for continued participation, highlighting the need for further long-term, controlled studies of this promising intervention.

P29.06

The effect of the dance DVD created for the rehabilitation of Parkinson's disease patients

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Introduction: In order to prevent the progression of symptoms of Parkinson's disease (PD) and declining function, continuous rehabilitation from the early stage is important. For that purpose, I think rehabilitation that can be done at home by yourself is very important. Therefore, we created a dance DVD that can be continued at home for rehabilitation of PD and verified its effect.
Method: 1) Created two dance DVDs with different difficulty levels for PD (Part 1 25min=Easy, Part 2 20 min=complexity). 2) 30 persons were randomly selected from the applicant. 3) Distributed the created DVD and continued dancing three or more times in a week for 3 months 4) Evaluation was conducted twice. Pre evaluation → Perform PD dance on DVD for 3 months at home → Post evaluation. 5) Analysis applied t-test.
Outcome measures: For motor function (Timed Up-and-Go Test : TUG, flexibility = forward bending of the sitting position), For cognitive function (Instruction manual of Japanese version of Montreal Cognitive Assessment : MoCA-J, Apathy Scale: AS). In addition, a questionnaire survey was conducted after the end of the intervention period.
Results: There were 19 subjects who were able to participate until the final evaluation. Age=65±6.7, Gender=male/female: 15/4, Hoehn and Yahr stage=2.7±0.6, Motor function (TUGT: time p=0.01, number of steps p=0.02, flexibility p=0.02) Cognitive function (MoCA-J p=0.007, AS p=0.007)
Results of a questionnaire (It became easier to get up from the chair, turning around in the toilet and became possible with no handrail. etc.)
Discussion: PD patient voluntarily carrying out dance DVD at home made a significant effect on motor function, cognitive function, mental symptoms. This result shows that even if a Parkinson's disease patient carries out at home, the effect appears, and the dance DVD is useful. From the questionnaire result, it has been found that it has a good effect on daily living behavior.

P29.07

Growing a Parkinson community-University collaboration through Rock Steady Boxing

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Introduction: Rock Steady Boxing was introduced to the Louisiana Tech University campus in September of 2016. The initial purpose of the Rock Steady Boxing program at Louisiana Tech was to provide a community exercise option for the Parkinson community. However, no one could have imagined the prospective growth of the program or the opportunities that Rock Steady Boxing brought to University students and faculty.
Description: This presentation will highlight the progress and achievements of students and faculty with regards to the experiential learning environment, service and the research benefits reaped from this collaboration with a Parkinson community. The alliance is illustrated through student work, projects, and research examples and reinforced in student, faculty and boxer reflections.
Results: University faculties seek out unique opportunities for student learning, scholarly work and research that are close to home and impactful. Campus-based programs such as Rock Steady Boxing can serve as a catalyst for University students that will seek answers and care for people living with Parkinson's long after

graduation. University campus resources are a deep well of opportunity that can further the goal of a healthy Parkinson community.

P29.08

On the reasons for participation of exercise continuation program – PD Cafe – for Parkinson's disease

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PD Cafe, Tokyo, Japan

The purpose: "PD Cafe" is an exercise class specialized in Parkinson's disease (PD) which started in Kodaira city in Tokyo from 2013. The patient and the medical staff act together to make a community where the patient can continue the exercise. I decided to understand why patients are continuously participating in exercise lessons, listen to objective opinions and provide a better place.
Method: We interviewed 20 people who participated in PD Cafe interviews about the reasons for participation through group work. We divided 20 people into 4 groups and talked with each other. Finally, we presented a presentation for each group.
Result: The opinions expressed in this group work were asked "I can work hard to keep exercising because I am with everyone" "I can hear about life" "Can share the same trouble".
Discussion: As a feature of PD Cafe, being able to share life troubles and prepare for it is considered as one of the factors to participate continuously. It was also suggested that exercising with the same sick people lowered participating hurdles. From now on, it is important to devise a program focusing more on life.

P29.09

Nutritional status in patients with Parkinson's disease in a tertiary teaching Hospital in Northeastern México

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Introduction: Parkinson's disease is a neurological disorder that affects more than 10 million people in the world; usually related to weight loss and malnutrition. Disease progression has been postulated to lead to risk of protein malnutrition.
Objective: To describe the nutritional status of patients with idiopathic Parkinson's disease in a tertiary teaching Hospital in Northeastern México.
Materials and methods: We recruited patients from the outpatient movement disorders clinic, ages 47 to 80, with diagnosis of idiopathic Parkinson disease. Nutritional status was evaluated with anthropometric measures: Body Mass Index (BMI), Tricipital Skin Fold (TSF), Muscular Arm Circumference (MAC) and Muscular Arm Area (MAA). Disease severity and progression was classified with Hoehn and Yahr stages (H&Y), in mild (H&Y 1), moderate (H&Y 2–3), and severe (H&Y 4–5) Descriptive and inferential statistics applied. Chi squared was used to contrast risk of malnutrition between stages. The risk of malnutrition and protein malnutrition was determine using the equations and tables elaborated by Frisancho (1981).
Results: We included 69 patients, 53.4% were male, with mean age 61±11 years; most frequent stage was moderate (73.9%), followed by mild (19.6%) and severe (6.5%). BMI was normal in 43.5% (n=30); 24.6% were underweight (n=17), and 31.8% (n=22) overweight.
Risk of malnutrition. We found a higher risk of protein malnutrition in patients with normal BMI, according to MAC (50%, vs 38.9% and 11.1%; p=0.013), and to MAA we found higher risk of severe malnutrition in underweight patients (50%, vs 40% and 10%; p<0.05).
Disease stages. When comparing nutritional variables between stages, we found that moderate stages had a higher risk of protein malnutrition than mild and severe, according to MAC (100% vs. 0% and 0%; p<0.05).
Conclusion: In patients with Parkinson's disease, normal below-normal weight, and moderate severity are factors associated with higher risk of malnutrition. Larger studies are needed to dilucidated the relationship between disease and nutritional status, so appropriate therapeutic measures are applied.
Keywords: Parkinson disease, nutritional status, Mexico.

Table 1 - Comparison of MAC risk classification according to BMI.

	Malnutrition Risk (n= 19)	Normal (n= 38)	P*
BMI, n (%).			<0.05
Underweight	7 (63.6)	4 (36.4)	
Normal Weight	9 (33.3)	18 (66.7)	
Overweight	2 (1.1)	16 (88.9)	

*Chi square test.

P29.10

Big for Life® exercise group for people with Parkinson's: The Australian experience

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Objective: To evaluate the experience of participants in a Big for Life® pilot program in Australia. To explore the potential influence Big for Life® had on motivation to exercise, mood, self-perceived fitness levels, mobility and occupational performance.
Background: Big for Life® is an exercise group for people facilitated by an Occupational Therapist and/or Physiotherapist. Eligible participants had already completed a four week intensive 1:1 program called LSVT Big®. LSVT Big® is a standardized treatment protocol, developed in the USA and used in many countries around the world, focusing on increased amplitude exercises to improve mobility, balance and ADL performance. Big for Life® sessions are intended to be fun, challenging and reinforcing large amplitude movements, as well as providing participants with opportunities for social interaction while they are engaging in exercise. This project was designed as an internal quality improvement activity.
Method: Four Big for Life® groups were conducted during 2018 in a private rehabilitation hospital in Victoria, Australia. A total of 24 people participated. Each group was one hour in duration and focussed on exercises and ADL tasks based from patients' goals. Carry over tasks were assigned for home practise. Pre and post assessments were conducted. The outcome measures used were Geriatric Depression Scale, Canadian Occupational Performance Measure, 6 Minute Walk Test & 10 Metre Walk Test and a subjective patient feedback form.
Results: Results will be finalized at the conclusion of the fourth group (Jan 2019). The trending results for the first three groups include that mood improved the most (approximately 25% improvement) followed by improvements in occupational

performance. Endurance, step length and step speed showed minor improvements. Most notably, the vast majority of participants reported the group experience as positive and increased their motivation to complete their LSVT Big® exercises at home.
Clinical Message: The Big for Life® exercise sessions appear to benefit people with Parkinson's and therefore will continue to be a treatment option at a private rehabilitation hospital in Victoria, Australia.

P29.11

Living with Parkinson's – My running story. Returning to running after diagnosis and a pathway to running faster than before diagnosis
*Ian McFarlane**
Eastern Masters, Melbourne, Victoria, Australia

Can you still run with Parkinson's?
My running had deteriorated markedly from running a long Sunday run of 17K down to 1K if I could run at all.
I was slowing down.
It was difficult to lift my feet efficiently.
My stride had shortened.
Other runners would run away from me up hills – and hill running had always been a strength.
I felt like I was running on one leg.
I had to physically lift my legs into and out of a car. We concluded that we would have to sell our car.
I had difficulty getting out of a chair.
Eventually leading to a diagnosis of Parkinson's disease at the age of 53.
I duly purchased my last pair of running shoes – it was a sad moment and for reflection after almost 40 years of running.
My Neurologist put me on Kinson Medication – and it helped!
My running group was not too sure what to make of me.
-Why did he not know how he was going to run until he started the run?
-Why would he drop out of training half way through a session?
-Why did he suddenly drop off the pace rapidly in training?
-Was it safe for him to run?
We finally concluded that running would not kill me. I had just ran out of Dopamine!
It took about 12 months to sort the medication out.
A chance encounter with a Physiotherapist who knew of a Person who took extra dose of meds for training and knew my Neurologist. An extra half dose was ordered and it worked a treat.
Discovered PD Warrior program and dramatic improvement resulted.
Slowly built up distance, running surface variety and speed. Progressed through running groups back to my running group level.
Park run times:
Before Parkinson's: 24 mins 12 secs
Park run with Parkinson's: 30 minutes +
After PD Warrior training: 24 mins 13 secs
Best now: 24 mins 1 sec
Future: Aim <23 mins.
Conclusion: Yes, you can still run with Parkinson's and quite successfully.

P29.12

Living with Parkinson's. Exercise and Parkinson's. A look at how through the power of exercise I can run up hills again
*Ian McFarlane**
Melbourne, Victoria, Australia

Does exercise help with Parkinson's?
I can no longer exercise without medication, but with exercise I can reduce the amount of medication required.
There are several schools of thought on this.
Parkinson's is a movement disorder!
In the past – how do you expect to move then?
Currently – much of the establishment agrees that exercise is useful but that it should be mild and within your limitations. Maintain your situation
Emerging (20 years in the making) programs that stretch your current level and are Parkinson's specific. The belief being that Parkinson's can be slowed down using the principles of Neuroplasticity and the ability for the brain to change its own structure and function.
I have targeted proactive Parkinson's treatments against feedback from the Health Industry – "Oh you have Parkinson's – there is nothing that we can do about that. We can treat the symptoms. It is progressive in nature. There is no cure."
There are groups around the world who have an interest in this space. Largely coordinated through Facebook Groups like 'Parkinson's Road Fitness Fun' or 'PD Warrior Global Tribe'. They motivate and feed each other encouraging positive engagement of exercise and improvement. People learn off other people's experiences with Parkinson's and how they addressed it and overcame it.
Which exercise is best?
There is no clear cut winner. The general rules of thumb are:
1. Any exercise is good exercise. Do exercise that you enjoy. Move it or lose it philosophy.
2. Strenuous exercise is better. Challenge yourself. Train hard. This will maintain your level of fitness and wellbeing.
3. PD specific exercise, amplitude and multi-tasking focused are better again.
4. Best of all is a combination of general exercise, strenuous exercise and PD specific exercise.

Exercises that I have tried include:
- Bike riding (static and road/trail)
- Balance
- Gym work
- Walking
- Running
- Ballroom dancing
- PD warrior

Rock steady boxing is receiving rave reviews in North America.
LSVT BIG is well regarded.
Parkinsong is well received.
Conclusion: I can run up hills again.

P29.13

Developing silver food which is easy to swallow in patients with Parkinson's disease
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Objectives: We want to develop elderly-friendly food which easy to swallow through the analysis of functional dysphagia in patients with Parkinson's disease (PD).
Methods: We compared 30 PD patients and 50 age-matched elderly healthy controls without swallowing disturbance. We evaluated functional dysphagia scale using Videofluoroscopic Dysphagia Scale (VDS), American Speech-Language-Hearing

Association National Outcome Measurement System (ASHA NOMS), and Modified Penetration Aspiration Scale (MPAS). Nutritional status of participants were checked albumin level, fat mass, muscle mass and body mass index (BMI) also checked through body composition test. The status of PD was checked with Hoen and Yahr (H&Y) stage, UPDRS motor scores (part III), disease duration (month), levodopa equivalent doses (LED). We evaluated the survey of satisfaction to determine tolerability and not inferiority of silver food than standard diet.
Results: The average H &Y stage is 2.83, UPDRS motor score is 24.18 and mean LED is 586.04. The muscle and fat mass showed no difference between two groups but albumin level was significantly lower in PD group. Tongue sensory, motor function of tongue and salivation was more decreased in PD group. Subscales of oral stage were significantly impaired such as bolus formation, mastication, premature bolus loss and oral transit time in PD group. The vallecular residue, pyriform sinus residue, penetration aspiration of pharyngeal stage was significantly impaired in PD group. The oral transit time and pharyngeal transit time was shorter, and pharyngeal delay time was significantly shorter in PD which tried elderly-friendly food than standard diet. The albumin levels correlated with total VDS score. A preference survey of our silver food, patients' satisfaction was high in texture, taste, odour of food. And aspiration risk of silver food which checked MPAS and VDS was lower than standard diet.
Conclusions: In this study, we observed that elderly-friendly food which easy to swallowing was tolerable to PD patients who did not show functional dysphagia.

P29.14

Body fat loss is associated with autonomic dysfunction in Parkinson's disease
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Objectives: Body weight loss is one of major non-motor complications in Parkinson's disease (PD), although the mechanism has not been elucidated. Ghrelin is a powerful orexigenic peptide, originally isolated from stomach. Ghrelin induces a positive energy balance and weight gain by simulating food intake and adiposity. The aim of the study is to investigate the association between body fat loss and ghrelin secretion in PD.
Methods: In 99 patients (52 females) with PD and 57 healthy controls (27 females), body mass index (BMI), body composition [(fat free mass (FFM), body fat percentage (BFP), body fat mass (BFM)], and serum leptin and plasma ghrelin were compared, stratified by sex. In addition, we compared ghrelin and body fat percentage divided by with or without orthostatic hypotension (OH) as one of the important symptoms of autonomic dysfunction in PD.
Results: BMI was significantly lower in PD subjects [BMI (males: PD 21.5±2.4, controls 23.4±2.6, p=0.002. females: PD 19.8±3.2, controls 22.1±4.0, p=0.006)]. In either males or females, BFM was significantly lower in PD than in control, although FFM was not different. Leptin was significantly lower in PD patients in both sexes, and ghrelin was significantly lower in male PD patients (males: PD 27.4±24.7 pg/ml, controls 41.9±31.2 pg/ml, p=0.019). Ghrelin and body fat percentage is significantly lower in patients with OH than without OH only in males [body fat percentage (males: with OH 16.7±5.1, without OH 21.7±5.8, p=0.003) ghrelin (males: with OH 18.1±17.1 pg/ml, without OH 34.2±28.0 pg/ml, p=0.026)].
Conclusions: Among body compositions, reduced body fat with maintained FFM was a distinctive feature in PD. Plasma ghrelin was significantly reduced in male PD patients, suggesting a dysfunction of homeostasis in lipid metabolism. Ghrelin secretion is regulated by autonomic nervous system. Some of the autonomic symptoms in PD is more dominant in males than females. Our results suggest that decreased ghrelin secretion in male PD patients is associated with autonomic dysfunction in PD.

P29.15

Impact of boxing-based training in Parkinson's disease: A new lifestyle for PD patients in Chile!
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Background: Parkinson's disease (PD) can affect movement, leading to the appearance of many motor symptoms. Balance related symptoms don't respond to medication as good as they respond to exercise. There aren't many options for rehabilitation in Concepción, Chile, and they are often not very motivating. To help solve this problem, we have developed a unique rehabilitation program for people with PD that uses fitness boxing as therapy. This approach is one-of-a-kind in our country.
Objectives: To develop a new therapeutic approach and to test its effects in a pilot study over local population.
Improving balance, mobility and Quality of Life (QoL) of PD patients of the city of Concepción
Increase the reach of NeuroboxingParkinson (NBP) as therapy.
Methods: February 2017: public workshop named "K.O Parkinson's"
April 2017: the pilot study. 15 PD patients (H&Y 1–3) enrolled into a 36 sessions of boxing physical therapy program, with a 3-times-a-week frequency. TM6, Timed Up & Go, DGI, functional reach, MiniBEST, Romberg test and unipodal stance (US) were tested before and after the training program. QoL was examined with the PDQ-39 questionnaire.
In 2018 our team was funded with USD$18,890 in order to enhance the NBP model and coaching of new NBP instructors.
Results: We found significate improves on the DGI, MiniBEST, Romberg test and US, revealing a lower fall risk, possibly due to a positive impact on balance. PDQ-39 showed a significant decrease in the average scores. Besides the improve in clinical outcomes, the participants had an enhanced sense of belonging.
NBP is now up and running in 3 different gyms, and counts with over 20 new instructors.
Conclusion: With NBP we've been able to not only impact over the motor symptoms of people with PD, but to help them to achieve important changes in their way to face the disease. Many of them have overcome severe depression, and every one of the NBP patients so far have developed new and strong bonds of friendship and partnership. NBP is unique in Chile and allows us to bring closer the physical therapy process to the patients and their family in an effective, safe, motivating and fun way.

P29.16

Motor performance and quality of life in a community exercise program for Parkinson's disease
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Objective: To present updated results of performance assessments of participants in physical activity programs at a dedicated community center for people with Parkinson's disease.
Background: Numerous studies in the past 15 years have demonstrated the value of physical activity for Parkinson's disease (PD) but data confirming the long-term value of such recommendations are lacking. InMotion, a nonprofit in the Cleveland

area, offers classes with certified instructors in a variety of physical activities free of charge.
Methods: Participants all carried a diagnosis of PD and were able to complete gait and balance assessments independently. Enrollment was otherwise unselected. Motor performance assessments were conducted at baseline and after 6 and 12 months. Assessments included a 2-minute walking test, 60-second sit-to-stand and lateral hurdle stepping tests, and 30-second bilateral single-leg, single-arm clean-and-press and rotational body turn tests. Participants also completed extended Timed-Up-and-Go (ETUG) test trials in alternate directions. We also assessed quality of life with a self-reporting instrument, the PDQ-39, at 6-month intervals. Mean figures of all data endpoints were derived. Statistical significance was determined using a paired t test.
Results: Enrollment in the program is ongoing. 163 subjects have had initial motor assessments; 63 have been reassessed at 6 months, and 36 again at 1 year. In this report, we present the results from the 36 participants who have completed all 3 assessments. All motor tests showed stability of improvement from baseline to 6 and 12 months. All but the single-leg stance showed stability or improvement from 6 to 12 months.
Conclusions: Motor performance in this cohort was stable or improved over a 12-month period, as measured by mobility and balance tests and the PDQ-39. 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. Our results support the practice of recommending physical activity as a therapeutic measure for persons with PD.

P29.17

Introduction of exercise class "PD Gym in KMC" for patients with Parkinson's disease
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Background: It's important for patients of Parkinson's disease (PD) to understand the necessity of exercise and acquire the habit of self-exercise to prevent the progression of disease. PD gym in KMC (exercise class for PD in Kanazawa medical center) is held mainly by neurologists and rehabilitation staff at this hospital.
Objects: The targets in the class are about 30 patients with Yahr scale 1–3 who live in Kanazawa.
Activity contents: A lecturer of PD treatment and exercise class by the hospital staff are performed 2 or 3 times a year. The round-table discussion in which patients and health care workers can freely exchange an opinion has been added as a new program since 2017. Participants put the PD exercise which can be done easily at home into effect with others through the guidance of rehabilitation staff in the class. There are 7 kinds of original exercises made up to now. That corresponds to the movement obstacle of PD and consists of the contents which can happily get exercise according to music.
Results: It was held a total of 15 times from 2013 July to 2018 July. The former exercise class participants are 590 in total. According to the questionnaire, we obtain useful opinions and comments such as "It's possible to forget sickness.", "I try to do stretching exercise even if somewhat unwell condition." There were many answers (half of the questionnaire) that the chance of self-exercise was increased.
Conclusion: We think that PD gym in KMC is closely related to the improvement of exercise motivation for PD patients from the results of the questionnaire. We have a lot of PD patients looking forward to this meeting as well as have a lot of voices for continuation of this meeting.

P29.18

A novel motor and cognitive program to retrain coordination and functional movement in Parkinson's disease: A study by Cleveland Clinic Lou Ruvo Center, Las Vegas and University of Nevada Las Vegas
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Objective: To test safety, feasibility, and effectiveness of the Recalibrate curriculum in people with Parkinson's disease.
Background: Recent research in Parkinson's disease shows a positive correlation between exercise and neuroplasticity and protection against brain degeneration. High intensity interval training can be beneficial for priming the brain to be more receptive to learning but without the integration of cognitive engagement or dual tasking, motor skills are not as easily acquired. This can pose a challenge when developing an effective exercise program that addresses the different subtypes of Parkinson's and that is translational. Recalibrate addresses this by breaking down the biomechanics of functional reach trajectories and connecting an internalized metronome to retrain coordination with cognitive overlay. The individual will learn to commandeer their body through tactile sensory feedback and sound by connecting the metronome to different parts of the kinetic chain where fluid and organized movement is impaired. Reaching is implemented at 3 different angles and 4 distances while accelerating and decelerating between 3 tempos. This occurs simultaneously with a moving base of support changing directions from front to back, linear, and rotational. This moving base extinguishes compromised foot positioning directly addressing the primary cause of falls.
Methods: 20 individuals with diagnosed idiopathic Parkinson's disease between the ages of 35–80 will be assigned to a delayed start adaptive randomization cross over design. They must have at least two of the following: UPDRS score of 20 or above, freezing of gait, and or more than one fall in the prior year. Each group will receive 36 hours of the Recalibrate curriculum. All participants will receive a baseline, mid, and post assessment. The assessments will test balance, self-efficacy, motor control, motor function, endurance and fatigue, strength, mood, functional reach, and quality of life.
Results: We hypothesize that the participants will notice improvements in their ability to make the proper postural adjustments in a changing environment, the ability to recognize where their weight is and how to shift and counteract momentum, better control over changes in amplitude and velocity during goal-based tasks, improved mindfulness, sharper cognitive skills, a heightened sense of awareness of environment, and improved quality of life.

COMPREHENSIVE CARE: Alternative & complementary therapies/ Creativity

P30.01

Dance for Parkinson's: Outcomes of a knowledge dissemination initiative

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In 2017–18, three events were held in Canada to disseminate the research related to the benefits of dance for people with Parkinson's disease (PD). The events were held at Toronto Western Hospital, Canada's National Ballet School, and the Canadian Neurological Sciences Federation Conference. They targeted people with PD, their families and carers, and healthcare professionals that work with people living with PD. The events included a series of posters and video display summarizing the research about dance for PD to date, an inclusive demo dance class so that participants could experientially understand the benefits, and a panel discussion. A mixed-methods study was conducted to explore the impact of these dissemination events on: 1) peoples' experiences at the events including people with PD, their carers, and other stakeholders; and 2) healthcare professionals' intentions to refer clients with PD to dance programs. Data collection methods including post-event surveys, interviews, and a comment board were used to understand the impact of the events. This presentation will report key outcomes from this project including the meaningful experiences it provided for people living with PD and the questions it raised about the role of healthcare professionals in connecting people with PD to dance.

P30.02

Dance for Parkinson's: Exploring a remote delivery model

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More than two decades of research has established that dance is a particularly beneficial and meaningful activity for people with Parkinson's disease. Yet, much of the world's Parkinson community does not have access to dance programming. In particular, those living with Parkinson's disease in rural areas and small towns may struggle to find a trained dance instructor in their communities that are able to offer such programs. For communities that do not have access to a trained dance instructor, Dance for Parkinson's Network Canada (DFPNC), a partnership between Parkinson Canada, Dance for PD®, Dancing with Parkinson's Canada, and Canada's National Ballet School (NBS), will explore a model in which NBS' Sharing Dance Parkinson's program is delivered to a remote community via video-streaming technology. The pilot will take place in Sault Ste. Marie, Canada, over eight weeks, in February and March of 2019. Post term questionnaires for participants and those supporting the program onsite will inquire about their experiences of this model. In particular, questions related to feasibility, safety, and enjoyment of the participants will be considered in this initial evaluation of the model. Insights from this pilot will speak to whether and how this remote delivery model could make dance more accessible to the Parkinson community in Canada and worldwide. Outcomes from this pilot will be provided in the presentation, and an i-pad demonstrating one of the video-streamed dance sessions will be attached to the poster during the presentation session.

P30.03

Dance and action representation: Experiences of a co-developed dance programme for Parkinson's

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Objectives: Evidence suggests that dance may help people with Parkinson's to overcome difficulties with movement as well as a range of non-motor symptoms. In addition to physical activity, dance involves internal representation of movement through action observation and motor imagery. These processes activate sensorimotor networks that facilitate movement, and are also thought to be involved in empathy and social interaction. Action observation, imitation and imagery may therefore contribute to both motor and non-motor benefits of dance. We explored the use of these processes within a dance class for people with Parkinson's.
Methods: A dance programme was co-developed by dance artists and researchers, with input from people with Parkinson's and a physiotherapist. The programme was trialled in a 6-week pilot study (approx. 1 hour per week). Classes drew on elements of Ballet and Bharatnatyam, using story-telling and themes to enhance imagery. At the end of the trial, participants were invited to a focus group to obtain qualitative feedback and to explore the involvement of observation and imagery in dance.
Results: Eight participants attended the focus group. Discussions were transcribed and analysed, using a combined hypothesis- and data-driven thematic approach. Reflections on the overall experience indicated that participants enjoyed being immersed in a creative activity and environment, rather than focusing on symptoms. Nonetheless, some were aware of achieving functional benefits, or wanted more information on how dance could help. Participants reported using observation and imitation to support movement in classes, and one individual had applied hand movements and imagery learned through dance to help with everyday tasks. The group setting provided a great source of support and motivation. Psychosocial benefits such as increased confidence and improved mood were also reported, and participants expressed a desire to continue with dance and other activities.
Conclusions: The dance programme was well-received and positive effects in physical and psychosocial domains were reported, consistent with previous qualitative studies. Moreover, the findings highlight the value of imagery, observation and imitation within dance, and potential benefits to everyday movement. For example, combining movements with imagery may encourage the development of strategies to apply outside of classes.

P30.04

Creativity and Parkinson's: Connections made pursuing creative endeavours

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Objective: This abstract explores the idea that People Living with Parkinson's (PLwP) benefit in many ways from being creative. It will investigate the idea that creativity and practicing new skills whilst in a group setting increases self-esteem, confidence and builds friendships. Much needed and often missed greatly once PLWP begin to limit their social activities for whatever reason.

Methods: Being creative is generally associated with artistic endeavours such as writing, drawing, painting, sewing, composing music, playing musical instruments etc.
Time spent on artistic and creative activities is wonderful for the soul, designing, planning, experimenting with new skills and journaling the process is an empowering and satisfying way to recall past activities. In Australia the Parkinson's Support Group, Young at Park, Brisbane subsidizes painting workshops as part of the ongoing pursuit of happiness and fun activities. During the class participants are totally absorbed in the process, allowing for relaxation and achievements to seep through the class environment. Working together on group projects is another way to make connections, spend time on conversations and problems whilst enjoying time developing new skills, confidence and friendships. This enables the PWP the chance to develop new skills in a comfortable and assessable environment. Stories are exchanged and histories are discussed, life and differences understood.
Results: As with all creative endeavours, it's not the end result, it's the process that's important, as is the satisfaction of crafting something that is unique. When the group made the patchwork, the quilting was outsourced, which enabled time spent on emerging skills.
The connections made through quiet time and social activities build supportive networks vital for mental health and confidence.
Other benefits: better hand eye coordination, gets you off the phone, organisation, goal setting, creates wonderful gifts. The understanding and acceptance that we can still do things, but just a little slower.

P30.05

Occurrence of spleen qi deficiency as defined by Chinese medicine in Parkinson's disease
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Objective: To find out the frequency of "Deficiency of Spleen Qi" (DSQ) in Parkinson's disease (PD) subjects as well as the correlation between DSQ and PD.
Background: In traditional Chinese medicine (TCM), patients can be classified as a main constitution according to their major signs and symptoms. DSQ is a significant and consistent syndrome occurring in people with PD.
Methods: This study comprised three parts: 1) Determining the frequency of DSQ in PD; 2) Comparing the frequency of DSQ in PD with non-PD subjects; and 3) Monitoring DSQ in PD subjects for 24 weeks. Outcome measurements were a modified DSQ scale and the Chinese version of the Parkinson's disease Questionnaire 39 (C-PDQ39).
Results: 187 PD subjects (mean ages 69.93±9.60 years) completed the assessment in Part 1. Of these, 170 (90.91%) were diagnosed as having DSQ. Thirty non-PD subjects (mean ages 66.63±10.24 years) completed the assessment in Part 2. Of these 11 (36.67%) were diagnosed as having DSQ. Positive correlations between DSQ total score and Hoehn-and-Yahr (H&Y) stage (correlation 0.316; $p<0.001$), as well as between DSQ and C-PDQ39 total score (correlation 0.572; $p<0.001$), were observed. For Part 3, 47 subjects from Part 1 were observed for 24 weeks. Variation of the DSQ was noted but all the subjects developed DSQ at the end of study.
Conclusions: DSQ is 2.5 times higher in PD subjects than in the normal population. More PD subjects had DSQ at the advanced H&Y stages. Further, larger study on the prevalence rate of DSQ in PD subjects is warranted.

P30.06

Art therapy may improve signs and symptoms of Parkinson's disease: Preliminary findings from the "ExplorArtPD Study"
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Background: Symptoms related to impaired visuospatial function are relatively common in patients with Parkinson's disease (PD). Restricted visual processing can directly hamper patients' motor function. For example, systematic biases in visual perception may influence navigational veering, thus directly affecting locomotion. In patients with PD, an impaired visual function is linked to negative feelings including depression, fearfulness and reduced self-efficacy. Art Therapy (AT) has the potential of recruiting different neural networks, including those concerned with high visual conscious perception. As such, AT may serve as a neurobehavioral intervention to improve multiple functional domains, including visuospatial functions and emotional wellness.
Methods: This is a dual-phase exploratory study. 1: cross-sectional, controlled, biomarker study on 30 non-demented PD patients (H&Y 2–3) and 30 age-matched controls; 2: prospective, open label study involving 20 sessions of AT (2sessions/week). Motor and gait functions were assessed by MDS-UPDRS, Timed Up and Go test (TUG), and wearable accelerometers. Cognitive and Visuospatial functions were assessed by neuropsychological inventories (MoCA, Rey-Osterrieth FigureTest, Benton Visual Test), computerized testing (Navon VisualTest, Visual Research Test, and visual reaction time), and binocular eyetracking (Eyelink 2). Psychological wellness was assessed by Beck Depression Index (BDI), Modified Fatigue Impact Scale, and PROMIS-Self-Efficacy scales. Brain imaging included T1-weighted 3D high resolution, DWI, and RS-fMRI sequences. Preliminary analyses were conducted on clinical data from 18 PD-patients and 14 controls completing the study. Eye tracking from 4 subjects was analyzed for exploratory purposes.
Results: PD-patients and controls were significantly different with respect to BDI score, Navon Visual Test, Rey Figure Test, UPDRS-III, and TUG-3 (maximum gait speed). Following AT, PD patients showed significant improvements in UPDRS-III, UPDRS-total, PROMIS (symptoms management), and Navon Visual Test (number of errors). A strong trend towards improved ReyeFigureTest was observed. On eye tracking analysis, significant increases in exploratory eye movements and fixation patterns were observed spatiotopically during examined stimulus regions.
Discussion: According to our preliminary findings, AT may improve visual-constructional abilities, visual recognition, and motor function. These improvements are accompanied by increased self-efficacy and changes in oculomotor behavior characterized by a more efficient visual exploration strategy. The duration of these potential benefits as well as their underlying mechanisms remain to be determined.

P30.07

Counselling program: Providing emotional support to those affected by Parkinson's across British Columbia

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Motivation: Statistics published from the Ministry of Health in 2014/2015, show there are over 13,300 British Columbians living with Parkinson's disease, a number that is expected to double by 2040 (Dorsey & Bloem, 2018). With the increasing number of patients diagnosed with Parkinson's, greater pressure is placed on the limited number of movement disorder specialists in British Columbia. The lack of available healthcare resources results in longer waitlists, leaving more patients without adequate care or access to educational resources.
Problem Statement: The motor and non-motor symptoms of Parkinson's can have a major impact on an individual's mental outlook and health, as well as the mental health of those around them. They and/or their family members may struggle to adjust to the social, emotional and personal changes brought on by the disease. The biochemical brain changes with Parkinson's can lead to depression and anxiety. The delayed treatment of depression and anxiety in Parkinson's can result in significantly reduced quality of life for the people diagnosed with Parkinson's and their carepartners.
Methodology: The availability of counselling to cope with this life altering news and physical changes, and to find support for how to live well with Parkinson's is essential for all individuals affected by the disease. Parkinson Society British Columbia (PSBC) offers free, short-term, confidential counselling services for people with Parkinson's and their carepartners. Counselling is available in person or via phone for those in remote communities or with mobility concerns. Counselling provides a safe, non-judgmental and structured environment to discuss challenges, process emotions and learn coping strategies.
Results: Since launching counselling services in April 2015, PSBC has provided over five hundred hours of free counselling to approximately 144 clients including couples and families. The feedback PSBC has received about this service has been overwhelmingly positive, including an increased interest in the service as we currently have a two months waitlist of individuals seeking counselling.
Conclusion/Implication: PSBC hopes to increase the number of counselling days in the near future to offer more support to this population.

P30.08

A black box model for Parkinson's disease (PD): Ayurvedic complementary methods and data science

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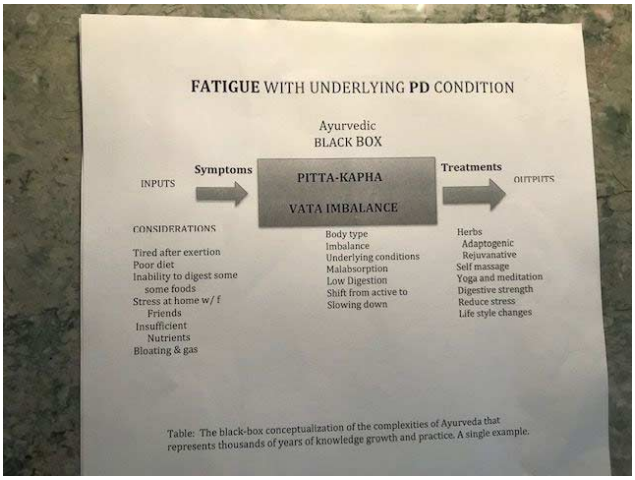
A black box is useful when a relationship between inputs and outputs is too complex to be understood in a short time frame. This is typical in software testing when the input-output relationships are complicated. Ayurveda, the traditional medicine of East India, is a complex system and can be modeled with a black box. Ayurveda is based on three universal constitutions: Vata, Pitta and Kapha. One cannot easily decode the many subtle aspects of Ayurveda without years of training. It is knowledge that has been practiced for thousands of years. The black box streamlines Ayurvedic complexities. It helps the healthcare professional concentrate on what works as a complement (augmentation) to the allopathic prescriptions of pharmaceuticals and surgeries. Ancient complementary treatments are still in use. There have been some clinical studies conducted and more are planned. The black box becomes a gray box if we look inside. The black box can be developed as a set of algorithms and verified as correct by a movement disorder specialist or PD database. Data science techniques, like neural networks, can be trained until they reach asymptotic performance. The black box then acts as a steady state classifier. The inputs are the PD symptoms and the outputs are the complementary treatment protocols. The set of complementary treatments that are the black box outputs include: herbs, yoga, pranayama, meditation, massage, diet and more. These are remedies that have been used for more than 2000 years. Ayurveda, in ancient times, targeted a set of PD-like symptoms that were known as kampavata. The herb that was used to remedy this condition then yields a precursor for Ldopa and is still used today. To utilize the model, a person with PD will fill-out a questionnaire, the results of which are entered as inputs into the black box. The outputs are customized plans of complementary treatments for the PD patient. In the attached table a single symptom (fatigue) with PD as an underlying condition is used as an example.



P30.09

Development of a music therapy protocol to enhance breathing, swallowing, and vocal/speech functions for individuals with Parkinson's disease: A pilot study

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Objective: This study is a pilot trial to develop and evaluate a music therapy protocol including vocal/singing training and physical exercises with music to improve breathing, swallowing, and vocal/speech functions of individuals with Parkinson's disease.
Method: Two female patients with Parkinson's disease at the age of 69 (Participant A) and 72 (Participant B) participated in a pretest, a 40-minute music therapy session, and a posttest. In the pretest, a series of questionnaires were administered to screen frailty, dysphagia, and custom to sing in daily life. The data for vital capacity (FVC), water swallowing test (WST), and maximum phonation time (MPT) were collected to assess breathing, swallowing, and vocal/speech functions. In the posttest, the measures except for the questionnaires were administered. The music therapy protocol consisted of physical exercises using

keyboard accompaniment to stimulate/facilitate motor movements of respiratory and laryngeal muscles, breathing exercises with wind instrument as auditory feedback for active breathing, and vocal/singing exercises to facilitate vertical movement of the larynx, oral/motor control, and phonation.
Results: In the initial assessment questionnaire, no frailty was detected from the both participants, while a small sign of dysphasia was reported by Participant B. FVC% was slightly changed in Participant A from 79% to 80%, while improved from 96% to 103% in Participant B. Swallowing speed of both participants enhanced from 3.03 ml/sec. to 4.00 ml/sec. in Participant A, and from 7.69 ml/sec. to 10.00 ml/sec. in Participant B. MPT also increased from 8.18 sec. to 9.42 sec. in Participant A, and from 12.30 sec. to 26.10 sec. in Participant B.
Conclusion: It is speculated that the music therapy protocol has the potential to improve breathing, swallowing, and vocal/singing functions of people with Parkinson's disease. Further inquiry with a larger sample size should be conducted considering the stage of Parkinson's disease, age, level of functioning, and normal/abnormal cut-off point in each measurement.

P30.10

Group singing improves quality of life in people with Parkinson's: An international Sing to Beat Parkinson's project
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People with Parkinson's may experience stigma, increased isolation, stress and anxiety due to the chronic nature of Parkinson's. Complementary therapies, such as singing, have been reported to have positive impact on quality of life in people with Parkinson's. Sing to Beat Parkinson's® is a community group singing programme especially developed for people with Parkinson's, practised for the last 10 years in the UK, to enhance their quality of life and psychological status. Recently, an international study was conducted in the UK, Australia and South Korea, to evaluate the effects of Sing to Beat Parkinson's® on quality of life and psychological status. People with Parkinson's (N=95; mean age=70.26; male 45%; 52% were diagnosed = 5 years ago) participated in a standardised 6-month weekly group singing programme, which included breathing exercises, vocal warm-ups and preferred song singing. PDQ39 and modified DASS21 were administered at baseline and follow-up. MANOVA, ANOVAs and t-tests were performed with SPSS v24 and significance was set $p<.05$ (2-tailed). In quality of life measures, some improvements were observed in a number of dimensions (Stigma, Social support, Cognitive Impairment, Communication and Single Index) of PDQ39. MANOVA revealed a multivariate effect of time ($p=.02$) and a time x country interaction ($p=.003$). There were univariate effects of time on Stigma ($p=.027$) and Social Support ($p=.002$). Additionally, there was a time x country effect for Activities of Daily Living ($p<.001$) and Social Support ($p=.004$); the improvements were larger in South Korean participants than UK or Australian participants. For DASS21, there was a multivariate effect of time: anxiety was significantly reduced after singing programme ($p=.004$); depression and stress also decreased albeit not significantly ($p<.08$). This first international, transcontinental singing study with people with Parkinson's affirmed that Sing to Beat Parkinson's® is a beneficial programme for people with Parkinson's. After a 6-month weekly group singing, singers experienced better social support, reduced stigma and anxiety. Although this study is limited by its design and the small sample size, the findings are encouraging and warrants further research. Group singing can play a significant role in improving everyday life of people with Parkinson's. (We also would like to include a singing workshop.)

P30.11

Effects of dance on cognitive functions, psychological symptoms and health-related quality of life in Parkinson's disease
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Background: Parkinson's disease (PD) is a neurodegenerative disorder of the central nervous system which manifests as a broad spectrum of motor and non-motor symptoms. While there is accumulating evidence supporting dance for improving motor features in PD, it is not yet clear if the benefits extend to non-motor features.
Objectives: To determine the impact of dance classes based on Dance for Parkinson's disease® (DfPD®) model, on cognition, psychological symptoms and Quality of Life (QoL) in people with PD.
Methods: A quasi-experimental parallel group, pre- and post-test design was used. The participants were allocated to a Dance Group (DG; n=17) or Control Group (CG: n=16). Participants had early-stage PD (Hoehn & Yahr: DG=1.6±0.7, CG=1.5±0.8) with no cognitive impairment (Addenbrooke's score: DG=93.2±3.6, CG=92.6±4.3). The DG undertook a one-hour class, twice weekly-12 weeks, while the CG had treatment as usual. Both groups were assessed for disease severity: MDS-Unified Parkinson Disease Rating Scale (MDS-UPDRS); cognition: National Institute of Health Tool Box (NIH-TB): cognition battery, Trail Making Test (TMT) A and B; psychological symptoms: Hospital Anxiety and Depression Scale (HADS), UPDRS–part-I; and QoL: Parkinson's disease Questionnaire- 39(PDQ-39) and UPDRS-part-II.
Results: A group comparison of the pre-post change scores for a majority of the measures showed that cognition (executive function and episodic memory), psychological, and non-motor PD symptoms, as well as QoL, were significantly improved by the intervention (DG>CG, p's<0.05, Cohen's d>.8, large effects). There were some trends towards improvement in selected cognitive measures, however, these were non-significant.
Conclusion: We conclude that the dance classes based on the DfPD® model had a clear benefit on psychological symptoms, QoL and limited benefits on cognitive function.

P30.12

Egaoshi® (“Smiling”) yoga: Invented by Kyoko Kimura, the first Egaoshi® in Japan, an all-in-one exercise introducing a combination of smiling, food, breathing, music, movement and beauty that tremendously improves the symptoms of Parkinson’s disease

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My name is Kyoko Kimura, the founder of the very first Egaoshi ® (“Smiling”) Yoga in Japan. My aunt died of Parkinson’s disease after enduring extensive suffering. I was diagnosed with Vitiligo Vulgaris, which causes my skin to lose its original skin color. My doctor told me that it would never be cured. On top of that, my son contracted kidney disease at the age of four, Thus, my quest to find a method to strengthen the immune system began. I researched the importance of food and grew organic rice and vegetables. I also traveled to India and was trained as a Laughter Yoga teacher under Dr. Kataria.

As my quest for health continued, I broke both of my hips in an accident and was in a wheelchair for many months. However, I saw this difficulty as an opportunity and received the inspiration to invent “Egaoshi® (“Smiling”) Yoga: an All-In-One-Exercise.” It has a combination of 6 elements, “Smiling, Food, Breathing, Music, Movement and Beauty,” which brings about a synergistic effect that strengthens the body’s immune system. I named it Egaoshi ® (“Smiling”) Yoga, with the exercises I named as “Ha! Dance®” and Pa-pi-pu-pe-po Dance ®. These exercises are combined with breathing that focuses on exhaling, which eliminates bodily waste.

This combined synergistic effect, brought about by these 6 elements, strengthens the power of natural healing, the immune system, and the dopamine levels. The results from these exercises have been remarkable! The typical symptoms of Parkinson’s disease improve tremendously, posture straightens beautifully and all the shaking stops. This is an amazing result like a miracle! My natural skin color was restored after losing it from Vitiligo Vulgaris.

Through these experiences, I was able to discover that the human body is not separated into unrelated parts but that it is, in fact, one life form! These discoveries made me see the potential in activating the body’s cells to restore youth and beauty. What I am aiming at now is the founding of, “Total Medicine,” which unites both western and oriental medicine, bringing to light the benefits of both.

P30.13

Dance workshop for Parkinson’s disease patients

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Dance is recently focused on as a treatment against incurable neurological diseases as Parkinson’s disease because it is enjoyable in nature and may offer multi-dimensional benefits. Previous clinical trials have shown that dance improves motor symptoms, particularly problems with balance and mobility, as well as overall physical fitness. In addition, dance also may improve cognitive function and mood by having shared the dance experience with others and by that they feel to be more accepted and be understand, which could improve emotional well-being and quality of life.

Recently, the opportunity of Dances for Parkinson’s disease are also increasing in Japan while the frequency is quite low compared to Western countries since it is not acknowledged well among physician as well as patients. Now, we can do it only by clinical research and/or some private workshops without using social security systems at any hospitals.

To inform the efficacy of dances to patients of Parkinson’s disease and their families, we performed a workshop of Dance for Parkinson’s disease at Minoh city hospital in April 2018. About fifteen patients of Parkinson’s disease with their families participated to the workshop. All of them were from outpatient clinic and their severities were from 1 to 3 of Hohn-Yahr stage classification. Two neurologists and four therapists of our hospital were also participated to it. Exercises and dance with some tools as balloons were performed together by taking some intervals between them. We also use easy music to make relaxed mood during the performance. Participants could tackle to the program freely depend on their body conditions. Efficacy was mainly evaluated by using a questionnaire at the end of the workshop and at each admission of outpatient clinic.

The patients felt amelioration of their symptom and feelings after the workshop, which lasted during about 1 month.

Our results suggest the efficacy of dance to Parkinson’s disease physically as well as psychogenic aspects as mood. More objective evaluations of symptoms are required to evaluate the efficacy. Information of Dance to the patients and physicians is also required.

P30.14

Group music therapy enhances positive affect in people with Parkinson’s disease

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Background: In recent years, studies show that music therapy may be beneficial for people with Parkinson’s disease (PD). In particular, there is increasing evidence of the individualized use of music on motor symptoms in neurorehabilitation. However, there has still

been less research attention to the impact of music therapy on psycho-social aspect of people with PD.
Objective: The purpose of this study is to investigate how Group Music Therapy (GMT) influences psychosocial aspect of people with PD and explore the meaning in participating group music therapy.
Methods: Participants were 65 both in-patient and out-patient at a local medical center. Monthly GMT was opened to the patients as well as their families. Music therapy interventions include musically-enhanced exercise, group singing, and improvisational ensemble for one hour facilitated by two music therapists. Nurses and rehabilitation staff were present for whatever they were needed. Before and after GMT, psychological states were measured using Two-dimensional Mood Scale (TDMS). Also, on the voluntary base, open questionnaire was performed in order to capture participants' experiences in a free format. All the texts were used as descriptive data for text-mining (KHCoder) and statistically as well as qualitatively analyzed.
Results: TDMS score showed that, after music therapy, positive arousal significantly increased and negative arousal decreased. Also, there was a significant difference in all items; vigorous, stable, pleasant arousal ($p<0.01$). Furthermore, the results from text-mining revealed that the participants were attracted to GMT focusing on their healthy aspect and recognized the benefit not only on the physical level, but also on the cognitive and psycho-social level.
We conducted frequency analysis, collocation analysis, and cooccurrence network analysis in order to clarify the difference between two Japanese synonymous words meaning dictionaries.
Discussion: Findings from this study suggest that GMT could strongly improve the participants' immediate psychological state. And, GMT could influence not only physiological aspect, but also multi-dimensional aspects of people with PD. Further analysis on the description of people with PD may provide insight into the meaning of the GMT.
Both statistical data and descriptive data will be presented.

P30.15

A study on the effects of a group dance and creative movement program using Indian dance techniques on symptoms of Parkinson's disease

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Background and Objectives: The importance of Dance and movement is being recognized in the management of Parkinson's disease. Dance and movement based interventions using western dance forms such as Tango, Waltz/foxtrot, Ballroom, etc. are found to be useful for people with Parkinson's (PwPs). Dance and music being culturally rooted art forms; PwPs in India may not relate as well to Western dance forms, as they would to Indian dance forms. The present study focused on developing a culturally specific dance based program using creative movements and Indian dance forms for PwPs in India. The purpose of the study was to assess the effectiveness of this culture specific dance intervention program on the motor and non-motor symptoms of Parkinson's and on the overall quality of life of PwPs in India.
Methods: 34 people diagnosed with Parkinson's disease (Hoehn &Yahr stage- II to IV) and attending Parkinson's support groups in Mumbai participated in the study. Using convenience sampling, 17 people were assigned to a 'dance program' group and 17 people continued with a traditional exercise group therapy. The participants attended a once a week, 1-hour group therapy sessions over a period of 12 weeks. Participants were assessed for their physical functioning, cognitive abilities, non-motor symptoms: anxiety and depression, mood and quality of life; pre and post intervention period using standardized tests for each domain. Differences in Pre and Post intervention scores were compared using Statistical analysis tests.
Results and Conclusions: Data of 16 participants from the dance group and 11 from the traditional exercise group (who met the 50% attendance criteria) were analysed. Participants in the Dance intervention group improved significantly on positive affect as measured by PANAS ($p=0.02$) and lowered the feelings of anxiety and depression measured by HADS ($p=0.02$), as compared to participants in traditional exercise group. Subjective reports from PwPs in the dance study group correlated with the objective findings as they expressed their joy, satisfaction, improved confidence and better group cohesion post intervention. Dance programs using Indian dance forms can be used as a supportive therapy along with traditional exercises for PwPs.

Domain	Tests/subscales used (outcome measures)	Dance therapy group (mean score ± SD)	Traditional exercise group (mean score ± SD)	t score	P value
Motor functioning	MDS-UPDRS	6.96± 14.67	-3.45±13.20	1.924	0.06
Quality of life	PDQ-39	- 4.37±14.73	5±10.18	-1.95	0.061
Depression and anxiety (mood component)	HADS- total score	4.6±8.98	-1±4.87	2.04	**0.05***
	Depression score	1.67±4.11	-1.81±3.02	2.487	**0.02***
	Anxiety score	2.93±5.11	0.81±3.25	1.28	0.21
cognition	ACE-III (total score)	2.75±4.23	2.45±7.84	0.114	0.91
	Attention subtest score	0.5±0.81	0.27±1.55	0.44	0.66
	Memory subtest score	0.62±2.91	2.63±5.85	-1.05	0.31
	Fluency subtest score	0.62±1.74	0.27±1.95	0.48	0.63
	Language subtest score	1.68±3.40	-0.90±2.46	2.29	**0.03***
	Visuo-spatial subtest score	-0.68±1.53	0.18±1.07	-1.72	0.09
Affect	PANAS (positive affect)	5.14	0.11	2.34	**0.02***
	PANAS (negative affect)	-3.21	-3.88	0.32	0.75

P30.16

From body, mind, to the integration: A mixed-method, randomized controlled trial of mindfulness yoga on physio-psycho-spiritual well-being of people living with Parkinson's disease

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Background: Clinical practice guidelines support exercise as rehabilitation for Parkinson's disease (PD), but no randomized trials have tested whether yoga – a mindfulness-based exercise intervention – is superior to conventional physical exercises for stress and symptoms management for people living with PD.
Methods: An assessor-blind randomized controlled trial was conducted at four community rehabilitation centers in Hong Kong,

with embedded process evaluation. A total of 138 people with idiopathic Parkinson's disease (H&Y stage I–III) were randomized into eight weekly sessions of mindfulness yoga (n=71) or stretching and resistance training exercise (n=67) groups between December 2016 and May 2017.
Outcome measures: Primary outcomes included anxiety and depressive symptoms (Hospital Anxiety and Depression Scale). Secondary outcomes included severity of motor symptoms (Movement Disorder Society – Unified Parkinson's disease Rating Scale motor score), mobility (Time-up-and-go test), spiritual well-being in terms of perceived affliction and equanimity (Holistic Wellbeing Scale), and health-related quality of life (Parkinson's disease Questionnaire-8). Assessments were done at baseline, 8 weeks (T1) and 20 weeks (T2).
Results: Participants included 65 men (47.1%); mean (SD) age was 63.7 (8.7) years. The participation rate of 88.5% with an attendance rate of 80% demonstrated that the mindfulness yoga program was well received. Both groups appeared to reduce motor symptoms significantly. Generalized estimating equation analyses revealed that the mindfulness yoga group generally had significant better improvement on various outcomes than the stretching and resistance training exercise group; particularly, anxiety, depressive symptoms, perceived affliction, perceived equanimity and health-related quality of life (HRQOL). From participants' narratives, the mindfulness practice of yoga helps redefine their illness experience through body-mind integration. Instead of struggling to get away from vulnerable health experiences, they practice being present with every sensation and thought non-judgmentally with a loving-kindness mind.
Conclusion: Among people with mild-to-moderate PD, mindfulness yoga was concluded to be as effective as stretching and resistance training exercise in improving motor dysfunction and mobility, with additional benefits on anxiety, depressive symptoms, spiritual wellbeing and HRQOL. Results support the implementation of mindfulness-based exercise interventions in PD care worldwide, which is essential to help people cope and live better with fluctuating PD symptoms that cannot be addressed pharmaceutically.

P30.17

Theoretical concept of impact of Tai Chi on falls in clients with Parkinson's disease
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Parkinson's disease (PD) is considered to be one of degenerative disorders of the central nervous system. According to the Parkinson's disease Foundation there is an estimated 60.000 Americans that are newly diagnosed each year with PD. Patients that have been diagnosed with Parkinson's disease encounter many side effects including freezing gait and poor balance. Freezing gait and poor balance were found to be correlated to an increased fall risk in patients with PD. Researchers are examining complementary and integrative therapies to lessen the symptoms and improve quality of life. Some studies indicate that Tai Chi (TC) could be utilized to lessen the symptoms of freezing gait and poor balance, decreased patient fall rate and increased patient general well-being. The main concept that will be presented within this paper includes Theoretical Concept of Impact of Tai Chi on Falls in Clients with Parkinson's disease.

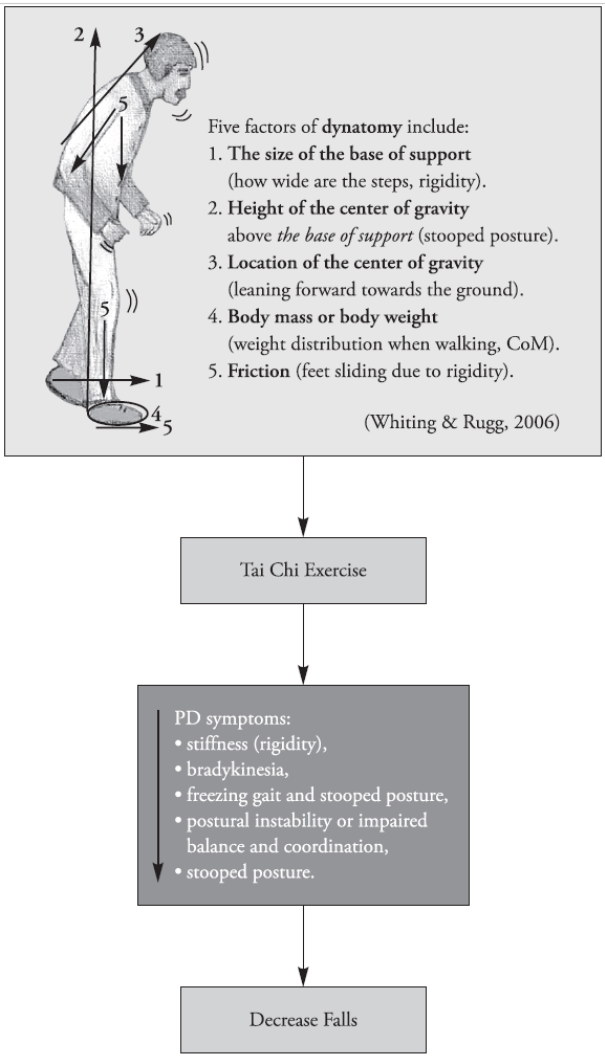

Figure. Cwiekala-Lewis Parkinson's Fall and Tai Chi Theoretical Framework

P30.18

Multidisciplinary care models for Parkinson's disease: The Parkinson's Foundation Centers of Excellence experience
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Objective: Parkinson's disease (PD) symptoms impact not only physical and motor function, but also mental health, relationships, and quality of life. Multidisciplinary approaches help treat motor and non-motor symptoms and improve clinical outcomes. However, less is known about how different care models influence referrals to

allied health professionals or affect clinical outcomes. Parkinson's Foundation Centers of Excellence (COEs) utilize three multidisciplinary team-based care models with allied health and center team providers working: 1) within the same institution ("all-in-one"), 2) within different but affiliated institutions ("affiliate"), and 3) for different and separate institutions ("independent"). We compared usage of allied health therapies across the three models and examined relationships between therapy usage and clinical outcomes.

Methods: With data from the Parkinson's Foundation Quality Improvement Initiative (QII), we examined frequencies of the three models and allied health professionals by COE models. We analyzed relationships between care models and allied health usage using chi-square test. Two level hierarchical linear models were used to investigate the effect of models on clinical outcomes including motor (Timed Up and Go, TUG), cognitive (composite z-score), PDQ-39, hospitalizations, and caregiver burden (Multidimensional Caregiver Strain Inventory, MCSI) among allied therapy users.

Results: The dataset included 10,058 patients from 22 COE for whom model and QII data were available. There were 18 "all-in-one" COE models, 18 "affiliate" models and only 2 "independent" models. Of the allied therapies, PT usage was most frequent (over 50%), but other allied therapies (e.g., OT, SLP, nutrition, social work, mental health) were utilized in 3–20%. There were significant differences in allied health usage across models ($p<0.0001$), with highest PT frequency in the "all-in-one" and "affiliate" models. There were significant differences in clinical outcomes for motor function, with lower TUG scores in "affiliate" model patients compared to "all-in-one" model and lower MCSI total scores among occupational therapy and psychiatrist users in the "all-in-one model" compared to the "independent" model.

Conclusions: Allied health service usage in COEs varies across different disciplines, with an emphasis on PT. Psychosocial and mental health therapies may be under-utilized. Among allied therapy users, there were significant differences in clinical outcomes across care models.

P30.19

The effects of non-invasive transcranial brain current stimulation (tDCS) on posture over stable and unstable surfaces in people with Parkinson's: A randomised double-blind sham-controlled crossover study

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Parkinson's disease (PD) is a degenerative disease of the central nervous system. Motor dysfunction is a primary feature of PD, with postural instability, one of the key features that leads to an increased likelihood of falls. When asked to perform concurrent motor and cognitive tasks, (e.g. standing while counting numbers), postural control can deteriorate further. Transcranial Direct Current Stimulation (tDCS) can be used to safely modulate cortical excitability without serious adverse effects.

The study aimed to investigate the effect of tDCS on dual-task performance over different standing conditions in people with Parkinson's disease.

tDCS was delivered with an intensity of 1 mA during 20 minutes using a constant current stimulator. The anode electrode was placed over the left dorsolateral prefrontal cortex (Left-DLPFC), and the cathodal electrode was placed over the right supraorbital area (R-SO). The sham condition consisted of 15 seconds of stimulation at the beginning and the end of the intervention period separately. 16 PD participants (age=65.38±9.722, ACE-R=91.88±4.177, MMSE=29.13±1.088, ABC=80.21±17.637), with a mean UPDRS of 37.69±18.311 and a mean Hoehn-Yahr score of 1.60±0.713 completed 4 single tDCS sessions in a randomised order. Under both real and sham stimulation conditions, participants stood either directly on the force plate or a foam placing on the force plate. Single task and dual task performance were assessed prior to, during, and immediately after possible stimulation. Path length, sway area, velocity, medial-lateral sway, and anterior-posterior sway were recorded during the performance.

Figure 1 presented the comparison between the real tDCS and sham tDCS under stable and unstable standings on all the outcome measures. There were significant main effects of stimulation (P=0.000) and task (P=0.000) on all measures under stable standings. However, under unstable standing, only significant main effect of task (P=0.000) was observed.

The results suggest a single session of tDCS targetting the left dorsolateral prefrontal cortex improved the ability to adapt posture to a motor-cognitive dual task under stable standing. There are no effects of tDCS on posture under unstable standing condition.

Figure 1 The main effects of stimulation and task on postural measures under stable and unstable standing conditions

		Stimulation			Task		
		Real tDCS	Sham tDCS	P	Single Task	Dual Task	P
Path length	Stable	297.965 (48.273)	324.075 (48.750)	0.000	268.870 (48.343)	353.170 (48.511)	0.000
	Unstable	525.090 (47.930)	526.784 (48.025)	0.721	471.992 (47.938)	579.882 (48.002)	0.000
Sway area	Stable	143.009 (50.177)	174.322 (50.811)	0.000	129.868 (50.275)	183.463 (50.586)	0.000
	Unstable	439.504 (48.386)	427.264 (48.503)	0.127	419.411 (48.420)	447.357 (48.435)	0.000
Velocity	Stable	9.932 (48.275)	10.806 (48.653)	0.000	8.966 (48.345)	11.772 (48.513)	0.000
	Unstable	17.501 (47.931)	17.559 (48.027)	0.712	15.731 (47.940)	19.329 (48.004)	0.000
Medial-lateral sway	Stable	11.240 (51.055)	12.602 (51.933)	0.000	10.203 (51.302)	13.639 (51.495)	0.000
	Unstable	22.636 (48.595)	22.746 (48.733)	0.703	21.798 (48.629)	23.584 (48.663)	0.000
Anterior-posterior sway	Stable	21.470 (49.522)	22.752 (50.016)	0.000	20.558 (49.596)	23.663 (49.848)	0.000
	Unstable	33.151 (49.376)	32.827 (49.570)	0.321	32.022 (49.459)	33.956 (49.436)	0.000

P30.20

Combating Parkinson's through the arts: The practice of origami

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Objective: Using Japan's traditional paper-folding art to maintain dexterity, motor recall, memory and equilibrium in persons with Parkinsons.

• Since about 600 AD when Buddhist monks brought the art of papermaking to Japan, Japanese artists have folded paper into sculptural, practical, and abstract shapes. Origami has become part of Japanese culture, and has aesthetic, social and even religious significance.

• The challenge of origami is to make the figure without cutting the paper, usually starting from a perfect square. This tight constraint forces the folder to use memory of the various techniques for crimping the paper to create form (legs, wings, arms, heads, etc.) from the paper available.

• The physical act of folding the paper practices finger and hand dexterity, and relies on motor recall that practices hand-eye coordination.

• Creation of new models, and re-creation of existing models, encourages new and abstract thinking, which may help form new brain connections and challenges recall of previously learned folding sequences. Just as when learning a new language or doing mental arithmetic, origami's three-dimensional thinking tests the plasticity of the brain.

• Origami holds the potential to practice fine motor dexterity, usefully challenges memory recall, and serves as a type of relaxation therapy akin to meditation for those who do it frequently.
• Teaching origami may be a useful tool in the fight to slow neuromuscular deterioration and fading of memory recall, and offers an economical therapy that can be utilized in the simplest of surroundings.
Training modules:
I. Valley/Mountain fold; the Geometry of Paper
II. Preliminary Base and the Waterbomb Base
III. Frog Base and Fish Base – the Squash Fold
IV. Bird Base
V. Inside Reverse Fold/Outside Reverse Fold
VI. Basic Crane and Models from the Bird Base
VII. Basic Frog and the Petal Fold
VIII. Advanced Folds: the Rabbit's Ear, and Sinking
IX. Advanced Bases: Stretched Bird Base, Blintzed Bird Base, Dog Base
X. Modular and Ornamental Origami
XI. Non-square Paper Origami
XII. The Zen of Origami

P30.21

Taiko drumming for individuals with Parkinson's disease: Performing artists partner with OT to promote community wellness

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Taiko, which means "large drum", is a musical instrument that originates from Japan. Taiko drumming combines music, dance, theater, and martial arts into an artistic and physical practice that is as fun as it is challenging. Players are encouraged to use whole-body movements and full arm extensions while striking the drum and loud vocals to transfer energy to the audience and the other performers.
While taiko originally comes from Japan, it is increasingly becoming popular worldwide. San Jose Taiko has been a contemporary ensemble since its founding in 1973, serving as a pioneer in the art form and fostering a community that now boasts more than 500 groups across North America. San Jose Taiko creates innovative performance, empowers diverse voices, and educates across cultures, promoting a more accepting and activated world. Aspiring to increase accessibility of taiko for special needs populations, San Jose Taiko consulted with an Occupational Therapist (OT) to develop and implement a safe and effective taiko workshop for individuals with Parkinson's disease (PD).
An introductory taiko workshop was designed by San Jose Taiko performing members in collaboration with the OT. The class included activities emphasizing large amplitude movements, full extensions, trunk rotation, variation of volume and tempo, and using a loud voice. There were nine attendees from across California, and feedback was unanimously positive with 100% of the participants stating that they would like to participate again. In an anonymous post-workshop survey, one participant stated, "I enjoyed everything. I noticed after the session that my hand did not tremble. I suspect Taiko increases dopamine which aids in our PD wellness."
Given this success and enthusiastic response, San Jose Taiko will offer six-week classes for the local PD community and their caregivers. The intention is that this program can serve as a model to other taiko groups in North America, expanding accessibility and further exploring therapeutic potential. This program also serves as an example of ways OTs and other healthcare professionals can partner with local cultural arts organizations to create more community options for exercise and social interaction among individuals living with PD.

P30.23

An approach to Parkinson's disease patient combined with yoga and pilates: PD Cafe – for Parkinson's disease

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Purpose: We report the results of approaching yoga and pilates on 2 patients with Parkinson's disease.
Case information: Case ①: 40's, female, median Hoehn-Yahr Stage III, symptoms have occurred 12 years ago. Case ②: 30's, female, median Hoehn-Yahr Stage Ⅰ, symptoms five years ago.
Procedure: We conducted posture assessment, TimeUP & GoTest (TUG), before and after intervention in two cases. Lessons were conducted for 20 minutes each for a total of 40 minutes, and the same poses and exercises were done. In addition, we got the consent of this report to the cases.
Result: Case ①: Before the intervention, the posture bent laterally to the left side and Stooped posture. But Improvement after intervention. In TUG, 16.58 seconds before intervention → 7.02 (-9.56) seconds after intervention resulted faster.
Case ②: Posture did not improve. In TUG,9.56 seconds → 8.98 (-0.58) seconds, which was not marked change. However, the improvement of the gait and the stability at the change of direction were improved.

Discussion: For 2 cases, In yoga, I chose a pose to increase the flexibility of the muscles around the hip joint and a pose to relax muscle tension around the neck. In Pilates, I focused on the flexibility of the spine and muscular strength of the trunk, especially the abdominal oblique muscles, in order to balance the posture. As a result, the improvement in posture of case ① resulted in correct

muscle activity during walking motion, improving balance ability. I think that it led to walking speed. This is also the reason why the case 2 is improved in gait and the stability at the time of turning has improved. Due to the difference in the results of the two cases, we think that poses and exercises that emphasize individuality are more effective. In addition, this time we report focusing on physical functions, but these two methods are to value the balance between the mind and the body. Combined use of yoga and Pilates is able to support the body and spirit of Parkinson's disease patients.

P30.24

Building international communities – Dance with Parkinson's

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[3] 21st Century Museum of Contemporary Art, Kanazawa, Japan
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[5] Dance artist – 21st Century Museum of Contemporary Art, Kanazawa, Ishikawa, Japan
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[7] Dance Well-movement research for Parkinson's, Bassano del Grappa, Italy
[8] Fresco Parkinson Institute Italia/Villa Margherita, Venezia, Italy

The presentation encompasses four unique experiences coming from Germany, Japan, Italy and the U.K., dealing with the topic of dance and Parkinson's. It illustrates not only the impact dance has on people confronted by the neurodegenerative, progressive movement disorder, but also how engagement in this field can positively impact well being, social inclusion, artistry, professional development, audience engagement and the shaping of a more diverse dance culture. The experiences include dance practices regularly held in museums and artistic contexts, the development of creative processes and presentation of dance performances to audiences, studies and researches of the impact that the practice of dance has on people living with Parkinson's, the creation of multicultural inclusive communities and the development of international dialogues and collaboration to progress approaches and practices. The presenters comprise a variety of perspectives spanning from dance artists, museum experts, institutions, scholars and local citizens, offering new approaches for building and connecting internationally communities.

P30.25

The effects of concomitant use of hydrogen water and photobiomodulation (PBM) to Parkinson's disease

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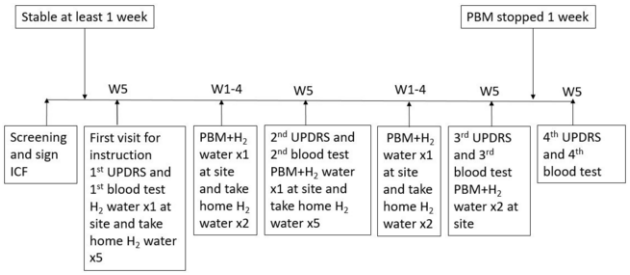
Introduction: Parkinson's disease is the second most common neurodegenerative disorder. Symptomatic treatments alleviate the motor deficit but do not stop the progression of disease. Photobiomodulation (PBM) directly affects cellular metabolic activity that is regulated by energy production within mitochondria. Near-infrared laser therapy (NILT) has been under development for the treatment of Parkinson's disease. On the other hands, the progression of PD is thought to be from oxidative stress. Recent cell and animal studies have confirmed that molecular hydrogen (H2) functions as a highly effective antioxidant. Drinking H2 -dissolved water (H2 -water) reduced oxidative stress. With the exposure of light, the enhanced mitochondrial activities might be accompanied by increase ROS (reactive oxygen species) production, which might have weakened or even offset the effect of the PBM therapy. We conducted a small clinical study to test if concomitant use of hydrogen water and PBM have therapeutic effects on PD patients.
Method: Eighteen PD patients diagnosed with Hoehn and Yahr stage II-III are recruited. The PBM is arranged for consecutive five days from Monday to Friday for each patient for consecutive 2 weeks and then withheld for the third week to see if the therapeutic effect will be sustained or declined. Patients also drink hydrogen water 200 ml in volume and contains 2.5 ppm in concentration concomitantly. (Study scheme uploaded)
Result: The overall severity of PD (sum of Part I, II and III in UPDRS) is significantly decreased after only one week of PBM+H2. This improvement is continuing following the second week of therapy. After cessation of therapy for one week, the total score is increased but still significantly improved as compared to the initial score.
Conclusion: The concomitant use of hydrogen water and PBM is helpful to patients with Parkinson's disease



COMPREHENSIVE CARE: Lay/professional health literacy & public thought

P31.01

Subjective observations on the effects of antibiotics on the PD symptoms of PWP William Curnow since previous PWC4 poster including data taken before and after FMT procedure plus three usages of antibiotics

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PWP William Curnow, diagnosed 2002, submitted to WPC4 the only poster dealing with the possible role of gut bacteria in the onset and development of PD.
His neurologist was startled when Curnow whom he knew was an architect, asked him if PD could possibly be an outcome from a gut micro-organism
Curnow was aware of the impact of an animal's biome on its host and on experimental outcome. He was involved in the development of CSIRO High Security Australian Animal Health Laboratory [AAHL], the CSIRO SPF Animal Production Unit Long Pocket, and as consultant to UN/FAO, and Indian, French and Canadian Governments on like projects.
To his surprise, years later, he was able to experience the remission of his own PD symptoms when he was hospitalised for an unrelated medical condition requiring treatment with antibiotics. He must be

imagining things., but his own GP confiemed the abatement of PD Symptoms. His Poster at WPC4 covered this period of his living with PD.
Since that time Curnow and Professor Borody have repeated the effect on two occasions by treating a bacterial gut infection of Curnow's at the CDD, Sydney. Following this period Borody carried out an FMT on Curnow who remained off all antibiotics for over a year.
Recently Curnow was again hospitalized with faecal impaction and pneumonia.
Curnow was treated with antibiotics and once more his PD symptoms disappeared for the duration of medical intervention.
His Poster for WPC5 will cover the period between PWC4 and PWC5
Curnow and Borody conclude that there is a strong relatonship betwen gut bacteria, Parkinson's symptom abatement, and one or more of the antibiotics used to treat conditions involving one or more gut bacteria.
That said, the next task is to identify which particular micro organism/s are involved and which antibiotics are appropriate to control the organism and more importantly PD. Curnow now 80 years old looks forward to developing the next poster on the subject for PWC6.
He believes in being too busy to let Parkinson's disease get in the way of a good research conundrum that has evaded conventional medical wisdom for 200 years.

P31.02

Development of a Massive Open Online Course (MOOC) to educate healthcare professionals about Parkinson's disease
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Approximately 60,000 Americans are diagnosed with Parkinson's disease (PD) each year and more than 10 million people worldwide are living with PD. Healthcare professionals can expect to encounter persons with PD in a variety of settings and should be aware of the complexities of this chronic neurodegenerative disorder and best practices in care. It is incumbent upon those working with this population to learn about its motor and lesser-known non-motor symptoms, as well as treatment modalities, including medication management and other strategies to reduce symptoms and enhance quality of life. Furthermore, there are necessary modifications to care when the person with PD is hospitalized to prevent or minimize negative outcomes, such as ensuring anti-Parkinson's medications are given "on time, every time" and that anti-dopaminergic medications are avoided.
To address the ongoing knowledge and care gap regarding PD among healthcare professionals, a massive open online course (MOOC) was developed and made available via the University of Maryland System's edX platform. A MOOC is an open access and interactive course offered via the web; it has emerged as a popular mode of distance learning education aimed at unlimited participation. This educational program titled, Parkinson's disease, is designed for healthcare professionals such as nurses, physical therapists and related practitioners. It consists of five distinct modules: Overview; Symptoms; Medication Management; Management/Other; and, Care of the Hospitalized Person with Parkinson's disease. For each module, there is a detailed PowerPoint with a short post-test to assess learning. There is also an unfolding case study to reinforce learning and handouts (where applicable) which highlight various care tips. Lastly, there is a 30-minute video interview titled, Living with Parkinson's disease, featuring a person with PD discussing his experience with symptoms, diagnosis, medication management, as well as, the importance of exercise, positive coping strategies and role of support groups. This formal packaged educational program utilizing the MOOC approach through edX is an innovative strategy that reaches a much larger audience. It can serve to enhance both the competence and confidence of healthcare professionals regarding best practices for working with this population.

P31.03

Exploring OFF experiences and communication with clinicians
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Background: The Davis Phinney Foundation is committed to helping people live well with Parkinson's. One way of doing this involves educating the community about detection and management of OFF states. The lack of a commonly held definition of OFF can lead to varying interpretations of symptoms and under recognition of OFF, by clinicians and people living with Parkinson's. This study explores the (1) experience of OFF among people living with Parkinson's and (2) their communication regarding OFF with clinicians.
Methods: This study included 1376 people living with Parkinson's (51.52% male) who completed an online self-report questionnaire. Respondents had an average age of 69.74 (range 37–96) and a mean disease duration of 6.68 years (range <1 year – 28 years).

Results: Most respondents (77%) reported experiencing OFF to some degree with 38% experiencing OFF "often". Almost half (48%) of respondents rated their OFF as moderate to high severity. The most commonly reported OFF experiences included: wearing off or end of dose deterioration (55%), non-motor fluctuations (30%), unpredictable OFF (21%), delayed ON (21%) and early morning akinesia/bradykinesia (19%). Less than a third of respondents (29%) reported discussing OFF often with their clinicians while 22% felt dissatisfied with their clinician's recognition and understanding of OFF. Thirty percent reported dissatisfaction with clinician recommended strategies to manage OFF.
Respondents who reported experiencing OFF more frequently and with more severity were:
- less likely to report frequent discussions about OFF with their clinicians (p<.001)
- more likely to report dissatisfaction with both their clinicians' recognition and understanding of OFF (p=.011) and the suggested management strategies (p<.001).

Those who reported more ability to predict their OFF were more likely to report:
- frequent discussions about OFF with their clinicians (p<.001)
- more satisfaction with their clinicians' recognition and understanding of OFF (p=.009) and suggested management strategies (p=.027).

Conclusions: Findings suggest that OFF is common among people living with Parkinson's and a need exists for more and improved communication between people living with Parkinson's and their clinicians to identify and successfully manage OFF and improve quality of life.

P31.04

In support of a fungal and related mycotoxin model contributory to Parkinson's
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The Parkinson's disease Fighters United community is about 5000 members and comprised of researchers, medical providers, and

clever, motivated patients. A “think-tank” atmosphere is fostered in a safe space where a vigorous exchange of ideas often daylights critical insight into the disease.
The momentum in PD research is swinging towards investigating dysfunctions within the gut and the micro-biome therein. Attention is being given to improper diet, insufficient exercise, and environmental stressors as causes of the disease. It is coming to light that these factors are involved years before symptoms and diagnosis. This is consistent with anecdotes within PDFU.
Realizing the significance of the work of Joy Milne, the Scottish lady who can smell PD, with near 100% accuracy up to 10 years prior to diagnosis, administrators Mr. David Spry, Mr. Glen Pettibone (both Parkinson’s sufferers with technical backgrounds) and others from the group have recently hypothesized that the potential exists for infectious fungi to disrupt the body’s dopamine production and compromise the host’s immunity. This may result in a deficit of dopamine which could lead to Parkinsonism, alone or in concert with other factors. What Joy can smell has been identified as malasezzia, a skin yeast normally associated with antibiotic resistant teenage acne.
If true this is very encouraging because drug, diet, supplement, and exercise programs, already exist that are anti-fungal.
The authors explain in this presentation the basis for a fungal contributor to Parkinson’s. The hope is to educate, increase awareness, inspire further research, and encourage safe, actionable experimentation with the patient community.
The journey begins with James Parkinson himself; with Joy Milne’s story; introduces the reader to the dogs detecting Parkinson’s; explains the results of the University of Manchester study; educates the audience as to the nuanced world of fungi, and their mycotoxins; suggests pathways for further research; and points out safe pathways for potential treatments generally considered safe.
The authors tie together all of this to demonstrate the plausible existence of fungal Parkinson’s and the potential for action.

P31.05

Service-learning as an introduction to Parkinson’s disease for pre-clinical medical students
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Service learning is becoming a common method for introducing medical students to certain populations. It is frequently used to educate students on preventative medicine, health in underrepresented populations, and international health. This model seeks to expose students to multiple aspects of a disease while also providing benefit to patient through socialization and community involvement. Parkinson’s disease (PD) is uniquely suited for a service-learning curriculum as socialization has been shown to improve quality of life for patients. In addition, exposure to PD is limited in medical education despite PD patients being seen in nearly all medical specialty clinics. We therefore began a student-directed service-learning program for PD.
We recruited 5 interested first year medical students to become leaders of a “Parkinson’s Partners” group at Boston University. We encouraged these leaders to independently design a curriculum for 4 unique 2-hour meetings per semester. Curriculum combined social activities with narrative-based education. Meetings took place monthly at BU medical school. A one-on-one meeting outside the institution was also incorporated to help foster the partner relationship. The students embedded a research project into the group to evaluate quality of life outcomes through PDQ-39 scores for patients and burnout scores for students. In addition, we expanded the service-learning program by partnering student leaders with patients undergoing Deep Brain Stimulation. Student leaders were successful in initially recruiting participants as well as implementing strategies for retention of participants throughout each semester. We feel that the this service learning group for PD has not only met the goals of the program, but has provided our leaders an opportunity to learn how to develop community programs for PD patients, a skill which they would not have gained in a classroom or clinic setting. In addition, this program may also stimulate students’ interest in Movement Disorders and lead more of them to pursue a career in this field.
[1] Shah, NS, et al. Development and evaluation of a service-learning model for preclinical student education in cardiovascular disease prevention. Adv Med Educ Pract. 2016; 7: 153–161
[2] Smith, KS, et al. Integrating service learning into the curriculum: Lessons from the field. Medical Teacher. 2013; 35:5, e1139–e1148; DOI: 10.3109/0142159X.2012.735383

COMPREHENSIVE CARE: Disability and quality of life outcome measures

P32.01

Quality of life in Parkinson’s disease patients may not improve with physical, social, or emotional interventions
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Background: Parkinson’s disease is associated with progressive decline in cognitive, and motor function, as well as alterations in mood, which leads to a poor quality of life for Parkinson’s patients. Many have called for cognitive, motor, and mood interventions as a way of improving quality of life in PD patients.
In this study, we tried to determine if interventions to improve physical, cognitive, and emotional needs would improve the quality of life of PD patients.
Method: 64 patients with PD were offered three intervention groups coordinated by social work, which include yoga, cognitive training, and support groups. The attendance for each group for each patient was calculated.
Social Work administered the Ferrans and Powers Quality of Life Index and as well as Lawton-Brody Instrumental Activities of Daily Living Scale.
Results: A univariate regression analysis was performed in an attempt to determine if attendance at Yoga, Cognitive Training, and Social support groups have an impact on QOL controlling for length of diagnosis and functional independence.
The Overall univariate regression model was significant, F=2.56 (df=5), P=.036(.05).
Partial correlation between Cognitive Training Group attendance and QOL (controlling for all other variables) was not significant, R-partial=+0.11, P=.38 (>.05).
Partial correlation between Yoga Group attendance and QOL (controlling for all other variables) was not significant, R-partial= -0.079, P=.55 (>.05).
Conclusion: The results of this study indicate that physical, psychosocial, and cognitive interventions did not have an impact on Quality of Life. As expected patients with more advanced

Parkinson's disease have a poorer quality of life; however, contrast to popular belief, when adjusted for disease progression and level of functional independence, the amount of attendance in interventional groups did not appear to lead to a better quality of life for our PD patients. Therefore, interventional programs in Parkinson's disease need to be re-evaluated in order to improve patient outcomes and quality of life.

P32.02

Life satisfaction in men and women with Parkinson's disease

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Background: Life satisfaction has been defined as "the degree to which a person positively evaluates the overall quality of his/her life as a whole; in other words, how much the person likes the life he/she leads" and should be the ultimate goal of health care in general. At present, there is limited knowledge on life satisfaction in people with Parkinson's disease (PD).
Objective: This study aimed to investigate how life satisfaction evolved over a 3-year period in men and women with PD.
Methods: Participants (N=255) were recruited from three hospitals in Sweden. A total of 164 persons with PD (35% women) had life satisfaction data at baseline as well as the 3-year follow-up. Their mean (SD) age and PD duration at baseline were 68 (±9) and 9 (±6) years, respectively. The first item of the Life Satisfaction Questionnaire (LiSat-11), which addresses satisfaction with life as a whole, was used. It has six response categories: 1; Very dissatisfied, 2; Dissatisfied, 3; Rather dissatisfied, 4; Rather satisfied, 5; Satisfied, and 6; Very satisfied. The responses were dichotomized into Not satisfied (1–4) and Satisfied (5–6), according to a previous study by Fugl-Meyer et al. (i.e., the developers of LiSat-11). Changes in life satisfaction from baseline to the 3-year follow-up were studied with McNemar's test. Exact, two-tailed p-values are reported.
Results: At baseline, 63% (n=103) of the total sample were satisfied with their life as a whole, which decreased to 50% (n=82) three years later (p=0.005). Among men at baseline, 67% (n=71) were satisfied with their life versus 54% (n=57) three years later (p=0.020). The corresponding numbers for women were 55% (n=32) at baseline and 43% (n=25) three years later (p=0.189).
Conclusion: This study suggests that life satisfaction decreases in people with PD after three years, in particular among men. Life satisfaction in women with PD seems to be somewhat more stable over time. Further studies are needed to identify predictive factors of life satisfaction.

P32.03

The association between non-motor symptoms and quality of life in Parkinson's disease

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Introduction: Parkinson's disease (PD) is the second most common neurodegenerative disorder. Whilst primarily perceived as a motor disease by many, non-motor symptoms (NMS) are also a major component of PD, reported in the vast majority of people with the disease. Quality of life (QoL) refers to the overall well-being of an individual, and is determined by the person and how they perceive their standard of life. This study aimed to explore the relationship between NMS and QoL in PD.
Methods: Individuals diagnosed with idiopathic PD (n=100) in South East Queensland, Australia, were recruited into this observational study. The Non-Motor Symptoms Scale (NMSS) was used to evaluate NMS, including severity and frequency, and the Parkinson's disease Questionnaire (PDQ-39) used as an assessment of QoL. The NMSS symptom and domain scores were assessed in relation to the PDQ-39 Summary Index (PDQ-SI) and respective PDQ-39 domains. Bivariate analysis was used to measure the associations between NMS and QoL.
Results: Participant demographics comprised of 62% male and 38% female with a mean age of 69.1 years (SD 7.35) and mean Hoehn & Yahr stage 2.34 (SD 0.59). Lower QoL was associated with higher overall NMSS scores, as well as total severity and frequency ($p<0.001$). Overall QoL was significantly associated with all NMSS domains (all $p<0.05$), as well as combined severity and frequency scores for all the NMSS domains (all $p<0.05$), aside from urinary domain frequency. All NMSS domains were significantly associated with at least two QoL domains. The Mood/Cognition domain was significantly associated with all PDQ-39 domains (all $p<0.05$). Furthermore, the PDQ-39 mobility domain was significantly correlated with all NMSS domains. 24 of the 30 NMSS symptoms were positively associated with the PDQ-SI, the most prominent being light headedness/dizziness, fatigue, lack of motivation, depression, flat moods, lack of pleasure, forgetfulness and dysphagia (all $p<0.001$).
Conclusion: This study found multiple associations between NMS with QoL. In particular, NMS domains of mood/cognition, attention/memory, sexual function and miscellaneous (unexplained pain, anosmia, hyperhidrosis, weight change) had the most associations with various QoL domains. Prompt identification and management of NMS will likely improve QoL of individuals with PD.

Table 1: Pearson's Correlations between NMSS and PDQ-39 Domains

NMSS	Cardiovascular including falls		Sleep/Fatigue		Mood/Cognition		Perceptual problems/ Hallucinations		Attention/ Memory		Gastrointestinal Tract		Urinary		Sexual function		Miscellaneous	
PDQ-39 domain	R	*p*	R	*p*	R	*p*	R	*p*	R	*p*	R	*p*	R	*p*	R	*p*	R	*p*
Mobility	**0.312**	**0.002**	**0.368**	**<0.001**	**0.442**	**<0.001**	**0.326**	**0.001**	**0.223**	**0.025**	**0.423**	**<0.001**	**0.320**	**0.001**	**0.288**	**0.004**	**0.398**	**<0.001**
ADL	0.156	0.121	**0.256**	**0.010**	**0.353**	**<0.001**	0.133	0.186	**0.274**	**0.006**	**0.321**	**0.001**	**0.217**	**0.030**	**0.303**	**0.002**	**0.342**	**<0.001**
Emotional wellbeing	**0.353**	**<0.001**	**0.275**	**0.006**	**0.512**	**<0.001**	**0.333**	**0.002**	**0.215**	**0.032**	**0.349**	**<0.001**	0.180	0.072	**0.246**	**0.014**	**0.258**	**0.010**
Stigma	0.185	0.065	0.172	0.086	**0.311**	**0.002**	0.093	0.359	0.173	0.086	0.167	0.097	0.178	0.077	0.172	0.087	**0.307**	**0.002**
Social support	**0.215**	**0.032**	0.184	0.067	**0.214**	**0.032**	0.043	0.671	**0.207**	**0.038**	0.172	0.087	0.153	0.128	**0.224**	**0.025**	0.188	0.060
Cognitive impairment	**0.292**	**0.003**	**0.364**	**<0.001**	**0.256**	**0.010**	**0.333**	**0.001**	**0.484**	**<0.001**	**0.362**	**<0.001**	0.098	0.334	**0.296**	**0.003**	**0.268**	**0.007**
Communication	**0.282**	**0.005**	**0.290**	**0.003**	**0.315**	**0.001**	**0.353**	**<0.001**	**0.382**	**<0.001**	**0.410**	**<0.001**	0.126	0.213	**0.337**	**0.001**	**0.308**	**0.002**
Bodily discomfort	**0.303**	**0.002**	**0.314**	**0.001**	**0.284**	**0.004**	**0.249**	**0.013**	**0.346**	**<0.001**	**0.380**	**<0.001**	0.155	0.124	**0.284**	**0.004**	**0.460**	**<0.001**

*Significant associations (p <0.05) in bold

P32.04

Differentiation of fatigue and tiredness vocabularies in US and UK patient samples

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Chronic fatigue is a major determinant of quality of life in Parkinson's disease (PD) with a third of people with PD (PWPs) reporting fatigue as their most disabling PD symptom. Fatigue is however difficult to define, particularly with respect to tiredness. The present study addresses the need for a PWP-friendly vocabulary able to differentiate fatigue and tiredness. A questionnaire-based study compared a US group (n=13, b1943-64) and a UK group (n=9, b1944-72). English was their first language and all were resident in the country where they completed the questionnaire. Study participants were presented with 39 words or phrases and

asked to state whether each mapped better to “fatigue” or to “tiredness”. PWPs were allowed to avoid giving a response if they did not know the meaning of a given word or phrase. When expressed in order of selectivity for fatigue over tiredness, the following terms showed the highest selectivity in the US group: fatigue (12:0 fatigue:tiredness), feeble (11:2), fatigued (11:2), debility (10:3) and lack of stamina (9:3). In the UK group, the terms showing highest selectivity for fatigue over tiredness were lethargic (9:0 fatigue:tiredness), lack of energy (8:1), fatigue (8:1), drain (8:1) and lack of stamina (7:2). Two of the top five terms for fatigue were common to both US and UK groups. Conversely when expressed in order of selectivity for tiredness over fatigue, the following terms showed the highest selectivity in the US group: tiredness (12:0 tiredness:fatigue), tired (13:0), drowsy (12:1), overtired (9:3) and enervation (8:3). In the UK group, the terms showing highest selectivity for tiredness over fatigue were: tiredness (9:0 tiredness:fatigue), tired (9:0), drowsy (8:1), overtired (7:2) and drained (7:2). Four of the top five terms for tiredness were common to both US and UK groups. A total of 7 participants (4 US, 3 UK) did not know the meaning of 8 words (6 US, 5 UK). These data may be helpful in operationalising a clinical scale for fatigue in PD that will distinguish fatigue from tiredness.

P32.05

The impact of Parkinson’s disease on quality of life: The JAQPAD (Japanese QOL survey of Parkinson’s disease) study

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Objective: To evaluate the impact of specific factors on the quality of life (QOL) in Japanese patients with Parkinson’s disease (PD).
Background: PD is a progressive disorder involving both motor and non-motor symptoms which impact the patient’s QOL. Previous studies have reported the impact of either motor symptom (MS) or non-motor symptom (NMS) on QOL of PD studies, however, evidence is lacking on the integrated impact of both MS and NMS and other PD related factors on QOL of PD patients.
Methods: All 8,183 members who belong to the Japan Parkinson’s disease Association were invited to participate in this survey. Questionnaire sheets were distributed to patients by mail. The survey included QOL questionnaires PDQ-8 and EQ-5D, and other disease related questions such as off-time duration per day, Hoehn & Yahr (H&Y) stages, presence of wearing-off (WOQ-9 score), troublesome dyskinesia duration per day, activities of daily living (SE-ADL score) and NMS (NMSQ total score). Multiple regression analyses were conducted using the PDQ-8 summary index score as the main outcome measure, with age, gender, H&Y stage, PD duration, employment status, troublesome dyskinesia duration per day, number of PD medications, frequency of PD medication per day, nursing care level, WOQ-9, SE-ADL, and NMSQ as independent variables.
Result: 3,753 patients responded to this survey (response rate: 45.86%). Of these, 3,494 patients were eligible to be included in the analysis. The largest H&Y distribution was stage 3. Mean age was 71.4±7.8 years with mean disease duration 10.3±7.1 years. Mean summary index score of PDQ-8 was 35.07±20.85. Before fitting the model, variables which were highly correlated with off-time duration per day such as H&Y stage, troublesome dyskinesia duration per day, frequency of PD medications per day, and SE-ADL were eliminated. From the multiple regression analysis following with the backward stepwise elimination, duration of off-time, age, disease duration, and NMS score, significantly contributed to the QOL.
Conclusions: This study highlights the importance of timely assessment and integrated management of both motor and non-motor complications to improve QOL in PD patients.

P32.06

“Where’s the ‘feeling better’ box?” Beyond PDQ39

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This author first encountered the PDQ39 when hearing an eminent movement specialist say there was no evidence that Parkinson’s dance increased quality of life. This ran so counter to my own experience as a PwP dancer that I asked what measure had been used: the PDQ39.
The PDQ39 was ground-breaking when developed in the 1990s, underpinning the shift to acknowledge and research non-motor symptoms including “the emotional and social domains of health” (de Boer et al 1996:70).
Now a second shift – a radical change in attitude and approach to patient self-management (Bloem 2011; 2016) – compels a critical revisit. This shift recognises that partnership with empowered patients can increase quality of life (Canoy et al 2015; Leicester 2018); and also acknowledges the pressure of increasing numbers of PwP (P-UK AGM 2018) against limited healthcare resources.
Rethinking Quality of Life: PDQ39 relates quality of life to degree of functional impairment: “PDQ-39 dimension scores […] are coded on a scale of 0 (perfect health as assessed by the measure) to 100 (worse health as assessed by the measure)” (Jenkinson et al 1997:354). It reinforces patient dependency on health professionals by measuring only what is lacking, what a PwP can no longer achieve.
The challenge, over twenty years later, is to reframe our understanding of quality of life, decoupling it from functional impairment, and identifying the values (Alexandrova 2017; Longino 1990) underlying and informing that reframed understanding. “Parkinson’s has opened up a whole new career for me” (Mayhew-Archer 2018), and my own Parkinson’s has unlocked areas of learning, activity and discovery, arguably increasing my overall quality of life.
Starting points for a new measure: I present the capability model (Sen 1999; Canoy et al 2015), already used in Parkinson’s research, and Measuring Humanity’s assets-based indicator framework (de Andrade 2017). These measures of capability and potential show how questions of assessing patient empowerment, responsibility, self-management, and choice might be framed, and how improvements in emotional and spiritual wellbeing could be measured. How might a questionnaire capture ‘feeling lovely’ (Houston 2015)?
“What we measure affects what we do – and what we think we can do” (Adams 2018).

COMPREHENSIVE CARE: Shared decision-making: PwP – caregiver – doctor

P33.01

Preparing future practitioners for interdisciplinary teams: An update on the collaborative study research at Concordia College, Moorhead, Minnesota, USA

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Introduction: The Institute of Medicine (IOM) Committee on Health Professions education (2003) emphasized the need for team-based interdisciplinary education strategies to create professionals that could collaborate effectively to provide quality care. The Committee endorsed a vision for education of health professionals that required professionals to be educated to deliver patient-centered care as members of an interdisciplinary team emphasizing evidence-based practice. As a result of the IOM recommendations Colleges and Universities across the country are exploring and integrating Inter-Professional Education (IPE) in their curriculum (IPEC, 2011). IPE has been found to improve multi-disciplinary team functioning by education students about the values, ethics, and principles of the various disciplines as well as developing the skills needed to foster professional relationships (Thistlethwaite, 2013).
Method: Six case studies were developed by faculty representing dietetics, nursing, social work, healthcare administration, exercise science, and education. The cases included: an older adult in a small rural ND town struggling with the diagnosis of Parkinson's disease, a 5 year old entering the school system with multiple disabilities, a middle aged gentleman with coronary heart disease, a middle aged woman with diabetes, an adolescent with an eating disorder, and a policy case study where students explore the impact of a specific policy on professional practice and the clients of that practice. During a common meeting time, students work together to identify priorities for their work with the client and their family. Differences between plans are noted and discussed.
Survey Instrument: Following the event, students participate in a survey to explore their knowledge and growth. They are asked about their understanding of the different disciplines prior to and then following the event. They also rate whether their ability to work with diverse professionals has been enhanced, and to rate their role and participation in the event.
Results: Students reported a greater understanding of other professional roles following the experience (38.09% = "moderate," 61.9% = "exceptional"). In addition, students reported that their ability to work with diverse professionals was enhanced by the experience (30.23% = "moderately", 69.76% = "exceptionally"). Finally, 89.25% of students reported that they agreed "exceptionally" that their role and voice was valued.

P33.02

emPowered! Tool: Enhancing communication systemwide – Building skills and expanding confidence for PwP and care partners in self-advocacy and care team planning

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During the 2016 WPC conference, in an informal survey conducted at the AbbVie booth, 63% of PwP reported that they forgot to share something important with their doctor, 57% reported that they minimize the impact of their symptoms when talking with their doctor, and 30% were concerned that they would be perceived as a complainer if they talk issues with their doctor. This data, combined with ethnographic research of more than 500 people with PD, care partners, and physicians, motivated PMDAlliance to develop its emPowered! ® Tool.
Not simply a symptom tracker, the emPowered! ® Tool addresses a much deeper issue – the differing perceptions of disease impact as experienced by various members within the person with Parkinson's ecosystem. This tool, presented in a workbook format, improves communications that usually become more challenging as the disease progresses and is designed for a year of use. The emPowered! ® Tool is distributed at PMDAlliance conferences and through a support group leader licensing program to our network of more than 800 support group leaders, who in turn reach more than 25,000 PwP. More than 2,000 have been distributed in the last 6 months. Version two is in development, expanding the care team planning.
Comments from providers with patients utilizing the tool: "We all get on the same page quickly and share a clear overview of what happened between visits." "Tracking symptoms progression or abatement over time allows for more effective monitoring of efficacy of interventions."
Comments from PwP and loved ones: "The tool allows me to be included in the conversation about what I see." "I'm often at a loss about how to help my parents. Now, when I visit, I use the tool as a guide to talk as a family about what's happening with Parkinson's."
emPowered! ® Tool recipients reported a 75% increase understanding the need to share in-depth information with physicians. 82% reported increased understanding of the value of tracking trends related to disease progression. 77% felt increased confidence in expressing themselves in conversations with physicians. 84% reported increased appreciation of the value of ensuring family members understands disease process, medications and symptoms.

P33.03

A national comprehensive survey study of Parkinson's disease psychosis patients and caregivers regarding time to Parkinson's disease psychosis diagnosis and treatment initiation

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Objective: Parkinson's disease psychosis (PDP) is a troubling non-motor symptom of Parkinson's disease characterized by hallucinations and delusions that is often unreported. Clinical approaches to the management of PDP include medication adjustments and initiations, but the experience of people with Parkinson's and of their caregivers is not well understood. The goal of this study was to understand the experience and management of PDP.
Methods: A survey was sent both to people with Parkinson's ("patients") and to caregivers indicating interest in PDP through (a) calls to the Parkinson's Foundation helpline or (b) registering for a webinar on PDP.
Results: 418 individuals completed the survey. Of the respondents, 199 identified as patients and 219 as caregivers. Of these, 266 (95 patients, 171 caregivers) reported the patient having experienced symptoms of PDP. Caregivers were significantly more likely to report delusions than patients (p<0.0001), but reporting of hallucinations and illusions was similar. Caregivers who reported delusions were more likely to identify as "worried" or "very worried" about PDP than those who reported only hallucinations (79% versus 48%, respectively; P=0.0001).
In total, 244 respondents contacted a healthcare professional (HCP). Discussions of PDP symptoms with the HCP were held by 81%; however, 12% waited several visits before discussing them. Of those engaging an HCP, 78% attempted strategies to manage PDP: (1) 34% utilized non-pharmacologic coping strategies, with 9% reporting improvement; (2) 55% adjusted PD medications, with 32% reporting improvement; and (3) 47% started an antipsychotic, with 24% reporting improvement. Overall, 48% indicated that at least one of the three strategies resulted in improvement, whereas none of 19% who did not report PDP symptoms to an HCP said that symptoms improved.
Conclusions: In this analysis, delusions proved to be of greater concern to caregivers than hallucinations. Management of PDP entailed multiple strategies, but improvement was dependent on reporting of symptoms to the HCP and appropriate treatment, both of which appeared in many cases to be unnecessarily delayed.

COMPREHENSIVE CARE: Palliative care/End of life care/Long-term care

P34.01

A comparative analysis of long-term custodial care utilization in patients with Parkinson's disease psychosis versus without psychosis within the United States

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Introduction: Parkinson disease (PD) impacts >4 million patients worldwide and will likely affect ˜9 million by 2030. Psychosis is a complication of PD that may contribute to nursing home stays >100 consecutive days (defined as Custodial Care [CC]). Currently, the association between Parkinson disease psychosis (PDP), PD, and use of CC has not been well studied or directly examined. This study analyzes utilization of CC among PDP patients in the US (phase 1) and compares it with a matched non-PD cohort (phase 2).
Methods: Using Medicare Part A, B, and D data from 2007–2015, phase 1 evaluated rate and duration of CC and related costs. Phase 2, comparing PDP vs non-PDP, is ongoing. In phase 2, a cohort of patients with incident PD will be created by finding the first occurrence of PD in claims from 2008–2015 and no prior evidence of PD within a one-year look-back period. PDP patients will be identified by 2+ claims of psychosis 30 days apart after PD index date. Using a direct matching method, PDP patients will be matched to non-PDP patients based on demographics and time since onset of PD. Cumulative incidence curves will be generated for the two comparative groups. Adjusted hazard ratios will be calculated using proportional hazard models. Additionally, costs and healthcare utilization will be described in the period before and after use of CC. Characteristics of patients who did or did not require CC will be compared between the two cohorts, and time to CC will be calculated using the Kaplan-Meier estimator.
Results: In phase 1, over a mean follow-up of 1.8 years for the overall PDP-only cohort, 32% and 40% of PDP patients required CC within 4 and 6 years, respectively, with a rate of 12.2 per 100 person-years among all PDP patients. Once in CC, mean stay was 1.4 years, and costs tripled relative to PDP patients not in CC.
Conclusions: Phase 1 provided information about the rate of CC, length of stay, and costs among PDP patients. The ongoing phase 2 is expected to provide important comparative analysis regarding CC in non-PDP vs PDP cohorts.

P34.02

Team-based outpatient palliative care improves patient and care partner-centered outcomes in Parkinson's disease

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Background: Palliative Care (PC) is medical care focused on improving quality of life (QOL) for people with serious illness that addresses medical symptoms, psychosocial needs, spiritual wellbeing and advance care planning. There is growing recognition that people living with Parkinson's disease or related disorders (PDRD) and their family care-partners have significant PC needs and a growing number of centers worldwide now offer PC services for PDRD. We report the results of the first multisite, randomized comparative effectiveness clinical trial to assess whether outpatient PC improves patient or care-partner outcomes in PD.
Methods: We randomized people with PDRD with moderate to high PC needs (and care-partners, if present) to either continue current standard care (including a neurologist) or receive standard care augmented by team-based PC for 12 months. Our PC intervention included care from a neurologist, nurse, chaplain and social worker with guidance and from a palliative medicine specialist. We collected data every 3 months on patient QOL (QOL-Alzheimer's disease), symptom burden (Edmonton Symptom Assessment

Scale-PD), grief (Prolonged Grief Disorder Questionnaire), mood (Hospital Anxiety and Depression Scale), spiritual wellbeing (Functional Assessment of Chronic Illness Therapy Spiritual Wellbeing) and care-partner burden (Zarit Burden Inventory). Our primary outcomes were change in patient QOL and care-partner burden at 6 months.
Results: We enrolled 210 people with PDRD, and 175 care-partners. Compared to standard care at 6 months, those assigned to the PC intervention had improved QOL (0.90 improvement vs 0.73 worsening, p=0.027), symptom burden (7.3 improvement vs. 0.3 worsening, p=0.0062), grief (2.9 improvement vs. 0.3 improvement, p=0.01) and less caregiver burden (0.75 worsening vs. 2.56 worsening, p=0.049). There were no significant differences in mood or spiritual wellbeing. Secondary analyses suggest benefits were greater for persons with higher needs.
Conclusions: Compared to standard care, outpatient PC provides significant benefits for people living with PDRD and their care-partners. This study supports efforts to make PC a part of standard PDRD care and provides a scalable model for implementation. Future research should examine implementation and dissemination of this and other models of PC in diverse communities and healthcare settings.

P34.03

The experience of care home placements for people with Parkinson's disease: A qualitative study in the North East of England
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Objectives: There are few previous data on the experience of living in a care home for people with Parkinson's disease (PwP). We investigated this within a cohort of PwP living in care homes in North-East England.
Methods: We conducted in-depth interviews within a cohort recruited to a larger study for all people with late stage Parkinson's. Interviews were conducted by a psychology trainee and analysed thematically.
Results: Ten PwP and two family members were interviewed. Key concerns were the lack of time to consider the move to a care home, loss of independence, meaningful social contact and concerns over staff knowledge of Parkinson's, particularly in relation to medication. Many PwP recognised the pressure felt by care home staff, and after allowing for this, reported many positive experiences.
Conclusions: Greater awareness by staff of symptoms and PwP's concerns, particularly in relation to medication, may help to improve care home experience.
Key points
• There are few previous data on the experience of people with Parkinson's disease living in care homes.
• Admission to care home was often rushed with very limited choice of where to go.
• Loss was a major theme, both in terms of loss of relationships and loss of independence.
• Awareness of Parkinson's symptoms by care home staff was a major concern, particularly the fluctuating nature of the condition.
• Understanding the importance of medication in Parkinson's by staff was also seen as a major contributor to good experience.

P34.04

Bridging the gaps in Parkinson's education for nurses in long term care facilities
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Background: PD is traditionally viewed as a motor disease consisting of tremor, bradykinesia, and rigidity. Adequate treatment of motor symptoms improves quality of life for people with PD in nursing homes (Geda et al., 2008), but NMS in PD are frequently under recognized, under treated, and are often more disabling than motor symptoms. Left untreated, NMS can lead to poorer quality of life.
Objective: The objective of this project is threefold: To educate nurses in Long Term Care facilities about the prevalence of NMS, improve the recognition of NMS and identify interventions for PD NMS.
Methods: The Nurse Practitioner at the San Francisco Veteran Affairs Parkinson's disease Research, Education, and Clinical Center met with Veteran Affair Community Living Centers (CLC) and provided them with an education in-service about PD. A pre-survey and post-survey were conducted to assess NMS knowledge.
Results: Preliminary pre-survey results of this ongoing project suggests that nurses were not aware of PD related NMS prior to the intervention. Results from the post survey suggested an immediate knowledge increase in NMS. However, impact of the education intervention was difficult to evaluate as there was a low response rate to the post survey.
Project challenges include short in-service, communication difficulties with nursing leadership, and difficulty collecting post intervention surveys. Results from the first CLC will be used to improve upcoming in-services at other CLCs.

COMPREHENSIVE CARE: Health accessibility/Underserved populations

P35.01

'No one has ever mentioned such word'': Knowing, or not knowing about Parkinson's disease in Kenya, sub-Saharan Africa
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Introduction: Research on Parkinson's disease (PD) in Kenya, sub-Saharan Africa (population 51.4 million), is scant, while knowledge about the disease among the population and health care professionals is very low. This qualitative study examines diagnosis and care amongst people with Parkinson's disease (PWPD) and their families in Kenya.
Objectives: To explore the experiences of PWPD with regards to their diagnosis journeys among public and private hospital settings in Kenya.
Methods: Ethnographic methods comprising interviews and observations were applied over nine months (March 2018 – December 2018) across urban and rural areas. Participants included PWPD (N=50), family members and caregivers (N=22),

medical consultants in private and public hospitals (N=13), pharmacists (N=28), community health volunteers (N=2) and herbal doctors (N=5). In addition, 12 PD support group meetings were observed in two urban locations.
Results: PD clinical pathways in Kenya are far from straightforward in all settings. The number of practicing neurologists is very low (N=20), clinics are overwhelmed by neurological cases in government and private hospitals and there are no PD nurse specialists. Interviews with PWPD and family members identified that information provided by health professionals about PD is limited, including the actual diagnosis. Support services and accessible information are very limited. Consequently, PWPD generally have a very poor understanding about disease, symptoms and progression, and if not told their diagnosis are unable to access any further information, support or research relating to PD. Lack of 'knowing' about PD impacts on an individual level, in terms of information availability, and a societal level, in terms of disease awareness. Support groups though currently fledgling, are important for support of PWPD and families, and for their role in advocacy.
Conclusions: The diagnosis journey of PWPD in Kenya is difficult, within private and public settings. Kenya has limited resources to invest into healthcare as well as huge pressures from other non-communicable and communicable diseases. However, as the population ages, the incidence of PD will increase. There is a need for more information about PD, increased awareness, and more structured neurology services to manage PD including integrated care involving neurologists, PD nurse specialists and support groups.

P35.02

Implementing a change of approach: From mono-to interdisciplinary follow-up of patients with PD
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ParkinsonNet is a multidisciplinary network that aims to deliver high quality and individualized healthcare and improve the patients' ability to self-management. ParkinsonNet was first introduced in The Netherlands in 2004, where it currently includes 15 different healthcare providers, including nurses, speech therapists, physiotherapists, social workers, occupational therapists, dieticians and others. Participating providers meet 2 to 4 times a year for training sessions and to strengthen the interdisciplinary network.
In April 2017, the Norwegian ministry of health launched a 30-month long pilot study to customize the Dutch ParkinsonNet model to the Norwegian social and geographic setting. The model was introduced in two designated regions of Norway: Rogaland, with 470 000 inhabitants and an area of 9378 km2, and the capital Oslo, with 635 000 inhabitants and an area of 427 km2. In each of the two regions 15 to 20 speech therapists, physiotherapists and occupational therapists were educated according to the ParkinsonNet model and taught to build a network.
Results: Achievements and challenges from the first training session and through one-year follow up will be presented. Preliminary results show that the level of knowledge across healthcare providers was uneven at baseline. Through focused targeting of the given needs and a practical approach, the overall knowledge of how to approach patients with PD and insight into the role of other healthcare providers increased by approximately 50% and more than 93% of the participants remained within the project.
Conclusion: Over all the implementation of the ParkinsonNet model in Norway seems to be feasible. There is a clear need and interest for an interdisciplinary approach to patients. Further expansion of the number of participants and continuation of the training and network building are necessary to achieve more quantifiable outcomes.

P35.03

Neuro Life Online: Live-stream community building therapeutic intervention (exercise, socialization, wellness and more) available worldwide, used in US, Australia, UK, Canada and Israel
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In 2016, PMDAlliance began testing Neuro Life Online® (NLO), a comprehensive service platform developed after piloting several initiatives to expand services in rural/underserved areas. NLO offers live-stream PD exercise, physician-based education, wellness coaching, social hours, and assistance in setting up telemedicine services for unserved and underserved populations across the US and internationally.
The need for more services is obvious. 19% of people in the US (60 million people) and 45% worldwide live in rural areas, based on a 2007 UN report. A 2015 study revealed severe depression and anxiety exists in 40–70% of people with PD and care partners – higher than most other chronic conditions. Only 20% receive treatment for their depression and anxiety, resulting in emergency room visits and increased mortality rates. A 2010 study linked overall physical and mental health to social relationships. Addressing health concerns without also addressing socialization and isolation issues results in poor outcomes. Conversely, when interventions are combined with community building and socialization, overall wellbeing is enhanced and follow through is improved.
After extensive literature and internet research and ethnographic interviews with 1,000+ people with PD, PMDAlliance did not find any far-reaching, comprehensive, disease-specific program that met the needs of people impacted by PD living in rural and underserved areas. Offered services were generally medical or didactic, not human-centric and dynamic.
Launched in 2017, NLO was designed as a partnership program. Any WPC attendee, physician or organization can engage as a partner and provide this program free of charge to their community, groups or patients and care system. Current users live across the US, in Canada, England, Australia, and Asia. Our growing network of 70 volunteer MDS physicians (called Physician Advisors) means that NLO live-streaming regularly offers the expertise of high-quality medical professionals to people living in areas not otherwise served.
It offers socialization without regard to geographic location and focuses on the whole person's health and wellbeing. In 2019 NLO also includes complementary therapy education sessions and care partner happy hours.
Medical professionals and community based providers are able to add a link to the NLO program via a complementary plug in on their website easing access.

MEET THE NEURO *LIFE* ONLINE™ TEAM

Maria C. Ospina, MD - Neuro *Life* Online™ Medical Advisor

Dr. Ospina brings more than 18 years of experience as a neurologist and movement disorders specialist in Phoenix, Arizona. She completed her fellowship in movement disorders at Louisiana State University Medicine School and graduated with honors from St. George's University in 1998. Practicing across Arizona and in Florida, Dr. Ospina, known for her holistic and practical approach to living with movement disorders, enjoys ensuring that people with neurological diseases and their support team are informed, empowered, and able to navigate care. She has also been an investigator in several clinical research trials in Parkinson disease and other movement disorders.

Judy Talley, MA Gerontology – PMDAlliance Program Director (*coordinates Care Partner Co-Op ™*)

Judy is Program Director for PMDAlliance. She draws upon two decades of experience in housing, services and healthcare for older adults. With leadership experience in assisted living, memory care, rehabilitation and rehab/nursing facilities, Judy brings a wealth of information about training, program design and delivery. Utilizing her expertise in developing educational programs for varied audiences, Judy leads the Certified Parkinson Disease Care™ program and provides guidance and information about navigating changes in care needs and lifestyle choices.

Mia Cooper – Neuro *Life* Online™ Move It! ™ Instructor

Mia is a certified personal trainer with more than 25 years in the exercise, fitness, health and wellness field. She has participated in more than 150 hours of Parkinson-specific training and is a partner in F.I.T. (Fall Intervention Training), a program that strives to keep clients living independently by improving each client's fitness level. Mia conducts Move It!™ classes three times per week, focuses on Parkinson-specific exercise, and always considers the safety of class members exercising at home.

Sarah Scott – Neuro *Life* Online™ Move It!™ (Rock Steady Boxing) Instructor

Sarah Scott is a graduate of ASU with a degree in education. She teaches Zumba, Yoga and certified by Rock Steady Boxing. Rock Steady Boxing Phoenix gives people with Parkinson's disease hope by improving their quality of life through a non-contact boxing based curriculum. Sarah engaged in Rock Steady Boxing after her parent was diagnosed with Parkinson disease. Known in the gym as Coach Sarah, she is active in the Parkinson community and is passionate about keeping people with Parkinson's moving!

Mandy Snell– Neuro *Life* Online™ Coach (Weekly Wellness).

Originally a farm girl from Illinois, Mandy now lives in Mesa, Arizona, where she uses her degree in Tourism Management and background in event planning in her program, *Meaning in Motion*. She mentors people through a journey of self-discovery that marries her love of the outdoors with her talent for bringing out the best in others. Her personal experience includes a loved one with PD who inspires her volunteerism.

Jennifer Anderson, Neuro *Life* Online™ Exercise Special Events Instructor PT, DPT, NCS.

Jennifer is a physical therapist with a passion for Parkinson disease. She founded Root Physical Therapy, which is specifically designed to empower people with PD. Jennifer earned her doctorate in physical therapy (DPT) from A.T. Still University. She is a board certified neurologic clinical specialist (NCS), which is a distinguishing certification attained by successful completion of a rigorous examination demonstrating specialized knowledge and advanced clinical proficiency in neurologic physical therapy practice. She is LSVT BIG® certified, and PWR! trained.

Perry Heilman, Neuro *Life* Online™ H! ™ Happy Hour Co-Host

An Arizona resident since 1953 and diagnosed with PD in early 2010, Perry retired in 2012. He said, "I avoided social interaction for a time until I made up my mind to venture outside my self-imposed comfort zone. I found a community with an ocean of love, support, and knowledge." He added, "We are each unique but with enough common experience to be friends, teachers and students with and for each other." Perry looks for forward to hanging out with you.

Judy Reynolds, Neuro *Life* Online™ H! ™ Happy Hour Co-Host

Judy moved to Arizona in 1997. Retired from the defense industry in 2005, she was diagnosed with PD in 2014 and became involved in several support groups and exercise programs. She believes that exercise is what keeps her healthy and helps delay the onset of symptoms. Judy regularly attends PMDAlliance Get Out! events and keeps active to boost her overall health. Social and welcoming, she likes to help people remember that PD doesn't define you.

Andrea Merriam, BA – Neuro *Life* Online™ Coordinator

Andrea's career has always been about establishing connections and building relationships. Andrea brings 15 years' experience in corporate sales and marketing to the PMDAlliance team. Andrea has an ability to look below the surface and discover hidden treasures that helps to translate the power of PMDAlliance programming. She coordinates the Neuro Life Online program and growing our audience and spreading the word about PMDAlliance's mission, programming, resources and events.

Sarah Jones, MPA, MS Strategic Design – PMDAlliance Executive Director (*Coordinates Learn It!™*).

With more than 25 years of experience leading non-profits and health care programs, Sarah's expertise extends to creating dynamic work cultures, systemic transformations, and blending passion for mission with innovative, high-quality business models. Sarah has designed programs and led trainings for local, national and international audiences, including groups in Canada and Botswana. Driven by the belief that life is too short to just show up every day, she strives to create a world that we are excited to live in and be a part of.

To view additional Lunch with Docs™ faculty and guest speakers.

RESEARCH AND BEST PRACTICES BASIS OF PROGRAM

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P35.04

Rural & regional Australia: The case for specialist Parkinson's nurse services

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Approximately 28% of Australians currently reside outside of major cities and this number is expected to increase (Australian Bureau of Statistics, 2017). However, 93% of neurologists are located in major cities. Consequently, access to specialist services for people with Parkinson's disease living in rural and regional Australia is extremely limited. There is no national approach to ensure equitable access to neurologist and specialist nursing services for people with Parkinson's disease (PD). This absence of a consistent approach to ensuring integrated specialist nursing services is especially apparent in regional and rural areas. Health related quality of life is worse in these areas, while management of PD is poorer when contrasted with that of people in urban areas.
Parkinson's NSW partnered with nursing researchers from Charles Sturt University to undertake a staged project to build the case for the implementation of sustainable specialist Parkinson's nurse services in rural and regional Australia.
Stage one utilised a four-stage integrative framework to guide an extensive literature review to identify evidence-based models of care specifically focused on the role of the community-based specialist neurological nurse caring for people with PD. Stage two employed a two-site case study design to investigate and contrast the impact of two models of specialist nursing care that are currently funded by Parkinson's NSW. Interviews were conducted with people with PD, carers, health professionals and the two nurses. Yin's 5-phases guided the qualitative analysis of the interview data with the findings from the literature review informing the interpretation of the data.
This presentation will provide a snapshot of stage one and report on the findings from the qualitative component of the two-site case study. Consumers and carers at both sites were unanimous in describing the positive impact of the specialist nurse position. However, the rigorous analysis informed by the literature review demonstrated the specific benefits of one model over the other. These research findings have relevance to both the wider Australian context and countries with similar geographical challenges. They are being utilised by Parkinson's NSW to advocate for the implementation of specialist Parkinson's nurse positions in underserved rural and regional locations.

P35.05

A closer look at the unmet needs, research and care priorities for women with Parkinson's

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Objective: Women and Parkinson's Teams to Advance Learning and Knowledge (Women and PD TALK) created the first patient-centered research agenda focusing on the unmet research and care needs of women with Parkinson's. The purpose of the agenda is to increase research that addresses women's needs and guide women with PD and medical professionals to make better-informed healthcare decisions.
Background: Parkinson's disease (PD) affects an estimated seven to 10 million men and women worldwide. However, research indicates that women with PD experience differences in risk, reported symptoms, medication side effects, and access to care.
Methods: Ten regional forum sites were hosted across the United States to collect unmet needs and research priorities for women with Parkinson's as it related to their perceived risk, symptoms, treatment and care. Forum participants consisted of women with Parkinson's, care partners and health professionals. Through convenience sampling, regional team leaders recruited a range of 25 to 53 registered participants to attend each forum. Breakout sessions were facilitated at each forum using scripted questions. In total, 243 women with Parkinson's and 174 care partners and health professionals shared their insights. Breakout sessions were audio recorded and analyzed through thematic analysis. In addition, seven of the ten regional forums used a topic questionnaire, in which the data were analyzed through frequency distributions.
Results/Outcomes: Forum participants reported several observational differences between men's and women's experiences with PD. Participants (irrespective of gender or PD status) most frequently reported: the role of hormones on the development and severity of PD, decreased activities of daily living, embarrassment about the visibility of PD, treatment complications and cultural norms not prioritizing women with PD (each with a frequency > or = 80%). Women with Parkinson's were significantly more likely to discuss impact on identity ($p<0.05$) and personality ($p<0.05$), medication side effects ($p<0.05$) and poor communication with

providers at diagnosis ($p<0.05$) than care partners and health professionals.
Conclusions: The Women and PD TALK project has created and is disseminating a research agenda to ensure better outcomes and improve the standard of care for women with Parkinson's while also educating and empowering women to advocate for themselves.

P35.06

Educational and outreach interventions to address neuropsychiatric issues in Parkinson's disease
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Objective: Neuropsychiatric issues are frequent and impact quality of life, relationships, and outcomes in Parkinson's disease (PD). Despite their importance, people with PD experiencing neuropsychiatric issues are under-served as these symptoms are frequently under-diagnosed, under-discussed, and under-treated. To address these gaps, we developed an innovative educational and discussion/support group series on neuropsychiatric issues in PD with live and virtual platforms. Our objective was to increase awareness of neuropsychiatric issues and examine changes in knowledge regarding symptoms and team management after educational intervention.
Methods: We hosted 8 educational and discussion/support group sessions on neuropsychiatric symptoms in PD, devoting each session to an individual topic. Sessions were led using a team approach with combinations of movement disorders neurology, physician assistant, nurse, social worker, neuropsychologist, and local/national guest speakers. Four sessions were in-person; four were web-based. We analyzed knowledge and experiential survey results (Likert) completed by participants before and after the educational intervention.
Results: Fifty-seven participants participated (n=34 PD, n=23 caregiver) in the series. Of these, 6% had PD diagnosed <1 year, 29% with PD duration of 1–5 years, 32% for 6–10 year, 23.5% for 11–15 years and 8.8@ for over 15 years. Pre-session knowledge was lacking in both people with PD and caregivers as about 60–87% of participants reported "average or below" knowledge on cognitive, behavioral, emotional issues of PD as well as who are allied health professionals, what they do, and who is on their PD care team. After the educational series, PD and caregivers alike improved significantly in knowledge with 70–100% now reporting "very high or above average." Comments were positive about both formats, though some had difficulty with technology and others with travel. Sessions were well received regarding content, format, and delivery.
Conclusions: Educational and discussion/support group interventions effectively increase awareness about neuropsychiatric issues and improve knowledge gaps in the PD community. Different presentation modalities may be better suited to certain audiences. However, regardless of format, education and discussions can help educate the PD community on neuropsychiatric issues, reduce stigma and fear, and increased important communications between patient and doctor and patient and caregiver.
Supported by Parkinson's Foundation Community Grant

P35.07

Use of a hybrid telehealth visiting nurse clinic to support the use of device assisted therapies for Parkinson's disease in a large rural and remote North Queensland area. A feasibility and a patient perception observational study
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The population of Queensland has a large non-urban distribution compared to the other Australian states and territories; by 2020, 20% of this population will be over 65. The Modified Monash Model criteria (MMM) provide a health economics model of healthcare access and places most of this group outside of well-developed MMM 1 regions with comprehensive health care. Australian government neurology workforce statistics from 2016 indicate that only 5.7% of neurologist work outside of MMM 1 areas. Observe PD suggested that a third of eligible patients do not have access to device assisted therapy. Australian practice is biased towards DBS, but in Queensland the tyranny of distance over a vast geography and geographic restriction of DBS to Brisbane centres limits state-wide equity of access to this and other advanced therapies.
Tele-neurology is a well-established Australian practice but does not provide a comprehensive solution for complex neurological patients with medical devices, such as apomorphine and LCIJ pumps whose care and adjustment requires a physical presence. The validation of routine Tele-Parkinson's clinics is incomplete, and it is possible some domains of Parkinson's disability such as non-motor symptoms may be underappreciated with remote patient medical service provider interaction.
We will present prospective observational data on a cohort of patients with PD attending a visiting PD nurse led clinic in which the neurologist is also present through a telehealth connection. We will provide data on patient demographics, and clinical features such as device assisted therapies in MMM 2–4 areas. We will present data to support the feasibility of supporting device assisted therapy for PD with this hybrid model, and patient satisfaction.

COMPREHENSIVE CARE: Daily life activities including working & driving

P36.01

A day in the life of...
*Clare Lindley**
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Aims: To present a poster discussing the impact of Parkinson's disease on young people.
A day in the life of a young person with Parkinson's disease- The daily struggles we endure, our determination to succeed and the continual quest for understanding not sympathy. It will include stories from the heart. Some will be light-hearted but all the stories will be real. It will capture the implications this disease has on the younger generation, working, family life and all the normal day to day tasks involved with living! This will give reassurance and guidance to others who are newly diagnosed. Promoting the notion that it's not all doom and gloom and despite the struggles we endure WE have the ability to take control. We can live our life to the best of our ability, whilst making some adjustments along the way.
10 years in, I was diagnosed with Parkinson's disease age 30. I am a nurse a passionate parkie advocate, who is proud of my journey and the things I have achieved. With ups and downs along the way the only thing that's certain is PD is here to stay! Let's celebrate our success even though it's a rocky road.
Outcome and objectives: Increase knowledge and understanding around the area of young onset Parkinson's diseases. Achieving this by presenting real life stories to raise awareness and abolish the myth that this condition only affects the older generation. To share stories that engage with the wider community, make people stop and think and ultimately change people's perception on the condition.

P36.02

Action imagery and observation in neurorehabilitation for Parkinson's disease (ACTION-PD): A pilot RCT of a home-based intervention to improve functional actions

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Objectives: Parkinson's can significantly affect manual dexterity, impacting on activities of daily living (ADL). We conducted a pilot randomized controlled trial (RCT) of ACTION-PD, which allows individuals to train everyday hand actions at home, using a tablet-based app. The intervention was developed with patient and clinician input and combines action observation and motor imagery, which have been shown to improve movement amplitude in people with Parkinson's in the lab. We aimed to assess feasibility and acceptability, and to collect preliminary outcome data, to inform a larger-scale study.
Methods: Participants with mild to moderate Parkinson's were randomized to the intervention (N=6) or control (N=4) group. Training consisted of video-based observation, imagery and physical practice of 5 functional manual actions (e.g., fastening buttons): "core actions" and 3 "personal actions" selected by the individual. Participants trained at home using the tablet PC app in a seated position, with a target training time of 120 minutes per week for 6 weeks (e.g., 30 minutes x 4 days or 20 minutes x 6 days), with telephone support from the researchers. Controls received a weekly telephone call to maintain contact. Participants completed pre and post questionnaires and lab-based assessments (including trained and untrained personal actions), and the intervention group were interviewed about their experiences.
Results: Post-training interviews indicated that the training schedule was acceptable and the app was usable. Participants reported greater awareness of motor imagery, but wanted the option to select different actions for training (e.g. more or less challenging). Preliminary outcome data indicated an 11.3% improvement in self-reported dexterity (DextQ-24) in the intervention group, compared to 9.8% decline in controls. The intervention group showed reduced difficulty ratings for trained personal (34.7%) and core (45.9%) actions, as well as untrained personal actions (22.1%), while controls showed increased difficulty for personal (6.8%) and core (7.0%) actions.
Conclusions: This study indicates that this home-based intervention is acceptable to participants and an RCT is feasible. Preliminary outcomes are also promising, with numerical improvements in self-reported dexterity (the primary outcome). Participants' experiences indicate that the intervention would benefit from a greater choice of actions and feedback.

P36.03

Falls during neurorehabilitation and beyond in people with Parkinson's disease

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Objectives: To understand which patients with Parkinson's disease (PwPD) fall during and after neurorehabilitation by investigating:
a) falls during neurorehabilitation
b) falls thereafter
c) severity of injuries.

Methods: All falls occurring in PwPD in our clinic during 2017 were analyzed retrospectively according to:
a) Barthel ADL index (BI)
b) Short Orientation and Memory Concentration Task (SOMCT)
c) age
d) gender
e) Hoehn & Yahr stages
f) number of falls
g) severity of injuries.

All PwPD were contacted by written questionnaire at least 10 months after in-patient neurorehabilitation to investigate their history of falling post neurorehabilitation.
Results: Of the 145 in-patients 18 fell during neurorehabilitation (=12.4%). The fallers presented as follows:
a) BI: mean 71, range 35–100
b) SOMCT: mean: 9.5, range 2–22
c) age: mean: 73, range 58–82
d) gender: 13m, 5f
e) Hoehn & Yahr stage with most falls: 12 patients between 3–4
f) number of falls: 12 patients with 1 fall each, 4 with 2 falls each, 2 with 3 falls each
g) severity of injury: all with no or minor injury.

Of the 145 questionnaires 105 were returned (72.4%). Out of 105 PwPD 42 fell within the first 10months post neurorehabilitation (=40%) with 8 of them already having had falls during neurorehabilitation. The fallers presented as follows:
a) BI at the time of discharge from neurorehabilitation: mean 85, range 55–100
b) SOMCT at the time of discharge: mean: 4.7, range 0–15
c) age: mean: 73, range 47–87
d) gender: 24m, 18f
e) Hoehn & Yahr stage with most falls: 11 at stage 3 and 11 between 3–4
f) number of falls: 11 patients with 1 fall each, 4 with 2 falls each, 27 with >2 falls each
g) severity of injury: 34 with no or minor injury, 8 with severe injury
h) location of fall: 22 at home, 12 at home and external, 8 external.

Conclusion: Extensive interdisciplinary efforts during in-patient neurorehabilitation seemed to have a positive effect on rate of falling and severity of injury. In our clinic every PwPD received tips and instructions on how to avoid falls and/or prevent serious injury. Nevertheless, 40% fell post neurorehabilitation, calling for additional efforts having to go into fall prevention, especially in the own home, as well as injury reduction, particularly as PD is a progressive degenerative disease.

COMPREHENSIVE CARE: Self-management, empowerment, coping strategies

P37.01

Mindfulness based stress reduction in Parkinson's disease

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Background: Parkinson's disease (PD) is a neurodegenerative disorder with no cure that affects approximately 1 million people in the US. PD patients suffer from motor and non-motor symptoms,

including disrupted sleep, pain, cognitive changes, and fatigue. These are known to significantly affect quality of life and can be difficult to treat.
Mindfulness involves "the awareness that emerges through paying attention on purpose, in the present moment, and nonjudgmentally to the unfolding of experience... [1]" Mindful practice may be beneficial in coping with psychological and physical conditions related to brain function, including depression, anxiety, and chronic pain [2]. Mindfulness meditation may also slow disease progression and improve quality of life in heart disease [3] and cancer [4]. A connection between mindfulness and PD has not yet been explored, though benefits in patients with chronic disease suggest that it may be a novel intervention for patients living with PD.
Objectives: We aim to determine the impact of Mindfulness Based Stress Reduction (MBSR) on specific, clinically meaningful endpoints in patients with Parkinson's disease.
Methods: We collaborated with Duke Integrative Medicine to create a MBSR course for individuals with PD. 15 Duke patients completed the study. Selection criteria included: 1) Hoehn & Yahr stage <2.5, 2) MOCA score of = 26, 3) willingness and ability to complete training, and 4) no recent mental health crises. Participants completed quality of life surveys and a qualitative interview prior to, just following, and three months following course completion. The UPDRS was completed in the pre and post assessments. This study design was approved by the Duke University Health System IRB. Financial support was provided by the Parkinson's Foundation.
Results: Study activities have been completed and data has been collected. Data analysis is pending at this time.
Conclusions: Once analyzed, the collected data may support MBSR as a valid, non-pharmacological intervention that improves quality of life for people with Parkinson's disease.
[1] Clin Psych: Sci Prac 2003; 10, 144–156.
[2] Psychophys 2016; 53:1366–76.
[3] Lancet 1990; 336:129–33.
[4] J Urol 2005; 174:1065–9.

P37.02

Life does not end where a diagnosis starts: Entraidons-nous (let us help each other)
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Entraidons-nous is a not for profit Canadian organization constituted of people afflicted, directly or indirectly, with a neurological disease. Its principal actors have all received the diagnosis of Young Onset Parkinson's. Together, they manage to retain their balance ("Team Funambulists").
Chantal, Linda, Nadia and François have more in common than a diagnosis.

- They feel empowered to keep going, individually and collectively.
- They have the will to confront the challenges that life put across their paths.
- By trial and experience, they are learning how to make their choices right.

Staying active is one of the messages that they keep repeating. Furthermore, it is a great opportunity to wonderful encounters. Socio-therapy is, as they say, a key element in staying stable.
A healthy mind in a strong body. True. Moreover a stable body in a steady mind is as imperative. Going from the dark cloud to the colorful arc is not painless, but achievable.
Neurologists prescribe physical activity. Not only do they keep propagating this recommendation, they support it by showing the example. François received much attention in Quebec during the summer of 2018 by traveling the province on his bicycle. In three weeks he pedaled over 2200 km and, accompanied by his Entraidons-nous partners, met with Quebecer's all across and spread the message that life does not end where a diagnosis starts. Benefiting significant media attention, they engaged to give explanations about this "unknown" malady and demystify existing myths. Having Parkinson's disease at 40 is not frequent but it does exist
Depression, isolation, abandonment, separation, double diagnosis, withdrawal from their careers, our 4 Funambulists do not hesitate to share their stories. On their web site they make available different resources intended for their well-being. Messages of inspiration are much published too.
Masterminds of this social aid movement across the Parkinson community of Quebec, their hope is to bring together people who have received all forms of diagnosis, from inception to mortality, and beyond their provincial borders
Let us help each other, together. This is what Entraidons-nous is… and much more
Because life does not end where a diagnosis starts.

P37.03

Impact of a self-efficacy enhancing program for recently diagnosed persons with Parkinson's disease and their care partners
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The Parkinson's Self-Efficacy Learning Forum (PD SELF) program was initially developed in 2013 as a clinical trial and has expanded to serve more than 17 communities across the United States over the last five years. PD SELF is designed to assist recently diagnosed individuals and their care partners use self-efficacy principles to adopt the healthcare behaviors that positively influence effective disease management and quality of life (QoL). Participants attend eight monthly 3-hour highly interactive sessions designed to teach and reinforce self-efficacy behaviors through a standardized curriculum led by two trained lay facilitators (one with PD) in each city. 590 persons with PD (PWP) and 382 care partners have

participated in the program. Research has been conducted with each cohort.
Results of QoL assessments across five data collection periods have been remarkably similar, suggesting that the integrity of the curriculum has been maintained at each site. Results of the most recent assessment for PWPs indicate that the total self-efficacy score improved statistically from baseline to post-course evaluation (P<.001) along with the total score assessing psychosocial functioning (P<.01). The total self-efficacy score for care partners also improved (P<.001) along with the QoL score (P<.01), which is remarkable since the curriculum is primarily directed at strengthening the self-efficacy of PWP's. A longitudinal study of the original group showed psychosocial functioning continued to improve at 4-year follow-up despite declining health.
Anecdotal results that have been observed over time are equally impressive:

- Nine participants have become group leaders in succeeding years
- A number of cohorts continue to meet after the program ends
- Participants are motivated to participate in clinical trials and become advocates for research
- Participants become role models for others with PD
- Social support for one another continues after program completion
- 125 individuals applied to be leaders of the program for the current year
- There is a waiting list in many communities for the next program cycle

PD SELF appears to be effective in assisting recently diagnosed PWPs and care partners increase self-efficacy and improve QoL Results also appear to be consistent across groups.

P37.04

Online support groups: Building a sense of community across British Columbia

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Motivation: Statistics published from the Ministry of Health in 2014/2015, show there are over 13,300 British Columbians living with Parkinson's disease, a number that is expected to double by 2040 (Dorsey & Bloem, 2018). Problem Statement: With the increasing number of patients diagnosed with Parkinson's, greater pressure is placed on the limited number of movement disorder specialists in British Columbia. The lack of available healthcare resources results in longer waitlists, leaving more patients without adequate care or access to educational resources. Methodology: In a 2017 survey, Parkinson Society British Columbia (PSBC) was ranked the number one resource for education and support on Parkinson's. PSBC's in-person support groups were ranked top four most valuable offered services. While our support groups are located throughout BC, not everyone has the ability and accessibility to these in-person groups. Results: In late 2016, PSBC started its first online support group, the Online YOPD Support Group. This came out of a need directly shared from our YOPD constituents in an evaluation form. Due to the latter's success, PSBC decided to create another online support group specifically for carepartners. This was the start of the first Online Carepartners Support Group, which has run every month since September 2017. Conclusion/Implication: These virtual groups provide our subpopulations (i.e., people with YOPD and carepartners) living across BC to come together on a monthly basis to connect and exchange valuable information. Online support groups allow us to reach a wider breadth of our Parkinson's population. They allow us to serve those in remote communities with limited resources, those with mobility and transportation concerns, as well as those who aren't able to leave their loved one with Parkinson's alone.

P37.05

Impact of nurse navigation on Parkinson's disease community wellness

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Objective: There is a great need to provide people with Parkinson disease (PD) not only quality medical care, but social support and disease-related resources, education, and management. High-quality nursing professionals knowledgeable about the disease and its unique characteristics are essential to the successful management of people with PD. The purpose of this project is to develop a nurse navigation program at an established Parkinson-specific community wellness center and evaluate its effect on quality of life and self-efficacy for managing chronic disease among people living with PD. This program works towards empowering participants to play an active role in their healthcare and aims to enhance communication between the wellness center and medical professionals.
Methods: Twenty-four members of a PD wellness center in Phoenix, Arizona were recruited to participate in the new nurse navigation program for a 12-week period. The intervention period, conducted by a nurse navigator, includes an initial visit and needs assessment, ten individualized visits focused on specific aspects of PD wellness, and a concluding visit. Individual weekly visits consist of 45-minutes with a nurse navigator for each participant and include discussion of various topics such as individualized PD specific education, advanced directive assistance, hospital preparedness, and medication review. Weekly visits with the nurse navigator ensure individual needs are addressed and communicated with healthcare providers.
Results: The intervention period for this study is currently underway and will conclude on December 7, 2018. To evaluate outcomes of nurse navigation in the target population, the Parkinson Disease Questionnaire-39 (PDQ-39) will be used to evaluate quality of life (QoL) and the Self-Efficacy for Managing Chronic Disease 6-item scale will be used to evaluated self-efficacy for managing chronic disease in study participants. Healthcare team feedback and system outcomes will be measured by utilization of an individualized satisfaction survey and communication log. Data analysis, project reports, dissemination, and a sustainability plan will all be completed from January through April 2019.
Funding: PF-NFA-1804, Parkinson Foundation

P37.06

Poised for Parkinson's: Group classes in Alexander technique for managing symptoms of Parkinson's disease

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[6] The Poise Project, Charlotte, NC, USA

Objective: To develop and test a group course using Alexander technique (AT) principles to improve functional mobility and quality of life for people living with Parkinson's disease (PlwPD).
Background: AT is an embodied mindfulness approach that aims to transform disruptive reactions to stress into adaptive responses, enhancing moment-to-moment performance of daily activities while improving confidence and reducing anxiety. Previous studies have demonstrated that private AT sessions can reduce motor symptoms and improve mood in PlwPD.
Design: We are delivering an adapted Alexander technique program in three cities in North Carolina (USA) to provide group instruction for 75 minutes, twice a week, for 8 weeks. We aim to recruit 36 PlwPD and care partners in total. Two-thirds of these will be allocated to a waitlist group, and will later participate in courses themselves.
Intervention: Coursework includes functional anatomy and self-management strategies, taught through verbal instructions and hands-on guidance for both PlwPD and their care partners. We aim to minimize physical symptoms such as stooped posture, bradykinesia, freezing, and speech impairments. Our strategy is to embed Alexander technique principles into real-life activities that PlwPD often practice in rehabilitation settings, such as balance and functional IADLs. A unique feature of our program is that all activities are prefaced with strategic thoughts and verbal prompts to inhibit disruptive automatic reactions PlwPD often exhibit on initiating and sustaining movement. These self-regulatory strategies, while neurologically sophisticated, are presented simply enough for both PlwPD and their care partners to be able to easily reinforce them in real-life daily circumstances. Therefore a unique aspect of this approach is that the PlwPD does not need to set time aside to practice skills, but rather incorporates them throughout their day.
Outcome measures: Results will be available from the multisite study in May 2019. We will assess balance (Brief BESTest), functional mobility (7-point Physical Performance Test), and mood (subjective surveys).
Conclusion: AT shows promise as a long-term self-management approach to reduce PD motor and non-motor symptoms, helping PlwPD to maintain an active lifestyle, and easing care partner burden. Group classes have the potential to provide cost-effective delivery with additional social benefits.
Funding: Parkinson's Foundation (USA)

P37.07

Improving self-management and management of daily life for people with Parkinson's disease through an educational intervention – the Swedish National Parkinson School (NPS)

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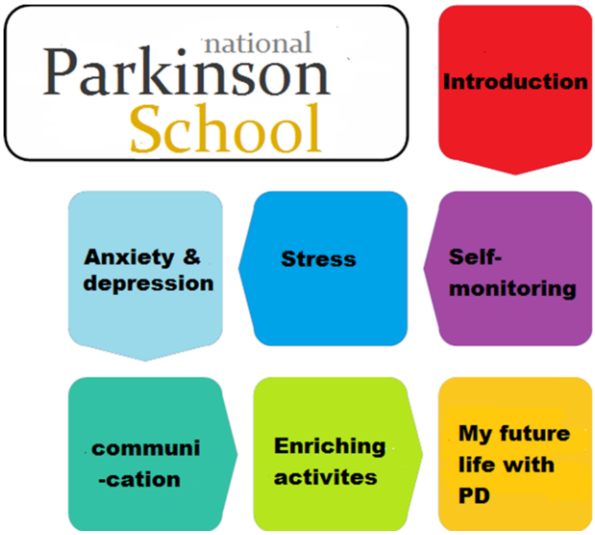
Despite availability of effective symptomatic therapy, Parkinson's disease (PD) has an increasingly negative impact on the lives of people living with the condition. As the disease progresses, fluctuating motor as well as non-motor symptoms affect daily functioning and satisfaction in life. There is a need for interventions that go beyond the traditional medical paradigm to provide adequate care and support. The National Parkinson School (NPS) is a Swedish self-management program aiming to improve the ability of persons with PD to manage daily life and thereby increase life satisfaction. The NPS is organized as seven weekly 2-hour thematic sessions (introduction to PD and medication, anxiety and depression, stress, self-monitoring, communication, enriching activities, and future life with PD). In between sessions participants apply and practice the new knowledge gained in their own every-day life through home assignments.
The objective of this study was to assess outcomes of the NPS program from the perspective of persons with PD.
Data from 48 persons with PD (29 women; median (min-max) age, 71 (52–83) years; PD duration, 5 (0.5–15) years; Hoehn & Yahr stage, III (I-IV)) from five outpatient clinics providing the NPS were included in these interim analyses. Pre- and post-intervention data were collected before the first and after the last NPS session, and included the health education questionnaire (heiQ; an outcome measure developed specifically for self-management programs), experience-based health valuation (EQ5D), PD related health problems (PDQ-8), fatigue (PFS), and life satisfaction (LiSat). Data were analyzed using the Wilcoxon signed-ranks test.
There were significant improvements in "Skills and Technique Acquisition" (heiQ; $p<0.001$), "Constructive Attitudes and Approaches" (heiQ; $p=0.002$), experience-based health valuations (EQ5D; $p=0.021$), and PD related health problems (PDQ-8; $p=0.027$). Other outcomes showed non-significant trends towards improvements.
In conclusion, these preliminary data show promising results in that the self-management program NPS is beneficial for participants' well-being and improving skills in handling daily life.



P37.08

'Mind the gap' – A scoping review of long term, physical, self-management in Parkinson's

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Abstract/Structured summary
Background: Parkinson's is a common progressive neurological condition characterised by impairments of movement and balance; and non-motor deficits. It has long been accepted that physical activity is a fundamental component of management for people with Parkinson's (PwP), despite this PwP remain inactive. There is a social and financial drive to increase physical activity for PwP through physical self-management, however little is known about this concept.
Objective: This scoping review aims to is to provide an overview of the literature concerning the apparent 'gap' between the robust evidence base to promote long-term physical activity for PwP and its provision, participation and uptake through physical self-management.
Design and sources of evidence: A systematic search of the databases; Medline, EMBASE, HMIC, CDSR, Cochrane Methods Studies, DARE, CINAHL, PEDro, PsycINFO and Cochrane Library using the search terms 'Parkinson*' and 'self-manag*' was undertaken as well as citation and grey literature searching and a consultation exercise with key stakeholders.
Charting methods: A narrative summary was then undertaken to describe the current state of the literature.
Results: A total of 1959 studies were identified with nineteen papers from seventeen studies meeting the inclusion criteria – Three reviews, four experimental studies, three pre-post test designs, six cross-sectional designs, one qualitative interview design and two mixed method designs
Conclusion: The findings of this scoping review suggest there is a need for clarity on what 'physical self-management' means and involves, with a gap between what the evidence promotes and what is being achieved by PwP. Further research should focus on the amount, type, intensity and duration of physical self-management models including behavioural change approaches and how, where and by whom this should be implemented.

P37.09

In Sync! Comprehensive support group network: Support group in a box

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Many people impacted by PD rely heavily on support groups and peers for support, socialization, tips and assistance. Most support groups are led by people with movement disorders or their care partners. They dedicate their time and energy over multiple years as volunteer leaders. Yet while they support so many others, they seldom receive the support they need. To address this need, PMDAlliance developed the In Sync!® Support Group Leader program, now in its fourth year.
We receive an average of 2–3 inquiries per month for assistance in starting a support group. With limited understanding of how to start, grow and sustain a group, the leaders are often untrained and isolated. This multifaceted program arms group leader with information needed to maintain a robust, connected and informed group.
PMDAlliance provides 2 tools to new and existing support group leaders as a part of its In Sync!® program: 1) In Sync!® Livestream Education & Networking Roundtables; and 2) Support Group in a Box® toolkit with 6 hours of web-based training included. These tools are available at no charge to anyone interested in starting a group, new leaders, and established leaders. All attendees at WPC are able to sign up for these two tools and will be informed about when a live In Sync! Conference will be available near them.
Support Group in a Box® offers resources to start, market, maintain and sustain a group. Particular attention is given to the needs of rural and smaller communities that are often without adequate resources. It is an excellent toolkit for new groups, as well as support groups that have been in existence for a long period of time. By ensuring each group has a solid foundation and utilizes support group best practices, PMDAlliance is able to help ensure groups grow and sustain, even when group leaders change.
In Sync!® Quarterly Roundtables provide an opportunity for PMDAlliance to educate leaders about medications, treatments and up-to-date information resources available to them. Roundtables also offer live-streaming conversations with MDS physicians, social workers, PTs, OTs, SLPs and other relevant professionals.

P37.10

Patient-centered care for people with Parkinson's disease in the context of a navigator program

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Backgrounds: People with Parkinson's disease (PwP) have various care needs in terms of self-management for clinical symptoms as well as psychological issues. Health care professionals should understand needs of PwP, and health care interventions must be provided with respect to individual characteristics such as motor and non-motor symptoms. Therefore, a systematic approach is required for PwP. The navigator program is expected to meet the Parkinson's disease-specific needs providing systematic and continuous care.
Objectives: To provide guidance for navigator program development and to suggest the evidence concerning navigator program for PwP in terms of acceptability and benefits on critical outcomes such as quality of life and continuum of care.

Approach: Development of the navigator program is recommended to start with careful design of preliminary program based on Professional Navigation Framework (Fillion et al., 2009). Also, there is need for a delphi method to verify content validity of the program.
Results: Navigator program for PwP may include contents such as living with Parkinson's disease (PD), planning future life with PD, symptoms and management of PD and environmental management of PD. It is tailored to patient across the health trajectory. Navigator program will be guided by primary health care professionals, providing advanced knowledge of information such as self-management, empowerment, coping strategies and supporting resources as well as social support.
Discussions and implications: Navigator program is a program that goes beyond the traditional care coordination or case managing program. Furthermore, navigator program improves access of health care services as well as heightening efficiency and sustainability of care. With this program, comprehensive management will be acquired by continuity of information and relationship with health care professionals. This program is expected to be the cornerstone of the health care services which ensures the continuum of care for PwP. Future health models will go in a direction with personal and participatory attributes so that navigator program for PwP will be very appropriate and evolving health care program.

P37.11

Living with Parkinson's. Support Groups. Don't feel so lonely. A look at the team of people required to live well with Parkinson's
*Ian McFarlane**
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It can seem lonely with Parkinson's. There have been numerous times that I have rung Parkinson's Victoria, complaining to Victor that "I feel so lonely. Who can I talk to? Where can I get help?"
But, you do not have to be lonely. There are many support groups and people who can help you. My experiences may help you to find some of them as follow.
Key support people:
-Neurologist. A general neurologist may be the person who diagnoses you. It is common for patient's to change neurologist to a Movement Disorder (Parkinson's) Neurologist or simply to one that meets your personal needs and preferences better. You will probably only see your neurologist 2 or 3 times per year.
-General Practitioner. Generally the Doctor who refers you onto a Neurologist for diagnosis. If you believe something is wrong then do not be afraid to push for a referral. I was seeing a GP for a year because I believed something was not right. As I could still run 10K they told me to go away. I went to another GP who did not think that I had Parkinson's but referred me to a Neurologist. I was diagnosed first visit to the Neurologist as having Parkinson's. A second Neurologist confirmed it. My GP told me later that she had not had a Parkinson's client on her books for 10 years!
Why use other support people/groups?
You can learn off of each other? Help those newly diagnosed? Ask for assistance. Listen and learn from others. This makes many communities with a common cause or association. Trained expertise can also help you achieve a positive outcome in a timely manner.
Other support people/groups that I have used:
- Physiotherapist
- Movement disorder program
- Incontinence nurse
- Rehabilitation Hospital
- Dietician
- Exercise physiologist
- Myotherapist
- Parkinson's Victoria
- Parkinson's nurse
- Young at Parkinson Group (those still working)
- Parkinson's specific Facebook groups
- Gym staff
- Sports (running) coaches
- Family
- Researchers/Clinical trials/information sessions
- Colleagues

Conclusion: You do not have to feel lonely.

P37.12

Parkinson's smell levels, symptom management and empowerment: When Joy met Alison
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Background: The smell of Parkinson's can make early diagnosis possible (Trivedi et al 2018). Joy Milne, the Trivedi paper's 'Super Smeller', detected changes in her husband's odour 12 years before his Parkinson's diagnosis. Subsequent research determined the smell was dominant in sebum rich areas, and mass spectrometry based metabolomics identified putative volatile organic compounds (VOCs) involved. The Trivedi paper concludes that these VOCs could serve as potential diagnostic biomarkers. Joy also realised she could detect 5 different levels of Parkinson's, rising in severity from level one (very low) to five (extreme).
Significance for one PwP: Alison Williams (PwP from Edinburgh) met Joy Milne in March 2016. We describe how Joy detected changes in Alison's Parkinson's smell over two years. Counter to the expected course of Parkinson's, the smell decreased from level 3 at their first meeting, to level 1 at their next in autumn 2017. Alison's physical and mental revival has been marked, and subsequently maintained to date (November 2018) with a continuing smell level 1.
We track Alison's smell level reduction over time, quoting email and face-to-face conversation, setting the reduction against lifestyle changes made over the same time period. We particularly examine amount and types of exercise undertaken prior and subsequent to each assessment, and refer to changes in medication.
We have, importantly, found that the smell is lessened if symptoms are well managed.
The psychological impact on Alison of knowing her smell level has decreased is described, noting the increased resilience (physical, mental and emotional) needed to maintain the lifestyle changes, and take responsibility for her own wellbeing. We describe the impact on Alison's partner, family, friends and colleagues.
Joy observes strict ethical guidelines, never revealing what she smells unless asked. Joy and Alison's growing personal trust allowed the question to be asked: "Can you smell me?"
Implications for the future: The Trivedi paper concludes that this work, extending sebum biomarkers beyond diagnosis, may "open new avenues of stratification" (Trivedi et al 2018:7). We welcome the potential for, among other benefits, enhanced symptom management, empowerment, and accurate assessments of interventional impact.

P37.13

Parkinson's care (coping, advocating, relating and engaging): A small group self-management educational and support group pilot program

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Objective: Many people diagnosed with Parkinson's lack the knowledge, skills and social support critical to managing Parkinson's disease (PD) impacting quality of life. While online educational resources are widely available, they lack the supportive component. Conversely, support group meetings offer needed support but may lack clearly defined education and self-management skill development. Self-management programs for other chronic diseases have been shown to help people cultivate skills to live well with their condition, however, there are limited programs available for Parkinson's patients. Parkinson CARE seeks to address these needs.
Method: Parkinson CARE pilot program offers patients a five-module small group education and support group. There were (n=11) participants in this ongoing initial pilot. Education modules cover disease education and self-management skills. Additionally, psychosocial topics are addressed through presentation, discussion, and exercises utilizing cognitive behavioral therapy approach addressing coping with the diagnosis, relationship issues, communication, intimacy, goal setting, social support, self-advocating and participation in research. Individual sessions with a clinical social worker are offered as well as connection to ongoing support programs. Participants are asked to complete a pre-class questionnaire and survey, a post-class survey, follow-up survey and questionnaire at three and six-months.
Results: Parkinson CARE pilot program sample included eleven people in two separate groups (n=7 class I and n=4 class II). All eleven attendees reported seeing a general neurologist, with none reporting ever having seen a movement disorder specialist. 36% (n=4) reported feeling their physician provided them with adequate information about the disease. 100% participants reported in post-class surveys (n=10 completed) the class provided beneficial disease education and increased their understanding of how to self-manage. However, few reported an improvement in their perceived ability to communicate with their physician. Improvements were noted through follow-up surveys in participants feeling empowered to manage their disease with 100% reporting engagement in support programs and exercise classes. Though results offer limited qualitative feedback as only one class at the time of this abstract has completed both the three and six-month follow-up surveys and questionnaires, the initial feedback supports ongoing analysis of the benefit of small group self-management education and support classes.

P37.14

Providing education and support for newly diagnosed patients and families in the community

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Evidence suggests that individuals with Parkinson's disease (PD) are dissatisfied with information received about their condition at diagnosis (Schrag 2018). This can adversely affect health related quality of life (GPDS Steering Committee). Combined with the complexity of a chronic progressive condition, this warrants the development and implementation of education and support programs in the community – early following diagnosis. This abstract describes two different programs introduced in Massachusetts. The "Parkinson Good Start Program" is a 2-part series developed by a team of PD specialists from Boston University Medical Center and Boston University. The target audience includes individuals newly diagnosed with PD and their family members. Participants receive up-to-date information on the diagnostic process, motor and non-motor signs, pharmacological and rehabilitative treatments. The evidence supporting the benefits of exercise is presented with recommendations on how to get started. The program is person-centered and emphasizes a secondary prevention, self-management approach. Participants are encouraged to establish their healthcare team early. A panel representing "team members" including a rehabilitation nurse, physical therapist, occupational therapist, speech therapist, dietician and social worker discuss how they collaborate with people with PD to help them live well. Participants voice common concerns, addressed by the panel. Community resources are provided to assist with managing and coping with PD. Recognizing the psychosocial support needs of an individual following a diagnosis, the American Parkinson Disease Association (APDA) has developed the Parkinson's Roadmap for Education and Support Services (PRESS™). This 8-week, in-person, closed support series was piloted in six communities and has expanded to over 20 sites across the US. This program features tailored content to address the psychosocial needs of persons with early PD and care partners. PRESS™ support groups are facilitated by healthcare professionals trained in group-facilitation and provide a structured setting for people to share their experiences, feelings, and strategies for coping with PD. Together, these programs address unmet needs of newly diagnosed persons with PD. Graded exposure to essential evidence-based content about PD, appropriately tailored psychosocial support and the opportunity to ask questions of experts are central elements needed to increase satisfaction with experiences associated with receiving a diagnosis of PD (Schrag 2018).

P37.15

Applying the extreme sport Art Du Deplacement (ADD)/Parkour into rehabilitation training to increase physical and mental wellbeing people with Parkinson's disease (PDP)

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The purpose of this study was to transfer ADD-training-methods into safe training paradigms for people with PD, and psychologically framed coping strategies for mood management through integrating the ADD therapy via the Esprit Concrete Method and the neuroprotective training through the Neurowerkstatt Method. A growing number of PD exercise studies show, that exercise is beneficial for mobility, strength and cardinal symptoms (1,2). ADD includes numerous physical tasks of motor learning. It improves physical fitness, and mental wellbeing (4,5). ADD can be considered a safe activity when practiced under expert supervision (6). A preliminarily ADD study with PDP reported that acceptance of body impairment was reflected as having changed in the daily livings. PDP underlined the fun factor in doing serious training, reported feeling safe while training, gaining insight into their coping styles and how to better manage these (7). We propose, that a weekly exercise program of an ADD specific group nature when combined with fortnightly 1:1-psychological therapy, is a potentially useful rehabilitationprogram that is beneficial in reducing secondary symptoms, but also for strengthening neuroprotective factors e.g. enriched ones environment and motor skill learning, through intensive exercise training paradigms while safeguarding ones

wellbeing and mental health. To our knowledge this is the first study that combines ADD informed psychological physical therapy as a useful exercise and wellbeing strategy for people with PD.
An 8 (60 min) weekly training session program will combine physical and psychological wellbeing areas of focus, supported by 4 (50Min) psychological support sessions. The questionnaires PDQ39, GAD-7, PHP-9, WSAS pre and post intervention will be used in conjunction with semi-structured pre and post interviews. 4 PDP H&YI-II will be included.
The questionnaires previously produced varied insights. There was a differentiated change in PDQ39 subscales according to PDP-individuals. Anxiety(GAD-7), degree of depression severity(PHP-9), and impaired functioning(WSAS) fluctuated positively in all PDP.
The pilot study preliminarily suggests, that ADD therapy is an exercise possibility for people with mild PD. It has potential to physically improve symptoms and it might optimize reduction in disease progression. It further suggests the potential to improve mental wellbeing though the above outlined study's research is needed to validate the intervention further.

P37.16

A treatment protocol for Parkinson's related fatigue using cognitive behavioral therapy approach

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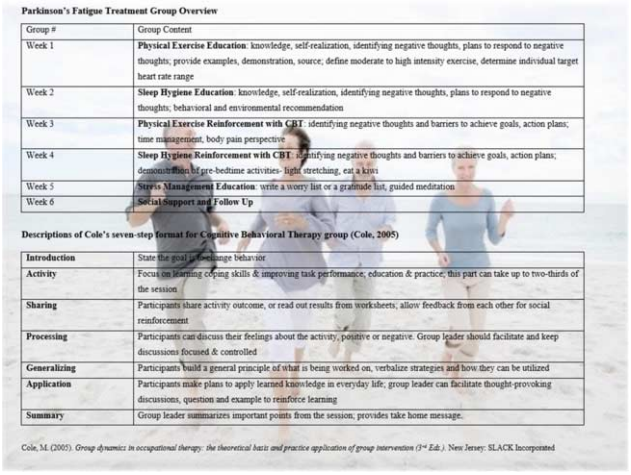
Fatigue affects more than half of people living with Parkinson's disease. Despite its prevalence, treatment options remain limited. To improve quality of life, a group treatment protocol was developed for Parkinson's fatigue management primarily using cognitive behavioral therapy, based on the best available evidence. The program focuses on assisting individuals with Parkinson's disease who experience fatigue to establish proper sleep hygiene habits and a physical exercise routine to meet the end goal of reducing fatigue. Participants are encouraged to perform moderate to high intensity physical exercise at least three times a week. Stress management is also included as a coping skill in this protocol. Participants meet in a group setting because utilization of social support is encouraged to achieve goals.
Cognitive behavioral therapy approach helps individuals change their unhelpful and dysfunctional cognition (thinking) and behavior, into positive and constructive thinking and behavior that leads to an improvement in mood and function. The aim of the treatment group is to change negative thoughts and behavior regarding changing sleep hygiene habits and exercise behavior into positive ones. Participants are trained to develop the skills to be efficient in self problem-solving and self management for their fatigue symptoms.
Cole's 7-step group development process is a seven-step format that incorporates the basic concept of "client centered care and facilitates engagement in occupation to support participation in life", as stated in the Occupational Therapy Practice Framework. The seven steps in group leadership include introduction, activity, sharing, processing, generalizing, application and summary.
Modified Fatigue Scale is the primary outcome measure for the study; sleep quality, sleep hygiene habits, and Parkinson's disease quality of life are also measured. This is an on-going feasibility study that aims to explore the effectiveness and feasibility of this protocol as well as to produce a treatment protocol that is able to be replicated by health professionals who serve the Parkinson's population.



Parkinson's Fatigue Treatment Group Overview

Group #	Group Content
Week 1	**Physical Exercise Education**: knowledge, self-realization, identifying negative thoughts, plans to respond to negative thoughts; provide examples, demonstration, source; define moderate to high intensity exercise, determine individual target heart rate range
Week 2	**Sleep Hygiene Education**: knowledge, self-realization, identifying negative thoughts, plans to respond to negative thoughts; behavioral and environmental recommendation
Week 3	**Physical Exercise Reinforcement with CBT**: identifying negative thoughts and barriers to achieve goals, action plans; time management, body pain perspective
Week 4	**Sleep Hygiene Reinforcement with CBT**: identifying negative thoughts and barriers to achieve goals, action plans; demonstration of pre-bedtime activities- light stretching, eat a kiwi
Week 5	**Stress Management Education**: write a worry list or a gratitude list, guided meditation
Week 6	**Social Support and Follow Up**

Descriptions of Cole's seven-step format for Cognitive Behavioral Therapy group (Cole, 2005)

Introduction	State the goal is to change behavior
Activity	Focus on learning coping skills & improving task performance, education & practice; this part can take up to two-thirds of the session
Sharing	Participants share activity outcome, or read out results from worksheets; allow feedback from each other for social reinforcement
Processing	Participants can discuss their feelings about the activity, positive or negative. Group leader should facilitate and keep discussions focused & controlled
Generalizing	Participants build a general principle of what is being worked on, verbalize strategies and how they can be utilized
Application	Participants make plans to apply learned knowledge in everyday life; group leader can facilitate thought-provoking discussions, question and example to reinforce learning
Summary	Group leader summarizes important points from the session; provides take home message.

Cole, M. (2005). *Group dynamics in occupational therapy: the theoretical basis and practice application of group intervention (3rd Edt.).* New Jersey: SLACK Incorporated

P37.17

Do education programs affect the quality of life of people with Parkinson's disease? A systematic review and meta analysis

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Purpose: Symptoms of Parkinson's disease (PD) may threaten quality of life (QOL) and functional status, and increase dependence on care and assistance. Given that provision of patient education may improve QOL by empowering patients to adopt active roles in their treatment, this study aimed to review the efficacy of disease-specific education programs in improving the QOL of people with Parkinson's disease.
Materials and methods: A systematic literature search was performed in electronic databases Ovid Medline, Scopus, PsycINFO, CINAHL, Cochrane Library and AMED up until August 2018. Both randomised and non-randomised controlled trials were eligible for inclusion. Methodological quality of studies was assessed using the PEDro scale. Continuous data on QOL outcomes was pooled in meta-analysis where possible.
Results: The search strategy produced 48 studies which underwent full text assessment for inclusion, yielding a final count of six studies, and a total of 490 participants. The mean participant age was 66 years, mean time since diagnosis 6 years, and mean disease severity 2 (Hoehn & Yahr scale). All studies investigated standardised education programs provided in an out-patient setting by multidisciplinary health professionals. All education programs were delivered in small group settings, with one study incorporating additional one-on-one sessions. QOL outcomes included the Parkinson's disease Questionnaire (PDQ-39) (n=5), and the Short-Form Health Survey (n=1). Meta-analysis showed that education programs produced a small, significant improvement in the QOL of participants (Standard mean difference: 0.35, 95% CI -0.55 to -0.16, p=0.0004).
Conclusion: Standardised, Parkinson's-specific education programs provided by multidisciplinary health professionals may improve the QOL of people with PD. Further research is required to determine the most effective forms of patient education in this population.

P37.18

The self-identified experiences and needs of people with Parkinson's disease relating to patient education: A qualitative study

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Study aim: To identify the self-identified experiences and needs of people with Parkinson's disease (PD) relating to disease-specific education programs.
Materials and methods: People with PD attending either of two metropolitan health networks' movement disorder programs were recruited to participate in semi-structured interviews to explore experiences and self-perceived needs in education. Thematic analysis was used to identify the main themes arising from the transcribed interviews.
Results: Nine people with PD, mean age 77 years, mean of 11.5 years post diagnosis, participated. Disease severity of eight of the nine participants was described as 3 (Hoehn & Yahr). Prior education content was classified as either 'active' (opportunities for clarification, consolidation and reinforcement following provision) or 'passive' (no subsequent follow up or reinforcement), with participant preference for 'active' educational delivery. Five key themes emerged from the data in relation to participants' past experiences and future preferences regarding patient education, namely: education early in the disease trajectory; experiences and preferences for providers of education, mode of education delivery, and curriculum; and barriers to accessing education.
Conclusion: The findings of this qualitative study suggest that people with PD may not routinely receive patient education. Further, this study identified that people with Parkinson's disease are interested in engaging with formal education, delivered by both health professionals and their peers, to assist in empowering them to self manage their condition. Specificity and individualisation of education delivered was valued. Further research is required to increase confidence in these findings beyond a predominantly metropolitan mid-disease stage demographic.

COMPREHENSIVE CARE: Pharmacy and/or social work

P38.01

Direct client care for individuals diagnosed with Parkinson's disease and their support systems

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Micro-level social work practice is defined as the direct interaction between client and social worker on a one-on-one basis. At Houston Area Parkinson Society (HAPS), direct care is the basis for all connections with clients. HAPS social workers' facilitate numerous support groups across various populations (including Newly Diagnosed, Caregivers, and Caregivers for those with Parkinson's disease with Dementia/Lewy Body Disease), but also conduct psychosocial assessments, family meetings and ongoing case management that allow individuals and HAPS licensed master-level social workers (LMSW) to focus on specific issues pertaining to the diagnosis of PD. HAPS social workers provide opportunity for meaningful dialogue and address pertinent issues to the individual – customizing conversation, outlook and planning for each person as their needs are addressed.
Through case management, HAPS social workers form lasting relationships and bonds that build rapport, foster communication and walk with the client to where they are in their Parkinson's journey. Case managers are equipped with knowledge of PD and its treatments, along with the mental, social, emotional, cognitive and spiritual effects that a chronic progressive diagnosis can have on a person. Armed with those tools and the desire to create a lasting bond, social workers are able to help troubleshoot and proactively assist in strategizing for an ever-evolving future.
Families are complex without the issues that can arise post-diagnosis – Parkinson's disease compounds and complicates issues that may already be present. With the support of a LMSW, families are able to have open conversations that can lead to breakthroughs in interpersonal relationships, greater connection, and forethought in planning. HAPS social workers also support client and family in the community – attending visits to physicians in order to assist with the articulation of home-based issues, providing information and referral for a variety of subjects, including household accommodations and therapies, and advocating not only for client and family but helping the client find ways to advocate for themselves.
Direct interaction is and will always remain a primary component of Houston Area Parkinson Society – as we continue to expand programming we will never lose focus of our connection to the individual and their importance to our mission.

P38.02

Priority setting in a Parkinson patient association – A mixed method approach

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Objectives: This priority setting study was commissioned by Parkinson's Quebec to encourage people with direct and personal experience of the condition to identify their needs, and then prioritize the top strategic developments of the organization for the upcoming years.
Setting: Province of Quebec, Canada.
Participants: People with Parkinson's (PwP), and their caregivers living in urban and remote communities.
Methods: Using a nominal group technique, 33 participants (66% PwP) were recruited to identify their needs to improve their daily living with the disease. The Fitch model was used to classify these needs. Then, a survey was designed using the list of unmet needs ranked as most important by the participants of the nominal groups, and completed by the most frequent topics addressed by Parkinson Quebec help line. Needs were scored on a 5-point Likert scale. 592 participants completed the electronic survey. Needs were prioritized by plotting the relevance of the need (i.e. the percentage of non-missing responses) against the need for training development (i.e. the inverse of the mean need score). Top priorities were identified in the upper right quadrant of the graph. Using logistic regression models, we identified respondents' characteristics to address subgroup specific needs.
Results: The top priorities for strategic developments included informational needs (better information at the time of diagnosis, alternative medicine, falls management, sexuality, speech and swallowing), tools to navigate the healthcare system (understanding of the role of the institutions supporting the continuum of care), financial support (prescribed and OTC medications, health professionals), social support (mentorship), physical activity programs, and emotional support. Discrimination at work or with insurances did not appear to be an issue. Respondents under the age of 65 had a hard time to identify with the existing documentation and programs. Younger age, remoteness, and early stage of the disease were correlated with lack of disease management skills.

Caregiver status and female gender were associated with needs for informational, emotional, functional, financial support.
Conclusions: This priority setting study identified the unmet needs of the PD community of Quebec. It will be used to guide the development of future educational material and programs.

LIVING WITH PARKINSON'S: Public education or awareness programs

P39.01

Introducing the clinical trial companion, a research engagement tool
*Catherine M. Kopil, Todd Sherer, Deborah W. Brooks, Holly Teichholtz, Rachel Dolhun, Kristin Demafeliz, Sarah Berk, Aleem Siddiqui, Emily Moyer, Amanda Melnick, Andrea Katz, Maggie McGuire, Kristen Teesdale, Brittany Greco, Tanya Simuni, Michael Schwarzschild, Claire Henchcliffe, Sohini Chowdhury**
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Background/Objectives: Clinical trial design has shifted towards patient centricity in the past 5 years,. For researchers this means using new technologies, increasing social media presence and meeting patients where they are. To address knowledge gaps created by these trends, The Michael J. Fox Foundation (MJFF), leading clinical trialists and people with Parkinson's developed the Parkinson's Clinical Trial Companion, a comprehensive suite of materials aimed at enhancing research participation among volunteer and researcher communities.
Methods: The Trial Participant Pack, part one of the dual-sided suite, addresses common misconceptions and frequently asked questions about clinical research among the patient community. Part two, the Trial Resource Pack, provides clinical trial teams with guidance for incorporating patient centricity into trial design. The Trial Participant Pack is comprised of a book and videos focused on research participation, importance of diversity in research and Parkinson's disease (PD) genetics. Readers are encouraged to visit Fox Trial Finder (FTF), MJFF's online trial matching platform, to learn about research opportunities and ways to participate. The Trial Resource Pack offers evidence-based best practices and a toolkit of customizable templates to support recruitment and retention. To raise awareness of these resources, MJFF utilized a multi-modal strategy that included paid advertising, social media, and email marketing and tracked efforts via unique identifier codes. The volunteer book and best practices manual are translated into five languages for international distribution beginning in 2019.
Results: Since launch in April 2018, the Trial Participant Pack received over 119,000 views and the Trial Resource Pack over 3,800 views. Paid advertising was most effective at generating awareness among volunteers (75% of referrals) while search engines (35%) were most effective among researchers. In April 2018 alone, 1,347 new volunteers registered for FTF – a 35% increase over registrations from April 2017.
Discussion/Future Directions: High volume viewership of the Trial Participant Pack demonstrates desire for education within the PD community. Accelerated FTF registrations during the campaign suggests awareness generation is important for engaging volunteers in research and that education can spur action. Continued promotion of the Clinical Trial Companion aims to speed Parkinson's trial recruitment by educating both volunteers and trial teams.

P39.02

An intraprofessional mock code: Nurse anesthesia and baccalaureate nursing students – Parkinson's disease patient missed/omitted/delayed medication simulation case study
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Ten million people worldwide suffer from Parkinson's disease (PD). It is estimated that PD will double from 6.9 million in 2015 to 14.2 million in 2040 globally. It is believed this estimate is an understatement of the true prevalence of PD. Missed/omitted/delayed medication occurs frequently in hospitalized PD patients, increasing length of stay and causing harm. Previous research indicates a priority concern of novice nurses is not knowing what to do in a code situation. Evidence shows interprofessional mock code simulations increase nurses' confidence in recognizing code situations, and improving the reaction time to life saving protocols. A literature review reveals the absence of an intraprofessional mock code simulation focused on nurses. To fill this gap, an unfolding mock code simulation focused on a PD patient experiencing care transitions was conducted among an intraprofessional team of undergraduate nursing (N=94) and master's level nurse anesthesia students (N=24) and clinical faculty (N=4). The purpose of this study was to increase awareness among an intraprofessional nursing team regarding adverse events as a result of missed/omitted/delayed PD medications, as well as to promote comfort in working with the intraprofessional team.
Using a pre/posttest quasi-experimental design, study results indicate that following the intraprofessional mock code simulation: undergraduate nurses increased knowledge related to Carbidopa/Levodopa administration route (pre-test 69.2%; posttest 88.3%; percent increase 27.7%), while nurse anesthesia students showed no change in knowledge (95.8%; 95.8%; 0%). Undergraduate nurses (57.5%; 100%; 74%) as well as nurse anesthesia students (75.0%; 95.8%; 27.8%) increased knowledge related to when it is acceptable to miss/omit/delay PD medication administration. Clinical faculty demonstrated no change in knowledge. Finally, 57.4% of undergraduate students reported minimal to no comfort level in working with the anesthesia personnel pre-simulation. Post-simulation 94% of the students who reported minimal to no comfort indicated a response of moderate to extreme comfort.
While this study was conducted in a simulation lab located in one mid-sized private University in the northeast section of the United States, it holds great potential for dissemination among clinical nurses for improvement of patient safety and intraprofessional

communication/collaboration specific to the PD population experiencing a care transition.

P39.03

Living solo with Parkinson's disease

*Sandra Elms**
Newcastle Parkinson's Support Group, Newcastle, NSW, Australia

"I often say now I don't have any choice whether or not I have Parkinson's, but surrounding that non-choice is a million other choices that I can make"
Michael J. Fox
Purpose: To raise awareness of the problems confronting people living alone with Parkinson's.
Problem: PD is a disease, which knows no boundaries, affecting all genders, ethnicity, ages, people with partners and carers, and those alone.
Carers have to confront the decline and changer of the person they knew, resulting in challengers and suffering. For this reason carer support organisations have been formed.
For those living alone, the problems of loneliness, isolation, depression, anger, and accidents have to be confronted alone. very little is on offer, resulting in feelings of being the "forgotten people".
Method: Establish a database of names and contact details of people living alone in the Hunter region of NSW (Australia) from available information.
Send out questionnaire to known 'solo PDP's.
Hold a National Conference, in Newcastle NSW, to ascertain the problems faced by living alone and strategies to alleviate them.
Advertise in the community, using flyers, local newspapers, magazines, local radio/TV to reach as wide an audience as possible to attend the conference.
To raise awareness in the indigenous and ethnic groups in the Hunter, who are under represented in support groups.
Outcomes: To help people living 'solo' feel supported with their problems and concerns taken into account.
To establish a network so people can reach out to others for support and help for their specific difficulties.
To provide a social network for mutual support.
To help to prevent major mental health problems.
Map of Hunter region NSW with Population numbers.

P39.04

"Let us go singing as far as we go: The road will be less tedious" Virgil

*Sandra Ems**
Newcastle Parkinson's Support Group Choir, Newcastle, NSW, Australia

Introduction: Singing, particularly in a group, benefits people with neurological disorders, like Parkinson's. It gives a feeling of pleasure, well-being and a sense of belonging. It enhances the quality, pitch, volume and clarity of the voice.
Background Information: Newcastle Parkinson's choir was formed in 2014. Named the "Shake, Rattle 'n' Roll Choir, it meets once a week, sessions consist of breathing exercises, voice practise, followed by ensemble practise for specific events, or singing just for fun.
Speech Pathology Dept., University of Newcastle, runs voice therapy classes. I attended in 2015 and recently a Refresher Course. It showed very little deterioration of my voice. This is not due to 'conscientious practise' but singing in the choir'.
Aim: Ascertain the benefits of singing in a group.
Encourage more people to join the choir.
Method: Collect data from choir members, using a questionnaire.
Obtain traces of recordings of my voice, from Newcastle University.
Seek a research program/student interested in the project.
Encourage more people to join the Choir. use new logo for Choir, designed by University students, to advertise locally, Radio/TV newspapers.
Encourage younger people to form own Choir, if preferred.
Target the Hunter Region of NSW. Contact Indigenous and Ethnic groups, under represented at Support Group.
Outcomes: To raise awareness of the benefits of singing in a group for people with ParKinson's.
To raise the profile of the Choir and Support Group.
To foster a feeling of companionship and support for all people with Parkinson's, irrespective of age, gender, ethnicity and faith.
Quotes: Some days there won't be a song in your heart. Sing anyway. Emory Austin.
If you're gonna sing, sing loud. Travis Tritt
Singing is such an excellent thing, that I wish all people would sing. Richard E. Byrd.
A song can be more than words or music, when sung with soul, a song carries you to another world, to a place where no matter how much pain you feel you are never alone. C. Aiken.

P39.05

Sidekicks™: An intergenerational program uniting people with Parkinson's and youth

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Background: The intergenerational program Sidekicks™ brings together people with Parkinson's and school-aged youth. Participants in the program share stories while working collaboratively on various art projects over the course of four highly interactive guided workshops. By fostering connections and promoting mutual understanding, this program may positively impact both people with Parkinson's and youth. The objectives of the Sidekicks program include increasing perceived social connectedness and self-esteem and reducing feelings of social isolation among people with Parkinson's. For youth, the program aims to increase youths' knowledge about Parkinson's, positive attitudes towards people with Parkinson's and a positive mindset. This program is a collaboration between the Davis Phinney Foundation and Lundbeck.
Methods: This investigation included data from 47 people living with Parkinson's and 51 school-aged youth who participated in the Sidekicks program in four cities: Chicago, Denver, San Diego and Reno. Participants completed pre- and post-program self-report surveys assessing the objectives of Sidekicks.
Results: Among those people living with Parkinson's, there was a significant increase in self-reported social connectedness from before the program (M=5.33, SD=1.24) to after the program (M=6.25, SD=1.12; p=.004). People also reported feeling less social isolation after the program (M=2.01, SD=0.80) than before the program (M=2.49, SD=0.62; p=.003). In youth, there was a marginally significant increase in positive attitudes of the attributes of people with Parkinson's after the program (M=5.26, SD=0.93) compared to before the program (M=4.86, SD=0.75; p=.073). Youth also reported significantly more positive attitudes regarding interacting with people with Parkinson's' after the program (M=5.79, SD=1.28) than before (M=4.93, SD=1.46; p=.006).
Conclusions: These findings suggest that intergenerational programs may positively impact people living with Parkinson's and improve their quality of life as well as positively impact youth participating in the program. Further work is needed with larger samples to continue exploring the impact of these programs.

P39.06

#UNITED for Parkinson's campaign

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Background: People with Parkinson's (PWPs) are too often depicted using one of two extreme models. One model portrays us as people in dire need of pity; while the other model shines the spotlight on PWPs that are performing incredible feats – climbing every mountain, rowing every sea. Neither of these models represent the majority of PWPs, and most of us fall somewhere in between. Furthermore, not only are the two depictions inaccurate, they are potentially detrimental to many PWPs, especially those of working age.
Aims: To change the perceptions and images of PWPs by launching a global campaign that generates new media images for PWPs, using input from PWPs.
Method: The campaign will launch on December 11, 2018 in Leicester, UK. Using simple, but effective and innovative mechanisms, it will take on two forms:
1.Celebrating the Lives of PWPs
This involves people around the world taking pictures of themselves and uploading them using provided electronic window frames. The frames allow for each person to indicate the individual they are hoping to find a cure for. As the images are being uploaded, they will be shown on a map, accompanied by each individual's "hopes" for PD. These uploaded images will also feed into a massive collage of "real PWPs" that will be displayed on billboards across the world on World Parkinson's Day (WPD) on April 11, 2019.
2.The #UNITED Race
10 captains with 10 physical #united hashtag signs will start a race in Leicester on December 11. The goal is for each captain to send their physical hashtags around the world between the launch date and WPD. Each time a physical hashtag arrives at a new destination, the recipient will take a picture and upload it online. This will help us track (like NORAD tracks Santa) where each hashtag is and how far it has travelled. The captain whose hashtag travels the furthest by WPD wins the race.
Outcomes:
- A fun and engaging campaign that concludes with a magnificent collage depicting real faces of real people with PD.
- A strong sense of and togetherness within PWP, their families, and their communities.
- Increased PD awareness.

A depiction of the finished collated artwork on 1 of 10 billboards

P39.07

Art as a vehicle for participation in the Spanish-speaking Parkinson community

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Muhammad Ali Parkinson Center at Barrow Neurological Institute, Phoenix, Arizona, USA

Objective: Give the Spanish-speaking PD community in the Americas an avenue for participation in the WPC 2019.
Methods: In the last 6 years, the Hispanic outreach program at the Muhammad Ali Parkinson Center (MAPC) has strengthened a network for Hispanic people with Parkinson's disease (PWPs) and their caregivers. It currently reaches beyond Phoenix, to various cities in the USA and several Latin American countries. The network has stayed active via social media and online conferences offered by the MAPC. These communities have shown great interest and appreciation for receiving education and avenues for participation.
Many network members wished to participate and represent their communities at the WPC 2019, but language, costs and other barriers impeded them to attend. In response, with the help of MAPC art instructor Gregory Pearce, we developed an avenue for participation using the universal language of art. Spanish speaking PWPs and caregivers were invited to use a variety of media to color the same drawing and support the WPC's Soaring with Hope for PD project. In our drawing, the 7 feathers in the background represent the 7 continents of the world. In the foreground, the word HOPE is housed within the Japanese structure of the WPC 2019 logo. We distributed the drawings at PD related events, via email and social media. Participants were asked to return cellphone photos of their finished drawings. Despite all barriers, the Spanish speaking PD community colored more than 1,000 feathers to symbolically strengthen the wings of the WPC 2019's origami cranes, so they can fly far and give hope to the worldwide Parkinson's community.
Results: We received a total of 224 drawings. All the drawings were used to create this poster, titled "Wings of Hope." An electronic version of the poster will be shared with all the participants to be used as an awareness tool in their communities. We include a map of the participating countries to help raise awareness about the large and diverse Spanish-speaking PD community in the Americas. We hope more avenues for participation can be created to give this vibrant community an opportunity to contribute to the WPC's vision for the future.

P39.09

Spanish-language educational programming: Serving diverse communities

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Background: Over 40 million people speak Spanish in the US, with 3/4 of Hispanics preferring to use Spanish in the home. While the incidence of PD in Hispanics is the highest of any ethnic group in the US, the population is one of the most under served in terms of language and cultural barriers.
Building upon a history of service to Spanish speakers through resources and educational materials, the Parkinson's Foundation held its first Spanish- only live event in Long Beach, CA, in January of 2017, hosting over 175 PWP, family caregivers and healthcare workers. A second educational event was held in Puerto Rico in April of 2018 with over 185 attendees, and most recently in November 2018, two events were held in Los Angeles and San Diego reaching over 250.

Objectives: Objectives were to provide comprehensive educational programs presented entirely in Spanish, facilitate networking and relationship building, and leave behind literature, information on local resources and other Spanish- language PD programming as follow up items and ways to continue engaging.
Methods: Through collaborative efforts, the Parkinson's Foundation, the Muhammad Ali Parkinson Center, and UCSD worked with community health workers, providers, patient and caregiver volunteers, and other medical centers to build programs that were culturally considerate, covered topics of interest to attendees, and provided actionable strategies to seek out specialists, support groups, and other resources in the community.
Program features included music, dancing, family, empowerment activities and open conversation.
Results/Outcomes: Live education programs in 2017–18 have reached 625- 650 participants, with more than half estimated as contacts not previously engaged with the Parkinson's Foundation. Hundreds of additional connections were made via Facebook live streams, social posts and through recordings of the events posted on the foundation website and YouTube Channels.
Outcomes include increased awareness of and engagement with resources as well as an increase in local Spanish support groups and exercise classes geared towards Hispanics.
Conclusion: In conclusion, the foundation will continue to build and expand resources and education and to find ways to best reach and serve Spanish-speaking communities in the US and beyond.

P39.10

Providing authentic learning experiences about Parkinson's disease: Bringing humanity into the classroom
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[3] University of PA Parkinson's disease and Movement Disorders Center, Philadelphia, PA, USA

Edmond J. Safra Visiting Nurse Faculty (V.N.F.) Scholars have joined in the educational effort to prepare nursing students to care for persons living with Parkinson's disease. Prior to V.N.F.'s effort, nursing schools across the USA reported a limited amount of time was spent teaching about Parkinson's disease in their didactic classrooms resulting in a lack of preparation of the nursing students to understand and develop skills for working with patients diagnosed with this disease. New effective strategies to convey the complexity of Parkinson's disease to nursing students is crucial to the development of competence in caring for these patients.
Purpose: To explore the feasibility and value of an in-class interview of Parkinson's patients for undergraduate nursing students.
Method: Senior nursing students were given the opportunity to participate in an in-class interview of a patient with Parkinson's disease. During the experience, students were able to see, hear and identify care issues from the patient's descriptive account of the disease. Following this experience the students, patient and faculty member detailed their experience in reflective narratives.
Results: All reflective narratives were coded for common themes. By sharing his journey, the patient stated that it gave him "a new insight into this complicated disease." Students described their experiences as a way to gain "a unique perspective on the strength of the human spirit"; the experience "provided an opportunity to apply knowledge of a disease to a personal scenario that goes beyond any textbook definition"; and "It was the ability to talk face to face that allowed me the opportunity to connect not simply to his words, but his true presence." Students valued the authenticity of the experience and reported that they would recommend this teaching approach because it "helped them learn new information and empathize with others."
Conclusion: With the aging of society, it is a priority for nurses to develop a deeper understanding of the patient's experiences and perspective of living with Parkinson's disease. The in-class patient interview technique is a valid and important method to convey knowledge and true understanding of the person with Parkinson's disease.

P39.11

Community engagement as stakeholder in improving student nurse awareness of Parkinson's disease support groups
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Increased awareness of support groups in nursing programs will enhance the student knowledge base regarding community resources available for Parkinson's disease (PD) patients and their families. The need for awareness is great. Adding Rock Steady Boxing and Lee
Silverman Voice Training (LSVT)-Big/Loud programs to support group visits in community outreach education is a dynamic geriatric/psychiatric mental health support group experience. Literature searches and meetings with key stakeholders led to this project. Faculty from 5 local Colleges of Nursing (CON), Rock Steady Boxing Coaches at Saads Health Care in Mobile, Alabama collaborates with patients, families, the health care community and the community at large.
Methodology: The project will be implemented by developing a relationship with local colleges of nursing and the host center providing Rock Steady and LSVT Big/Loud programs. The sample will consist of nursing students invited to participate in a pre and post visit student survey. Based on a participatory design, interprofessional collaboration with local support group/s information will be gathered, determining outcomes of student participation. A pre and post survey will measure student knowledge at baseline, and stakeholder satisfaction.
Learning Objectives: 1) Recipients of this presentation will identify a model of improving awareness for nursing students visiting community based support groups such as Rock Steady Boxing/LSVT- Big/Loud therapy.
2) Recipients of this presentation will identify ways to introduce Rock Steady Boxing to nursing students to improve awareness and increase knowledge of access to wellness for PD patients/families.
3) Satisfaction survey results will be discussed.
Conclusion: Initiation of improved awareness for community support groups is a step toward increased awareness of wellness programs for PD patients/families. Use of community resources brings awareness to student nurses/new graduate nurses. Education which includes interactive experience with community resources for PD assists patient encounter in graduating nurse future careers. Engaging with PD patients brings alive didactic lectures pertinent to PD, promoting symbiotic effects, catalyzing increased wellness resource awareness and disease processes for students in local CON.

P39.12

The Edmond J. Safra Visiting Nurse Faculty Program at the Parkinson's Foundation

*Gwyn Vernon**
Edmond J. Safra Visiting Nurse Faculty Program at the Parkinson's Foundation, Wallingford, PA, USA

Background: Parkinson's disease (PD) is the second most common neurodegenerative disorder of adults with over 60,000 new cases yearly. Yet, little content is offered in nursing school curricula. An unpublished study (Bunting-Perry and Vernon, 2007–8) showed that less than 43% of schools of nursing included education on PD, and in those that did, more than 97% of content was outdated, irrelevant to current practice or evidenced based. The same survey showed that the barrier to including content on PD in nursing schools is competence and confidence of nursing faculty to deliver this content.
Methods: The Edmond J. Safra Foundation provided funding to develop a faculty development program, The Edmond J. Safra Visiting Nurse Faculty Program at the Parkinson's Foundation, or "VNF". Program emphasis includes building faculty confidence in caring for the patient and family suffering from this disease process and enhancing comfort in teaching students about PD. The 40-hour accredited program combines didactics, clinical time with patients and families, involvement in a PD support group and the completion of an independent project to benefit nursing education in PD and/or patient care. Seven to eight programs are held yearly at large academic multidisciplinary PD Centers which are chosen for their internationally known expertise in research, patient care and education. Host nurses at these sites are all experts in PD nursing. A standard program curriculum is delivered at all sites and is updated yearly.
Results: To date, 228 nurse faculty scholars have completed the "VNF" and through their efforts evidenced based content on PD is being introduced to their respective schools of nursing and within their professional organizations. Over 20,000 nursing students benefit from their professor's knowledge of PD yearly. Evaluations from faculty show that 100% learn new skills and knowledge and 100% feel a new confidence in applying their knowledge of PD in the classroom and clinical teachings. The inclusion of time spent during the program in actual patient care and involvement with an expert team at the host centers makes this continuing educational program for nursing faculty unique and successful.

LIVING WITH PARKINSON'S: Government advocacy/Campaigns/Public policy

P40.01

Actual status of support for Parkinson's disease patients in our hospital

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Background: Patients with designated intractable diseases have a large economic burden of medical expenses due to long-term medical care, and so a medical expense subsidy system is necessary. In Japan, medical expenses are paid to some patients with designated intractable diseases based on the "Medical Law Concerning Patients with Intractable Diseases." The medical expenses to be borne by the patient vary depending on the income of the patient, but it is from 2500 yen per month to 30,000 yen per month. The burden on the patient using the ventilator is 1000 yen per month. In case of Parkinson's disease, patients with Yahr III stage or daily functional dysfunction level of 2 or more are indicated for the medical expenses subsidy system. People with mild conditions, who need to continue expensive medical care, are also eligible for medical expense subsidies.
Objective: To examine the role of the medical expense subsidy system for Parkinson's disease patients. We will examine how to use this system for patients with Parkinson's disease.
Methods: In our hospital, we surveyed patients who applied for a designated intractable disease due to Parkinson's disease in 2017 and investigated the actual status of subsidies for them.
Conclusion: The number of patients with Parkinson's disease who applied for medical expense subsidy at our hospital was 126 in 2017. Among them, at least 5 were eligible for subsidy within 2 years of disease onset. In such cases, it was estimated that the probability of developing dementia was high.
Discussion: The Medical Expenses Subsidy Program reduced the economic burden of patients with Parkinson's disease. In some cases, it is necessary to introduce this system from early onset diseases. Early diagnosis of Parkinson's disease and early evaluation of degree of daily life impairment should be conducted, and the subsidy system should be utilized without delay. Using it in combination with other systems is considered beneficial.

LIVING WITH PARKINSON'S: Living well with PD

P41.01

The effects of tango on well-being and functional mobility in Parkinson's disease

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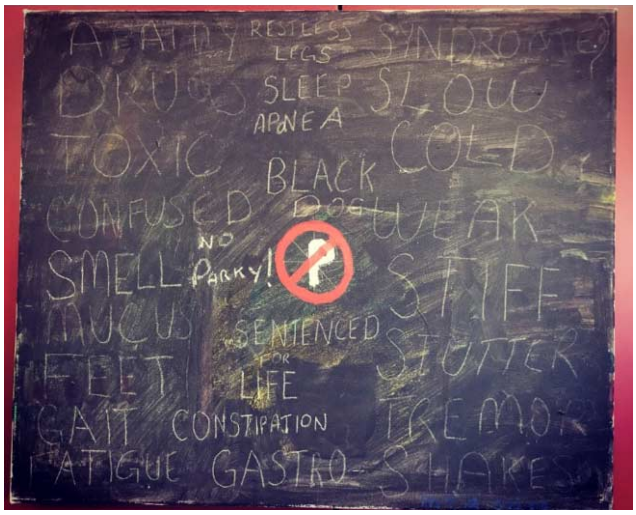
This study aims to clarify the effects of tango on well-being and functional mobility in Parkinson's disease. Difficulties with gait and balance are common among patients, contributing to an increased incidence of falls. Dance used as a therapeutic tool may be beneficial. Because dance is an activity performed to music, the music may serve as an external cue to facilitate movement, thus addressing the first recommended component which is the use of external cues. Dance also involves the teaching of specific movement strategies, which is the second recommended component. Argentine tango therapy is suitable for participants with PD because they can be taught a very specific strategy of walking backward. Gait changes may include not only slowness of walking with short, shuffling steps and a flexed posture, but also festination and/or freezing of gait. Aspects of walking that appear to be particularly impaired include dual tasking, such as turning and walking backward. Dance is an enjoyable and socially engaging activity. In fact, in a social setting may enhance motivation. For these reasons, it may be an excellent form of exercise for those with PD (Earhant, 2009). A single case of basic and dance therapy was applied to a male participant (83 years of age). A Basic A-B-A design was used in this tango dancing therapy, with a baseline(A) period of one week, a tango therapy session(B) lasting one week, and a return to the baseline period of one week; this designs were applied for three weeks. Tango dancing therapy lasts for 40minutes. It comprises a greeting embrace, warming up, rhythmic training, and practicing steps in a seated position to tango music. The participants then practice steps in a standing position in pairs, which is followed by a cool down/closing routine. The data were based on the participant's score on the Functional Balance Scale (FBS), Time

Up and Go Test (TUG), Unified Parkinson's disease Rating Scale (UPDRS), Hasegawa Dementia Scale-Revised (HDS-R), and a physiological functions scale and well-being scale. The participant's physiological functions and behavior were also analyzed.

P41.02

Parkinsons, a bugger of a way to make new friends
*Michael Atkinson**
Parkinsons Australia, Parkinsons Victoria, WPC Amassador, Torquay – Surf Coast, Vic, Australia

Along the beautiful Surfcoast region Painting with Parkinsons' sessions sees various opportunities present themselves to the participating parkys looking to let go of the unwelcome intrusion into their lifestyle and treat the beast with the contempt it deserves.
My motivation in presenting this work was a day when my head was particularly cloudy and I was particularly angry towards this stupid disease that follows its own rules.
I seized the colorful "happy shot" painting I had been completing and washed it over in black watercolor and whilst it was wet I recorded in faint white the "negatives" I face daily deliberately letting them soak away in the black wash.
In the middle of the painting is a clean white spot that parodies a "No Parking" sign, "No Parky" drowning out the contempt the words express



P41.03

Shaking through the tulips
*Michael Atkinson**
Painting with Parkinsons, Parkinsons Australia, Parkinsons Vicoria, WPC Ambassador, Torquay – Surf Coast, Vic, Australia

James Parkinson Tulip
The James Parkinson Tulip, a cardinal red species, with small feathered white edges and a white outer base, was designated as the symbol for Parkinson's disease.
In 1980, a Dutch horticulturist afflicted with Parkinson's disease, named the tulip for Dr. James Parkinson, an English doctor who in 1817 first described the condition in an "Essay on the Shaking Palsy."

The distinctive red tulip was introduced on April 11 2005, at the ninth World PD Day Conference in Luxembourg as the Worldwide Symbol of Parkinson's disease.
At my Painting with Parkinsons group to acknowledge the event various participants created multiple abstracts of the Tulip Symbol and I consolidated the 21 paintings to create the picture, reflecting a variety of interpretations. (1.2metres x 75cm).

P41.04

Calling All Artists: A program for artists with Parkinson's disease
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Some patients with Parkinson's disease (PD) are reported to experience enhanced artistic creativity after starting dopaminergic treatment. These patients come from a variety of artistic backgrounds, ranging from artistically naïve to professional artists. Despite this shared experience, patients with PD do not routinely network with fellow artists, and there are no widely adopted programs for artists with PD in the United States. In response to this need, a program called "Calling All Artists! Cultivating Art, Music, and Creativity in the Parkinson's disease Community of Greater Boston" was developed by the Parkinson's disease and Movement Disorders Center at the Beth Israel Deaconess Medical Center (BIDMC) in Boston, MA. This program has grown from a grass-roots gathering inspired by one patient to a Parkinson's Foundation grant-supported program that touches the lives of many. "Calling All

Artists!" networked artists with PD together in bimonthly meetings, inspired educational events, led to the creation of a video, offered small grants to participants, and hosted a gala event that featured these artists. One of the educational events was the 2018 BIDMC Annual Parkinson's disease Symposium titled "The ART of Living with Parkinson's disease". This symposium featured presentations by "Calling All Artists!" participants and welcomed over 100 attendees. "Calling All Artists!" group members include over 20 persons with PD who identify as painters, musicians, poets, quilters, photographers, a potter, and a professional cook. The group meetings focus on the participants' passion as artists and strategies to continue their art as they live with the challenges of PD. Discussions include the joy of art, feelings of isolation, fears of exhausting their creativity, and sources of strength. At these meetings, participants enjoy sharing their art and their stories, effectively learning from one another and fighting PD together as a group. "Calling All Artists!" has provided a much needed social, cognitive, and emotional platform to artists with PD in the greater Boston area. A future goal is to expand "Calling All Artists!" to the national level to further connect artists who have PD with each other at Parkinson's Foundation Centers of Excellence around the country.
Previously presented at the 2019 Center of Excellence Leadership Conference, Phoenix, AZ, USA

P41.05

Live, not just survive with Parkinson's disease: An Edmond J. Safra visiting nurse faculty program presentation
*B. Suzy Diggle**
University of North Carolina, Wilmington, North Carolina, USA

Parkinson's disease is an expensive and extensive healthcare issue in the U.S. as well as worldwide. All healthcare providers who care for adults need to know important aspects of Parkinson's disease patients care in order to assure that these individuals receive the best possible care. People with Parkinson's disease have the potential to live out their normal life span. The majority of our care for this population of people consists of education, preparation and managing the signs and symptoms that occur along the disease process. A significant portion of their care is preventing the common side effects of the disease and some of the treatment. The proposed talk and poster will include all the above aspects regarding how to treat and care for individuals with Parkinson's disease throughout their life span. Some of the areas that will be included are sexuality, impulsiveness and many others. In addition, this article will discuss what non-pharmacological and pharmacological treatments are either safe or not safe to administer to Parkinson's disease patients. Lastly, this article will incorporate resources for patients and their family.

P41.06

Innovative model of care for persons with Parkinson's disease in rural India
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This poster illustrates the process and strategies used by Neurology Foundation (NF), a not for profit organization to develop a program for underserved People with Parkinson's disease (PwP) and other neurological diseases living in villages in rural India. This population required the development of a program that ranged from diagnosis to rehabilitation.
Networking with Government and NGOs in the village was the first step. This enabled identifying grass root community workers (CWs) with some exposure to health related issues. An analysis of their experience and ability resulted in the development of a training program by NF with support from PDMDS that would equip them with skills to conduct door-to-door surveys to identify the target population. This was followed by a medical camp to confirm the diagnosis of those identified. The next step was development of the training program which included training in information on PD and stroke, simple physiotherapy techniques and exercises for PD and stroke, how to help the beneficiaries and how to work in the community. Strategies used for training were audio-visuals, demonstration, discussion and printed resource material in local language. An important component was the on-going evaluation and training of the community workers by the team of health professionals including physiotherapists and psychologists.
The NF has set up rehabilitation centres for senior citizens with neurological diseases in the village where the group sessions are conducted by the community workers under supervision and monitoring by NF. The outcome and feedback from the members of the group showed that the program impacted not only physical but also social and emotional well-being. This model has been documented and is being replicated in several other villages.
In summary, implementation of the rural program by NF through its community model improved quality of life of people with Parkinson's and other neurological diseases in rural India. The key factor in this program was designing training programs for community workers who had no knowledge about neurological diseases. Training of various stakeholders and using different awareness strategies helped in creating awareness about PD and other neurological diseases.

P41.07

Parkinson's disease. A patient's perspective
*Rob Hagen**
Parkinson Vereniging, Nieuw Vennep, The Netherlands

Slow moves, rigidity, tremor, stoop posture, we just need a few words to characterize people with Parkinson's disease (PD). And although in the last few decades it is well onderstood that Parkinson's disease is more than just a movement disorder, the emphasis is still on lack of motor control. PD is the disease of the motor system and everything else may seem of secondary importance.
What doctors and even some neurologists don't realize is that not motor but behavioral problems cause the most devestating consequenses of the disease. In my experience as a patient representative for five years, and having been involved in some tens of studies on PD, I think we should care more about those among us who face difficulties to start a conversation or take action when they want to and embrace their loved ones when they want to. Because this is also what PD is about. PD is the visitor that you take along with you whether you like it or not. It is there 24/7 in the head and mind, in brain and behaviour. The mere fact that physical symptoms are dominant in diagnosis and require easier treatment than mental and cognitive problems shoud not distract our attention from mental and cognitive problems in every day life.
Why is this important to stress non-motor symptoms?
For people with PD and their partners it is relief to know that their thoughts and feelings are common. Their personality change, anxiety and confusion belong to the disease just as falling and freezing.

P41.08

Multidisciplinary musical approach for the treatment of Parkinson
Rachel Heffez Ayzenfeld, Orit Lif Kimhi, Ahmed Daka, Nirit Lev, Irit Alon, Omri Lapidot*
Meir Medical Center, Kfar Saba, Israel

Background: Parkinson Disease (PD) is a progressive neurodegenerative disease that results in combination of symptoms, which cause physical limitation, dependency and suffering to the patient in his family. In the past fifteen years alongside the standard medical treatment, patient with PD in our hospital are getting supportive, rehabilitating treatments in group therapy.
Although patients in geriatric rehabilitation suffer from motor and non-motor injuries after cerebrovascular accidents or other conditions, constitutes a different population, the purpose of the intervention is similar to that of PD patients and is to improve the daily function and adopt copping patterns that promotes quality of life.
Methods: Our multidisciplinary team includes professionals from variety and complementary fields that work in a dynamic way by sharing their evaluations, goals and treatment plans using direct communication. The multidisciplinary involvement addresses sensor-motor field, coordination, mobility, balance, daily function, cognition language and emotion.
The unique multidisciplinary treatment in our department is long termed and typically not time bounded. It includes multidisciplinary team working in a weekly meeting of PD patients support group and along the routine of the geriatric rehabilitation, and sees the patient and his family as partners. We works across the psycho-educational- functional therapeutic sequence using a variety of therapeutic approaches that proved their effectiveness in proir studies, such as "Think Big" and "Think Loud" with the addition of a supportive element named "Feel Big". On top of that we employ specialized music and movement treatment methods such as RGRM and therapeutic drumming. The use of music and rhythm is assumed to be a stimulus that allows the activation of certain areas of the brain which can be either cortical or subcortical.
Results: The effectiveness of such intervention was evaluated in an experiential way. It contributes to the wellbeing of the patients, improve their mood and motivation.
We intend to examine the effectiveness of the multidisciplinary music approach in a comparative study using excepted measurements in PD patient's supportive groups and geriatric rehabilitation patients.
Remark: We will be happy to conduct a drumming workshop and show a three minutes movie about our multidisciplinary music approach.

P41.09

If you can dream it, you can do it: A selfstudy in living well in Denmark
*Elisabeth Ildal**
Cure4Parkinson, Vedbæk, Denmark

In November 2013, I was elected for the municipal Rudersdal elections in Denmark. I was happy, but I had a secret. June 20, 2013, five months before I was diagnosed with PD. We were in shock. Following my husband's advice, I decided to keep my Parkinson's diagnosis a secret. I was worried about the stigma that comes from having a chronic illness. The November 2013 election came and I won. There I was, on the front page of the newspaper, with my secret. The same day, I went into my Parkinson's closet and stayed there until April 2016. Three years in the dark, afraid that someone might figure it out and use it in politics. It finally happened in 2016.I was attending the Social and Health Committee Meeting when I decided that I had had enough. I did not consult with anyone. I interrupted the meeting and announced for the first time, "I HAVE PARKINSON'S" and started crying. Everyone was astonished, but after the shock many people came up to me to say that they were sorry to hear that I had the disease. That same day I wrote a long post on Facebook – it was a big shock for everyone. I called the local newspaper and the next day I was on the front page again, but this time with the title of the article "Ildal has Parkinson's". My secret was out. The years of darkness were over after my announcement.
Throughout the three years in the closet in the dark, I had followed the MJF and WPC2016.I went to WPC2016. After Portland, I flew to Spain for three weeks of rehabilitation. In November 2016 I established Cure4Parkinson, a trainingcenter where people with Parkinson's train people with Parkinson's through boxing, gymnastics, table tennis, and strength training. WPC 2016 Portland saved and changed my life forever.
2017, I campaigned proudly as a PwP and was re-elected as head candidate for the election of November 2017. I was re-elected as a politician, even with my Parkinson's. Now I live with items PD 24/7 with full public

P41.10

The benefits dance activities bring to the daily lives of people with Parkinson's disease
*Yayoi Koga**
Kyushu Sangyo University, Fukuoka City, Japan

This presentation is concerned with the activity of dance for patients with Parkinson's disease and people involved with performing in Japan.
Manizia, a dance artist who is based in Fukuoka, has organized a dance group for patients with Parkinson's disease since 2016. This

activity is called 'PD dance', and was aptly named by a member of the group to mean both 'Parkinson's Dance' and 'Perfect Dance'.
PD dance raises the expressive and creative activities of the patients, as well as being effective to their bodies and spiritual aspects of them. There are no examples yet in Japan of this activity and it is placed as one kind of community dance which utilizes the power of dance widely in society.
They have performed three times so far, in addition to holding workshops once a month, and the members of PD dance are now planning to perform in the Opening Ceremony of this World Parkinson's disease Congress. Some new members are being solicited for WPC. Their activity will be reported on, including any change in the participant's daily life.

P41.11

What are the most important factors for living well with Parkinson's disease? An informal survey from a women's Parkinson's Facebook group
*Sharon Krischer**
Twitchy Woman blog, Beverly Hills, CA, USA

Background: Online media is a growing area of information and support for Parkinson's disease (PD). Online groups allow people to share successes and challenges with other people with Parkinson's.
Objective: The purpose of this project was to survey women about what they felt most contributed to and hindered their ability to live well with PD.
Method: The following question was asked to a women's Facebook group in November, 2018.
"Please list the top 3 things that help YOU to live well with Parkinson's. Then the flip side – the top 3 things that are obstacles for you:
For example:
Positive: Exercise, Advocating for myself with my doctors, Friendships with other women with PD.
Negative: Poor sleep, Tremor gets in the way of doing things, Daytime fatigue"
Results: 55 women with Parkinson's have responded to the question. Of the responses, the most frequently reported positive aid for PD was exercise (n=37). Several types of exercise were shared, including, Rock Steady Boxing and yoga. The second most frequently mentioned response was friendships with other women with PD (a supportive peer group). Family, especially a supportive spouse and other friends, and faith (church, prayer, faith in God) were not far behind. Less frequently discussed responses included spending time with grandchildren, good access to medical care and medications, a good attitude, diet and adequate sleep.
The most frequently mentioned obstacle for many of the women were sleep challenges (n=34). Women shared that lack of sleep and fatigue were a major obstacle for them. Balance and Gait, including falls, were the second most frequently mentioned with Anxiety mentioned as the third biggest obstacle. Many other symptoms of Parkinson's were mentioned such as constipation, dyskinesia, off times, as well as lack of PD resources in their area.
Conclusions: This informal survey identified sleep and exercise as important factors for living well with Parkinson's disease. This survey was limited by the small sample size and that it was only open to women in one FB group.

P41.12

Inspirational reading to enrich your journey with Parkinson's disease
*Deanna Krywy**
Person with Parkinson's, Duncan, BC, Canada

When I was diagnosed with Parkinson's ten years ago I turned to the internet to glean information. I quickly became disillusioned with the information that was too scientific for me. Next, I journeyed into the realm of forums. I soon found them discouraging with their all too often depressing nature. I was already anxious and depressed!
What I needed as a newly diagnosed person, was someone or something to tell me that my life going forward would be all right.
As an avid reader, I ventured to my local book store and there found "Always Looking Up" by Michael J. Fox. This was the start of my library of inspirational books! My library grew to over 25 books which encompassed the theme "living well with Parkinson's". These books, written by people with Parkinson's from all walks of life, with different stages of Parkinson's, have inspired me in many ways. It has made me realize the importance of optimism and that I can live a full and good life with a diagnosis of Parkinson's.
I donated my library to The Barbados Parkinson's Support Group and hope they will find these books as inspirational as I did. Returning to Canada, I have already begun my new library purchasing "Perseverance – the seven skills you need to survive, thrive, and accomplish more than you ever imagined" by Tim Hague. Many blogs are written by PWP but I need my inspiration from a physical book, something I can hold.
"Inspiration, move me brightly, light the song with sense and color, hold away despair (Robert Hunter, Terrapin Station (1977); "Lady With a Fan")"

This quote has meaning for me in two ways as I am holding a physical book and what is in the book is holding away despair.
I want to share titles of inspirational books written by people with Parkinson's with the hope that others will find these books as helpful as I do. The poster will include a photo of the book cover with a short explanation about each book. I will be asking for each author/publisher's approval to include them on the poster.

P41.13

Living with Parkinson's: Dealing with other Parkinson's symptoms. A look at the life of someone with Parkinson's and how to deal with day to day issues

*Ian McFarlane**
Melbourne, Victoria, Australia

Parkinson's to the patient is more than just seeing a Specialist Neurologist several times a year, taking medication and sitting in the corner hoping for the best.
There are many symptoms that need to be considered and dealt with to improve quality of life and to (hopefully) slow the disease progression down.
I liken it to the Boy with his finger in the dyke. Holes to plug are symptoms. He addresses one symptom then another and then another, plugging the holes with his fingers as he goes. Eventually he runs out of fingers but the holes reform or additional holes form and require plugging again and again.
Which symptoms do we address first? This can be difficult to determine but it is important to work through them in a sequence, preferably one symptom at a time. Address those with the biggest impact first.
The key symptom to manage is constipation. If you are constipated then your medications may not be able to reach the part of the gut where they are absorbed and transported to where they are needed in the required timeframe before breaking down and becoming ineffective. This may lead to falsely believing that the medication either does not work or is not strong enough. Ongoing management of constipation is important to get consistency of medication effect. Also use the Bristol Stool Chart & always aim for a 4 on the scale.
Other symptoms to address include:

- Urgent urination finding a 'toilet' and wetting yourself
- Balance issues leading to falls
- Sleep issues at night time.
- Variation in medication impact
- Stessful situational shaking
- Pains in the stomach impacting daily activities
- Pains in the arms and hands
- Freezing of arms
- Daytime sleepiness
- Extreme fatigue
- Deteriorating voice quality making it difficult to be heard
- Co-ordination difficulties
- Loss of hand dexterity
- Medicinal side effects
- Difficulty looking after yourself. Shaving, personal hygiene.
- Difficulty maintaining your own property

It is recommended to start addressing your other symptoms as soon as possible with an aim of prevention.

P41.14

A walk in the park: The lived experience of Parkinson's disease and the role of Lifestyle Redesign® occupational therapy in addressing unmet needs

S. Hanlon Newhall[*1], Jim Elyea*[2]
[1] Johns Hopkins Bayview Medical Center, Baltimore, MD, USA
[2] History for Hire, Inc., North Hollywood, CA, USA

Background: Throughout his illness course, Jim, a person with Parkinson's disease (PWP), has learned to compensate for motor and non-motor changes he experiences. Through the Lifestyle Redesign® for Parkinson's disease (PD) occupational therapy (OT) program, Jim has implemented strategies to address unmet PD needs. Alongside his OT, Jim tells his story of how lifestyle changes can dramatically improve health outcomes, independence, and quality of life for PWP.
Objectives: To inform PWP, carepartners, and healthcare professionals about the lived experience of PD, and how the Lifestyle Redesign® for PD program helps improve health-related quality of life (HRQOL) for PWP through improved functional performance in home and community activities and enhanced communication and self-advocacy skills.
Methods: The presentation will discuss outcome data and themes from a semi-structured interview with Jim, who participated in nine sessions in the Lifestyle Redesign® for PD program, an outpatient OT program located in Los Angeles, CA at the USC OT Faculty Practice. The program addresses PD self-management through implementation of health-promoting lifestyle changes. In individualized sessions, PWP receive education and engage in problem solving to develop strategies to address barriers to participation. Based on Lifestyle Redesign® principles, participants are guided through the process of developing healthy habits and routines to improve symptoms and lifestyle factors such as sleep, depression, and stress.
Results: Jim's pre and post-outcomes indicate HRQOL and functional performance changes. Canadian Occupational Performance Measure (COPM) scores indicate clinically significant improvements in performance (2.8 points) and satisfaction (3.4 points). Unified Parkinson's disease Rating Scale (UPDRS) activities of daily living (ADL) scores indicate decreased impairment (-2 points) and Schwab & England ADL Scale functional independence scores increased by 10%.
Conclusion: Through compensatory strategies, lifestyle changes, and occupational therapy, Jim maintains a meaningful and fulfilled work and home life. This presentation will discuss successful treatment interventions, including: energy conservation/fatigue management, compensatory cognitive strategies, and sleep hygiene.

P41.15

An opportunity for healthcare professionals to guide and untangle discussions about delusions and hallucinations

James Norton[*1], Daniel Kaiser*[1], Stephen Bell*[2]
[1] ACADIA Pharmaceuticals Inc., San Diego, CA, USA
[2] AplusA Bell Falla, New York, NY, USA

Discussing psychosis associated with Parkinson's disease (PD) can be difficult for healthcare professionals, people with PD, and their caregivers. Cultural stigma makes it hard for sufferers to talk about psychotic symptoms. A trusting physician relationship helps, but how sufferers think and feel about symptoms may obscure the path toward recognizing and treating PD psychosis.

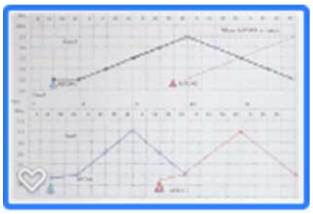
210 people with PD ("patients") and 422 unmatched caregivers completed a Market Research survey on their experiences with PD, their caregiver–patient relationships, and how well they cope with the disease. Patients and caregivers were classified into three groups based on the disease and its treatment: (1) PD without hallucinations or delusions; (2) PD with untreated hallucinations and delusions; and (3) PD with hallucinations and delusions that were being treated. For many questions, patients and caregivers were asked to answer from their own perspective and then each other's.
Responses revealed the difficulty physicians might have in evaluating whether sufferers wanted to treat hallucinations and delusions associated with PD, with seemingly contradictory responses from both patients (PT) and caregivers (CG). On one hand, respondents described hallucinations and delusions as sometimes positive (PT 23%, CG 7%) and other times negative (PT 33%, CG 37%) or neutral (PT 45%, CG 56%), yet overwhelmingly both patients and caregivers wanted the hallucinations and delusions to stop (84%, both groups). For patients who believed their caregivers did not want symptoms to stop, several reasons were offered, the most frequent being that the caregiver did not know how disturbing the symptoms were (31%). Nevertheless, both caregivers and patients believed the caregiver to be very concerned about the symptoms.
The difficulty of discussing hallucinations and delusions associated with PD may be aided by acknowledging the confounding ways sufferers think about these symptoms. Simple diagnostic questions may oversimplify and obscure these complexities: "Have you seen something others do not see?" "Does that bother you?" Sensitive, regular probing about the impact on daily life and emotions of PD symptoms–both motor and non-motor such as psychoses–may start the conversation and prepare all involved to speak openly as symptoms progress.

P41.16

Graphical approach to predict response of Parkinson medicine using the coefficient named the Walk-Disability-Level (WDL) which can be easily felt by patient by himself without using any special equipment

Mitsushige Oda, Yuya Oda*
Retired, Ryugasaki-shi, Ibaraki-ken, Japan

1.Introduction
I was an engineer in the aerospace engineering for more than 40 years. However I was suffered by the Parkinson's diseases (PD) for 12 years. Since then, I am taking PD medicine (MPD) every day. It is also said that the PD patients must not forget taking MPD periodically. However, it is not easy to take MPD periodically and if MPD is not taken at the specified timing, patient's body condition will become completely different from the predicted one. This relationship is usually explained by the dopamin density level within blood. However, patients can not get his dopamin density data by himself. However, since I believed there would be similar relationship between the disability level and the needed MPD to suppress the disability which will be observed by patients without using any special equipment.
2. Definition of the walk disability level
PD patients are often suffered by troubles when they want to walk. the walk disability level (WDL) can be defined as severeness of inconvenience level or difficulty level which PD patients feel when they want to walk. WDL can be defined as follows and can be observable by patient by himself without using special equipments.
(WDL) (status)
0.0 quite good and can run
0.5 good and can retry
1.0 normal, can walkf
1.5 feel some minor difficuliy
2.0. Feel some difficulty
2.5 Feel large difficlty
3.0 unable to walk by small stepping
3. Way of estimating WDL
Patient will periodically (at least each hour, hopefully each quarter hour inter) walk a few steps and checks the most likely WDL and the time when the WDL is observed.
4. Data example
Figure shows change of WDL when I was not hungry (case 1) and when I was hungry (Case2).
At the final presentation, detailed data analysis results will be shown.
Fig. Mitsushige Oda
5. Author is a member of the Japan Parkinson's Disease Association, and this abstract submission was approved by Ibaraki-ken division of JPDA.



P41.17

The profile of long-term Parkinson's disease survivors with more than 30 years of disease duration in Japan

*Yoshiko Okada**
JPDA (Japan Parkinson Disease Association), Hakusan, Ishikawa, Japan

Background: The profile of PD survivors with more than 30 years duration (PD-30) are not well known.
Objective: To evaluate PD-30 patient characteristics and to know about their life.
Methods: The questionnaire was posted to know the long-term survivors' way of living and their strains. The collected data were analyzed
Results: I posted 30 people from my address book and asked JPDA for the information of long-term PWPs. I identified 20 of PD-30 subjects
1) 3 men and 17 women. The majority (85%) was women
2) the present age was 46~78 years. Mean present age was 66.2 years.
3) age at PD onset was 13~43 years. Mean age at the onset was 28.3 years
4) PD duration was 30~60 years, the longest duration was 60 year, mean years.
5) They were diagnosed at the mean age of 39.3 year.
6) The first symptom was tremor 3, walking difficulty 7, writing difficulty 4, tremor and walking difficulty 4, others1.
7) 40% of them (8/20) have PD in their family.
8) They keep the average of 8.94 hours duration of on phase.
9) They are Hoehn Yahr stage 3 during on phase, stage 4 during off phase.
10) 4 people undergone DBS and 1 is on LCIG.
11) All are on levodopa, average amount is 383.3mg a day
12) 4 people can walk without aid, 14 need caregivers, cane or some aid. 2 do not walk, and 7 uses wheelchair. Nobody was bedridden.
Conclusion: PD-30 keep the better QOL in spite of long-term PD duration. And they think the factors to keep good QOL are as follows.
Good relation with your doctor.

The knowledge of the medication.
To have hobbies or something worth living.

P41.18

Parkinson's Roadmap for Education and Support Services™: PRESS. A how-to for developing early coping skills
Rosa Peña, Robin Kornhaber*
American Parkinson Disease Association, Staten Island, New York, USA

Objective: A review of the professional literature indicates that 8-week consecutive closed session psychosocial groups are not offered in the Parkinson's community. Groups of this type have been very effective with other disease states to provide early access to professional support and information and the development of a peer group of individuals living with the disease.
The APDA engaged a committee of healthcare professionals to develop a model program that would be piloted in APDA Chapters and Information and Referral Centers in several geographic areas.
Methods The committee decided on the format of an-8 consecutive week psychosocial group for people with PD and their care partners. The curriculum includes suggested topics and speakers for each session. Discussion within the group focuses on the sharing of information and resources, as well as the exchange of coping strategies to live the best quality life with PD.
The group is a closed group after the second session with a maximum of 16 participants. There is a pre-test administered at the first session and a post-test administered at the last session.
The program was piloted in six locations in 2017, which included a 3-month post program evaluation to determine whether participation in this program had led to changes in knowledge, attitude and behavior.
The PRESS™ program expanded to 18 national programs in 2018.
Results: The pilot post evaluations indicated that 91% had met the goals that they had set at the start of the program. All respondents reported improvement in the way they addressed day-to-day challenges.
The pilot 3-month post program evaluations had 85% indicating that they had made changes to accommodate living with PD.
Group participants (from 2018) reported making positive changes to their daily coping strategies and expressed interested in continuing to participate in a similar group in the future.

P41.19

Women and Parkinson's – Through a new lens
Kim Nitz[1], Lou Eisenbrandt[2], Megan Feeney[3], Karlin Schroeder[,3]*
[1] Parkinson's Foundation, Leawood, KS, USA
[2] Woman with PD, Overland Park, KS, USA
[3] Parkinson's Foundation, New York City, NY, USA

Objective: Empower local women living with Parkinson's disease (PD) through education on the unique aspects of how women experience PD, and examine related strategies for self-advocacy and emotional wellness.
Background: The Parkinson's Foundation Heartland Chapter hosted an education event in response to participating in the national forum for the Parkinson's Foundation Women and Parkinson's Teams to Advance Learning and Knowledge (Women and PD TALK) project. This project, funded through the Patient-Centered Outcomes Research Institute (PCORI), created the first national, patient-centered Women and PD research agenda and action plan to raise awareness and implement change in the way Parkinson's disease is studied and treated in women. In conjunction with this national effort, the Heartland Chapter is continuing to raise awareness about women's disparities in Parkinson's disease through grassroots educational efforts.
Program: The one-day educational event included a panel of speakers who presented on women's risks of developing PD, differences in symptom presentation and treatment response, and disparities in care. The panel of experts included a female Movement Disorder Specialist, a Speech Language Pathologist and PD fitness instructor working with rural PD communities, and a registered nurse who is a Vietnam veteran with PD and leads a class on emotional wellness. The program drew more than 90 women with PD, their friends, family and care partners, with 98% of responding participants agreeing the program increased their understanding of women-specific PD treatment and care strategies.
Outcomes: This event sought to strengthen local awareness of the unique experiences of women with PD, and also act as a catalyst for engaging women in an initiative to build on this knowledge through continued education and dialogue. One recently diagnosed woman has stepped up to help launch a women's-only support group, with several program participants interested in further involvement. The Parkinson's Foundation Heartland Chapter is partnering with a community organization to explore follow-on programming to further empower area women, and to provide a sounding board for the national initiatives and research agenda development. By connecting the local community with national efforts, the Heartland Chapter can help women with PD in the area feel more knowledgeable and supported to advocate for optimal care.

P41.20

Happier now: How positive psychology changed how I live with Parkinson's disease, a caregiver's journey
*Suzette Shahmoon**
UCL, Queen Square Institute of Neurology, London, United Kingdom

Background: Caring for a husband, with young onset Parkinson's disease for 20 years, affected my physical health and mental health. Learning about what underpins happiness through the study of positive psychology has helped me and my family to live better, improving our levels of happiness and physical health.
Objective: This poster will focus on the difficulties that arise when a loved one has Parkinson's. Living with PD means that life is unpredictable making life at home challenging as everyone struggles to cope with the consequences of that unpredictability. The degenerative nature of PD can make it hard to remain optimistic about the future. These elements alone can give rise to certain amounts of physical exhaustion, mental exhaustion and empathy fatigue.
Not knowing what to expect from moment to moment lead to fear, negative thoughts and self-isolation, which in turn lead to guilt and shame because "How dare I feel this way when I'm not suffering?" These thoughts and attitudes contributed to feelings of loneliness and at times despair.
Positive psychology has various interventions that can help counteract these symptoms of carer-burden and in turn contributed to my improved happiness and wellbeing.
Methods:
Various themes will be explored
1. Difficulties coping
2. Pessimism
3. Lack of motivation regarding self-care and living well
4. Self-dislike, guilt and shame
5. Loneliness and lack of engagement with life

The positive psychology interventions that will be explored as a means of improving these issues are
1. Mindset
2. Gratitude

3. Character Strengths
4. Self-compassion
5. Goal setting and hope theory

Results: Applying the theories and adopting various practices into our daily routine as a family have improved my physical and mental wellbeing as well as that of my husband and our four children. This has driven me to pursue a research project showing how these elements can help other people with Parkinson's and their loved ones.

P41.21

Tikvah for Parkinson, a community model for a non-pharmaceutical intervention program

Debbie Shapiro[*1], Ariel Simantov[2], Tanya Gurewitz[3]*
[1] Tikvah for Parkinson, Jerusalem, Israel
[2] Tel Aviv University Sackler School of Medicine, Tel Aviv, Israel
[3] Tel-Aviv Sourasky Medical Center, Tel Aviv, Israel

Background: As a result of the stigma associated with PD, the resulting social isolation and the lack of non-Pharmaceutical Parkinson activities in Jerusalem, few people with Parkinson (PWP) in Jerusalem were engaging in Parkinson specific exercise programs.
Action: Inspired by the WPC 2016, reports of the Ezrah LeMarpeh intense Parkinson rehabilitation project in Bnei Brak, Israel, and encouraged by Hadassah Hospital's Parkinson Clinic, a group of PWP decided to establish an open-ended non-pharmaceutical Parkinson rehabilitation program in Jerusalem.
In February 2017, Tikvah for Parkinson opened its first rehabilitation program with five participants. Today, over 100 PWP participate in at least one of Tikvah's daily three-to-four-hour intensive rehabilitation programs. Programs include a wide range of Parkinson specific exercise, Lee Silver Voice Therapy (LSVT) sessions, and Occupational Therapy sessions. Participants include PWP at all stages of the disease and are representative of all sectors of Jerusalem's population. In addition, several participants travel from other cities to attend the program. Funding is mainly via small donations and a symbolic participation fee.
The monthly lecture series, as well as informative newspaper and magazine articles and informal talks to schools and community groups about the challenges of living with Parkinson, has appeared to significantly reduce the stigma associated with the disease. Support groups for family members allow caregivers to talk about their challenges in a safe environment. As a result, the PWP community in Jerusalem feel more comfortable integrating into society and being more socially active.
Conclusion: The Tikvah for Parkinson program appears to be effective in improving the quality of life in people with Parkinson, as well as decreasing the stigma and demoralization associated with the disease. Despite the absence of research data confirming the effectivity of the Tikvah model in improving the quality of life and overall functioning of PWP, we believe, based on the program's growing popularity, glowing accounts of the participants and their care-partners, as well as the repeated referrals from neurologists, that the Tikvah for Parkinson model may serve as a blueprint for a community-based program that can be recreated in other communities and be led by a highly motivated and enthusiastic PWP.

Schedule
Week of October 7 - October 12

WOMEN'S PROGRAM

Monday:
10-11 Tai Chi (Lois)
11-12 Dance for Parkinson
12-13 Speech Therapy Group (Avigail)
13-14 Exercise (Nava)

Tuesday
14:00-15:30 Exercise (Nava)
15:30-16:30 Speech Therapy group (Avigail)

Wednesday
10:30-11:30 Boxing & Exercise (Debbie)
11:30-12:15 exercise and stretching with sticks (Tamar)
15-13:15 Singing (Shani)

Location:
Mercaz Shatner 3 (off of Kanfei Nesharim)

Please call Chani 058-3262-487 for directions for accessible entrance.

MEN'S PROGRAM

Sunday
10-11 Speech Therapy Group (Avigail)
11-13 Tai Chi, boxing, stretching, aerobics (Avi)

Tuesday
10:00-11:00 Singing (David)
11:-13 Tai Chi, boxing, stretching, aerobics (Avi)

16:30-17:30 Speech Therapy Group (Avigail)
17:30-19:30 Tai Chi, boxing, stretching, aerobics (Avi)

Thursday
10:00-11:00 Streching & Breathing (Solly)
11:00-13:00 Tai Chi, boxing, and exercise (Avi)

The support group for women caring for husbands with Parkinson takes place this Monday at 16:00 pm

P41.23

PD Link Northwest: A peer-to-peer support network for people with Parkinson's disease and carepartners

Melissa Tribelhorn[*1], Terry Harrigan[2], Maria Cole[3], Sarah Winter[4]*
[1] Northwest Parkinson's Foundation, Seattle, WA, USA
[2] Person with Parkinson's, Seattle, WA, USA
[3] Formerly with Northwest Parkinson's Foundation, Chicago, IL, USA
[4] Northwest Parkinson's Foundation, Bothell, WA, USA

PD Link Northwest is an innovative program by the Northwest Parkinson's Foundation (NWPF) that provides support and encouragement to people affected by Parkinson's, regardless of where they live.
A peer-to-peer support network, the program matches individuals impacted by Parkinson's with volunteers who have Parkinson's or are caring for someone with Parkinson's. PD Link volunteers share their experiences of living with Parkinson's; they offer tips on coping; they provide local community resource information; but above all, they lend a listening ear.
NWPF launched PD Link in 2013, inspired by the experiences of a woman with Parkinson's who was single, living alone, and looking for connections with other people with Parkinson's. While support groups are helpful for many people, not everyone impacted by Parkinson's chooses to attend or has access to one nearby. In the vast expanses of the Northwestern United States, connecting in-person is not a viable option for everyone. PD Link creates another opportunity for connection, in complement to support groups, that is not dependent on physical proximity. No matter where someone lives, PD Link can connect individuals impacted by Parkinson's with volunteers who have first-hand understanding of the Parkinson's experience.
PD Link volunteers connect with PWPs and carepartners over the phone, via email, or in-person, depending upon the preferences, location, and mobility options of the client. Clients and volunteers are matched based on demographical information, such as geographical location, gender, or age; age of disease onset; interest in DBS surgery; and other factors such as shared interests or hobbies.
NWPF provides volunteers with training, orientation, and support throughout the match process, typically 2–3 calls or meetings. Before matching with a volunteer, clients are screened for issues such as significant depression that would be beyond a volunteer's purview. Clients whose emotional needs exceed the scope of PD Link Northwest are connected to professional mental health providers.

NWPF has 20 active volunteers, annually training 4–8 new volunteers and providing 30–50 client matches.
PD Link could easily be replicated in other regions or altered to reflect language and/or cultural differences in other countries.

P41.24

Sábados en movimiento (moving Saturdays): Empowering patients with Parkinson's disease

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Objective: To evaluate the impact of continuing education programs on the perception of quality of life of patients with PD.
Background: In Colombia, the approximate prevalence of Parkinson's disease (PD) is 47 cases per 100,000 inhabitants. Currently, there are no government or public health programs for the rehabilitation of PD patients. Due to economic limitations, most patients cannot access to a continuous follow-up with neurologists or assist to educational programs. Fundación Valle del Lili (FVL) is a University Hospital and a highly complex medical center located in Cali, Colombia. Since 2014 and until 2016 the neurology service of the FVL treated 1033 patients with PD. Moving Saturdays is a nonprofit initiative of a multidisciplinary working group (neurology, neuropsychology, physical therapy) created for patients and caregivers of patients with PD. With a year of trajectory (September 2017–2018), and developing activities one Saturday each month, a group of specialists meets with families (70–120 people) with the aim of empowering people's knowledge about PD motor and non-motor symptoms.
Methods: A cross-sectional study was conducted in the fourteenth month of development of Moving Saturdays, some of the attendees of the meeting were invited to participate. The subjects answered a survey that included questions about the disease, the quality of the activities carried out during the Saturdays and the perception of quality of life.
Results: 60 people were invited to answer the survey, 48 subjects aged 52–92 answered it completely, 27 were men (56.3%) and 21 were women. 66.7% of the subjects attended at least 6 times. Most patients attend with a family member (75%). The most preferred activities were the educational ones (60.4%), followed by stretching exercises (58.3%), group activities (41.6%) and yoga (37.5%). 89.5% rated the activity as excellent. 87.9% consider that the activities have improved their quality of life. 54.1% want Moving Saturdays activities to be done more frequently. All patients would recommend this program to other patients with PD.
Conclusion: in our experience, the development of continuous education programs can improve the perception of quality of life and promote the empowerment of patients with PD.

P41.25

Using physical excercise to improve quality of life, postural balance and physical function in general. A study by University of Kent, England

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Background: Parkinson's is a chronic neurodegenerative disease, which usually leads to disability and disengagement with active lifestyles. There is good evidence that exercise is effective at improving and sustaining cognative and physical function in people with Parkinson's. Few studies have assessed long term effects of exercise and it's unclear the optimal dose for PwP. In October 2016, a collaboration with Parkinson's Equip and Medway Working Age Group, and a University of Kent reseach team started a community based exercise programme for PwP. Using data collected over one year, we evaluated the effects of multi-model exercise on physical function, cognition and wellbeing outcomes in PwP.
Methods: 22 participants, mixed gender, 65 +- 8 years, attended a once a week multi-model group exercise session (60 minutes). Health and functional assessments were completed at the start and repeated every three months for one year. Measurements, resting heart rate. blood pressure, height and weight, waist circumference, six minute walking test, timed up and go, 1 minute sit to stands and bilateral grip.
Results: Scores for 6MWT, TUG, and bilateral GS did not significantly change, (p=0.175, 0.143 and 0.333 respectively). The number of STS significantly increased during the year. specifically between baseline and the first three months (p=0.012).
Scores for CDT, TMT-A, TMT-B and OPQOL – Brief did not significantly change across the three different assessments, equivalent to half a year (p=0.769, 0.205 and 0.091, respectively). MMP increased significantly between baseline and the last assessment (=0.017).
Conclusion: A once-a-week multi-model group exercise programme for PwP showed an improvement in STS and MMP scores (notably, MMP scores significantly increased from 26.21 to 28.89 but no other significant changes, (i,e. no decline) in health or physical function over one year. That functional and cognitive performance were increased or maintained is a positive outcome, given the progressive nature of PD.
Outcomes from qualitative data capture the psycho-social factors that support engagement with the programme, how exercise helps PwP and evidence about 'real-world' feasibility. This project is on going (now running for two years), which is testament to its sustainability as a collaboration between a support group for PwP and a higher educational institute.

P41.26

Parkinson's Fitness – Paying it forward

*Brett Warthen**
Parkinson FIT, Bluffton, SC, USA

I am thankful for the inspiration of those who received a Parkinson's disease diagnosis before me. The people who challenged the perception of what it meant to live with Parkinson's. People like Scott Newman, who founded Rock Steady Boxing, and David Blatt, whose skiing and exercise videos challenged me to not just survive, but thrive with Parkinson's. These are just a few of the unsung heroes who have inspired my PD journey thus far.
I am also thankful for the internet bloggers who share their experience, insight, and coping strategies.

In 2016, I attended to the World Parkinson Congress in Portland, and I was intrigued by the posters and abstracts, in particular those created by people who were living with Parkinson's. The brief discussions that I had with those individuals were the highlight of the Congress for me. I hope that my participation at WPC 2019 can help inspire someone to share their story at WPC 2022.
For the past 5 years of living with Parkinson's, I've made exercise a priority in my life. I understand how hard it is to stay motivated, especially when struggling with soreness and stiffness, or facing one of those days where your body won't move the way you want it to.
There is far more to be exercise than the mechanics of which specific types of exercise are best for PwP. As a PwP, How do you stay motivated to keep exercising? As a trainer, how can you keep your participants motivated and attending classes regularly?
I am launching the Parkinson FIT foundation to help explore these issues...to motivate, encourage and inspire PwP and their trainers. There is a lot we can learn from each other, and I am interested in finding ways to promote dialogue and cooperation between different Parkinson's exercise programs.
It's time to pay it forward and help Mr. Parkinson's new recruits not just survive, but thrive with Parkinson's disease.

P41.27

Creating a virtuous cycle of PwP support
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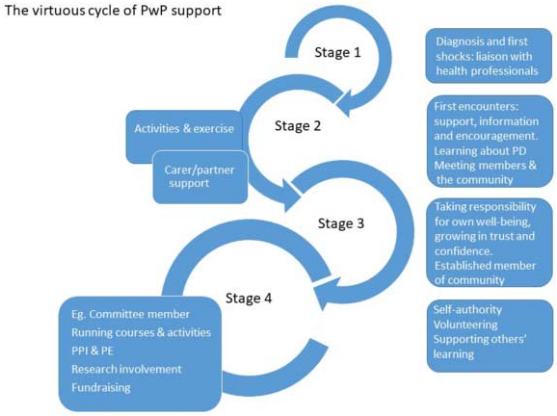
How do people newly-diagnosed with Parkinson's (PwP) make the journey from shocked and fearful patients to confident, engaged and empowered people, working in partnership with health professionals and support services, taking responsibility for their own well-being?
We present a four-stage model, derived from our analysis of Edinburgh Branch members' marketing ideas, in which a newly diagnosed PwP and their partner and family move from initial isolation to community. We track these against Rogers' (1967) stages of process, and the Dalai Lama's concept of wise selfishness, where our long-term individual interest lies in the welfare of everyone in the Parkinson's community and beyond into the wider society. We ascribe to Petzinger's (2009) position that while 50% of our well-being depends on our medication, the other 50% is our individual responsibility.
The model describes how a newly diagnosed person moves from Stage 1's dismay when their focus is inward – what will happen to me? – and an absolute dependence on their health professionals; through Stage 2's first tentative meetings with other PwP and the local community, joining in activities and learning about the condition from others' lived experience; to Stage 3 'coming into themselves' and taking responsibility for their own wellness; to the final Stage 4 when their focus moves beyond self, to contributing to the community. These empowered PwP support the newly diagnosed, repaying the debt they owe to the PwP who supported them in the first stages of their own journey and growth: creating the virtuous cycle of support. We acknowledge Edinburgh's lively and active local branch, built up over many years of volunteer commitment, and its strong underlying attitude of positivity.
We track the links between personal wellness, community health, appropriate support, learning and individual and community activities, and the development of a partnership with our health professionals rather than dependency.
We conclude by cataloguing community structures, activities, and contexts necessary for PwP, partners and families to navigate the journey with maximum possibility of quality of life – physically, mentally, emotionally and spiritually.



P41.28

Perak Parkinson's Association's efforts in creating awareness and helping PWP 6 years after establishment
*Lam Swee Yeoh**
Perak Parkinson's Association, Ipoh, Perak, Malaysia

Objectives: To review the activities organized by Perak Parkinson's Association(PPA) in creating awareness, training of health care professionals and caregivers as well as improving the quality of life of PWP and the challenges it had to face and methods of improvement.
Methods: PPA conducts almost daily activities for PWP who come to the centre for dance movement, circuit exercise, tai chi, Qi gong physiotherapy and karaoke. On Sunday mornings PPA also conducts yoga exercises at the river front. PPA also organized the Perak Parkinson's International Symposium in October 2017 by inviting local and foreign experts to give talks on PD to health care professionals, care givers, PWP and the general public. In addition, family days and simple celebrations were held during Chinese New Year, Moon cake festival and Christmas for members and PWP to enjoy themselves. Several fund raising events were also held by other organizations to generate funds for our activities. PPA had also participated in a government organized pensioners fair in Ipoh where PPA was given a booth to distribute leaflets and information on PD and display posters and photos of our activities along side Alzheimer and dementia societies. Despite some challenges and misunderstandings which PPA had to endure, it emerged stronger in the light of the lessons learnt from mistakes made. Empathy, patience, tolerance, compassion, forgiveness, good communication and understanding are qualities gained by working with PWP. In the spirit of helping PWP lead a better quality of life many PPA members including PWP and volunteers had put aside differences and sacrificed precious time and energy to help out in various activities and programs organized by PPA. As an NGO we still have lots to learn.
Results: Growing number of PWP coming to the centre for activities since establishment 6 years ago proves the effectiveness of what PPA is doing.
PPA hopes to slow down the progression of Parkinson's through exercise and improving quality of life of PWP.
Good fellowship was observed among PWP especially in helping each other and sharing of ideas in the management of Parkinson's disease

LIVING WITH PARKINSON'S: Advancing research: Fundraising, trials, campaigns

P42.01

The Fox Insight Study: An empowering opportunity to fuel Parkinson's research and help advance scientific breakthroughs from the comfort of home

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NO ONE UNDERSTANDS PARKINSON'S BETTER THAN THOSE LIVING WITH IT EVERYDAY. The first of its kind, Fox Insight is an online clinical study collecting patient-reported outcomes about health-related experiences from volunteers with and without Parkinson's disease (PD). Fox Insight (FI) aims to create the world's largest database on the day-to-day experience of living with PD, from 125,00 participants across the globe. This comprehensive dataset has great potential to help researchers better understand unmet needs of PWP, redefine therapeutic priorities and optimize clinical trial design. Anyone 18 years or older, with a computer, an Internet connection, and ability to read English can participate. FI is open to PWP worldwide. People without PD are also invited to participate as a comparison group, to help guide data interpretation. During the first study visit, interested volunteers consent to participate and provide information about their personal experience living with PD, through a guided online evaluation made up of simple questionnaires. FI then prompts participants to come back every 90 days for subsequent "virtual visits." A variety of built-in tools are also available to registered participants to help them most effectively manage their own health. For example, an Appointment Keeper, Physician Report, printable summaries of questionnaires, and access to other recruiting PD clinical trials all are offered within FI's dashboard. To date, approximately 30,000 people have enrolled across 52 countries worldwide, 62,000 study visits have been completed, and 600,000 survey responses have been captured. The Fox Insight study opens new doors to research participation and gives every person with PD the chance to tell their unique story over time; 75% of registered FI participants have never previously participated in research. Through Fox Insight, people with and without PD can connect with researchers and the broader Parkinson's community, to work together toward a more complete understanding of Parkinson's and potential treatment breakthroughs. PWP expertise on living with Parkinson's can help point to trends and associations and help lead researchers to important and potentially new areas of study. Fox Insight is supported by the Michael J. Fox Foundation for Parkinson's Research.

LIVING WITH PARKINSON'S: Other

P43.01

William James, psychologist: the latest James Parkinson doppelgänger

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Background and Objectives: Although James Parkinson is considered the world's best known '(emeritus) neurologist' [1], his physical appereance is still unknown [2, 3]. At least two popular doppelgängers have been identified and reported in the literature: James Parkinson dentist, treasurer of the British dental association; and James Cumine Parkinson, a lighthouse keeper, physician wannabe [4]. We describe the latest misidentification of the author of 'An essay on the shaking palsy'.
Design/Methods: Narrative review.
Results: On the XLII Annual Meeting of the Mexican Academy of Neurology (November 2018. Mérida, Yucatán) venue halls were named after Alzheimer, Babinski, Charcot, Ramón y Cajal, Oliver Sacks and James Parkinson. A photograph of—allegedly—James Parkinson, welcomed the visitors, encircled by a Kukulkán-ouroboros (a self-eating feathered-serpent), celebrating the city's Mayan past. As Parkinson died before daguerrotype was invented, photographs were unavailable, and this could only be another impostor. Using a reverse image search engine we identified the doppelgänger as William James (1842–1910), the "Father of American psychology". We were told by the organizers the picture was found online as that of James Parkinson, though the exact source was unknown. By searching "James Parkinson" on common engines, we found the photograph in question, on a peruvian webpage [5], regarding ephemerides of april 11th, James Parkinson's birthday (Figure 1).
Conclusions: William James is the latest Parkinson impostor, as we did not find previous reports of this mistaken identity. Let us not forget that Parkinson's looks will probably remain a mystery, as he died before invention of Daguerrotype, so no photographs on him exist. For the sake of historical accuracy, it is important to clarify these mistakes, although they might contribute to the mystery aura that surrounds James Parkinson.
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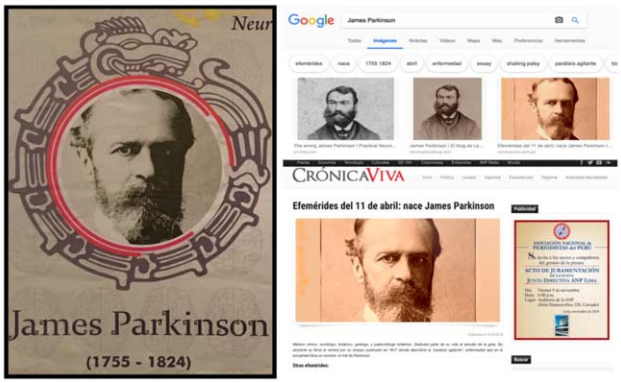

P43.02

PRISM: An ongoing pan-European exploratory, cross-sectional, web-based survey of people living with PD and their care-partners

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While core healthcare resource use and drug spending in Parkinson's disease (PD) have been widely studied, there is a paucity of data on the wider use and costs of support services/therapies, the true patient and care-partner burden of PD in Europe, and real-world treatment patterns.
PRISM (Parkinson's Real-world Impact aSsessMent) is an ongoing exploratory study addressing this gap in the knowledge base. It aims to inform potential improvements in PD management and evidence-based resource allocation in France, Germany, Italy, Portugal, Spain and the UK, as well as better characterize the burden of PD on people with PD and their care-partners. The study has been developed and executed as a collaboration between the Cure Parkinson's Trust, a Scientific/Medical team and Bial, with support from Wickenstones.
The study is a cross-sectional web-based survey capturing clinical characteristics, past/current treatment patterns, patient/care-partner QoL, impact of impulse control/sexual issues and costs including: direct (healthcare professional time, inpatient, emergency care, medicine), indirect (support services, productivity) and those paid out-of-pocket. Standardised PD measurement instruments, including the PDQ-39 and Zarit Caregiver Burden have been used or adapted where relevant for their strong psychometric properties and representation of clinical and social burden, as well as to set results in the wider context of the literature. The survey is structured to elicit data from both the person with PD and their care-partner, and respondents have the option to omit certain potentially sensitive questions. The survey was first developed in English, and then translated and validated before use in each country.
Respondents enroll in the study voluntarily, following receipt of literature from a patient group or clinic. The study aims to recruit a broad representation of real-world people living with PD and extend beyond the profile of a typical clinical trial population; as such data are monitored to characterize various sub-groups (e.g. demographics, nature of therapeutic intervention and severity of disease).
We present an update on study recruitment, as well as exploring patterns in the initially enrolled cohorts (e.g. demographics) and potential sources of bias/modifications to ensure our study makes a valuable addition to the literature exploring the burden of PD.

P43.03

Investigation of effect of LRRK2 kinase activity on the GLUT4 membrane translocation in adipocytes

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Background: Parkinson's disease (PD) is the second most common neurological disorder after Alzheimer's disease. Although recent genetic studies have revealed a genetic basis for familial and sporadic PD, the pathological mechanisms are not fully understood. A recent study showed that many PD patients have glucose metabolism abnormalities and reported association of PD with type-2 diabetes. However, the physiological interaction between neurodegeneration and abnormal glucose metabolism in PD pathogenesis remains to be elucidated. Results of our preliminary experiments showed increased expression of PD-casual molecule LRRK2 (leucine-rich repeat kinase 2) in the differentiated 3T3-L1 adipocytes. Therefore, in the present study, we investigated the effect of LRRK2 kinase activity on the membrane translocation of glucose transporter 4 (GLUT4).
Methods: GLUT4 membrane translocation was analyzed by immunofluorescence using the 3T3-L1 cell line stably expressing Myc-GLUT4-ECFP. Insulin resistance was induced by dexamethasone treatment. Effect of LRRK2 kinase activity on the membrane translocation of GLUT4 was determined by treatment with LRRK2 kinase inhibitors, CZC24156 and MLi-2. Moreover, the effect of LRRK2 kinase inhibitors on the expression and phosphorylation state of glucose metabolism related molecules, such as AKT, AMPK, and Rab10 was also determined by western blotting.
Results and Discussion: We confirmed whether insulin resistance was induced by dexamethasone treatment in insulin resistance (IR) adipocytes. Under our experimental conditions, dexamethasone inhibited insulin-stimulated recruitment of GLUT4 to the cell surface and also decreased AKT phosphorylation. Therefore, we used dexamethasone treated adipocytes as an IR-adipocyte model in the present study.
We found that LRRK2 inhibitors stimulated membrane translocation of GLUT4 and decreased the GLUT4 expression in IR-adipocytes. Furthermore, phosphorylated AKT (AKT-pT473) was also increased by LRRK2 inhibition, whereas the phosphorylation of LRRK2 (LRRK2-pS935) and Rab10 (Rab10-pT73) were decreased and phosphorylated AMPK (AMPK-pT172) was upregulated by LRRK2 inhibitors. These results suggest a novel role of LRRK2 in regulating the insulin-dependent membrane translocation of GLUT4 in adipocytes.
Conclusion: LRRK2 may play an important role in insulin-dependent glucose uptake through the regulation of GLUT4 membrane translocation in adipocytes.

P43.04

Characterization of the role of LRRK2 in the regulation of glucose metabolism

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Background: Parkinson's disease (PD) is a neurodegenerative disorder that affects movement due to progressive loss of dopaminergic neurons in the substantia nigra. Accumulating evidence suggests that long-term influences of interaction of environmental and genetic factors pose increased risk of PD. Epidemiological studies show that PD patients have abnormalities of glucose metabolism, and type-2 diabetes is linked to risk of PD. However, the effect of causal risk factors of PD on the glucose metabolism, and the physiological significance of abnormal glucose metabolism in PD pathogenesis needs to be studied mechanistically. In the present study, we investigated the role of leucine-rich repeat kinase 2 (LRRK2) in the glucose metabolism using a obesity model.
Methods: C57BL/6J wild type (WT), LRRK2 knockout (KO), and G2019S-knock-in (GS) mice were used in this study. These mice were fed a normal diet (ND) or high-fat diet (HFD). At the periods of 1, 3, and 5 months post-feeding with these diets, the oral glucose tolerance test (OGTT) was performed. Serum levels of insulin and leptin were analyzed by ELISA. The expression of LRRK2 and glucose metabolism-related proteins in adipose tissue, skeletal muscle, liver, and pancreas were determined by western blotting.
Results and Discussion: In the present study, we found for the first time that GS mice have impaired glucose tolerance in HFD fed condition. In contrast, KO mice display improved glucose tolerance compared with HFD-fed WT and GS mice. ELISA analysis showed that serum levels of insulin and leptin in HFD-fed KO mice were significantly lower compared to WT mice. In addition, KO mice showed improved HOMA-IR. Next, the LRRK2 protein expression levels in glucose metabolism-related tissues were evaluated. Higher expression of LRRK2 was noted in the adipose tissues compared with skeletal muscle, liver, and pancreas. Furthermore, GLUT4 protein expression in adipose tissues of KO mice was higher than WT mice. These results suggest that LRRK2 may regulate insulin-dependent glucose uptake through the regulation of GLUT4 expression in adipose tissue. It is well proven that the G2019S mutation in LRRK2 enhances the kinase activity. Therefore, we conclude that increased LRRK2 kinase activity exacerbates the glucose intolerance in mouse models of obesity.

P43.05

Implementing the nurse navigator model within an interdisciplinary team at the McGill University Health Center: A patient and caregiver reported outcome survey

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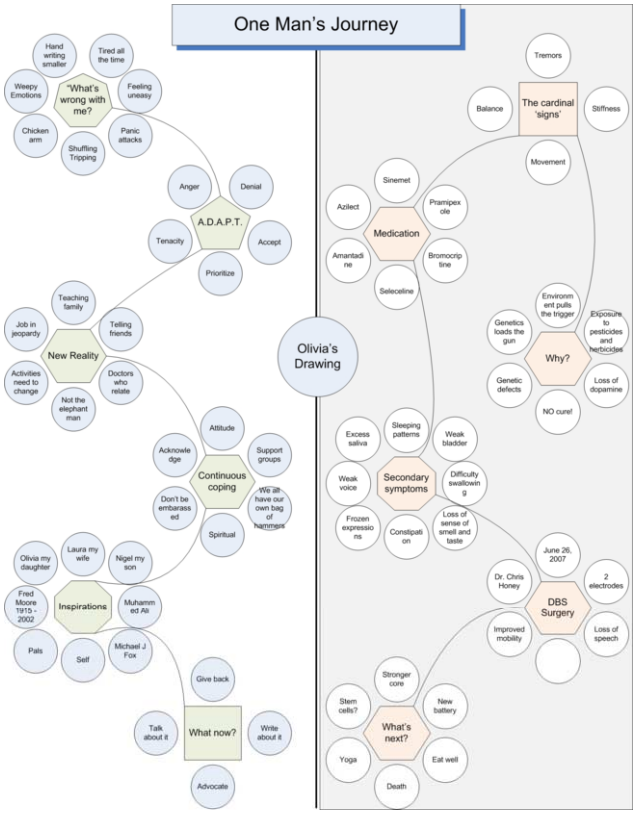
This survey was to evaluate patient/caregiver experience with a new model of care introduced within the Movement Disorders clinic in 2013: the Nurse Navigator Model. Inspired by its success in oncology around the world, the Navigator Model has specialized nurses acting as the main contact person for the patient within the healthcare team. The trajectory of care differs greatly when managing Oncology versus Parkinson's, and so it was necessary to ensure the model was sustainable, effective, and appreciated by patients and their families.
The NN contacts the patient as soon as a referral is received, providing an immediate link to the clinic even before they are seen. Furthermore, the NN is available to answer questions, provide support and education, and to advocate on patient's behalf during this time of uncertainty. Patient experience surveys provide valuable information for team-based clinics. To determine effectiveness and satisfaction, surveys were conducted during clinic hours targeting the patient experience. Patient participation was voluntary, aided by a facilitator. The surveys were completed in a consecutive manner throughout several clinic days during a span of 6 weeks. They included dichotomous questions, Likert scales, a semantic differential scale, and an open-ended question. While the facilitator knew who participated, the results remained anonymous as no name or code tied a specific patient to a specific set of answers.
118 completed surveys were returned to the facilitator. Results were overwhelmingly positive, reinforcing the NN as a patient friendly approach to care. Considering all the results in this report, the data strongly suggests patients accept and appreciate the Navigator Model. Patients expressed confidence in nurses being the front line.
A significant portion of respondents had a negative perception of their own health and wellness. The clinic's population does not differ from the general Parkinson's population, since those statistics are aligned with the known averages for individuals with Parkinson's disease and other movement disorders. Following that survey, the nurses in MDC wanted to start a project on more specifically the Description and Exploration of the role of the Parkinson's disease Nurse Navigator within the Movement Disorders Program of the McGill University Health Centre.

P43.06

One man's journey: Living with Parkinson's

*Rex Moore**
Vancouver, British Columbia, Canada

My proposal for an abstract under the "Living with Parkinson's" category is a personal power point [see image] of my life to date after a young onset diagnosis in 1993 at 41 years of age.
I am not a scientist, doctor or researcher. I am a 66 year old man who has survived 25 years of living with PD and one who still plays tennis and golf. I have been an inspiration to many people with Parkinson's, through my articles, speeches and one on ones with those just diagnosed or those considering DBS surgery. I served [4 yrs.] on the board of directors for the P.S.B.C. and attended the first World Congress in Washington D.C. At that congress the emphasis was on research, with scientists speaking to other scientists. There were many PWP in attendance and though there were some areas to display various creative endeavors and a separate meeting area for those afflicted, I felt at the time, that there needed to be more opportunity for the PWP to communicate with those professionals about the bottom line of PD. A chance for some interchange between those with PD and those without. A chance for the generals to get "on the ground" with the troops. I trust that this has come about in the subsequent Congress's. My presentation is focused on my journey from start to present with the initial symptoms, medications, life changing [ADAPT] and life saving [DBS], plus ways to cope and an inspirational poem "The Heroes of Parkinson's". I have built a 16 slide power point presentation to go along with my poster and I am an experienced speaker who has written over 50 articles for magazines, newspapers and Parkinson's newsletters as well as speaking in front of small and large audiences. Except for a couple of quotes, all my material is original.
Thank you for your consideration, I trust you will find my abstract not "out of the Box" but "in the wheel house" for those who suffer under the weight of PD and a life interrupted yet one that still must be lived to the best of our abilities.



P43.07

Being the patient at the centre of a multi-disciplinary team approach to Parkinson's care: A personal perspective

*Janet Niven**
Person with Parkinson's, Forfar, Angus, United Kingdom

Objective: To demonstrate the advantages to patients who attend a multi-disciplinary Parkinson's review clinic and how it empowers patients to take an active role in their own wellbeing.
Background: In Angus, the rural Scottish county where I live, the NHS Parkinson's clinics are based in three geographical locations. The team involved in the patient's care is multi-disciplinary with the patient being very much at the heart of it.
The annual review clinic takes place over one morning, lasting approximately 2 ½ hours. The patient spends around thirty minutes with each of the following:

Parkinson's Consultant
Parkinson's Nurse Specialist
Physiotherapist
Occupational Therapist
Nurse/H.C.A.

Over the course of the morning, the patient's condition is assessed by discussion, tests and questionnaires e.g. cognitive tests, non-motor symptom scores, dyskinesia, difficulties with tasks of daily living, medication and side-effects, gait, posture and movement and postural hypotension.
There is adequate time for the patient to discuss any concerns they may have and also possible coping strategies. Family members are encouraged to attend and be involved in the meeting. The team has good working relationships with other departments and patients can be referred to other disciplines such as Speech and Language Therapy, continence services and the falls service. Although the appointment may appear long, as a patient I find it less stressful and tiring than attending five separate appointments. Angus is a rural area and travelling to appointments can be problematic. The "one-stop" approach also allows the medical staff to assess the patient on the same day.
At the end of the clinic, the team meets to discuss the patient's progress and their score on the Unified Parkinson's disease Rating Scale (UPDRS) is calculated.
As a patient with Parkinson's, I feel very grateful for the level of care given to me and for the holistic approach of the team. Because of the variations in the condition, the MDT approach allows patients to have individualised care. If I have difficulties between appointments, I can easily contact my Parkinson's Nurse who can then arrange a meeting with the appropriate health professional. I really feel that I am at the centre of this multi-disciplinary team.

P43.08

Parkinson's – No longer the shaking palsy

*Gunvant Patel**
Self-employed, Melbourne, Victoria, Australia

Background: I was diagnosed five years ago with Parkinson's and as a psychiatrist it has been not only a time of personal reflection and re-evaluation but also an opportunity to bring a professional interest to my condition.
My experience of motor and non-motor symptoms over the last few years and the impact on my quality of life and functioning has brought to light limitations in how the condition is currently conceptualised; especially during the early stages before movement disturbance prevents independent functioning.
Objective: James Parkinson's 'An Essay on the Shaking Palsy' continues to influence current views that no longer hold. I wish to highlight the importance of moving away from Parkinson's as primarily a movement disorder and as a disease due to lack of dopamine. My professional knowledge of the major psychiatric disorder schizophrenia leads me to conceptualise Parkinson's as a neuropsychiatric syndrome. Neuropsychiatric meaning three broad domains of equal importance are involved – motor, mental and peripheral; and syndrome in that unlike with a disease we do not as yet know its cause.
In both conditions there are dopaminergic and non-dopaminergic features that require attention; yet in both the more dramatic and treatment-responsive aspects (motor in Parkinson's and delusions/hallucinations in schizophrenia) have influenced the perspective on diagnostic criteria, research and in particular management. Rating scales such as the gold standard MDS-UPDRS perpetuate this perspective with their predominance of items for movement disturbance.
Conclusion: The development of an assessment instrument that comprehensively captures the full range of symptoms would assist in progressive evaluation of the actual severity, impact on functioning and hence treatment/support needs. A targeted integrated multifaceted dynamic approach that optimises care and quality of life at all stages could then be offered to the person with Parkinson's.

P43.09

Little bits of big data for Parkinson's disease and co-morbidities: A computer programmer takes on his Parkinson's disease

*William Patterson**
Retired, Somerdale, NJ, USA

On my being diagnosed with Parkinson disease (PD) in 2010 I was shocked by the gravity of the diagnosis, and upset with how long it took to get the diagnosis as I had been asking various doctors, including neurologists, about various symptoms for years. This motivated me to go to work to learn and do as much as I could to reduce its impact on my life. I learned a lot.
Among many other things I learned is that there are significant benefits from high intensity aerobic exercise.
An example of such high intensity exercise is bicycle riding. Human experiments had shown high cadence biking to be successful at reducing symptoms. Animal model experiments had suggested intense aerobic exercise to be neuroprotective, i.e. stop or slow disease progress (although the US FDA has not approved any medications as being neuroprotective). I conjectured that bicycling, especially high cadence bicycling, COULD be neuroprotective. Further, I also conjectured that better effects, both symptomatic and neuroprotective could come from even higher cadences than had been used in experiments to date. (One big caveat is that at high cadences the risk of injury is greater and one has to be careful.)
Why conjecture? Why not insist on proof? I did not see a reason to wait 10 or 20 years for further research to take place, only to be told that both conjectures were correct and told that I would be far better off to have exercised during that time. I would have lost the benefits of neuroprotection and symptom abatement for those 10–20 years. The situation seemed to favor accepting the conjectures. If they were wrong, I would simply be healthier and have more fun.
I have used the information I could develop from a database of metrics from my exercise (1) to improve my exercising, (2) to deal with a co-morbidity, and (3) to develop a measure of the time-effectiveness of my medication for my movement disorder specialist.
I plan to provide downloadable copies of my written works at www.parkies.org.

Exercise optimization table / shows where and with what I got best cadences.

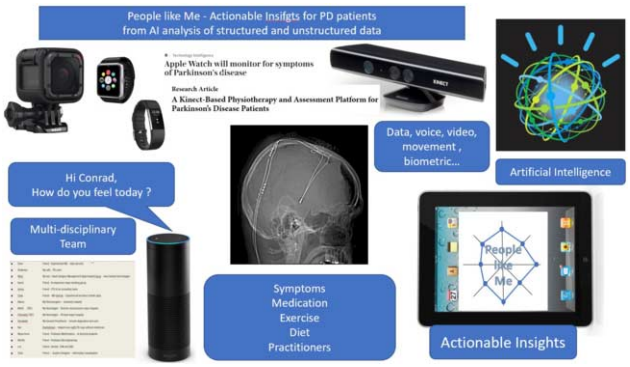
avcad	loc	equipment	shoes	num_sessions	num_data_points
110.04	gym	Spinning(TM)	cleated	96	296543
106.43	gym	Spinning(TM)	ordinary	38	99547
104.27	home	bike on stand	cleated	106	236402
101.11	gym	stationary cycle	ordinary	145	334077
94.87	home	bike on stand	ordinary	197	436584
90.35	gym	Expresso VR	ordinary	2	4029

P43.10

People like me: Voice-activated actionable insights for PD patients from AI analysis of structured and unstructured data such as voice, image, movement and biometrics

*Koen Van den Brande**
Patient, Mumbai, India

Background: Most PD patients are only seen by their doctor every few months, because it is a slowly advancing condition.
What data is collected is based on pre-defined parameters which reflect current understanding of the disease. The opportunity to collect unstructured data such as voice, video or movement, are limited.
Patients can only occasionally compare their personal progress against that of others through meetings and not in any systematic manner.
Objective: The People Like Me programme offers patients an opportunity to compare themselves against roughly similar individuals on dimensions of their choosing in order to identify differences that could lead to actionable insights.
Method: By using a voice-activated agent, patients can collect daily observations of voice, video and motion through an interactive dialogue about symptoms, medicines, exercises etc.
The integration of readily available technologies such as Alexa (or other voice activated agents) for voice activated interactions, Kinect for observing motion, Apple Watch and Fitbit to record biometric data and an iPad (or other tablet) to display results creates a daily stream of data which can be used by an AI engine like Watson to generate new insights and build up a People Like Me picture.
Results: Feasibility is confirmed by a number of studies such as …
Londoño, Sebastian. (2012). Parkinson Kinect System. 10.13140/2.1.1421.1846.
Ravindranath, Pradeep Anand et al.
A step forward in integrating healthcare and voice-enabled technology: concept demonstration with deployment of automatic medical coding model as an automatic medical coding model as an Amazon 'Alexa' skill.
Alzheimer's & Dementia: The Journal of the Alzheimer's Association, Volume 14, Issue 7, P955
...
A multi-disciplinary team of patients, carers, medical practitioners and technology specialists is working on refining the requirements.
A prototype will be available for demonstration at WPC, assuming arrangements can be made in advance.
Conclusions: By engaging proven, off-the-shelf and relatively inexpensive technologies under the control of the patient, we will be able to provide patients and the wider community alike with a much larger data set to draw new actionable insights from, using Artificial Intelligence.



P43.11

Development of a new seating system for postural deformities caused by Parkinson's disease

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Osaka-city Rehabilitation Center Assistive Technology Department, Osaka, Japan

Postural deformities are frequent and disabling complications of Parkinson's disease (PD) and atypical parkinsonism. These deformities include camptocormia, antecollis, Pisa syndrome, kyphosis, lordosis and scoliosis, and these deformities occur in complicated combinations. These postural deformities adversely affect various activities in daily living. We developed a new seating system for postural disorder caused by Parkinson's disease. This system provides seven problem solving methods to them. The first function is to provide CUE to get the proper posture. The second

function is to be able to select the posture required for daily living behavior. The third function is to help transfer to the chair. The forth function is to rotate the chair freely and be fixed every 90 degrees. The fifth function is to adjust the distance between the chair and the table. The seventh function is to help stand up from the chair. The seventh function is to provide an appropriate resting posture using posture conversion mechanism. This system has been adapted to people with stature from 150 to 185 cm. The load capacity is 120kg. Posture conversion can be electromotive type or manual type. Evaluation chart dedicated to this system will help you when you adapt to the patient. The following four evaluation methods are used to compare before and after adaptation, Guide to Seating Measures (ISO16840-1), Measurement weight load & weight transfer rate, Assessment of Subjective Visual Vertical, and Assessment of Activities of Daily Living.

We applied this system to 32 patients and evaluated the effect. As a result, we were able to confirm the effect of this systems for all patients. Almost every patients were able to obtain a proper posture and could improve daily living, and furthermore the burden on the body and the pain could be reduced. Although it was not able to obtain a direct effect on antecollis, it was able to reduce the burden on neck by getting a stable sitting posture. We will outline this system through this paper and report on the use effect. In the future we will decide the final specification and consider commercialization.

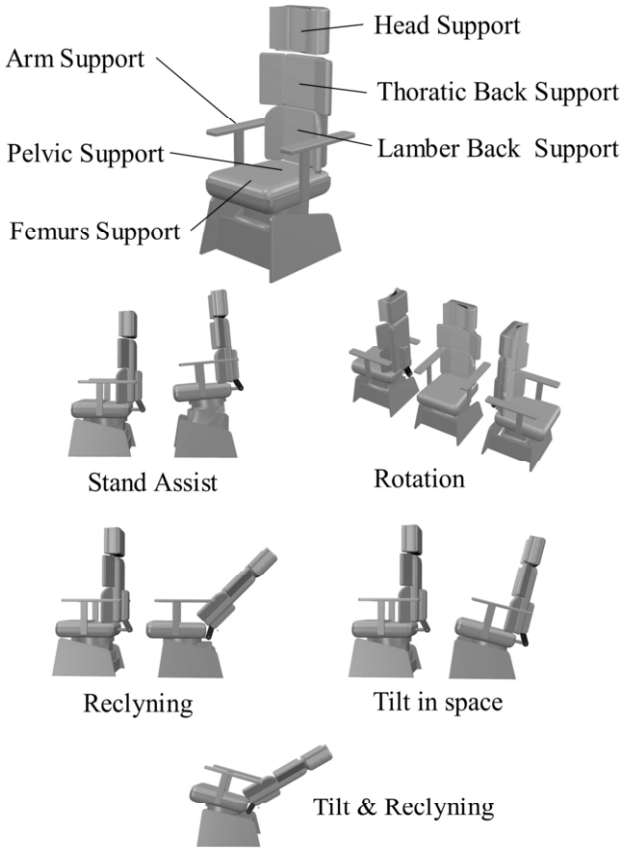

Fig.1

Late-Breaking Poster Presentations

BASIC SCIENCE: Etiology, genetics, epidemiology and toxicants

LBP.02

Association between SNPs of SLC41A1 and Parkinson's disease risk in the central Europe population

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Background: It has been proposed that loss of dopaminergic neurons in the pars compacta of the substantia nigra is connected to alteration of magnesium (Mg) homeostasis in brain. Mg2+ is required for numerous cellular processes including growth, proliferation and metabolic pathways. Intracellular Mg2+ homeostasis is strictly regulated. One of the transporters involved in regulation of Mg2+ balance is Na+/Mg2+ exchanger – SLC41A1, an integral protein located in the cytoplasmic membrane. The majority of Parkinson's disease (PD) cases are idiopathic. Several loci associated with idiopathic PD have been identified. Gene encoding Na+/Mg2+ exchanger is also located in PARK16 locus, which was found to be associated with susceptibility to PD.

Objectives: The purpose of this study was to analyze allele and genotype frequencies of single nucleotide variant rs11240569 (G>A; p.Thr113Thr) in Slovak cohort of PD patients (Caucasian origin) and matching control, non-PD group of probands. This variant has been associated with lower risk of PD development within certain populations.

Methods: TaqMan genotyping probes for qPCR were used to determine the presence or the absence of the variant in the cohort of Slovak PD patients and non-PD individuals, serving as control group.

Results: Our results indicate that the AA genotype is more prevalent in patients with PD compared to non-PD individuals. Presented data are consistent with previous observations of rs11240569 being associated with the risk of PD development. Presence of analyzed variant might modify regulation of transcription and thus alter total magnesium transport capacity of SLC41A1. This effect might contribute to magnesium deficit, previously described in both animal models and patients with PD.

Acknowledgement: This study was supported by grant VEGA 1/0277/18 and grant scheme of the government of SR – "Return home" to MK.

LBP.03

Analysis of SLC41A1 promoter sequence in Slovak cohort of Parkinson's disease patients

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Background: Magnesium (Mg) homeostasis was shown to be associated with numerous pathologies, including (neuro)degeneration. The most important regulator of Mg2+ homeostasis is Na+/Mg2+ exachanger SLC41A1. When over-activite, SLC41A1 leads to cellular Mg2+ deficit, which correlates with decreased survival of neurons. Transport capacity of SLC41A1 might be affected by alterations of SLC41A1 expression.
Objectives: Aim of the presented study was to perform sequencing analysis of the pre-defined fragment of SCL41A1 promoter region, located close to the transcription start site, in 100 patients with idiopathic Parkinson's disease (PD). Mutations in this region might affect binding capacity of various transcription factors and influence SLC41A1 expression pattern.
Methods: 100 Slovak patients with sporadic PD were involved in the study. DNA was isolated from peripheral blood samples. Sequenation analysis was performed by using Sanger sequencing. Pre-defined promotor fragment was divided into 4 regions by 4 pairs of primers. These regiones were individually amplyfied in Polymerase chain reaction (PCR) and subsequently used in PCR reaction with ddNTPs. Fragments were separated by capillary electrophoresis (ABI 3500 analyser). Sequences were analysed with BLAST.
Results: Genetic analysis did not revealed any variants in fragment 1 and 2 in any of 100 samples. However, two single nucleotide variants were present in fragment 3. These variants might affect the binding capacity of transcription factors and thus alter the expression of SLC41A1. Taken together, variants in promoter region of SLC41A1 might lead to change of Mg2+ transport capacity of SLC41A1 and thus contribute to the process of neurodegeneration. We have identified 2 candidate SNP in SLC41A1 promoter that will be further examined in regard to expression activity of SLC41A1.
Acknowledgement: This study was supported by grant VEGA 1/0266/18 and grant scheme of the government of SR – "Return home" to MK.

LBP.05

Genetic basis of inherited Parkinson's disease in Finland

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Introduction: Approximately 5 to 10% of Parkinson's disease (PD) is estimated to have a hereditary etiology. In recent years, at least 23 gene loci have been linked to monogenic PD. In Finland, however, only a few disease linked gene variants have been found so far, which may be related to the unique genetic heritage of the population.
Aims and methods: To find out if there are previously known gene variants in PD genes in the Finnish population, we searched for variants found in literature search in a new genetic database, SISu (1), which contains genetic data of over 10 000 Finns. In addition, to confirm our population findings and search for new gene variants, we sequenced 47 patients with suspected monogenic disease with a panel of 82 PD-associated genes. Another cohort of 147 idiopathic patients was used to investigate one promising variant found in the population data further.
Results: We found 16 possibly pathogenic variants in five PD genes (LRRK2, HTRA2, PARK2, PINK1, DJ-1) in the population data (2). Three of them were considered likely pathogenic and six likely benign after our pathogenicity analysis. From the patient cohorts we found nine potentially disease linked variants in known PD genes (PARK2, PINK1, SNCA, LRRK2, ATP13A2) in eight patients. Four of these were novel and two we have already published in collaborative studies (3,4). In addition, we found several possibly deleterious variants in candidate genes, which we are currently validating further.
Discussion: Finns carry only few previously described variants in known monogenic PD genes. Our results suggest that Finnish patients carry their own unique disease variants, some of which we also found in our study. We were also able to evaluate the disease risk of many known PD variants further by simply studying their occurrence in Finns. The study of novel disease variants may also bring valuable information about the pathogenic processes related to PD, which was clearly demonstrated by the discovery and recent functional study of Parkin p. S65N (3).
References:
[1] http://sisuproject.fi
[2] Palin E. et al. (poster), Euromit, 2014, Finland
[3] McWilliams T. et al., Open Biol. 2018
[4] Pasanen P. et al., Neurobiol Aging. 2017

LBP.06

Potential blood based biomarkers for Parkinson's disease by genetic and epigenetic analysis

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Parkinson's disease is a devastating age-related neurodegenerative disorder mainly affecting dopaminergic neurons of the nigral-striatal pathway. Behavioral symptoms of the disease do not occur until many of the neurons have already been lost. Moreover, direct methods to measure neuronal damage in humans are invasive,

complex, and not always feasible. Therefore, disease biomarkers based upon non-invasive and simple yet practical methods are desirable. We have previously exploited publically available gene expression and other epigenetic data from databases that measured gene level changes in blood of PD patients and compared to controls. These efforts resulted in a panel of 85 genes that identified potential biomarkers by integrating their gene expression and methylation patterns. Since 85 genes remain a large number for investigative studies into basic mechanisms and relationship with brain degeneration, and development of assays, we further refined the list of potential biomarkers for PD by filtering and orthology analysis. First, we investigated the expression patterns of these genes in other human tissues. Secondly, we evaluated their expression levels and splicing patterns. Thirdly, we identified orthologs of these genes in model animals. Finally, we evaluated their potential regulation by miRNAs and other noncoding RNAs. These data provide a more concise and feasible list of genes for use as a PD biomarker panel. Moreover, orthology and splicing data may provide insights into the neurodegenerative processes taking place during PD. Taken in combination with other nongenetic or epigenetic based biomarkers the ability to accurately predict PD in humans should potentially become markedly improved. This study was supported by University of Macau grant MYRG2016-00101-FHS.

BASIC SCIENCE: Cell death, disease modification, and trophic factors

LBP.07

Analysis of Parkinson's disease at a single neuron level

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[2] NIH, Bethesda, MD, USA
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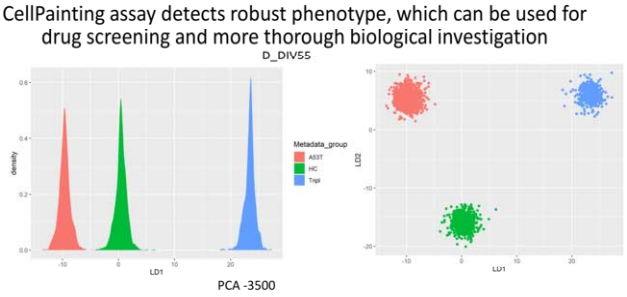
Parkinson's disease is the second most common neurodegenerative disease worldwide. However, no available therapies alter the underlying neurodegenerative process, characterized by loss of dopamine neurons in the substantia nigra pars compacta and subsequent degeneration of cortical neurons.
Stem cell differentiation methods progress rapidly, creating good models where we can obtain human dopamine and cortical neurons from induced pluripotent stem cells derived from patients with mutations in the α-synuclein gene. These models allow exploration of the effects of the mutations in the α-synuclein gene whilst retaining the patient's genetic background. We have developed versatile and scalable dopaminergic and cortical neuron differentiation protocols that successfully produced electrophysiologically active neurons carrying mutations in the SNCA gene (A53T and triplication of SNCA), suitable for single neuron high-throughput image analysis. We have tested, adapted and implemented the image based Cell-Painting assay (Bray et al., 2017), which allow us to quantify multiple molecular and phenotypic changes of stem cell derived neurons with mutations in the α-synuclein gene (A53T and triplication of SNCA). Firstly, we demonstrated that Cell-Painting assay is very sensitive analysis method, which is able to detect fine differences between toxin treatments. Secondly, we developed data profiling tools to cluster treated cells and extract biological reasons for clustering of the cells. Thirdly, we applied these methods to analyse stem cells derived neurons with mutations in SNCA gene, where found the distinct differences between neurons with and without mutation. Lastly, by comparing observed phenotypes with published databases, we selected and screened compounds, which have opposite effect to the phenotypes observed in dopaminergic neurons having A53T mutation and triplication of SNCA. Some of the compounds have reversed differences observed between "heathy controls" neurons and A53T mutation and triplication of SNCA, therefore we are currently extending screening by selecting even more specific compounds.
In this work, we show how to apply high-throughput microscopy to reveal significant differences and delineate fine changes at single neurons. In addition, we developed tools allowing us to manipulate and reverse those difference. This is a novel, non-biased and non-specific Parkinson's disease analysis approach, which revealed novel drug targets and potentials compounds to modulate observed differences!



BASIC SCIENCE: Protein misfolding, handling, and transmission

LBP.08

The Cryo-EM structure of amyloid fibril formed by full-length α-synuclein

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[2] School of Life Sciences, Tsinghua University, Beijing, China

Alpha-synuclein (α-syn) fibrils serve as the major component of Lewy bodies as the pathological hallmark of Parkinson's disease (PD) and other synucleinopathies. High-resolution structure of pathological fibril formed by α-syn is important to understand the pathological mechanism. By using cryo-electron microscopy, we determined a fibril structure of full-length α-syn (1–140) at the resolution of 3.07 Å. The fibrils are highly cytotoxic and transmissible for inducing α-syn aggregation in primary neurons. Based on the EM density map, we unambiguously built the fibril structure of α-syn comprising residues 38–102. The fibril structure features two protofilaments intertwining along an approximate 21 screw axis into a left-handed helix. Each protofilament features a Greek key-like topology. Notably, five early-onset PD familial mutations are located at the dimer interface of the fibril (H50Q, G51D, and A53T/E) or involved in the stabilization of the protofilament (E46K). Furthermore, these PD mutations lead to the formation of fibrils with polymorphic structures distinct from that of the wild-type. Our study provides molecular insight into a fibrillar assembly of α-syn at the atomic level and illuminates the molecular mechanism underlying familial PD mutations of α-syn.

LBP.09

Interplay between α-synuclein and lipids in Parkinson's disease

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[2] Bio-X Institutes, Key Laboratory for the Genetics of Developmental and Neuropsychiatric Disorders, Ministry of Education, Shanghai Jiao Tong University, Shanghai, China

Abnormal α-synuclein (α-syn) aggregation in Lewy bodies is the pathological hallmark of Parkinson's disease (PD) and other synucleinopathies such as Infantile Neuroaxonal Dystrophy (INAD), and idiopathic Neurodegeneration associated with Brain Iron Accumulation (NBIA)1. Despite its high propensity to aggregate under pathological conditions and when isolated in vitro, native α-syn is a highly abundant soluble neuronal protein in the CNS (~1% of the total proteins) and resists aggregation in normal intracellular environments. However, little is known how α-syn maintains its native structure. Here we systemically investigated lipid-binding partners of α-syn using untargeted global lipidomic profiling. We found that different α-syn species (e.g. monomer, oligomer and fibril) have distinct binding preferences to lipid molecules. We identified a class of lipid molecules which specifically bind with the N-terminal of α-syn monomer, induce a compact α-helical conformation and stabilize α-syn monomer from aggregation. Importantly, this lipid mediates physiological function of α-syn in synaptic vesicle trafficking. PD familial A30P α-syn mutant shows reduced binding affinity with the lipids. Furthermore, decreased production of this class of lipids dramatically promotes α-syn aggregation in cells. Our study suggests that dysfunctions in the lipid homeostasis might be critical in the development of Lewy body diseases.

LBP.10

Protein aggregation and exosomal release induced by α-synuclein: new insights into protective mechanisms of Drp1 inhibition

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[1] Florida International University, Miami, Florida, USA
[2] Fudan University, Shanghai, China
[3] Plymouth University, Plymouth, United Kingdom

Targeting α-synuclein (α-syn) as a therapeutic strategy for Parkinson's disease (PD) has been intensively pursued largely due to its well-recognized pathogenic role. We report here that blocking dynamin-related protein 1 (Drp1) improved autophagic flux in experimental models of α-syn. Using the rat N27 dopaminergic neuronal cells with inducible wild-type human α-syn, we observed proteinase-K resistant α-syn aggregates two days after the induction of α-syn expression. Consistently with the effects of α-syn on blocking autophagy, we observed higher levels of LC3 and p62 levels in these cells. However, knocking down Drp1 with siRNA drastically attenuated the accumulation of these autophagic proteins and reduced protein aggregation. To more directly monitor autophagy flux, we utilized the autophagy reporter HeLa cells with stable expression of mRFP-GFP-LC3. These cells were then either treated with human α-syn preformed fibrils (PFF) or co-transfected with a plasmid encoding wild type human α-syn in the presence or absence of siRNA-Drp1. Drp1 knockdown significantly attenuated autophagy impairment induced by α-syn. Impaired autophagy flux has been reported to increase the release of exosomes containing α-syn. Consistently with the observations above, we obtained data showing that Drp1 inhibition reduced exosomal release and spread of α-syn pathology from neurons to neurons and from microglia to neurons. To investigate how and at what stage of autophagy flux Drp1 inhibition had an impact on, we transfected the autophagy reporter HeLa cells with siRNA-Drp1 and then treated them with chloroquine to block lysosomal function. Drp1 inhibition partially improved lysosomal function as evidenced by an increase of autolysosomes. We also assessed mTOR activity by quantifying the levels of phosphor-4E-BP1, which is a downstream substrate of mTOR. We observed α-syn activated mTOR, and strikingly, knocking down Drp1 inhibited mTOR activity to an equivalent extent as rapamycin. In summary, his study highlights new insights that Drp1 inhibition confers neuroprotection through the autophagy-lysosomal pathway, further strengthening the therapeutic potential of targeting Drp1.

BASIC SCIENCE: Mitochondria, oxidative stress, and pathogenesis

LBP.11

Dissecting the effect of Parkinson's disease-related Miro1 mutations in mitochondria-associated membranes and mitophagy

Clara Berenguer-Escuder[*,1], *Paul Antony*[1], *François Massart*[1], *Philip Seibler*[2], *Christine Klein*[2], *Anne Grünewald*[3], *Dajana Großmann*[1], *Rejko Krüger*[1]
[1] Clinical and Experimental Neuroscience, Luxembourg Centre for Systems Biomedicine (LCSB), Belvaux, Luxembourg
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Background: Miro1 protein is not only a well known adaptor for mitochondrial transport, but also regulates mitochondrial function and quality control. Miro1 is associated with the endoplasmic reticulum (ER)-mitochondria contact sites, called mitochondria-associated membranes (MAMs). MAMs were shown to be key regulators of cellular calcium homeostasis and autophagy, and the alteration of these mechanisms was linked to neurodegeneration in Parkinson's disease (PD). Recently, we identified four PD-associated variants of RHOT1/Miro1. We hypothesize that these variants disturb MAMs function and mitochondrial dynamics, resulting in an alteration of the cellular activity and integrity.
Methods: Human skin fibroblasts were reprogrammed into induced-pluripotent stem cells (iPSCs) for subsequent differentiation into iPSC-derived midbrain dopaminergic neurons. Cells were maintained in chamberslides for live-cell imaging of mitochondrial degradation and starvation-induced autophagosome formation. Cells were seeded on coverslips for immunostaining of mitochondria and ER to analyze co-localization. Intracellular and extracellular protein amount was quantified by immunoblotting.
Results: Quantification of ER-mitochondria juxtapositions showed a significant alteration of the amount of MAMs in mutant fibroblasts and iPSC-derived neurons. Live-cell imaging results revealed altered autophagosome formation and LC3-dependent autophagy flux in mutant fibroblasts, as well as impaired mitochondrial degradation in mutant iPSC-derived neurons. Western blot analysis demonstrated increased protein levels of an autophagy-related small GTPase in mutant fibroblasts. α-synuclein protein levels were altered in mutant iPSC-derived neurons.

Conclusions: Miro1-mutant cells display an altered ER-mitochondrial tethering compared to control cells. We speculate that this alteration interferes the lipid transfer from MAMs to ER for the synthesis of autophagosomes in fibroblasts, contributing to a general impairment of LC3-dependant autophagy flux. Miro1-mutant fibroblasts may facilitate mitochondrial turnover via an alternative autophagic mechanism. Miro1-mutant neurons show defective autophagy flux, which may result in a disrupted mitochondrial turnover and an altered α-synuclein protein levels.

LBP.12

Role of metformin in diabetic aging female rat brain: A future therapy for neurodegenerative diseases

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Background: The emerging view is that diabetic brain features many symptoms that are best described as accelerated brain aging. Metformin is the most frequently used oral anti-diabetic drug, which apart from hypoglycaemic activity, improves serum lipid profiles, positively influences the process of haemostasis, and possesses anti-inflammatory properties.
Objective: The objective of this study was to investigate effects of metformin on glucose transporter (GLUT1, GLUT3) expression, intracellular calcium levels, expression of synaptic molecules synaptophysin and synapsin I, biomarkers of oxidative stress such as antioxidant capacity (FRAP), malondialdehyde (MDA), reduced glutathione (GSH), protein carbonyl (PCO), reactive oxygen species (ROS) and neurolipofuscin in diabetic aging brain of female rats.
Methods: Young (3 months) adult (12 months) and aged (24 months) rats will be diabetic by using alloxan monohydrate. Metformin was administered i.p. at a dose of 200 mg/kg/day for 30 days to both control and diabetic aging rats. A detailed study was carried on expression of glucose transporter, calcium levels, biomarkers of oxidative stress. Morris water maze with expression of synaptic molecules synaptophysin and synapsin I and ultrastructural studies of brain region by magnetic resonance imaging.
Results: Present study shows that there was a similar pattern of increased intracellular calcium levels, neurolipofuscin, MDA, PCO, and ROS levels, and a decrease in levels of FRAP, GSH and (GLUT1, GLUT3) expression in brain of both aging and diabetes. On the other hand, metformin treated groups exhibited significant reduction in helped to reverse the age related changes studied, to normal levels. Metformin treatments improved attention and memory functions with enhanced the levels of synaptic molecules synaptophysin and synapsin I. Our data showed that exogenous administration of Metformin brought these changes to near normalcy in diabetic aging female rats.
Conclusions: The results of this study will be useful for pharmacological modification of the aging process and applying new strategies for control of age related disorders including metabolic syndrome and neurodegenerative diseases.

LBP.13

Maintenance of lysosomal homeostasis by LRRK2 and Rab GTPases: implications for the pathomechanism of Parkinson's disease

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LRRK2, a causative gene product for autosomal dominant Parkinson's disease (PD), has been implicated in the regulation of lysosomes. LRRK2 harbors kinase activity, and recent studies have identified a subset of Rab GTPases, including Rab8, Rab10 and Rab7L1, as bona fide substrates. Here we investigated the roles and mechanisms of LRRK2 and its substrate Rab GTPases in the regulation of the lysosomal morphology and functions. We revealed that lysosomal overload stress induced the recruitment of Rab7L1 and LRRK2 onto the enlarged lysosomes, where endogenous LRRK2 was activated depending on Rab7L1. The family-wide screening of Rab GTPases that may act downstream of LRRK2 translocation revealed that Rab8a and Rab10 were specifically accumulated on overloaded lysosomes dependent on their phosphorylation by LRRK2. Rab7L1-mediated lysosomal targeting of LRRK2 attenuated the stress-induced lysosomal enlargement and promoted lysosomal secretion, whereas Rab8 stabilized by LRRK2 on stressed lysosomes suppressed lysosomal enlargement and Rab10 promoted lysosomal secretion, respectively. Of note, the expression of familial PD-associated mutant LRRK2 commonly increased its ability to attenuate lysosomal enlargement, when compared with that of wild-type LRRK2. These results suggest that the lysosomal homeostasis is maintained by a stress-responsive pathway composed of Rab7L1, LRRK2 and phosphorylated Rab8/10, and that the dysregulation in this pathway may contribute to the pathogenesis of PD.

LBP.14

Functional studies of mitochondrial protein p13 in the experimental parkinsonism model

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Mitochondrial dysfunction in the midbrain dopaminergic system is known a crucial hallmark of Parkinson's disease (PD). In the basic science field, rodents administrated with mitochondrial toxins has been used as an useful animal model since that shows cellular and behavioral dysfunctions resembling those in patients with PD. Previously, we identified a novel 13-kDa protein (p13) and showed p13 is highly expressed in midbrain, localized in mitochondria matrix, and may be involved in mitochondrial oxidative phosphorylation. Here, we addressed the functional roles of p13 by using mitochondrial toxin-induced PD models and p13 knockout mice. In dopaminergic cell line, p13 overexpression induces mitochondrial dysfunction, and apoptosis and p13 knockdown attenuates toxin-induced mitochondrial dysfunction and apoptosis via the regulation of complex I. In heterozygous p13 knockout mice, toxin-induced motor deficits and the loss of nigrostriatal dopaminergic neurons are markedly ameliorated. Accordingly, these results characterizes functional properties of p13 in midbrain and represent that manipulating p13 expression is a promising approach for therapeutic intervention in PD.

LBP.15

Mitochondrial fitness: novel diagnostic tool for patients with Parkinson disease

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Mitochondrial diseases are characterized by deteriorated mitochondrial functions. Clinical diagnostics is focused mostly on a group of relatively rare primary mitochondrial diseases (PMDs). PMDs are usually linked to pathogenic mutations in mitochondrial and/or nuclear DNA that negatively affect oxidative phosphorylation and the proper function of mitochondria.
Deviated mitochondrial homeostasis hallmarks also heterogeneous group of mitochondrial diseases known as Secondary Mitochondrial Diseases (SMDs) that involve progressive metabolic, cardiovascular, muscular or neurodegenerative diseases, Parkinson disease included. Even thought the worldwide prevalence of SMDs is significantly higher than of PMDs, the detection of physiological status of mitochondria is rarely considered in PMDs and overall remains underestimated in clinical praxis.
The aim of our project was to establish a clinically applicable algorithm reflecting the nunc tempus physiological state of mitochondria (mitochondrial fitness; MF). A complex evaluation protocol for determination of personalized MF will help: (1) to diagnose the disease, (2) to draw a complex clinical image, (3) to make a prognosis of the disease progression, and (4) to adjust the therapeutical regimen according to stage of the disease. MF is determined in PBMC (peripheral blood mononuclear cells) using three separate molecular methods.
Physiological analysis is performed in intact and permeabilized cells with high-resolution respirometry to measure the oxygen consumption in different states induced by combination of substrates and inhibitors of respiratory chain components. Molecular evaluation of mitochondrial integrity is based on TaqMan multiplex qPCR with two mitochondrial (D-loop, ND4 gene) and one nuclear (β2M) targets to identify the mitochondrial copy-number ratio and the stage of heteroplasmy. Biochemical analysis identifies the activity of individual respiratory complexes through enzymatic reactions that are detectable spectrophotometrically.
MF could serve as a dynamically responding marker reflecting the current status of mitochondria in initialization/progression of pathological process and subsequent therapeutical response of patients with PD.
Supported by the projects APVV-16-0033 and VEGA1/0554/19.

BASIC SCIENCE: Animal and cellular models of Parkinson's disease and Parkinsonisms

LBP.16

Robust generation of oligodendrocytes from pluripotent stem cells: a platform for studying disease mechanisms

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Oligodendrocytes are the brain cells responsible for myelinating axons in the CNS. Oligodendrocytes are produced during the development and postnatally. During their differentiation, oligodendrocytes undergo morphological changes and express specific markers. Developing oligodendrocytes are characterized by co-expression of transcription factors SOX10, OLIG2 and NKX2.2. Oligodendrocyte Progenitor Cells (OPCs), are the first cell type of the oligodendrocyte lineage; they express PDGFR-alpha. The transition of OPCs to immature/non-myelinating oligodendrocyte is marked by modification of cell-surface sulfatide recognized as O4 antigen. Mature-myelinating oligodendrocytes express Myelin Basic Protein (MBP), which is necessary for the myelination of axons. An important challenge in the field of disease modelling using stem cells is to generate oligodendrocytes in quantity enough for studying oligodendrocyte-related disease mechanisms. Moreover, recent evidence suggests that oligodendrocytes may play an important role in Parkinson's disease, Alzheimer's disease, Multiple System Atrophy and Amyotrophic lateral sclerosis. Scaling up the production of oligodendrocytes is therefore of paramount importance.
Here, we report the development of new protocols for generating oligodendrocytes from both rodent and human pluripotent stem cells, yielding up to 60% O4-positive oligodendrocyte lineage cells, measured by fluorescent activated cell sorting. The scaled-up production of oligodendrocytes from diseased pluripotent stem cells should allow us to perform omic studies, in order to identify whether or not oligodendrocyte cellular networks are altered in neurodegenerative diseases, including PD, thereby revealing oligodendrocytes as potential new targets for therapeutic intervention.

LBP.17

CLR01 protects dopaminergic neurons in vitro and in vivo in mouse and human models

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Parkinson's disease (PD) is the second most common neurodegenerative disease affecting thousands of patients worldwide. The molecular tweezer CLR01 has shown great promise as an anti-aggregation therapy, therefore we investigated whether this molecular tweezer could provide significant relief in vitro and in vivo in human and mouse models. In vitro, this compound was capable of decreasing α-synuclein aggregation in induced pluripotent stem cell-derived dopaminergic cultures. We insulted dopaminergic cultures with synuclein aggregates purified from post-mortem PD brain extracts, which had been pre-treated with PBS or

CLR01. CLR01 pre-treatment resulted in a reduction of synuclein aggregates and toxicity. Through microfluidic analysis, we found that CLR01 reduced α-synuclein aggregation in cells somas, when axonal terminals were exposed to α-synuclein oligomers. These data prompted us to test this compound in vivo in a human α-synuclein overexpressing model that had previously been shown to exhibit motor defects due to dopaminergic cell loss as well as synaptic defects. At 18 months of age, when dopaminergic cells have already been lost in this model, we found that 1 month of CLR01 treatment could reduce α-synuclein oligomeric burden. Finally, when we treated mice for two months at 12 months of age, when motor defects are only very mild, we observed an improvement in motor defects as well as a decreased oligomeric burden. Altogether, these results highlight that CLR01 could be helpful in the development of a disease modifying therapy for PD.

LBP.18

iPSC-derived dopaminergic neurons reveal LRRK2 mutations impair clathrin mediated endocytosis and help identify novel LRRK2 substrates

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Mutations in LRRK2 have been associated with numerous cellular pathways in PD. To investigate dysregulated pathways in an unbiased manner, we performed dual proteomic and transcriptomic analysis of iPSC-derived dopaminergic neurons from LRRK2-G2019S patients and controls. The endocytic pathway was the most significantly affected (p=1.89E-09). Western blot analyses confirmed that members of this pathway, including Endophilin and Dynamin-1, are downregulated in LRRK2-G2019S and LRRK2-R1441C iPSC-derived cultures. Furthermore, we demonstrated a functional deficit in endocytosis in these cells using FM dyes.
To further validate our findings we investigated endocytosis in LRRK2 BAC transgenic rats expressing either the human R1441C or G2019S mutation. In striatal tissue, we identified age-dependent alterations in levels of the same key endocytic proteins that were dysregulated in our iPSC model and changes in synaptic vesicle distribution. We have also demonstrated perturbations in the same pathway in human post-mortem tissue from G2019S patients.
As LRRK2 mutations increase its kinase activity it is important to understand its kinase substrates. No such studies have yet been carried out in dopaminergic neurons that degenerate in Parkinson's. We therefore carried out a phosphoproteomic study using control and G2019S derived-iPSC dopaminergic neurons. To avoid off-target effects we used two LRRK2 kinase inhibitors and analysed inhibitor treatment in LRRK2 KO iPSC neurons. This approach identified a 29 LRRK2 kinase substrates mostly implicated in neurite outgrowth and vesicle trafficking.
Together, our findings implicate LRRK2 in endocytosis and vesicle trafficking, and demonstrate that LRRK2 mutations lead to perturbations in these pathways.

LBP.19

Assessment of potential neuroprotective effects of nicotine in a human dopaminergic in vitro model of Parkinson's disease

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Over the past 50 years, retrospective epidemiological studies have consistently demonstrated an inverse association between the risk of developing Parkinson's disease (PD) and history of tobacco use, with a two-fold risk decrease among tobacco smokers and snus users. An increasing number of studies on cellular and animal toxin models of PD, as well as clinical trials, also suggest that nicotine could act as a neuroprotective agent via activation of nicotinic acetylcholine receptors, but the specific underlying mechanism remains largely unknown. In PD, the aggregation of α-Synuclein (α-Syn) into intraneuronal inclusions called "Lewy bodies" represents a major pathological hallmark of the disease, and several studies now indicate that nicotine could attenuate α-Syn aggregation kinetics in a test tube as well as in yeast. In this study, we aimed to determine whether nicotine and other tobacco compounds could exert a neuroprotective role against α-Syn-induced toxicity in a human dopaminergic neuronal model of PD. We differentiated human-induced pluripotent stem cells into dopaminergic neurons and then treated neuronal cultures with increasing doses of α-Syn Preformed Fibrils (PFF) or α-Syn monomers as controls. Various experimental conditions were tested using real-time and medium-throughput approaches: (i) neuronal adhesion/neurite outgrowth was assessed by impedance-based measurements using the xCELLigence® Real Time Cell Analyzer system, and (ii) mitochondrial respiration functions were evaluated using the Agilent Seahorse® analyzer. Our results show that α-Syn PFF treatment induces dose-dependent neurodegeneration, neuritic pathology, and mitochondrial dysfunction in human dopaminergic neurons, thereby demonstrating the utility of this system to model molecular features of PD. Importantly, nicotine pretreatment for one hour was able to protect against multiple features of α-Syn PFF-induced toxicity in dopaminergic neurons in a dose-dependent manner. Current efforts are directed toward dissecting the mechanism through which nicotine exerts this observed beneficial effect. Together, our results provide a robust medium-throughput in vitro model of α-Syn PFF-induced toxicity in human dopaminergic neurons and pave the way toward a better understanding of mechanisms underlying the observed beneficial effects of nicotine in PD.

LBP.21

Suppression of autophagic activity by Rubicon is a signature of aging

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The activity of basal autophagy, an evolutionally conserved cytoplasmic degradation system decreases with age in many organisms, while autophagy has emerged as convergent downstream mechanism in different longevity pathways. However, the molecular mechanism by which autophagy is regulated during aging is unknown. In addition, it remains largely elusive if the forced activation of basal autophagy suffices to extend animal lifespan and healthspan. Recently, we found that Rubicon, a negative regulator of autophagy is increased with age in worms, fly and mouse tissues, suggesting that age-dependent increase of Rubicon could be a reason for age-dependent impairment of autophagy(Nakamura et al., Nat Commun, 2019). Consistent with this idea, knockdown of Rubicon extends lifespan in worms and fly. Moreover Rubicon knockout mice ameliorate several age-associated phenotypes including α- synuclein pathology in mice. Interestingly, Rubicon expression is suppressed by several lifespan-extending conditions including calorie restriction in worms and mice. Our current results strongly suggest that suppression of autophagic activity by Rubicon is one of signature of aging.

LBP.22

Differential neuroprotective properties of nilvadipine enantiomers in experimental models of Parkinson's disease

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Parkinson's disease (PD) is the second most common neurodegenerative disease with an average age of onset of around 65. It is characterized by a progressive loss of dopaminergic neurons in the substantia nigra, which leads to debilitating motor and non-motor symptoms. This occurs alongside chronic neuroinflammation and α-synuclein-rich inclusions that present as Lewy-body pathology. Epidemiological and experimental evidence suggests that calcium channel blockers could play a protective role in the disease process. However, the mechanisms by which calcium channel blockers could elicit neuroprotection have not been elucidated. In our study, a safe and clinically approved L-type calcium channel blocker, nilvadipine, which has been used for treating hypertension, was used to study its efficacy in experimental PD. We carried out both in vitro and in vivo studies, where pre-treatment with nilvadipine showed protective effects, which were enantiomer dependent. In vitro treatment of N27 dopaminergic neuronal cells with nilvadipine demonstrated reduced cell death induced by Parkinsonian neurotoxicants MPP+ and 6-OHDA. Crucially, daily dosing with nilvadipine at 8 mg/kg significantly improved behavioural deficits and striatal dopamine levels in the 6-OHDA model of PD. Interestingly, the protective effects of nilvadipine were more pronounced in the (-)-nilvadipine enantiomer. Collectively, our studies suggest that nilvadipine reduces neuroinflammatory responses in microglia while also directly mitigating dopaminergic neuronal cell loss suggesting that it could elicit neuroprotection by multiple mechanisms. Therefore nilvadipine could have potential to be repurposed for Parkinson's disease.

LBP.23

Neuroprotective potential of curcumin along with piperine against MPTP induced Parkinsonism in rats: behavioral and neurotransmitter analysis

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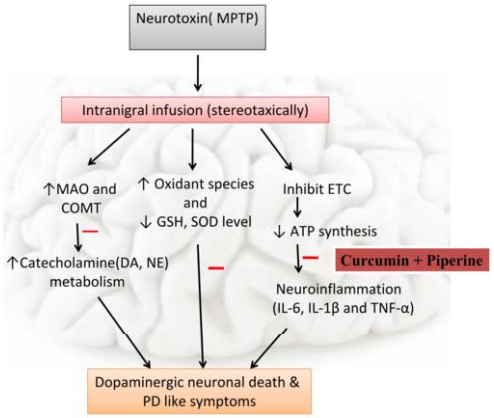
Purpose: MPTP is a neurotoxin affects dopaminergic neurons and produce Parkinsonism both in human and rodents. Studies evidenced curcumin possesses neuroprotective potential but major complication is its poor oral bioavailability. Thus present study was designed to study neuroprotective effect of curcumin in combination with piperine against MPTP induced Parkinsonism in rats.
Methods: Rats were administered MPTP (100).



LBP.24

PET imaging reveals early and persistent dopaminergic deficits after intra-striatal injection of preformed α-synuclein fibrils

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α-synuclein (αSyn) can aggregate and form insoluble fibrils which are the main component of Lewy bodies. Intra-neuronal Lewy bodies are the characteristic pathology of Parkinson's disease (PD). These fibrillar structures can act as seeds and accelerate the aggregation of monomeric αSyn. Indeed, recent studies show that injection of Preformed αSyn Fibrils (PFF) into the nigrostriatal system can induce aggregation of the endogenous monomeric αSyn resulting in dopaminergic neuronal death.
In this study, we injected 8 µg of mouse αSyn PFF, or soluble monomeric αSyn into the right striatum of Sprague Dawley female rats (total n=25). The rats were monitored behaviourally using the cylinder test, which measures forelimb use, and the corridor task that measures lateralised sensorimotor response to sugar-treats. In vivo PET imaging was performed after 3 and 5 months using 11C-DTBZ, a tracer of the vesicular monoamine 2 transporter (VMAT2). After the final scan, histology was performed using tyrosine hydroxylase (TH) as a marker of dopaminergic neurons, and the antibody MJF14 that can detect aggregated αSyn.
While, no paw asymmetry was found in the cylinder test, in the corridor task, the PFF rats had a tendency to wait longer to approach the 1st treat-container, approach less containers and eat less treats. Analysis of the DTBZ PET imaging showed that PFF αSyn injection led to a significant unilateral reduction of VMAT2 binding after 3 and 5 months (45% and 55% reduction, respectively), but not in the monomer- αSyn injections. Preliminary histology data show loss of dopaminergic (TH+) axons in the striatum (neuronal cell death in nigra is currently being quantified) and αSyn PFF pathology in nigral neurons.
Our histology data is consistent with the dopaminergic degeneration and αSyn PFF pathology observed in earlier studies, although this appears to be unilateral, vs the bilateral degeneration reported by others. We show here that this degeneration correlates with mild lateral neglect and an early but persistent significant reduction in VMAT2 in the PFF injected striatum. This model therefore replicates some of the changes present in human PD and can be useful for the testing of new therapeutic agents.

LBP.25

Synaptojanin 1 (SYNJ1) haploinsufficiency causes impaired autophagy and age-dependent decreased dopamine release in the dorsal striatal slices

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Mutations in SYNJ1 gene have been described in autosomal recessive early-onset Parkinson's disease (PD). This gene encodes for "synaptojanin 1," a phosphoinositide phosphatase known to play an important role in phosphorylation and the recycling of synaptic vesicles. In this study, we found age-dependent motor function impairments in SYNJ1 heterozygous (Het) deletion mice. We measured dopamine (DA) release using fast-scan cyclic voltammetry in acute striatal slices from both Het and wild-type (WT) control mice. We found that single pulse-evoked DA release in the dorsal striatum from the Het mice was decreased in an age-dependent manner when compared to their WT controls. There was no difference for single pulse-evoked DA release from mice at the age of 3–4 months, whereas single pulse-evoked DA release was decreased by 30% from aged Het mice (>17 months old). Recent studies suggest that synaptojanin 1 is involved in autophagy regulation. We therefore examined the autophagy pathways. We found that LC3II was increased in the Het mice at the basal condition. With baflomycin A1 treatment, LC3II accumulated in WT slices but not in the Het slices. Therefore, autophagy is blocked in the Het mice at a later step of lysosomal fusion/clearance of autophagosomes. Our findings suggest that down-regulation of SNY1 predisposes mice to PD, an age-dependent neurodegenerative disease via autophagy impairment.

BASIC SCIENCE: Dopamine, receptors, and other neurotransmitters

LBP.26

GABA potently inhibits platelet activation: ex vivo and in vivo studies

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Gamma-Aminobutyric acid (GABA) is the major inhibitory neurotransmitter in the central nervous system and it also appears in peripheral tissues. Platelets have been shown to possess a GABA uptake system. However, until the present study, no published reports had documented the characteristics and functional activity of GABA in platelets. This study was to examine the cellular signal events associated with GABA-mediated platelet activation. The aggregometry, flow cytometry, immunoprecipitation, and electron spin resonance were used in this study. GABA specifically antagonized collagen-induced platelet activation accompanied by PLCgamma2, p47, Akt phosphorylation, [Ca2+]i mobilization, and hydroxyl radical formation; in addition, GABA interfered with FITC-collagen binding to platelet membranes. Furthermore, GABA produced a concentration-related rightward displacement of the collagen concentration-response curve, indicating specific antagonism. Furthermore, GABA markedly inhibited platelet activation stimulated by convulxin. Immunoprecipitation revealed

that GABA directly associated with glycoprotein VI but not with integrin α2β1 in platelet membrane. Moreover, GABA significantly prolonged the closure time of whole blood and the occlusion time of platelet plug formation in vivo. We calculated the amount of endogenous GABA in platelets and found that GABA is a novel inhibitor of collagen glycoprotein VI. It is possible that an imbalance in the generation and/or release of GABA might contribute to pathological vascular diseases associated with platelet activation.

LBP.27

Dopaminergic denervation in PD is higher in the striatal region corresponding to the upper limb

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Objective: To determine whether the regions of the striatum corresponding to different body parts are differentially affected by dopaminergic denervation in PD.

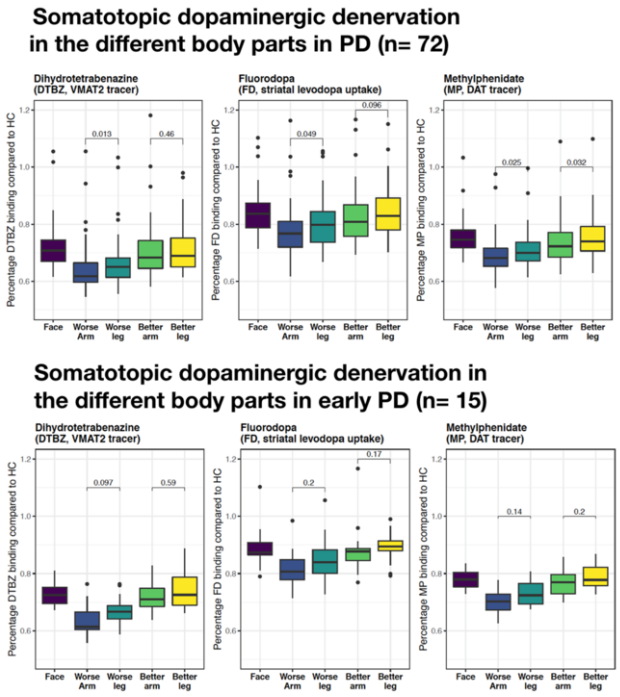
Background: The precise pattern of striatal dopaminergic denervation in PD may have important clinical consequences for several reasons: (i) The striatum has different functions and, from the motor point of view, a somatotopic organization. It would be expected for the pattern of denervation to correlate with clinical manifestations. (ii) The morphological analysis of dopamine-denervated areas in different stages of the disease may offer new insights into the pathophysiology of PD and its progression.

Methods: We analyzed previously obtained PET data from PD subjects and age-matched Healthy Controls (HC) with different dopaminergic tracers (DTBZ, FD and MP). First, we identified the regional striatal activation for each body part (face, right and left upper limb, right and left lower limb), based on the fMRI of 1200 healthy subjects from the Human Connectome Project. Secondly, we obtained the binding ratios (BR) in the region corresponding to each body part, weighted by the voxel-level striatal activation map. Finally, we compared the BRs in the regions corresponding to each body part between HC and PD. To further determine the temporal progression, we performed a subanalysis including only early PD (=2 years duration).

Results (see figure): 72 subjects with PD and 35 HC were included. We found reduced BR in the striatum of PD subjects in all the analyzed regions, greater in the hemisphere contralateral to the more affected clinical side. The upper limb region showed relatively reduced binding compared to the lower limb region for all three tracers in the more affected side ($p<0.05$), and for MP only in the less affected side ($p=0.03$).

In the subanalysis of 15 subjects with early PD, we observed the same trend, but the p-value did not reach statistical significance.

Conclusions: People with PD have a relatively greater dopaminergic denervation in the area corresponding to the upper limb compared to the lower limb. This could suggest that factors other than synaptic contiguity may contribute to a somatotopically-selective vulnerability in the initiation and/or progression of disease.



BASIC SCIENCE: Neuropharmacology

LBP.30

Discovery of small molecule inhibitors against α-synuclein aggregation via Mass Spectrometry-based screening

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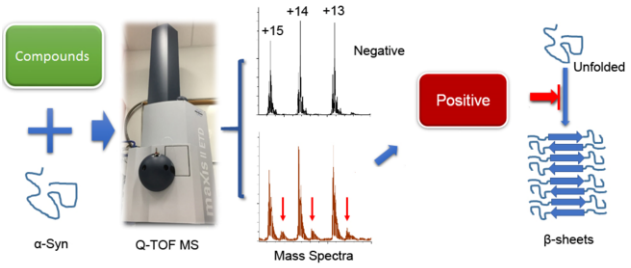
The accumulation of α-synuclein aggregates is a pathological hallmark of Parkinson's disease and also a priority target for drug development given its hypothesized contribution to neurodegeneration. As a result, discovering molecules that may act as imaging probes for α-synuclein and identifying inhibitors of α-synuclein aggregation are both hot research areas in PD drug development. An important and also common feature of such diagnostic and therapeutic agents is specific binding to the target protein. Therefore, developing new screening techniques which can directly detect the binding of molecules with α-synuclein will greatly help to discover novel and effective α-synuclein imaging probes and aggregation inhibitors. Here by establishing a mass spectrometry-based screening system, we were able to screen over 4,000 compounds and have identified several small molecules that not only bind to α-synuclein but also inhibit α-synuclein aggregation in the Thioflavin T assay. Further evaluations, such as circular dichroism and transmission electron microscopy were conducted to consolidate the inhibitory effects of these compounds on α-synuclein aggregation. These compounds also exerted protection against the α-synuclein toxicity in a neuroblastoma cell line. We

propose that the screened scaffolds may also have the potential to be further developed into α-synuclein imaging probes.



BASIC SCIENCE: Neurophysiology, functional imaging, human studies

LBP.32

Effective connectivity changes during processing of predictive information in Parkinson's disease

Noa Fogelson, Pablo Diaz Brage*
University of La Coruña, Oleiros, A Coruña, Spain

We examined the coupling between brain regions during the processing of predictive information in Parkinson's disease (PD). Previous studies have demonstrated contextual processing deficits in PD patients. Here we investigated the mechanisms underlying these deficits by evaluating the effective connectivity during the performance of a local contextual processing task, while Electroencephalography (EEG) was recorded. We used transfer entropy, a novel model-free method based on information theory to examine the pattern of information processing between brain regions during the processing of predictive stimuli. EEG recording blocks consisted of targets preceded by either randomized sequences of standards or by sequences including a predictive sequence signaling the occurrence of a target event. Subjects pressed a button when detecting target events. PD patients ("ON" medication) and healthy controls showed shorter reaction times for predicted versus random targets. Effective connectivity measures showed that the detection of predictive stimuli was associated with weaker effective connectivity between frontal and parietal sites, in the theta band, in PD compared to controls. The findings suggest that processing of predictive contextual information is altered in PD patients and that this may be associated with connectivity abnormalities within top-down frontal networks. These electrophysiological findings may contribute in establishing potential biomarkers for cognitive deficits in PD patients, and in further understanding the mechanisms underlying these deficits.

LBP.33

Transcranial direct current stimulation and yoga for functional movement disorders

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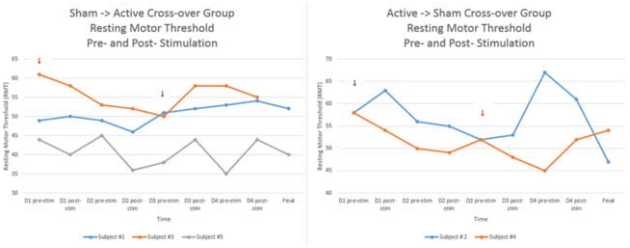
[2] Dongguk University, Goyang, South Korea

Background: There is lack of effective treatment for functional movement disorder, a disorder characterized by involuntary abnormal movements which is regarded to have a psychiatric cause.
Objective: We aimed to achieve improvement of FMD symptoms by using a combination of transcranial direct current stimulation(tDCS) and yoga.
Methods: This study is a randomized, double-blinded, sham-controlled, cross-over trial. Five patients participated in the study. Subjects received a total of four stimulation sessions (two active tDCS days and two sham tDCS days), with a wash-out period of 3 weeks. Subjects were instructed to attend a one-hour yoga class twice weekly during the study period. Both clinical evaluation and quality of life assessment via survey were conducted. Resting motor threshold values were obtained via transcranial magnetic stimulation pre- and post- tDCS.
Results: Mean age and disease duration of the patients were 53 and 6 years, respectively. Despite the lack of significant improvement in quality of life measures, 4 out of 5 subjects were clinically noted to have mild improvement.
Conclusion: There were no significant results in our study; we did observe mild clinical improvement which did not correlate with subjective quality of life. Future studies with more frequent stimulation sessions may help to determine if tDCS is effective for this neurological disorder.



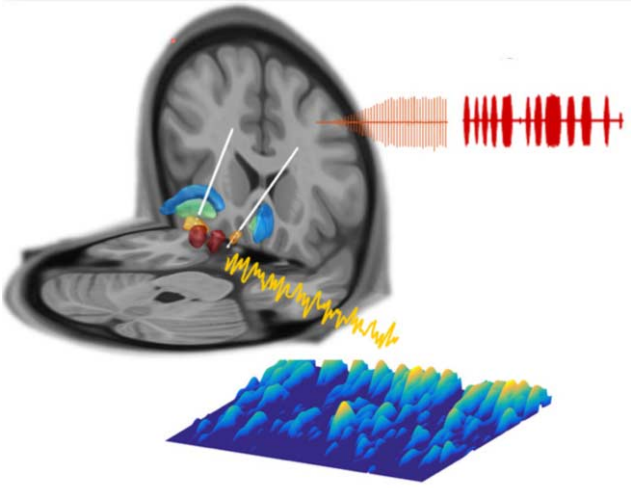
LBP.34

The prediction of dystonia patients' state based on machine learning and deep learning

*Zhang Zhao**
Fudan University, Shanghai, China

Background: Deep brain stimulation is a widely used treatment for patients with Parkinson and Dystonia. The ability to detect tremor over time from neural activity could be useful control signals for closed-loop deep brain stimulation. For tremor, neurobiological studies suggest that neural circuits underlying tremor mostly resides in subthalamic nucleus and globus pallidus, but less involve multiple, distributed corticolimbic regions.
Aim: This paper presents a human behavior prediction of dystonia patients by using local field potential(LFP) signals recorded from subthalamic nuclei(STN) and globus pallidus(Gpi). We try to use different machine learning algorithms and recurrent neural network to characterize the complicated relationship between neural activity and behavioral symptoms.
Method: I analyze recordings of local field potentials(LFPs) from the subthalamic nucleus and globus pallidus in 12 Dystonia patients with essential tremor. I select some internationally accepted nonlinear features to extract from EEG signals. By combining Chebyshev type I filters and adaptive filters, I map LFP signals to the time-frequency domain using time-frequency analysis and corresponding to the sEMG signals, selecting the appropriate threshold value through the statistical characteristics of the sEMG signal will divide the patients into two parts: tremor-free rest and essential tremor.
Then, the features of the neural information are preprocessed: the noise signals are filtered, and the normalized processing eliminates

dimension differences between different features, and drop out features with high correlation. Due to the serious tilt, we enhance the original data set. Afterward, the accuracy of k-nearest neighbor is 0.68, the AUC is 0.74;The accuracy of support vector machine that select Gaussian kernel function is 0.5618, the AUC is 0.54;Principal component analysis selects the front seven variables with the largest variance contribution rate before logistic regression and the accuracy is 0.528, the AUC is 0.54; The accuracy of the Adaboost model based on decision tree is 0.53; The accuracy of LSTM is 0.76, the AUC is 0.78. Within-patient training yielded better accuracy than across-patient training.
Conclusion: It is obvious that deep learning works better and there is a relationship between neural activity and behavioral symptoms. It can be used to help cure the Dystonia patients.



CLINICAL SCIENCE: Symptoms, signs, features & non-motor manifestations

LBP.35

Quantifying the influence of DBS on the bradykinesia in patients with Parkinson's disease during the peri-operative period by using wearable sensors
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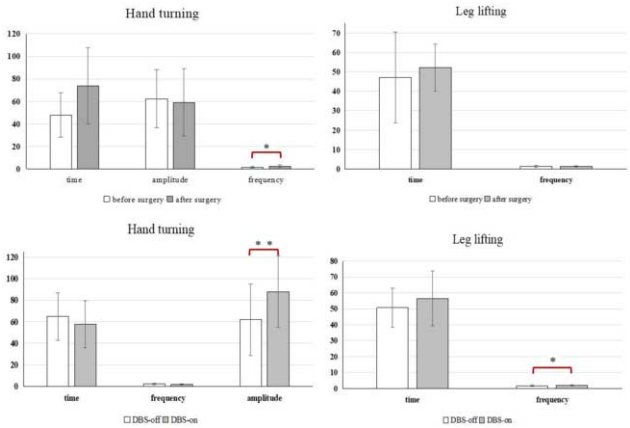
[2] Nanjing Brain Hospital, Nanjing, Jiangsu, China

Background: Bradykinesia is one cardinal symptom seriously influences patients with Parkinson's disease (PD). However, only a few studies concern about the precise quantification of this symptom in PD patients during their peri-operative periods. Therefore, we focus on the change of bradykinesia in PD cohort in different peri-operative time.
Method: Fourteen PD patients completed this piloting study. Their bradykinesia symptom was tested at three time points (before and after surgery, and DBS-on) without taking any medicine. Four wearable sensors set on both wrists and ankles were used to record the kinematic characteristics in two tests, including hand turning and leg lifting. In hand turning, patients were asked to raise their arms at the horizontal level, then incessant turn their palms up and down for 30 seconds. For leg lifting, patients were required to repeatedly step on a wood plank for 30 seconds.
The motion amplitude, frequency and time of hand turning, and the frequency and time of leg lifting were measured to evaluate the bradykinesia of upper and lower limbs. The differences of these motor features between the time before and after surgery and the time of DBS-on and DBS-off were used to assess the severity of bradykinesia respectively.
Result: Compared to the severity of bradykinesia before surgery, the frequency ($t(6)=2.55$, $p<0.05$) of hand was significantly increased after surgery, but the other features were no striking changes. In contrast with DBS-off, the hand turning amplitude ($t(13)=3.22$, $p<0.01$) and the leg lifting frequency ($t(13)=2.69$, $p<0.05$) were significant enhanced while the DBS was turned on.
Conclusion: Our results indicated that the microdamage caused by bilateral STN-DBS surgery was insignificant, and DBS has a positive effect on bradykinesia of four limbs. In conclusion, it is necessary to quantitative assess the severity of bradykinesia in four limbs during PD patients' peri-operative periods for monitoring disease and postoperative care.



LBP.36

Shuffling gait may be pitfall in neurologic examination in Parkinson's disease
*Hee-Tae Kim**
Hanyang University Hospital, Seoul, South Korea

Background: Gait disturbance is a cardinal symptom in Parkinson's disease (PD). However, gait disturbance is frequently unveiled in early stage PD especially in tremor dominant type. With technical development, gait analysis is enable to measure and discriminate gait pattern objectively. We compare gait parameter from 3D motion capture in PD patients with and without gait disturbance and control group. The purpose of this study is to investigate the gait in early stage of PD who did not complained of gait disturbance using three-dimensional (3D) motion capture.
Methods: 46 patients diagnosed as PD and 19 age-matched control were enrolled. 31 PD patients were suffered from gait disturbance and 15 patients did not. All participants were asked to walk under three 3D motion capture, and were performed several clinical scales including Unified Parkinson's disease Rating Scale (UPDRS), Hoehn and Yahr (H&Y) stage, Tinetti mobility test (TMT), Timed-up and go test (TUG). We compare the gait parameter among groups.
Results: Among various gait parameters, foot height is significant different in PD without gait disturbance compared to control. Other parameters including step, stride length and walking speed did not show differences between PD without gait disturbance and control. TMT and TUG is significantly correlated with foot heights than UPDRS scale or H&Y stage.

Discussions: We found that foot height which reflect shuffling gait is decreased in PD without gait disturbance. These findings suggest that shuffling gait may be easily underestimated, and clinician judge gait status based on walking speed or step length. Our results support that gait analysis may provide helpful information to detect subclinical gait disturbance in early stage of PD.

LBP.37

A novel tool to assess stereopsis in Parkinson's disease and its clinical implications

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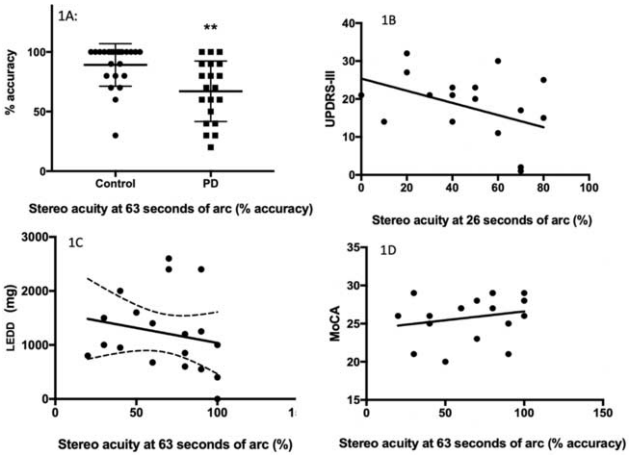
Objectives: To assess Parkinson's disease (PD) patients' stereopsis function using better and more physiologically meaningful tools; To reveal specific eye behaviors of stereo acuity impairment and whether it can be used as a biomarker of PD progression.
Introduction: PD patients suffer not only from motor symptoms, but also sensory visual dysfunctions. Visual disturbances are common, including higher-level depth perception (stereopsis) and the ability to judge distance. The hampered visuospatial judgment ability in PD patients could further limit their motor navigation and cause falls and injuries. Despite its significance in early detection and progression surveillance of PD, there is still scarce scientific research on stereopsis function in PD. In addition, the widely used Titmus Stereo Fly Test and Random Dot Stereogram do not consider the monocular cues, nor accommodation and vergence. We see a clear need of developing a new protocol to assess stereopsis for PD patients.
Methods: Twenty PD patients, Hoehn and Yahr stage 1–4, were recruited from the Parkinson and Movement Disorders Program at the University of Alberta. They were compared to 22 sex- and age-matched control subjects. The primary outcome measures of interest were abnormalities in stereopsis and eye behavior of stereo acuity. Visual testing included visual acuity (VA), visual field, extraocular movements (EOM), contrast acuity, stereopsis with Titmus Fly and a 3D TV system. MoCA test and UPDRS were also assessed. Levodopa equivalent daily dose (LEDD) was calculated.
Results: There were no differences in VA, visual field or contrast acuity between the 2 groups, nor in the Titmus Stereo Fly test. Using the 3D TV system, PD patients showed a significant stereo disparity when compared to control. At 63 seconds of arc and higher acuity (figure 1a), the deficit in PD was evident. The depth perception abnormalities show a trend correlating with the UPDRS-III, LEDD and MoCA (Figure 1 B-D, respectively).
Conclusion: Stereopsis deficit is associated with PD disease severity and cognitive status. Assessment of stereopsis using more reliable techniques may be a tool for early diagnosis and to monitor disease progression and responsiveness to treatment. Future behavioral study of gait/falls risk to correlate with stereopsis will be conducted.



LBP.38

Prevalence of advanced Parkinson's disease in Thai patients with Parkinson's disease using the Consensus on the Definition of Advance Parkinson's disease (CEPA Study): A single-center study

Jindapa Srikajon, Prachaya Srivanitchapoom, Yuvadee Pitakpatapee, Apichart Pisarnpong, Tanita Sangpeamsook, Arpakorn Suengtaworn*
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Background: Parkinson's disease (PD) is divided into 3 stages including early, mid, and advanced stage. However, the border zone between each stage is not clear. Identifying the stage of the disease is clinically important because the selection of advanced therapies such as continuous infusion or deep brain stimulation surgery (DBS) could improve motor, non-motor symptoms and quality of life in advanced PD (APD) patients. Recently, there was the statement addressed the definition of APD published from the CEPA study. The advantage of this consensus may help us to estimate the prevalence of APD and guide the physicians to employ more suitable treatments to the APD patients.
Objective: To identify the prevalence of APD according to the CEPA study in Thai PD patients who were registered to Movement disorders clinic at Siriraj Hospital, Thailand and to describe clinical characteristics of APD patients
Method: A retrospective chart review of all registered patients, total 452 patients, at our clinic from January 2016 to December 2018 was done with approval by the IRB. All data were collected during "ON" time. The demographic data and modalities of treatment including oral and advanced non-oral therapies were also collected.
Results: The prevalence of APD using CEPA's definition was 36.7% (166 out of 452) with male predominance (59.6%). The mean age of APD was 65.53±9.59 years. The mean of disease duration were 13.9 + 6.2 years and median of motor complication duration were 6.97 years. The APD patients were mostly in H&Y stage 3 (56.1%). Mean score of total UPDRS was 67.83±24.10 which mean score of UPDRS part III was 3.15±0.83. Seventy-nine patients (47.6%) received advanced non-oral therapies which mainly was an bilateral STN-DBS (89.9%) [table1]. The most factor that prevents the APD from the advanced therapies was the financial and psychosocial problems (54.9%).
Conclusion: Prevalence of APD in our population was one-third. Less than half of APD could achieve the proper treatment for controlling their symptoms. This current results may rise of the

awareness of identifying APD and make an impact to the level of the policy to provide proper care which APD patients deserve.

Table 1: Demographic data and clinical characteristics of the patients with APD

Variables	Mean ± SD or Median (min, max) (n=166)
Sex: male (n, %)	99 (59.6)
Age (years)	65.53 ± 9.59 (41.1-87.1)
Age at onset of disease (years)	51.49 ± 12.29 (24.27-75.71)
Disease duration (years)	14.04 ± 6.67 (0-40.85)
Duration of motor complications (years)	6.97 (0.05-22.2)
Antiparkinsonian medication in the past 2 weeks (n, %)	166 (100)
Monoamine oxidase B inhibitor	30 (18.0)
Dopamine agonist	102 (61.4)
L-dopa	162 (97.6)
Cathechol-O-Methyl transferase inhibitor	77 (46.4)
Apomorphine	1 (0.6)
Anticholinergic	21 (12.7)
Levodopa Equivalent Dose (mg)	927.85 ± 455.75 (150-2729)
Number of levodopa doses per day (times)	5.31 ± 1.63 (0-10)
Hoehn and Yahr stage (n=132)	3.15 ± 0.83 (2-5)
H&Y stage 1 (n, %)	0
H&Y stage 2 (n, %)	25 (18.9)
H&Y stage 3 (n, %)	74 (56.1)
H&Y stage 4 (n, %)	21 (15.9)
H&Y stage 5 (n, %)	12 (9.1)
UPDRS total score	67.83 ± 24.10 (22-119)
UPDRS-I score	11 (0-20)
UPDRS-II score	14 (1-38)
UPDRS-III score	34.67 ± 15.0 (10-77)
UPDRS-IV score	6 (0-14)
Underwent advance therapy (n, %)	79/166 (47.6)
Deep brain stimulation surgery (n, %)	71/79 (89.9)
Continuous infusion therapy (n, %)	5/79 (6.3)
Levodopa/carbidopa intestinal gel (n, %)	4/5 (80)
Subcutaneous apomorphine (n, %)	1/5 (20)
Ablative pallidotomy (n, %)	4/79 (5)

APD advanced Parkinson's disease, UPDRS Unified Parkinson's Disease Rating Scale

CLINICAL SCIENCE: Progression & prognosis

LBP.39

Ping Pong Parkinson: Testimonial, the diagnosis and activity that prolonged my life

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[2] Ping Pong Parkinson, Pleasantville, New York, USA

I always wanted to slow down, but I hoped that it would be on my own terms. I lived too fast. My body asked me to slow down but I didn't listen, and that is how PD saved my life.
In 2014, I was introduced to PingPong where I played sporadically, but after 6 months noticed an improvement in my PD symptoms. A year later, I started to play the guitar publicly again.
On March 1st 2017, Ping Pong Parkinson, a non-profit organization was established with the goal of halting the progression of Parkinson's disease by utilizing ping pong and an eclectic mix of other exercises as a form of physical therapy. Our model is based on the research-proven concept of neuroplasticity – the brain's capacity to make new neurons and connections through challenging physical exercise. Our program is underpinned by compelling evidence for the need for a regular exercise program for people with Parkinson's disease (PwP).
Methods: Our approach in achieving the aforementioned goal revolves around ping pong, a sport which is ideally suited in targeting, not just the motor symptoms of PD, but some non-motor symptoms, as well (depression, anxiety). By the nature of the activity, ping pong is fun but also addresses such Parkinson's issues as balance, agility and some aerobic activity. Our weekly 75 minute sessions begin with specific exercises specifically adapted and suited for PwP, including some Tai-qi and yoga derived callisthenics, as well as specific aerobic drills (e.g., marching to music). Our sessions conclude with juggling, another dopaminergic activity, and a group sing which enhances the volume of speech.
Conclusion: Videos of our "Ping Pong Pongers" (PwP) engaged in playing ping pong has been ongoing and provides an objective method of validating the positive motor effects of our program. Improvement has also been cited by some of the treating neurologists of members of our group. Positive changes in coordination are clearly apparent. Our module has evolved and been improved through trial and error. Our approach and model can be used as a basis for the nucleus of an exercise program designed for PwP.
https://vimeo.com/309645164
https://www.youtube.com/watch?v=cJd5H5IIbMY Dr.Russell(Yale)
https://www.youtube.com/watch?v=3hlWDNQe2HM CBSNews
https://www.youtube.com/watch?v=BjnokZlkbw8
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LBP.40

The management of Parkinson's disease: Benefits of a three-legged stool

*Peter Conrad**
Brandeis University, Waltham, MA, USA

Managing PD has changed in the last 50 years, from mostly medical approaches to include exercise.
Exercise emerged in the 1970s having general and specific health value, buoyed by public health findings and popular support for jogging and aerobics (Paffenbarger, 1975). There was very little specific about exercise for PD until 1990s (exceptions being "forced cycling" and some individual PT).
In the 2000s, two exercise-related innovations specific for people with PD emerged: Rock Steady Boxing (RSB) founded 2006 in Indianapolis and Dance for PD (DFP) 2001 in Brooklyn. RSB is noncontact boxing training for persons with PD. DFP is dance-based activity using dance and music to help develop rhythmic movement to counter PD symptoms. Both innovations showed remarkable national growth and popularity: RSB now has over 750 US affiliates with over 37,000 participants, while DFP is in 250 US communities and over a dozen abroad. Both only accept people with PD and their caregivers.
I began attending RSB in 2015 and started interviewing participants in 2016 (N=30). For a comparison, I attended 4 DFP classes, interviewed directors and participants, and reviewed written and electronic material (Butt, 2018).
Camradarie
Boxing and dancing appear to be very different, but participants' experiences have important similar characteristics, which nurture "Camradarie". Our interviews repeatedly demonstrated great value for participants beyond the exercise in these activities.
This Camradarie benefit encompasses sharing challenges, solidarity, collectivity, and social capital.
It is nurtured by common characteristics in both experiences:
- Mild to moderate movement-based activity
- Self-motivated participation
- Unique and specific for people with PD
- Focus on "fun" activities and positive and nonjudgmental interactions
- Participants not referred to as patients but in these environments as "boxers" and "dancers"
- Trained and committed leaders and coaches
- Not-for-profit organizations and local affiliations

Camradarie is a valuable PD personal gain and intrinsic to these groups' success. Camradarie has benefits for PD beyond exercise; public health research shows the more social relations and interactions individuals have, the healthier and happier their lives are. Managing PD benefits from a three-legged stool: Medicine,

Exercise, and Camradarie, each contributing to improved quality of life with PD.

LBP.41

Survival and development of dementia in the Parkinson's Incidence Cohorts Collaboration (PICC): An individual-patient-date meta-analysis of six incidence cohorts with 931 patients

Angus Macleod[*,1], Guido Alves[2], Marta Camacho[3], Lars Forsgren[4], Rachael Lawson[5], Ole-Bjorn Tysnes[6], Caroline Williams-Gray[3], Carl Counsell[1]*

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[2] Stavanger University Hospital, Stavanger, Norway
[3] University of Cambridge, Cambridge, United Kingdom
[4] Umea University, Umea, Sweden
[5] Newcastle University, Newcastle, United Kingdom
[6] University of Bergen, Bergen, Norway

Background: Most previous longitudinal studies in Parkinson's disease (PD) have used cohorts from hospital clinics or clinical trials. These have selection biases that tend to exclude older and frailer people with PD, which tends to underestimate the severity of prognosis/outcomes in this condition. Individual representative population-based studies have all been small. We therefore aimed to perform an individual-patient-data meta-analysis of incidence cohorts of PD – those studies which aim to identify and follow-up all new cases of PD in a defined geographical area and time period – to describe long-term prognosis in terms of mortality and dementia.
Methods: From a systematic review of incidence studies, we identified six incidence cohorts of PD with long-term follow-up: CamPaIGN & PICNICS (Cambridgeshire, UK), ICICLE-PD (Newcastle, UK, NYPUM (Umeå, Sweden), ParkWest (Western Norway), and PINE (Aberdeen, UK). 931 patients with PD recruited between 2000–2011 were followed for up to 16 years. Dementia diagnosis and deaths were recorded. We used Kaplan-Meier survival estimation and Cox regression with adjustments for age and sex.
Results: Of 931 participants, 314 developed dementia and 401 died after median 6.7 years follow-up. Figure 1 shows Kaplan-Meier survival plots, adjusted for age and sex, of A) survival and B) dementia-free survival. There was only weak evidence that survival, and no evidence that dementia, varied by study after correction for age and sex (p=0.12 and p=0.28 respectively, likelihood ratio tests). Median survival and median time to dementia across all studies were 9.2 years (95% confidence interval [CI] 8.7–9.8) and 9.1 years (95% CI 8.9–11.8) respectively. Hazard of dementia increased steeply with increasing age (hazard ratio [HR] for 10-year increase 2.38, 95% CI 2.05–2.75) but did not vary with sex (p=0.82). Hazard of death also increased steeply with increasing age (HR for 10-year increase 2.95, 95% CI 2.56–3.40) but women had about 30% lower hazards of death (HR 0.69, 95% CI 0.56–0.86).
Conclusions: We have provided estimates of mortality and dementia with low risk of bias. Further work with the PICC collaboration will identify prognostic factors for these and other outcomes and develop prognostic models in PD, which could be used for patient stratification and personalisation of treatment.

CLINICAL SCIENCE: Behavioral disorders

LBP.42

Structural connectivity and impulsivity after subthalamic deep brain stimulation for Parkinson's disease

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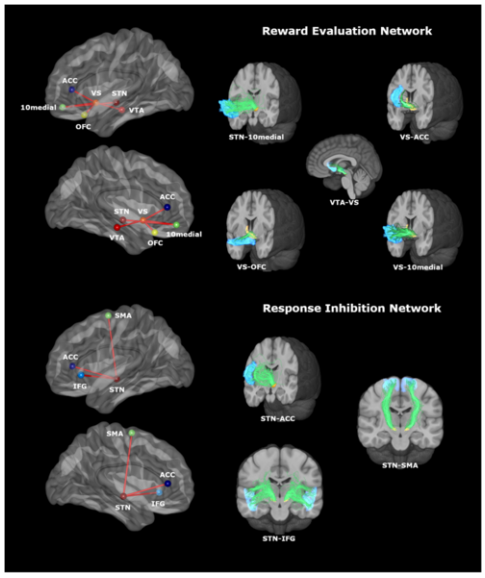
[2] Queensland Brain Institute, Brisbane, Queensland, Australia

Deep Brain Stimulation (DBS) of the Subthalamic Nucleus (STN) is an important advanced therapy for Parkinson's disease (PD), which alleviates motor symptoms and improves quality of life. However, some individuals develop postoperative neuropsychiatric symptoms such as impulsivity and mood elevation. This may arise from the central role of the STN in cognitive and affective, as well as motor, inhibition. Our group has previously demonstrated that the locus of subthalamic stimulation is a key determinant of postoperative neuropsychiatric symptoms; here we sought to delineate brain networks responsible for this phenomenon.
Fifty-eight, non-demented persons with PD undertook high-resolution diffusion brain imaging prior to subthalamic DBS. Each participant completed a battery of neuropsychiatric instruments at baseline and at three-months post-STN-DBS to quantify trait impulsiveness, compulsivity, disinhibition and impatience. Participants also played a played a slot-machine in a virtual casino prior to subthalamic DBS (whilst on medication) and three-months postoperatively (whilst on stimulation). This allowed ecologically-valid measures of impulsive behaviour to be expressed in the form of bet increases, slot machine switches and double or nothing gambles. Fibre-bundles within pre-determined "response-inhibition" and "reward-evaluation" networks were reconstructed using probabilistic tractography and the influence of network connectivity on impulsivity and gambling behaviour was examined with partial least squares path-modelling.
At baseline, the connectivity of the STN with cortical regions including the pre-SMA (supplementary motor area), IFG (inferior frontal gyrus) and ACC (anterior cingulate cortex) was significantly associated with elements of impulsivity requiring cognitive control ("stopping"). Connectivity of the STN with the ventromedial prefrontal cortex (vmPFC) and connectivity of the ventral striatum (VS) with the orbitofrontal cortex (OFC), ventral tegmental area (VTA), vmPFC and ACC was significantly associated with elements of impulsivity connected to compulsivity and reward seeking. However, individual connectivity profiles prior to STN-DBS did not predict changes in impulsivity postoperatively. Instead, these were significantly associated with connectivity between a stimulated neural volume of activated tissue (based on individualised DBS parameters) with these cortical regions.
These results demonstrate that post-DBS impulsivity is determined by the influence of stimulation on response-inhibition and reward-evaluation networks. Tractographic methods should integrate information from the site of stimulation in the postoperative modelling of non-motor outcomes.



CLINICAL SCIENCE: Cognition/Mood/ Memory

LBP.43

Cognition and gait in Parkinson's disease

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[1] WeCare MC, Lahore, Pakistan
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Motor-cognitive dual tasks (DTs) like (walking while talking) are used to explore the intersecting relation between gait and cognition. Evaluating DT situatio in Parkinson Disease is helpful since cognitive functions and motor control—both often impaired in PD—are examined at the same time. However, it is unclear if DT gait performance is indicative for cognitive impairment. Therefore, the objective of this study is to find if cognitive deficits are reflected DT costs of spatiotemporal gait parameters using MoCA.
Methods: Cognitive function, single task (ST) and DT gait performance were investigated in 80 PD patients. Cognition was assessed by the Montreal Cognitive Assessment (MoCA) followed by a standardized, sensor-based gait test and the identical gait test while subtracting serial 3's. PD patients were stratified according to the established MoCA cutoff score <26 (cognitively impaired) and =26 (cognitively unimpaired). DT costs in gait parameters [(DT – ST)/ST Å~ 100] were calculated as a measure of DT effect on gait. Correlation analysis was used to evaluate the association between MoCA performance and gait parameters. In a linear regression model, DT gait costs and clinical confounders (age, gender, disease duration, motor impairment, medication, and depression) were correlated to cognitive performance. In a subgroup analysis, we compared matched groups of cognitively impaired and unimpaired PD patients regarding differences in ST, DT, and DT gait costs.
Results: Correlation analysis revealed weak correlations between MoCA score and DT costs of gait parameters. DT costs of stride length, swing time variability, and maximum toe clearance were included in a regression analysis. The parameters only explain 10% of the cognitive variance. In combination with clinical confounders, regression analysis showed that these gait parameters explained 33% of MoCA performance. Group comparison revealed strong DT effects within both groups (large effect sizes), but significant between-group effects in DT gait costs were not observed.
Conclusion: These findings suggest that DT gait performance is not indicative for cognitive impairment in PD. DT effects on gait parameters were substantial in cognitively impaired and unimpaired patients, thereby potentially overlaying the effect of cognitive impairment on DT gait costs. Therefore, DT gait parameters as marker for cognitive performance should be carefully interpreted

LBP.44

Clinical practice of brain SPECT for early detection of subjective memory impairment in Parkinson's disease

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Cognitive dysfunction is a common feature of Parkinson's disease (PD). Recent research has focused on the detection and management of subjective memory impairment (SMI) as the stage that precedes Mild Cognitive Impairment (MCI). Nevertheless, there have been few clinical studies of biomarkers of SMI in PD. Therefore, we designed this study to investigate differences in perfusion brain SPECT between PD with SMI (PD+SMI) and PD without SMI (PD-SMI) to identify a potential prodromal biomarker of progression to dementia in patients with PD.
We recruited 30 PD patients with SMI and 24 PD patients without SMI. All subjects underwent perfusion brain SPECT and neuropsychological testing. Brain SPECT images were analyzed using the SPM program and were compared for patients with PD+SMI and PD-SMI.
The PD+SMI and PD-SMI groups did not show any statistically significant differences in neuropsychological tests except for MMSE. Despite a significant difference in MMSE scores, all scores of both groups were in the normal range. Brain SPECT analysis of PD+SMI patients showed hypoperfusion in the frontal and inferior temporal regions, anterior cingulate and thalamus compared with PD-SMI patients.
This pilot study evaluated the role of decreased brain perfusion SPECT findings in PD+SMI patients compared with PD-SMI patients as a predictive biomarker of pre-dementia as the stage that precedes MCI in PD. Future large, prospective studies are needed to investigate the pathophysiology of neuronal systems during cognitive decline.

Table 1
Demographic data and cognitive functions in the pAD and PDD groups and normal controls

Variables	PD+SMI	PD-SMI	P-value
Subjects	30	24	
Men	13	11	0.736
Mean age, years	64.17±10.14	65.96±10.99	0.541
Mean education, years	11.87±3.56	11.21±5.85	0.612
Mean duration of PD, months	36.13±30.22	28.63±21.62	0.293
H-Y stage	1.67±0.51	1.73±0.68	0.71
Daily dosage of levodopa(mg)	340.58±162.86	285.42±235.98	0.315
MMSE score	28.36±1.03	29.63±0.58	<0.001
CDR score	0.2±0.24	0.13±0.22	0.253
SOB score	0.35±0.60	0.16±0.32	0.159

Values are mean ±standard deviation
PD: Parkinson's disease, SMI: subjective memory impairment, PD+SMI: PD with SMI, PD-SMI: PD without SMI, MMSE: Mini- mental state examination, CDR: Clinical dementia rating, SOB: Sum of box of CDR

CLINICAL SCIENCE: Sleep disorders/ Fatigue

LBP.46

Identification of cerebrospinal fluid proteins associated with impaired sleep quality in Parkinson's disease

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Sleep disturbance, especially impaired sleep quality due to frequent nocturnal arousal leading to sleep fragmentation and a decrease in deep non-rapid eye movement (NREM) sleep, is a common symptom associated with patients with Parkinson's disease (PD). A recent epidemiological study demonstrated an association between sleep fragmentation and PD pathology, suggesting that impaired sleep quality may be a prodromal marker or risk factor for PD pathology. In this study, we aimed to explore biochemical alterations in the components of cerebrospinal fluid (CSF) collected from patients with PD and impaired sleep quality, which could reflect the biochemical changes in the brain related to PD pathology under impaired sleep quality. We performed an unbiased proteomic analysis of the CSF of 20 PD patients, who underwent objective sleep assessment using polysomnography (PSG) and subjective sleep assessment using within three months of CSF collection. In addition, detailed clinical assessment of PD by expert neurologists was performed at the timing of CSF collection. We then categorized the 1,388 proteins in total that were identified in the CSF into those that were significantly up- or down-regulated in PD patients with impaired sleep quality. This categorization was performed using multiple parameters of PSG including Arousal Index (ArI), an indicator of sleep fragmentation, or percentage of stage N3 sleep (%N3), the deepest NREM sleep, per total sleep time. Through these analyses, we identified CSF proteins that are associated with an increase in sleep fragmentation or decrease in stage N3 sleep in patients with PD. Intriguingly, enrichment analyses of these proteins revealed that proteins that are associated with sleep fragmentation or decreased stage N3 sleep have a different enrichment profile, suggesting that different components of sleep may differently alter proteins in the brain. Further analyses of these components would lead to a better understanding of the relationship between impaired sleep quality and the pathomechanisms of PD.

CLINICAL SCIENCE: Co-morbidities

LBP.47

Hip fractures in patients with Parkinson's disease

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Objective: Patients with Parkinson's disease (PD) had a higher risk of hip fracture due to fall and higher mortality than age-sex matched general population. We perfomded a study to identify the characteristics of patients with PD and important factors related to hip fracture and the status of treatment for prevention of fracture. So, We investigated the following studies: 1. Characteristics of PD patients with type of hip fractures, 2. Relationship between types of hip fracture and the degree of bone loss, the body mass index (BMI), 3. Relationship between the severity of PD and Bone mineral density (BMD), 4. Clinical status of osteoporosis management.
Methods: Data on patients with PD was collected from Jan, 2002 to Jan, 2017. The data used KCD-6 (Korean Standard Classification of Diseases) for its diagnostic code and it was obtained using G20 for PD and S72 for hip fracture. Finally, 31 patients were included in the study.
Results: Femur neck fracture was the most common type of hip fracture (51.6%). Neck fracture had a higher proportion of obesity (25% vs. 15.4%) than intertrochanteric fracture, and intertrochanteric fracture had higher proportion of osteoporosis (92.3% vs 62.5%) than neck fracture. As the stages of PD advances, the degree of BMD get worse. At the time of diagnosis of the hip fracture, only 22.5% of patients had taken osteoporosis medicine and the number of patients receiving postoperative rehabilitation was less than 30% of the total patients.
Conclusion: For prevention of fall related hip fracutre in patients with PD, not only the diagnosis and pharmacologic treatment of osteoporosis but also physical rehabilitation should be taken into consideration to both medical staffs and patients

LBP.48

Features of autonomic failure in elderly patients with Parkinson's disease and dementia with Lewy bodies on emergency hospitalization

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Objectives: Recently, the number of elderly patients with Parkinson's disease (PD) and dementia with Lewy bodies (DLB) visited emergency ward has been increasing. Along with a rise in the aging rate, PDD and DLB have been regarded as Lewy body diseases (LBD) belonging to the same spectrum disorders. It is necessary to make attention to the dysfunction of central and peripheral autonomic nervous systems, regulated from a hypothalamus and sympathetic ganglion respectively, strongly relate to motor and non-motor symptoms in the elderly. In this study, we investigated the background of admission in LBD patients by focusing on the symptoms of autonomic dysfunction.
Methods: Among total 588 patients who were admitted to the neurology ward from January 2013 to December 2014, 51 patients (PD 20, PDD 17, and DLB 14) were examined the reason for hospitalization, the severity and duration of disease, and mortality rate.

Results: The average age was 80.3±6.7 years. The disease duration was 4.95±3. 68 years. LBD patients accounted for 8.67 percent of all hospitalized cases in neurology ward. Reasons for hospitalization were; motor fluctuation, fall, pneumonia and other infections, dehydration, appetite loss, drowsiness, syncope, and ileus. 31 percent of the reasons correlated with autonomic dysfunctions. Mortality rate of LBD was significantly higher than the others.
Conclusions: An emergency visit with PD is caused by various symptoms. However there are few reports focused on the autonomic dysfunction previously. Therefore correct diagnosis and rapid emergency response require for autonomic failures in elderly LBD.

CLINICAL SCIENCE: Biomarkers

LBP.49

Metabolomics-based identification of metabolic alterations in PARK2

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Objective: Parkin is the causative gene for autosomal recessive familial Parkinson's disease (PD), although it remains unclear how parkin dysfunction is involved with the general condition. Recently, serum and/or plasma metabolomics revealed alterations in metabolic pathways that might reflect pathomechanisms of idiopathic PD (iPD). Thus, we hypothesized that serum metabolomics of patients with homozygous or compound heterozygous parkin mutations (namely, PARK2 patients) might reflect metabolic alterations due to parkin dysfunction.
Methods: We enrolled 15 PARK2 patients (52±17.6 years) confirmed with homozygous (7 cases) and compound heterozygous (8 cases) parkin mutations, along with 19 healthy age-matched controls (51±11.52 years). We analyzed 830 metabolites from participants' serum using well-established metabolomics technologies, including ultra-high performance liquid chromatography/tandem mass spectroscopy.
Results: Based on metabolic profiles, hierarchical matrix analysis can divide samples between control and PARK2 subjects. Profiles from PARK2 patients showed significantly higher levels of Fatty Acid (FA) metabolites and oxidized lipids, and significantly lower levels of antioxidant, caffeine, and benzoate-related metabolites.
Interpretation: Metabolomics can identify specific metabolic alterations in PARK2 patients compared with controls. Alterations of FA metabolites suggest a relationship between parkin function and lipid metabolism. Elevation of oxidized lipids in combination with decreasing antioxidants may reflect general hyperoxidative stress. Decreasing benzoate-related metabolites might be due to alteration of gut microbiota. Consequently, caffeine and its metabolite may be decreased due to malabsorption. These findings are similar to metabolic alterations in iPD. Thus, metabolic analysis may reflect the association between parkin dysfunction and parkinsonism.

LBP.50

Canine aromatic detection of Parkinson's disease: Can dogs identify PD early?

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Objective: The ultimate goal of this project is to develop an effective screening tool for Parkinson's disease.
Background: The onset of Parkinson's disease (PD) predates the emergence of cardinal motor symptoms by decades. Earlier detection of preclinical disease is an important unmet need due to the lack of validated biomarkers of PD with reproducible sensitivity and specificity. Canine detection of aromatic signatures of several human diseases has been increasingly explored as biomarkers of disease that may be developed for early diagnosis. We have trained dogs to identify the scent of Parkinsonism, although their accuracy has yet to be determined.
Methods: The goal of this study was to determine whether canine aromatic detection could be used to detect patients with clinically diagnosed PD. In order to determine the sensitivity and specificity of canine aromatic detection of PD, 46 earwax samples were obtained from 28 individuals with PD and 18 healthy controls. The canine breed Lagotto Romagnolo has a long-recognized (>900 years) ability to detect the scent of underground ripened truffles. Two Lagotto were trained using the ParK-9 training program, which includes bringing the dogs to a Parkinson's clinic to be exposed to people with and without PD; the canines are rewarded each time an individual with PD was positively identified.
Results: The canine(s) correctly identified 27/28 PD samples as positive (96.43% sensitivity; 95% CI: 81.65% to 99.91%) and identified 13/18 heathy controls as negative (72.22% specificity; 95% CI: 46.52% to 90.31%) when using ear wax samples. The overall accuracy for the diagnosis of PD was 86.96% (95% CI:73.74% to 95.06%).
Conclusions: Biomarker detection of PD is urgently needed. In this preliminary study, the canine Lagotto Ramagnolo was able to distinguish ear wax samples from individuals with PD from controls with high sensitivity and moderate specificity. Ongoing validation of canine aromatic detection of PD as a potential biomarker is ongoing. Further research is also warranted to attempt to identify a molecular signature of the PD volatilome.

A. Using the PRO-PD scale, the solid black line shows the approximate rate of patient-reported PD progression. The dotted lines below demonstrate the lifetime impact of a 50% reduction in slope when PD is diagnosed by motor symptoms, or ~20 years earlier, when this disease is actually thought to start.
B. Bottom photos demonstrate the ParK-9 track system and signaling positive samples.

ParK-9 SPC, 2019

CLINICAL SCIENCE: Pharmacological therapy

LBP.51

Pharmacokinetics of ND0612 administered at different infusion sites and with different cannula lengths: An open-label, randomized, cross-over study in healthy volunteers

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Background: ND0612 is under development as a non-surgical drug-device combination providing continuous delivery of carbidopa/levodopa subcutaneous (sc) solution (CLSS) for patients with Parkinson's disease (PD) experiencing motor fluctuations. The impact of infusion sites location and cannula length on Pharmacokinetics (PK), dermal safety and tolerability were assessed to offer more options for patients.
Objective: To evaluate the impact of sc infusion site location and cannula length on LD PK administered as a single 16-hour sc infusion of ND0612 (LD/CD 60/7.5 mg/mL) in healthy volunteers.
Methods: This study was a single center, open-label, randomized, single-dose, 4-period, crossover study to assess the effect of the infusion site location and of the cannula length on the PK of ND0612 infused to 24 healthy subjects (16 male and 8 female). Subjects were randomized 1:1:1:1 into one of four sequences. Each subject sequentially received ND0612 at three different infusion sites, with the abdomen infused twice, once with a long cannula (the reference route of administration) and once with a short cannula. The outer thigh and back sites were assessed with long cannula. Each of the 4 individual 16-hour dosing periods were separated by 32-hour washout time. Blood samples for PK analysis were collected before, during, and after administration of ND0612 up to 12 hours after the end of infusion.
Results: Mean plasma drug concentration-vs.-time profiles were similar for ND0612 infused with long cannula at the abdomen (reference) and each of the other treatments (abdomen with short cannula, outer thigh with long cannula and back with long cannula). The 90% confidence intervals for all PK parameters were within the pre-defined bioequivalence limits of 80–125% between all tests and the reference. The most common Treatment-Emergent Adverse Event (TEAE) was infusion site nodules. No TEAE led to study discontinuation and none were classified as serious or severe.
Conclusions: This Phase 1 study confirms that both the rate and extent of absorption of ND0612 are similar when administered using different injection site locations and cannula lengths. Infusion to back and outer thigh is not expected to affect efficacy of LD, offering alternative infusion locations for long-term ND0612 use.
Funding: NeuroDerm

LBP.53

Zonisamide ameliorates motor symptoms and sleep problems in patients with Parkinson's disease: a 3-month open-label study

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Objective: We aimed to evaluate the effect of Zonisamide (ZNS) on motor symptoms, depressive symptoms and sleep problems in patients with Parkinson's disease (PD).
Background: ZNS has been licensed for treating motor symptoms in PD; however, a few studies have assessed effects of ZNS on non-motor symptoms.
Methods: We planned a 3-month, open-label study to assess the effects of ZNS on motor symptoms, depressive symptoms and sleep problems. Levodopa-treated 18 PD patients with motor fluctuation were included. Patients received 25–50 mg/day of ZNS and were assessed for the Japanese version of the Movement Disorder Society Revision of the Unified PD Rating Scale (MDS-UPDRS) parts I, III, and IV, PD sleep scale (PDSS)-2, Beck depression inventory-2, and PD Questionnaire (PDQ-8) at baseline, 1 month, 2 months and 3 months.
Results: At 3 months, scores of MDS-UPDRS parts I, III and IV significantly improved and off-time reduced compared to baseline. Also, PDSS-2 total score significantly decreased at 3 months.
Conclusion: We showed the beneficial effects of ZNS on motor symptoms and sleep problems in levodopa-treated PD patients with motor fluctuation.

CLINICAL SCIENCE: Rehabilitation sciences (PT, OT, SLP)

LBP.54

The effect of speech rate on lip kinematics in Parkinson's disease

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Objective: To characterize the lip kinematics (amplitude, velocity) during speech produced at 3 speaking rates among individuals with PD in an ON or OFF medication state, in comparison to age and sex matched neurotypical adults.
Method: Ten individuals with idiopathic PD (69.80±10.38 years old, 60% male) and 10 neurotypical adults (70.18±8.93 years old, 60% male) participated in this study. They were instructed to produce "pa" at slow (2 syllables/sec), typical (3.5 syllables/sec), and fast (5 syllables/sec) speech rates as synchronized by a metronome. A 4-D a motion capture system was used to measure upper lip and lower lip kinematics. Multivariate analysis of variance was conducted to examine differences between groups (PD ON, PD OFF, control) and speech rates (2, 3.5, 5 syllables/sec) in labial kinematics (amplitude, velocity) for "pa" production.
Results: Only the [LL+J]y differed significantly between the PD ON and PD OFF groups (adjusted $p<.05$), indicating that inferior-superior (y) dimension appeared to be the dominant dimension for speech production. PD subjects showed significantly lower labial movements compared to neurotypical controls, indicating the presence of hypokinesia in the labial structure. As the speech rate increased to 5 syllables/sec, PD subjects produced syllable trains with labial movements at significantly lower displacement amplitudes compared to controls. In terms of velocities, the PD OFF group consistently showed a reduction of 30%-48% velocity movement for both opening and closing gestures compared to

control. When comparing the 2 Hz and 5 Hz rates, lips velocity increased but amplitude decreased at the higher rate.
Conclusions: Similar to the clinical symptoms in the upper and lower limb, a reduction in the range of motion (hypokinesia) and velocity (bradykinesia) was evident in the PD orofacial system. Administration of dopaminergic treatment improved hypokinesia and bradykinesia. As the speech rate increased, PD subjects down-scaled lip movements in both amplitude and velocity compared to controls, reflecting a compensatory mechanism to maintain the target speech rate. Utilization of these objective assessments will be helpful for diagnosing, assessing, and monitoring the progression of PD and further for evaluating the efficacy of pharmacological, neurosurgical, and behavioral interventions.

LBP.55

Effects of computerized cognitive training, with and without concurrent exercise, on executive functions in Parkinson's disease

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PD patients manifest motor deficits but also a wide spectrum of cognitive impairments. Several studies have suggested that the combination of both cognitive training and physical exercise can improve cognitive function in PD more efficiently than cognitive training alone. To explore this hypothesis 41 PD patients were allocated randomly to two groups, a cognitive training group (CT), and a cognitive training with concurrent physical exercise group (CTE). Cognitive training was implemented using a computer-aided training software that included a batery of cognitive tasks to target executive functions. We ensured the same cognitive load across the groups by adjusting the dificulty level of each cognitive task to the maximal cognitive capacity of each patient. Patients in the CTE group perfomed the cognitive training while walking on a treadmill. The training programs consisted of a total of 24 sessions (3 sessions/week). The executive performance were blindly assessed using standardized neuropsychological tests (Wisconsin Card Sorting Test, Word fluency test, Digit Span backwards test, Tower of London test, Stroop test, Trail Making test, Corsi Block test) two months and one week before the training programs, as well as one week and one month after their cesation. We showed a deterioration of the cognitive performance in the CT group across the evaluation time points, while the CTE group showed the reverse effect with a cognitive improvement as a result of the combined training program. Our findings suggest that the combined effect of treadmill walking and computerized cognitive training improves the executive functions in PD, while cognitive training on its own may not be effective.

LBP.56

'PDSAFE' – a multi-dimensional model of falls rehabilitation for people with Parkinson's. A mixed methods analysis of therapists' delivery and experience

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Objective: To explore the clinical reasoning choices made by physiotherapists and their experiences of treatment delivery in a large fall-prevention trial for people with Parkinson's – 'PDSAFE'.
Design: A mixed method design with descriptive statistics of frequency of the intervention plus combinations and patterns of exercises was adopted. Semi-structured interviews were utilised to explore the therapists' experiences of the delivering PDSAFE. Combined analysis enabled comparison of the content delivered against therapists views.
Method: Setting: PDSAFE was a multi-centred, single-blinded, randomised control trial.
Participants: Physiotherapists with a background in neurology and older person rehabilitation were trained in the delivery of PDSAFE.
Intervention: The intervention was multi-dimensional, physiotherapist delivered, individually tailored and a progressive, home-based programme.
Results: Fifteen physiotherapists contributed to the 2587 intervention sessions from the PDSAFE trial and six of those physiotherapists took part in the interviews. The falls strategies most commonly adopted were 'Avoiding tripping', 'Turning' and 'Freezing Cues' with a range of exercise combinations reflecting the personalised nature of the intervention design. All possible combinations of the intervention content were selected.
The therapists were positive about the conceptual underpinning of the PDSAFE programme and its holistic, patient centred focus. They identified cognitive deficits, co-morbidities and dyskinesia to be the most challenging aspects of the intervention delivery with those having support, good cognitive ability and motivation likely to gain the most.
Conclusion: Falls management for people with Parkinson's is complex and compounded by the progressive nature of the condition. PDSAFE is feasible to deliver and positively received by therapists and participants.

LBP.57

Cochrane Systematic Review on singing for people with Parkinson's

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A Cochrane Systematic Review protocol has been recently published to compare the efficacy and effectiveness of singing interventions on quality of life, wellbeing, and speech and communication among people with Parkinson's disease (PD). https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013279/full?highlightAbstract=singing%7Cwithdrawn%7Csing
Singing involves physical functions, such as engaging the vocal apparatus and respiratory system (Leanderson 1988), as well as mental functions through emotional expression (Welch 2005). From a neurological point of view, singing is a complex activity that integrates auditory and sensorimotor processes in the brain (Wan 2010). When singing, speech-related mechanisms, such as respiration, phonation, articulation, and resonance, are directly stimulated (Sundberg 1987).
Non-pharmacological treatments for people living with PD play an increasingly important role (IQWiG 2015). As discussed above, evidence suggests that singing can be a beneficial complementary

therapy for people with PD (Vella-Burrows 2012). The number of singing groups for people with PD in the community has been fast-growing in high-income countries.
A recent review of music-based interventions in neurological rehabilitation highlighted the benefits of music for people with neurological conditions, including PD (Sihvonen 2017). However, the review did not examine the specific effects of singing for people with PD. Another recent review on singing for people with PD reported benefits of singing in people with PD, but this was a narrative review and included non-randomised studies (Barnish 2016).
It is therefore timely to conduct a robust systematic review of the efficacy of singing for people with PD, including an examination of the effect of 'dose' of singing on relevant outcomes.
We will include Randomised Controlled Trials (RCTs) of singing interventions versus non-singing interventions, or usual care. Primary outcomes are quality of life and wellbeing measures; secondary outcomes include speech, respiratory, motor functions; psychological status.
Given our review protocol has just been published, we plan to undertake extensive literature searches during March, and we will extract data during April. Then, we will have some preliminary findings by May.
During the Congress in June, we would like to present our preliminary findings on our Cochrane Sytematic Review on Singing for People with PD.

LBP.58

Translational research platform for intelligent deep brain stimulation

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Deep Brain Stimulation (DBS) is a widely-used and effective therapeutic strategy for Parkinson's disease (PD). However, many previous studies observed non-significant effects and/or reported severe side effects of DBS. One possible reason is that the continuous DBS with a constant simulation pattern cannot provide an appropriate modulation to the neural network, of which the dynamics switch rapidly between different neural states and changes gradually along with the progression of disease. A novel intelligent DBS with neural feedbacks holds great promise to improve the effects and efficiency of DBS.
We thus developed a translational research platform for intelligent DBS (iDBS), which is capable for local field potential (LFP) acquiring and micro electrode recording, data transmitting, analyzing and deep brain stimulating. Through this platform, researchers can focus on the key problem of iDBS — algorithms and models. This platform supports multiple coding language, such as Matlab and C/C++, meeting the demand to transfer the innovative theoretical algorithm to engineering implementation. Moreover, this iDBS platform is compatible for commonly-used commercial DBS systems, which are Alpha Lab SnR and Neuro Omega systems. Through this platform, an innovative algorithm can be applied to animal experiments and clinical experiments with one deployment.
For a real time iDBS system, one crucial technical specification is the response time — total time delay from waiting data to stimulation, the average response time (without the time cost of iDBS algorithm) of our iDBS platform is 6.28 ms with a standard deviation of 2.61 ms. This platform can be applied to translational researches of DBS, from basic science research, pre-clinical research to clinical research.

LBP.59

Measures of vocal effort in Parkinson's disease: self-perception, and feedback on performance

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Introduction: Vocal quality of life can be measured based on self-perception and on feedback from others.
Objectives: To determine if vocal quality of life improves after vocal strengthening treatment with singing using two measures.
Method: Twenty-eight persons living with PD received twice weekly "vocal strengthening including singing" treatment classes for 6 weeks (Tanner, 2012). A single pretest-posttest design was used. Two rating scales to test for self-perceived changes in "vocal quality of life": (1) the Speech Intelligibility Inventory: Self-Assessment Form or SII (Kent, 1994) and, (2) the Voice Related Quality of Life or V-RQOL (Hogikyan & Sethuraman, 1999) were completed before and after treatment.
Results: Differences in self-perceived changes in vocal quality of life were statistically significant ($p<.05$) improved after treatment.
Discussion: Both outcome measures are useful, but employ different approaches to rate vocal quality of life in this population affected by hypokinetic dysarthria. The SII asked participants to remember feedback from other people about their own vocal production; this focused on dysarthria, a composite of speech and voice disorder. The VRQOL examined self-perception of one's own vocal production, which is different from remembering feedback from others.
Conclusion: This study supports the use of two types of measures for assessment of vocal quality of life, one based on memory for feedback from others, and another based on self-perception. In this study, both measures showed improvement after treatment. It is not clear whether this would continue to be the case if memory or self-perception were to change with disease progression.
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Test Name	Level of statistical significance	# of questions (# of choices in rating scale)	Statement type to be rated "example"	Target population
Voice Related Quality of Life (V-RQOL) (Hogikyan & Sethuraman, 1999)	0.5	10 (5)	Self-perception: "I have trouble speaking loudly or being heard in noisy situations"	Voice disorders
Speech Intelligibility Inventory: Self-Assessment Form (SII) (Kent, 1994)	0.1	22 (5)	Comments from others: "People find it hard to understand my speech in noisy places"	All types Dysarthria

LBP.60

Effects of combined auditory cues and treadmill training on cortical excitability and gait performance in Parkinson's disease

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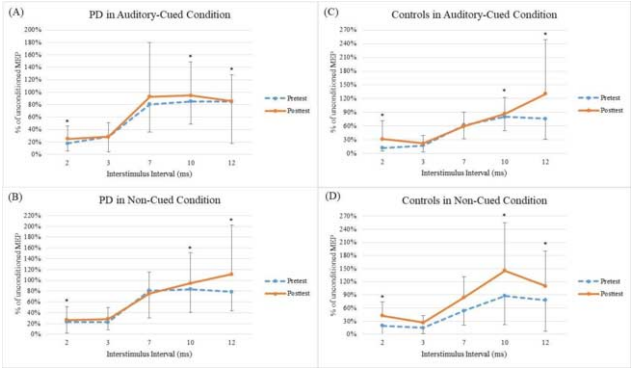
Background: Rhythmic auditory cues assist in overcoming gait disturbances, such as Freezing Of Gait (FOG), associated with Parkinson's disease (PD). However, the immediate effect of auditory cues on cortical excitability could be relative to training-induced plasticity, which plays a crucial role in PD rehabilitation.
Aim: This study investigated cortical excitability and gait performances in patients with PD (including freezers and nonfreezers) who received one session of auditory-cued treadmill training.
Design: Randomized crossover trial.
Setting: University laboratory.
Population: Twenty-six participants (17 individuals with PD and 9 healthy adults) were recruited into freezer (n=8), nonfreezer (n=9), and control groups.
Methods: Participants randomly participated in intervention under two conditions with a 1-week washout interval. The two conditions were treadmill training for 30 minutes with rhythmic auditory cues (AC condition) and without rhythmic auditory cues (NC condition) (cued frequency: 110% of subject's comfortable cadence on the treadmill), respectively.
Results: Patients with PD presented with a lengthened Cortical Silent Period (CSP) compared with the control group, both with and without the use of auditory cues ($p<0.001$ and $p=0.392$). The CSP increased with the AC condition ($p=0.032$) for the freezer group but not with the NC condition ($p=0.257$), whereas there was a significant lengthening of the CSP in the nonfreezer group with both AC and NC conditions ($p=0.007$ and $p=0.008$). The participants with PD showed an increase in speed ($p=0.006$) and stride length ($p<0.001$) after training.
Conclusions: One session of treadmill training either with or without auditory cues played a major role in modulating cortical excitability and increasing step length and gait velocity for patients with PD. The use of auditory cues with treadmill training enhanced corticospinal inhibition in both freezers and nonfreezers. However, this phenomenon was not identified in freezers when they participated in treadmill training without cues.
Clinical Rehabilitation Impact: Treadmill training may benefit only participants with PD without FOG; however, treadmill training with an auditory cue may benefit those with or without FOG.



CLINICAL SCIENCE: Clinical trials: Design, outcomes, recruiting, PwP involvement, communications

LBP.61

The Australian Parkinson's Mission: Integrating genomics, biomarkers and patient cell phenotyping into disease modifying clinical trials

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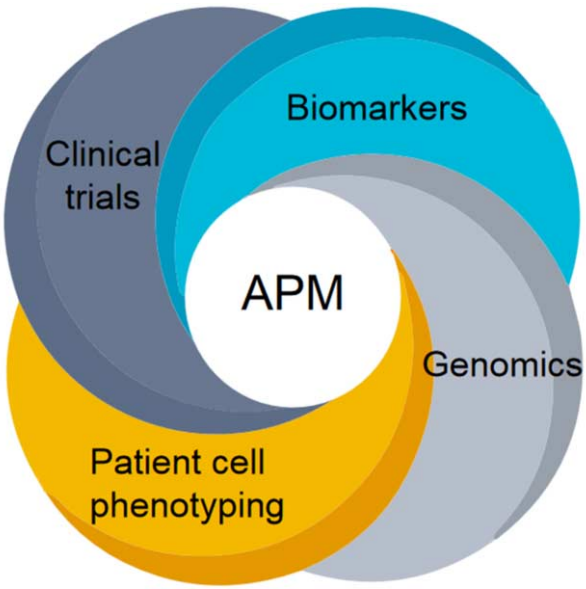
We currently face multiple challenges in identifying disease modifying therapies that slow or stop disease progression in people with Parkinson's disease. These challenges negatively impact clinical trials and include:
1. Insufficient insight into the molecular pathogenesis of PD
2. Variability in measures used in clinical trials to quantify disease progression
3. Possible misdiagnosis
4. A lack of biomarkers for early and accurate diagnosis and to measure disease progression
5. Parkinson's disease is a heterogeneous disorder with the significant likelihood of disease subtypes which renders ineffective a one-size-fits-all therapeutic approach
6. The lengthy timeline from drug discovery to patients
The Australian Parkinson's Mission (APM) will initially see a five-year program supported by the Commonwealth government of Australia that is designed to identify potential treatments and develop precision medicine approaches towards tackling Parkinson's disease by fully integrating the following approaches:
(a) A series of multi-arm, multi-drug clinical trials in multiple sites across Australia that will involve hundreds of patients in an effort to test repurposed and novel drugs that have been identified by an international panel of experts.



(b) Participants' genomic information, biomarkers and phenotyping of patients' cells will aid to advance our understanding of the molecular pathogenesis of PD and potentially stratify patients into disease subtypes. Genomic/biomarker-based subtyping would provide a major step towards personalized medicine for individuals with Parkinson's by identifying patients that will benefit from a drug and those patients for whom a specific therapeutic strategy would likely be ineffective.
(c) Assess blood biomarkers for their ability to accurately identify patients and detect drug efficacy with greater sensitivity than existing clinical measures.
The APM is an Australian-led international collaborative of scientists, clinicians, industry and people living with Parkinson's whose goal is to identify effective drugs that slow or stop disease progression and fast track them into clinical practice.

LBP.62

Neuropsychiatric complications as key components of Parkinson's disease: A critical framework for enhancing engagement in PD mental health research

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Objectives: The objectives of the project were to 1) identify barriers and facilitators to participation in Parkinson's disease (PD) mental health research, 2) describe factors that influence study dropout, and 3) develop tools to enhance accuracy of self-report and participant retention in PD mental health clinical trials.
Background: Common problems affecting mental health clinical trials include reluctance to take part, early termination, and inaccurate, inconsistent, and/or under- reporting of emotional concerns. These problems have the potential to reduce the impact of research, slowing the development of effective mental health treatments for people with PD (PWP). Enhanced understanding of these barriers represents an important step towards optimizing care for PWP.
Method: Three focus groups (N=16 total, 4–6 participants per group) were completed between December 2017 and March 2018 (Phase 1), transcribed, and analyzed via qualitative methods. Specific deliverables were developed in response to key themes, and two focus additional focus groups (Phase 2) were completed in June and July 2018 to gather further input on revised research tools and procedures. One Phase 1 group and 1 Phase 2 Group focused specifically on the unique needs of Veterans with PD.
Results: Limited knowledge about the common and central role that neuropsychiatric symptoms play in overall PD management was identified as key barrier to engagement. Perceived stigma was reported to be a major driver of self-report bias. Peer-to-peer research ambassador programs, improved educational materials regarding PD mental health, quarterly wellness newsletters, and mixed-media testimonials from prior study participants were examples of tools that may enhance the longevity and quality of PWP participation in mental health research, based on focus group results.
Conclusions: Once refined, deliverables from this project may support the collection of high quality clinical trial data, ultimately improving available mental health care resources for PWP.

LBP.63

BouNDless: An active-controlled randomized, double-blind double-dummy study of continuous ND0612 infusion in patients with fluctuating Parkinson's disease

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[3] Institute of Neurology, IRCCS San Raffaele Pisana, Rome, Italy
[4] NeuroDerm, Rehovot, Israel

Background: ND0612 is under development as the first non-surgical drug-device combination that provides continuous delivery of Carbidopa/Levodopa Subcutaneous Solution (CLSS) for patients with fluctuating Parkinson's disease (PD).
Objective: Determine the efficacy, safety, and tolerability of continuous subcutaneous ND0612 infusion in comparison to oral carbidopa/levodopa (CD/LD) in patients with PD experiencing motor fluctuations.
Methods: A total of 288 PD patients (Hoehn and Yahr =3) on =4 doses/day of CD/LD oral therapy (=400mg of LD), experiencing motor fluctuations (average of at least 2.5 hours daily, with a minimum of 2 hours every day) in the OFF state during the waking hours) will be enrolled. The study comprises 6 periods:
Period 1: Screening (1–4 weeks)
Period 2: Open-label oral CD/LD adjustment period (6 weeks)
Period 3: Open-label ND0612 conversion period (6 weeks)
Period 4: Double-blind, double-dummy, active-controlled, maintenance period where patients are randomized to either ND0612 infusion + Dummy IR CD/LD, OR to Dummy infusion + IR CD/LD (12 weeks)
Period 5: Optional open-label extension period (1-year)
Period 6: Safety follow-up (12 weeks)
Results: The primary endpoint is the change from Baseline (start of Period 3 = start of ND0612 infusion) to end of the maintenance period (Period 4, Week 12) in mean ON time without troublesome dyskinesia, normalized to 16 waking hours, using patient-rated ON/OFF diary assessments. Secondary outcome measures include changes in: OFF time (key secondary), UPDRS (Parts II and III), Patient's and Clinician's Global Impressions of Change, ON time without dyskinesia, PDQ-39 and Parkinson's disease Sleep Scale (PDSS) scores. Clinical assessments are by blinded-rater. Safety and tolerability are assessed via adverse event reporting, including local skin safety assessments, rates of premature discontinuation, and study treatment compliance.
Conclusions: BouNDless will be the first Phase III randomized, active-controlled trial to establish the efficacy and safety of maintenance treatment with continuous subcutaneous ND0612 in comparison to oral immediate-release CD/LD in patients with PD experiencing motor fluctuations.

LBP.64

Directional versus omnidirectional Deep Brain Stimulation for Parkinson's disease: 12-month results of a multi-center, prospective, blinded, crossover study

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Background: Deep Brain Stimulation (DBS) has been delivered through circumferential electrodes for over a quarter century to treat symptoms of levodopa-responsive Parkinson's disease. Recently introduced directional leads for DBS have the two middle rings divided into three segments, which allows for axially asymmetric stimulation. The Infinity DBS system (Abbott) delivers conventional omnidirectional stimulation to all three segments of the ring, or directional stimulation to only one or two segments. Progress is the first large, prospective, multi-center study conducted to evaluate safety and clinical performance of directional DBS.
Methods: Directional and omnidirectional stimulation were compared in 66 subjects receiving DBS in the subthalamic nucleus for Parkinson's disease. Subjects were programmed with omnidirectional stimulation for 3 months, followed by directional for 3 months and blinded to stimulation type for the first 6 months. The primary endpoint was the difference in Therapeutic Window (TW) for directional vs. omnidirectional stimulation assessed at the 3-month follow-up visit. Subjects were blinded to stimulation type for the first 6 months, and a blinded assessment was made for therapeutic window. Additional endpoints included blinded UPDRS part III motor examination scores, UPDRS part II for activity of daily living, PDQ-39 for quality of life, safety, subject and clinician stimulation preference and subject and programmer satisfaction with product usability.
Results: There was a wider TW for directional stimulation in 59 of 66 subjects (89.4%), meeting the endpoints for both non-inferiority and superiority. Single-segment activation produced wider TW than omnidirectional stimulation in 56 of 66 subjects (84.8%). Directional stimulation was able to produce a 35% wider TW, and therapeutic current strength was 30% lower using the optimal directional configuration. When asked for their preferred period, more than 2 times as many subjects and 4 times as many clinicians chose the period using directional stimulation. Additional results will be reported for activities of daily living, quality of life and patient satisfaction with using the DBS system.
Conclusion: Progress met its superiority endpoint, with 89.4% of subjects having a wider TW using directional DBS stimulation. This international prospective blinded crossover study is the largest clinical evaluation of directional DBS to date.

LBP.65

Communicating clinical trials to scientists, health professionals, study participants and the public: Hype, hope or despair?

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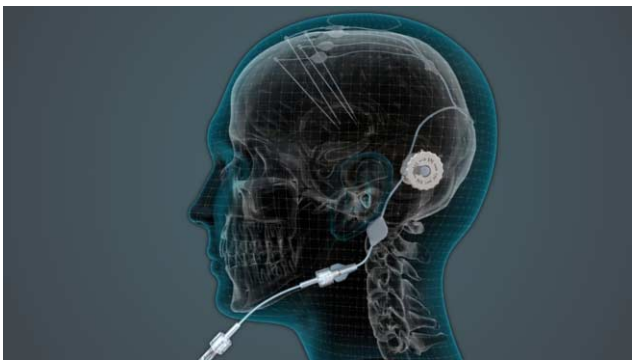
Background: Funding bodies require that clinical trials are reported to the scientific community, study-participants and the public. Securing publication in cases where the science has been robust but the primary and secondary trial outcomes are not met can be challenging, and thoughtful scientific and public dissemination is required, to balance participant experience with realistic scientific discovery from exploratory or post hoc measures. These studies might not be the most evidently appealing for publications to publish.
Methods: The latest reported Glial Derived Neurotrophic Factor (GDNF) investigations, funded by Parkinson's UK and the Cure Parkinson's Trust, offer a potential case study of the need for a joined-up approach to dissemination to prevent over-hyping study results given a consumer documentary following the trial was to air in conjunction with the results.
A dissemination strategy that linked journal editors, investigators, funders, study-participants, print journalists, documentary-makers and broadcasters was employed. An embargoed press conference was held on March 26th 2019, at the Science Media Centre, London. Study Participants were sent article proofs' and an extended lay-summary the same day. The two original open access articles published in Brain and the Journal of Parkinson's disease, occurred concurrently March 27th. The first of a two-part BBC documentary, that followed the trial throughout, aired February 28th, with the second episode revealing the results broadcast March 7th.
Results: At present, extensive coverage has occurred in all UK national newspapers with further coverage internationally and on social media with impact to be evaluated by the end of March.
To date, one article appearing before the press-embargo projected hype. Nine UK papers reflected disappointment in the top-line results but hope that key-learnings could be leveraged into future research. One UK lay-science publication (subsequently retracted) accused investigators and funders of spin and one article reflected only despair.
Discussion: The aim of the investigators and funders was that public dissemination in the lay-press, radio and television and in the BBC documentary mirrored the "hopefully" balanced reporting in the original scientific articles. Eleven days post publication of the original articles this appears to have been achieved. The above seems a topic worthy of further discussion.



CLINICAL SCIENCE: Neuroimaging

LBP.66

Usefulness of cardiac MIBG scintigraphy and midbrain/pontine ratio to differentiate Parkinson's disease from multiple system atrophy and progressive supranuclear palsy

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Objective: The purpose of this study was to evaluate the usefulness of cardiac 123I-metaiodobenzylguanidine (MIBG) uptake and midbrain/pontine ratio (M/P ratio) on magnetic resonance images (MRI) in differentiating Parkinson's disease (PD) from multiple system atrophy (MSA) and progressive supranuclear palsy (PSP).
Background: Clinical differentiation between PD and MSA or PSP is sometimes difficult.

Methods: Cardiac MIBG scintigraphy and brain MRI were carried out in 77 patients with PD (age, 68.8±10.0 years), 18 patients with MSA (age, 67.6±9.4 years), and 14 patients with PSP (age, 72.4±9.1 years). M/P ratio was manually measured using MRI sagittal section of T1 weighted images by the same neurologist blinded to the diagnosis and other clinical information.
Results: To differentiate PD and MSA, the delayed heart-to-mediastinum (H/M) ratio of cardiac 123I-MIBG uptake was significantly lower in patients with PD compared with those with MSA (2.04±0.98 vs. 3.25±0.51, P<0.001). M/P ratio was lower in patients with PD than those with MSA (0.24±0.036 vs. 0.31±0.087, p=0.005). To differentiate PD and PSP, the delayed H/M ratio of MIBG was significantly lower in patients with PD than those with PSP (2.04±0.98 vs. 2.79±0.85, p<0.001, p=0.012). M/P ratio was significantly lower in patients with PSP than those with PD (0.24±0.036 vs.0.20±0.51, p=0.002).
The area under the ROC curve for cardiac MIBG scintigraphy and M/P ratio in differentiation of PD from MSA was 0.84 (95%CI, 0.75–0.92), 0.75 (95%CI, 0.58–0.91), respectively. To differentiate PD and PSP, the area for MIBG and M/P ratio was 0.72(95%CI, 0.59–0.86), 0.80(95%CI, 0.64–0.97), respectively.
Conclusion: Cardiac MIBG scintigraphy and M/P ratio may be useful in distinguishing PD from MSA and PSP.

LBP.67

Distinctive MRI patterns of brain iron accumulation in atypical parkinsonian syndromes

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Recent data suggest mechanistic links among perturbed iron homeostasis, oxidative stress, and misfolded protein aggregation in neurodegenerative diseases. Iron overload and toxicity toward dopaminergic neurons have been established as playing a role in the pathogenesis of Parkinson's disease (PD). Brain iron accumulation has also been documented in atypical parkinsonian syndromes (APS), mainly comprising multiple system atrophy (MSA), and progressive supranuclear palsy (PSP). Iron-sensitive magnetic resonance imaging (MRI) has been applied to identify iron-related signal changes for the diagnosis and differentiation of these disorders. Topographic patterns of widespread iron deposition in deep brain nuclei have been described as differing between patients with MSA and PSP and those with PD. A disease-specific increase of iron occurs in the brain regions mainly affected by underlying disease pathologies. However, whether iron changes are a primary pathogenic factor or an epiphenomenon of neuronal degeneration has not been fully elucidated. Moreover, the clinical implications of iron-related pathology in APS remain unclear. In this review study, we collected data from qualitative and quantitative MRI studies on brain iron accumulation in APS to identify disease-related patterns and the potential role of iron-sensitive MRI.

COMPREHENSIVE CARE: Caregiving, relationships, respite care, families

LBP.68

Caregiving 101: A solution-oreinted guidebook for those providing care to persons living with Parkinson's disease

*Marjorie Getz**
Methodist College, Peoria, Illinois, USA

Approximately 43.5 million Americans provide care for another person; many for someone affected by Parkinson's disease. Receiving support/care allows persons, especially someone with PD, to live in their own homes or with family members. Our resource, a caregiver manual, allows unique care plans to be developed/modified to continue to meet a person's personal, financial, social and healthcare needs. Caregiving support depends on reliable resources for provision of competent care. Designed by healthcare providers for use by family caregivers, the manual was pilot tested and distributed throughout a small city in the Midwestern United States by local agencies on aging and adult daycare center staff. Feedback has been positive. Designed to assume no prior nursing care/medical care experience, the manual does assume that users have received some training or instruction in basic care from qualified healthcare professionals. There are nine sections of relevant caregiving topics and a section providing additional information on special caregiving needs for a person with PD. Detailed schematics are included showing how to carry out various procedures. One or two-sided waterproof fact sheets introduce each section; each of which is followed by more detailed information. Triage sheets to help users determine how serious a particular situation might be are included. Each section also includes a subsection especially relevant for the physical health care needs of the care provider. This poster describes this practical resource designed with the special needs of an at-home family caregiver for a person living with PD in mind.

COMPREHENSIVE CARE: Fitness, wellness, nutrition

LBP.69

Exercise behavior among patients with Parkinson's disease

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[2] Texas State University, San Marcos, Texas, USA

Introduction: Diverse exercise programs have been found to be effective in terms of improvement of postural control, balance, motor

function, fatigue, mood, executive control, and quality of life among patients with Parkinson's disease (PD). Multiple types of and modalities have been found to have beneficial effects in these patients. Some other studies have identified barriers to exercise in PD patients, including lack of informational support, lack of referral to physical therapy services, disease-specific limitations, and community-related issues. Our objective is to identify the exercise behavior of our PD patients and identify barriers.
Methods: Cross-sectional study done through telephone surveys in a random sample of Parkinson's disease patients that follow up at our Movement Disorder clinic.
Results: A total of 48 responses were included. 60.4% of our PD patients reported being engaged in regular physical activity, while 30.6% were "non-exercisers". 79.2% of all patients reported having received information regarding exercise by their physicians, and 75% had heard about the diverse benefits of exercise. Only 27.1% had received any written material. Among the "exercisers", 75.9% noticed benefits, including mobility (34.5%), balance (31%), improved tremors (10.3%), mood (6.9%), gait (6.9%) and strength (6.9%). 79.3% of them reported an improvement in their quality of life. The main barriers for our non-exercisers were mobility issues due to PD (68.4%), lack of interest (52.6%), pain (47.4%), perceived lack of benefit (47.4%), lack of time (31.6%), lack of community resources (31.6%), fear of injury (26.3%) and PD medication side effects (15.8%). 52.6% were interested in starting exercise.
Discussion/Conclusions: It is important to stress the importance of exercise to our PD patients, as there is growing evidence of the multiple physical benefits. Patients should be encouraged to exercise, information regarding benefits should be provided and limitations should be addressed. There is not a single modality of exercise that has been shown to be better over other types, so exercise should be tailored to patients' preference. Most of our patients who exercise noticed a benefit in multiple areas and the majority felt that physical activity improved their quality of life.

COMPREHENSIVE CARE: Alternative & complementary therapies/ Creativity

LBP.70

Effects of yoga on oxidative stress, motor function, and non-motor symptoms in Parkinson's disease: A pilot randomized controlled trial

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[2] University of Minnesota, Minneapolis, Minnesota, USA

Objective: To examine the feasibility, acceptability and preliminary effects of Hatha yoga on oxidative stress, motor function, and non-motor symptoms among individuals with Parkinson's disease (PD).
Methods: A pilot randomized controlled trial design with 2 arms: an immediate treatment group and a wait-list control group. The yoga-for-PD program was implemented via twice weekly 60-minute group-based classes for 12 weeks. Participants were assessed at baseline, 12 weeks, and 6 months post-intervention. Outcome measures included oxidative stress, motor function, physical activity, cognitive function, sleep quality, and quality of life. Data on program acceptability and yoga adherence were collected during the intervention and at 6 months post-intervention.
Results: Participants (n=20) had mean age of 63 years (SD 8, range 49–75) and disease duration 4.8 years (SD 2.9, range 1–13). All participants had mild-moderate disease severity; 18 (90%) were on dopaminergic medications. Seventeen participants (85%) attended at least 75% of the classes and 4 (20%) attended all classes. Most participants (n=17) reported they "definitely enjoyed" the intervention program. No adverse events were reported. At 12 weeks, there were no major differences in blood oxidative stress markers between the two groups. Motor function based on the Unified Parkinson's disease Rating Scale was better in the treatment group but their scores on Sleep and Outlook in Parkinson's disease Quality of Life (PDQUALIF) Scale, and the physical activity levels based on the Longitudinal Aging Study Amsterdam Physical Activity Questionnaire were worse than the control group. In within-group comparisons, motor function, cognitive function and catalase improved but three PDQUALIF domains (Social & Role Function, Sleep, and Outlook) and physical activity level worsened by the end of the yoga intervention program compared to baseline. The response rate for the 6-month follow-up survey was 74% (n=14) with six participants (43%) signed up for a yoga class and four (29%) practiced it independently. Health problems were the main barrier to yoga practice.
Conclusion: Yoga is feasible and acceptable, and may serve as a complementary method for improving motor function in PD. Further research using a larger sample size is needed to determine its impact on oxidative stress and non-motor symptoms.

Table 2. Between Group Comparison of Effects of Yoga on Oxidative Status, Motor and Non-motor Functions at 12 Weeks Adjusting for Baseline Measurement and L-dopa dose

Variable	Yoga (n=10)	Wait-list Control (n=10)	Difference	95% CI
Oxidative Status				
↑Total GSH (µg/ml)	211.4 (7.4)	207.5 (7.8)	-3.9 (10.9)	(-26.8, 19.0)
↑GSH:GSSG ratio	12.4 (.7)	13.1 (.7)	0.6 (1)	(-1.5, 2.7)
↓MDA (µM)	42.7 (4.6)	46.5 (4.9)	3.8 (6.9)	(-10.7, 18.3)
↓SOD (U/ml)	375.9 (37.5)	485.7 (39.5)	109.8 (55)	(-6, 225)
↑Catalase (nmol/min/ml)	41826 (3045)	42583 (3249)	757 (4936)	(-9613,11127)
↓Protein Carbonyl (nmol/ml)	17 (2)	19.2 (2.1)	2.1 (3)	(-4.2, 8.4)
↑GPx (nmol/min/ml/mg)	16.2 (1.6)	15.3 (1.7)	-.8 (2.3)	(-5.6, 4.0)
Motor Function				
↓Motor UPDRS (0 - 108)	17 (1.7)	22.5 (1.8)	5.4 (2.6)	(-0.1, 10.9)
↑LAPAQ Level, in minutes	2563 (756)	5749 (800)	3187 (1141)	(790, 5584)
QOS and QOL (range of scores)				
↑PD Sleep Scale (0 - 150)	112.2 (4.1)	106.3 (4.3)	-5.8 (6)	(-18.4, 6.8)
↑MoCA (0-30)	28.1 (.4)	27.5(.4)	-.8 (.6)	(-2.1, 0.5)
↓Beck Depression Inventory (0-63)	8.9 (1.1)	8.6 (1.2)	-.3 (1.7)	(-3.9, 3.3)
↓PDQUALIF				
Social & Role Function (0 - 100)	44 (3.8)	41.8 (4)	-2.2 (5.6)	(-14.0, 9.6)
Self-image & Sexuality (0 - 100)	37.6 (3.9)	41.5 (4.1)	3.8 (5.8)	(-8.4, 16.0)
Sleep (0 - 100)	35.1 (3.1)	24.7 (3.3)	-10.4 (4.6)	(-20.1, -0.7)
Outlook (0 - 100)	45.8 (2.9)	35.2 (3)	-10.6 (4.3)	(-19.6, -1.6)
Physical Functioning (0 - 100)	33.9 (3.2)	36.2 (3.4)	2.3 (4.7)	(-7.6, 12.2)
Independence (0 - 100)	10 (5)	5.4 (5.3)	-4.5 (7.4)	(-20.0, 11.0)
Urinary Function (0 - 100)	50.8 (4.9)	47.7 (5.3)	-3 (7.7)	(-19.2, 13.2)
Global (0 - 100)	52 (6.3)	53.3 (6.6)	1.2 (9.3)	(-18.3, 20.7)

Values are the mean (SE) unless indicated otherwise. ↑or ↓sign indicates better status.

CI= Confidence Interval, UPDRS = Unified Parkinson's Disease Rating Scale, MoCA = Montreal Cognitive Assessment, LAPAQ = Longitudinal Aging Study Amsterdam Physical Activity Questionnaire, GSH = total glutathione, GSSG = glutathione disulfide, MDA = Malondialdehyde, SOD = Superoxide dismutase, GPx = Glutathione Peroxidase, PDQUALIF = Parkinson's Disease Quality of Life Questionnaire.

LBP.71

'Digital Dancing' – Can you see what you feel?: An exploration of the physical 'experience' of dance for Parkinson's through 3-D motion analysis

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[2] Controlled Frenzy Ltd, Plymouth, United Kingdom

Background: Research has consistently shown dancing has positive impacts on those living with Parkinson's. Improvements are shown in both motor and non-motor symptoms such as improved balance, walking quality and distance, turning, quality of life and feelings of wellbeing. However, people living with Parkinson's who dance report current research does not represent the full, holistic effect of dance and fails to express individual experiences.
Objective: The objectives of this explorative, mixed methods study were to determine the feasibility of collecting measurements of

movement in the whole body in someone with Parkinson's dancing, and their experience of the effect of the dance at the same time?
Method: Three people living with Parkinson's wore a commercially available 3-D movement analysis system – 'Mocap' during three, one-hour dance classes following the 'Parkinson's Dance Science' approach (a Creative/Physiotherapeutic collaborative dance model). A set dance sequence was recorded pre-and post-class, alongside semi-structured interviews with each participant and a focus group with their peers after each class. A 'Convergent Parallel' mixed methods design following the principles of 'Joint categories and themes display' was used to ascertain the feasibility of collecting any quantitative changes in movement in relation to personal experiences of dancing.
Results: The quantitative variables; velocity of upper limb movements, rotation of the trunk, gait quality, posture and whole body extension were successfully extracted from the movement analysis data. Using a framework approach, emergent themes from the interview and focus group data were mapped against these variables. Results were presented visually for each of the three participants in respect of the explorative nature of the design.
Conclusion: The unique mixed methods approached, for the first time enabled quantification of immediate, physical, biomechanical effect of a Parkinson's Dance Science class alongside the personal, psychosocial, experience of dancing in a class environment. This novel method will allow future studies to not only explore the therapeutic potential of dance for Parkinson's as previous, but begin to determine what physical effects ('what you see') may drive positive personalised 'lived experience' ('what you feel') and unpack the holistic power of dance for people living with Parkinson's.

LBP.72

How does the contribution of movement as an artistic and expressive medium improve the quality of life of both the person with Parkinson's and their caregiver?
*Natalie Muschamp**
Step up for Parkinsons, Attard, Malta

The last decade as seen a significant increase in research into the therapeutic effect dance has on people with Parkinson's disease. On the basis of evidence provided by healthcare practitioners, dance scholars, neurologists and psychotherapists, it is now widely recognized that creative and expressive movement has a beneficial effect on people with Parkinson's disease and their caregivers. The aim of this Practice as Research project was to establish and explore the specific ways in which creative and expressive movement improves the quality of life for people with Parkinson's disease and their caregivers. The intervention took place over a period of twelve weeks – twice weekly one and a half hour creative and expressive movement classes focussed on both the person with Parkinson's disease and the caregiver. Due to the progression of the disease, caring for the person with Parkinson's disease typically becomes increasingly emotionally and physically straining. The spouse or family member often becomes the informal caregiver and the existing literature on the subject shows clearly that in general there is not enough support for this role. A methodology was formulated and put into practice whereby the person with Parkinson's and the caregiver took part in dance movement classes together. It quickly became clear that besides the physical benefits for the person with Parkinson's, there were psychological benefits for the caregivers too. Both have has a space in which they feel safe, can move and express themselves, and this in turn tended to strengthen significantly the connection between the caregiver and Parkinson's sufferer. When a person is diagnosed with Parkinson's disease this does not only change the life of the person diagnosed, it changes the dynamics in the whole family. If we want to improve the quality of life for the person with Parkinson's disease we need to make sure that the person caring has sufficient support.

LBP.73

Effects of vibrotactile stimulation on resting tremor in Parkinson's disease
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Resting tremor is a cardinal symptom of Parkinson's disease (PD) that contributes to the physical, emotional and economic burden of the disease. This pilot study investigated whether vibrotactile stimulation of the wrists and ankles delivered using wearable devices was a tolerable intervention stimulus to PD patients, and whether this vibrotactile stimulus produced any attenuation of resting tremor severity. The study involved a randomized cross-over design with all subjects receiving both high amplitude patterned (HA-P) and low amplitude continuous (LA-C) vibration on two separate visits to the laboratory. On each visit, resting tremor was video recorded for 10 minutes at baseline and while the vibrotactile stimulation was applied using the wearable devices. Tremor severity was scored using item 20 of the Unified Parkinson's disease Rating Scale (UPDRS) by a blinded clinician. Thirty-seven of the 52 enrolled subjects were included in the data analysis. Both vibration paradigms caused a reduction in resting tremor severity with a moderate effect size (HA-P: $P=0.01$, $r=0.31$; LA-C: $P<0.01$, $r=0.42$). No difference between the two vibration paradigms was observed ($P=0.10$). All subjects tolerated the vibrotactile stimulation with no reports of adverse events or discomfort. In conclusion, short durations of vibrotactile stimulation of the wrists and ankles delivered via wearable devices may attenuate resting tremor severity in individuals with PD, however, this study did not contain a sham condition and so the responses to the vibrotactile stimuli cannot be compared to a potential placebo response.

COMPREHENSIVE CARE: Lay/professional health literacy & public thought

LBP.74

Association between health literacy and health-related quality of life in patients with Parkinson's disease who participate in an ongoing group exercise program
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This study aims to clarify the association between health literacy and health-related Quality Of Life (QOL) in Parkinson's disease (PD) patients participating in an ongoing group exercise program.
Scores (total and subclasses) were calculated using basic information, functional, communicative and critical health literacy (FCCHL), and the 39-item Parkinson's disease Questionnaire (PDQ-39) in 34 PD patients participating a group exercise program. Univariate analysis was performed on association between basic information and FCCHL plus PDQ-39, followed by multivariate analysis on basic information and FCCHL and PDQ-39 scores of

pairwise combinations given by a correlation between FCCHL and PDQ-39.
Results showed that the following correlations are significant: between disease duration and communicative health literacy, PDQ-39 total score, stigma, cognition, and communication. There were significant correlations between Functional Health Literacy (FHL) and athletic ability and between Critical Health Literacy (CHL) and motor disorder. Predicted R-Squared in multiple regression analysis between FHL and athletic ability was 0.12. Multinomial logistic regression ratio between CHL and motor disorder reached a low predictive accuracy of 67.6%.
This study indicates the importance of providing easily comprehensible information on exercise methods or ingenuities for life in PD-specific motor symptoms and specialized knowledge in PD-specific non-motor symptoms.

Table 1：Demographic table by matching data, n=3,210

Variables	Case Parkinson's patient with Dementia (n=1,605)		Control Parkinson's patient without Dementia (n=1,605)		p value
	Male (n=731)	Female (n=874)	Male (n=731)	Female (n=874)	
Age (years) (n, %)					
Total mean±SD	76.8±7.8	78.2±6.4	76.8±7.8	78.1±6.4	
Modified Hoehn-Yahr Stage (n, %)					
Stage 3	267, 36.5%	213, 24.4%	267, 36.5%	213, 24.4%	
Stage 4	304, 41.6%	389, 44.5%	304, 41.6%	389, 44.5%	
Stage 5	160, 21.9%	272, 31.1%	160, 21.9%	272, 31.1%	
WHODAS 2.0 (mean±SD)					
Cognition (Domain 1)	62.7±27.7	64.5±27.7	50.0±29.1	54.5±30.1	<.0001
Mobility (Domain 2)	59.2±28.3	62.9±28.5	59.6±27.5	65.2±26.5	<.0001
Self-care (Domain 3)	40.2±31.6	42.8±33.8	40.0±30.9	42.1±33.4	0.2302
Getting along (Domain 4)	69.3±28.4	69.7±28.3	60.9±30.4	62.6±31.8	<.0001
Life activities (Domain 5-1)	76.8±35.6	76.9±35.0	70.2±38.7	74.1±37.8	0.0010
Participation (Domain 6)	47.1±24.1	49.0±24.8	48.7±24.7	50.5±25.2	0.0540
Summary	58.0±21.5	59.9±22.1	53.8±22.4	57.2±22.5	<.0001

COMPREHENSIVE CARE: Disability and quality of life outcome measures

LBP.75

A cross-sectional assessment of function and disability in patients with Parkinson's disease and Parkinson's disease dementia using WHO Disability Assessment Schedule 2.0
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Background: Parkinson disease (PD) is a common neurodegenerative disorder which affected more than 4 million individuals worldwide. Annually, about 10% of patients with PD developed Parkinson disease dementia (PDD). Both PD and PDD did cause functional decline and increase care burden to their families, especially PDD. Therefore, early awareness of PDD may help early prevention and management, as well as decrease economical loss and care burden. WHO Disability Assessment Schedule 2.0 (WHODAS 2.0), which was developed by WHO, provided a standardized disability levels and profile evaluation with high reliability and validity. Through WHODAS 2.0, we could assess the function and disability of participants with short, simple, and easy administration.
Method: Preliminary data was collected from the registry of disability evaluation, functional assessment, and by provision of Taiwanese Social and Family Affairs Administration—a ICF framework–based database established by the Ministry of Health and Welfare in Taiwan between July 2012 and October 2018. Patients with ICD-9-CM 332 and ICD-10-CM G20 were included, and patients with ICD-9-CM 332.1 or missing answer in any question were excluded. Included patients were divided to PD and PDD group, which was then matched by age, sex, and Parkinson severity in order to minimalized the baseline difference. We compared the difference in WHODAS 2.0 score between 2 groups by using chi-square test, fisher exact test, ANOVA F test and post hoc test using Scheffe method.
Result: In our study, the major difference between PDD and PD patients in WHODAS 2.0 was obviously in domain 4 (getting alone, 69.7±28.3 vs. 62.6±31.8, P<0.001) and domain 5-1 (life activities, 76.9±35.0 vs. 74.1±37.8, P=0.001), except domain 1 (cognition) which was also higher in PDD group. There was no significant difference in domain 2 (mobility), domain 3 (self-care), and domain 6 (participation) between PDD and PD group. Male and female in PDD group had no significant difference in all WHODAS 2.0 domain.
Conclusion: PDD patients has more difficulty in getting alone and life activities as compare as PD patients.

LBP.76

Assessment of psychosis in patients with Parkinson's disease
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Background and aims: Psychosis plays an important role among patients diagnosed with Parkinson's disease. It is believed that unto 70% of PD patients are affected with psychosis. Although many different hallucinations, illusions, and delusions are reported in PD, the majority of episodes are visual hallucinations. To better quantify PD psychosis and aid in future therapeutic trials, our study aims to designed a PD specific psychosis scale and undertook psychometric evaluations in order to rule out psychosis associated with PD.
Materials and methods: A cross sectional study was conducted in Sir GangaRam Hospital Lahore during May 2017 to August 2018. Total 80 patients diagnosed with Parkinsonism syndrome were included in the study. A questionnaire was established. The first five questions identify the type of hallucination (visual, auditory, olfactory, sense of presence) or delusion while the second five questions further quantify the intensity, frequency, insight and impact of the worst psychotic feature on the life of the patient and family. Analyses were performed using SAS 9.3.
Results: Sixty different PD patients with psychosis and 20 PD patients without psychosis were included in the study. In psychosis subjects, results were normally distributed: mean 19.23. In those without psychosis 12% scored >0. The intra-rater, inter-class correlation coefficient was excellent (N=28 pairs of observations seven days apart, ICC=0.87). Inter-rater reliability (two different raters, N=48 pairs) was outstanding for the entire group, ICC=0.92). As expected visual hallucinations were most common (mean=4.19). The presence of delusions was associated with greater total scores.
Conclusion: We report very good intra-rater reliability and excellent inter-rater reliability on a 10 question scale designed specifically for PD associated psychosis.

COMPREHENSIVE CARE: Health accessibility/Underserved populations

LBP.77

Cost-effectiveness of a Parkinson's nurse specialist position in rural and regional Australia: A pilot retrospective analysis

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Limited access to specialist services for people living in rural and regional Australia has been shown to contribute to decreased health related quality of life. In contrast to people living with Parkinson's disease (PD) in urban areas, disease management is poorer in rural and regional areas. With 93% of neurologists practicing in major cities and no national approach to ensuring equitable access to neurology and specialist PD services, it is challenging for those in rural and regional locations.
In late 2017, Parkinson's NSW partnered with nursing researchers from Charles Sturt University to undertake a staged project to build the case for the implementation of sustainable specialist Parkinson's nurse services in rural and regional Australia. The findings from an integrative literature combined with evidence from a qualitative project demonstrated the benefits of the nurse-led model in Coffs Harbour, New South Wales, Australia. The research team then undertook this project examining the financial impact of the Parkinson's nurse specialist model on health care costs.
A four-year retrospective medical record audit was undertaken. Patient outcomes prior to the employment of the Parkinson's nurse specialist (calendar years 2013–2014) were compared with outcomes after the establishment of the nurse position (2016–2017). The target population were people with a diagnosis of PD (as determined by a neurologist and/or geriatrician, rehabilitation and medical physician) identified in medical records and living either in the community or in an aged care facility in the Local Health District. A rigorous four-step process was designed to guide data collection and analysis, sample size was determined to achieve a medium effect size and an alpha level of 0.05. Pre and post results were compared using descriptive statistics.
Preliminary findings demonstrate a reduction in hospital length of stay and readmissions post the establishment of the specialist nurse position. When combined with the detailed findings expected from this retrospective audit, the data will form the basis for the economic analysis essential to advocate for the implementation of specialist nurse positions in underserved rural and regional locations.
These findings have relevance to the wider Australian context and for countries with similar geographical challenges.

LBP.78

Health services for Parkinson patients in five hospitals in South Sumatera, Indonesia

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Background: In 2007, Dorsey et al estimated that the number of PD cases worldwide would be doubled by 2030. It is caused by the increase of elderly population. In 2010, Indonesia's population was 237 millions and also increase in elderly population. This study aim to evaluate how health services for Parkinson's patients in Indonesia are, especially in South Sumatra.
Method: Descriptive studies that were conducted in 5 hospitals.
Results: Average number of Parkinson patients hospital visit per month is mostly in Hospital C, 31 patients. While the number of hospital visit in Hospital D, only 6 patients. Almost all patient has the hospital visit once per month, only in Hospital D the number of hospital visit once per week. Three hospitals are available for 4 types of Parkinson drugs, while others are only 3 types. Most hospitals do not have parkinson diagnostic tools, only hospital A has MRI.
Discussion: The highest number of hospital visit was found in hospitals B and C. Moreover Hospital A, located in the city of Palembang, the number of hospital visit per month is only 11 patients. This is probably because of implementation of referal system. With this system, the number of visits in class A hospital experienced a significant decrease. The number of hospital visits in Palembang City is greater compared to other cities, that probably due to easier access to health care services. In rural area, only 13% of elderly has the access to hospitals, 65.3% of the elderly did not seek any health services and 27.3% the elderly consider that unnecessary to visit health care services. These factors might influence the less prevalence data of Parkinson's disease in Indonesia. Almost all hospitals have incomplete service facilities for parkinson patients in both diagnostic and therapeutic. It could lead to underdiagnose and undertreatment of Parkinson's disease in Indonesia, particularly South Sumatera.
Conclusion: Health care services for Parkinson's patients in five hospitals in South Sumatra is not adequate yet. It should be considered to develop appropriate diagnostic and comprehensive management strategy of Parkinson's disease for underserve country.

Table 1. Description of health care services in five hospitals in Sumatera Selatan

Hospital	Class	Location (from capital city)	Visitation per month (average)	Frequency	Age (mean)	Parkinson drug	Diagnostic	Service	Neurologist
A	A	Palembang (0 km)	11,2	Once a month	61,1	L/B L/C/E Pramipexole trihexylphenidil	MRI 1,5 T	Rehabilitation clinic, Geriatric Clinic	10
B	C	Palembang (0 km)	26,2	Once a month	63,2	L/B L/C/E Pramipexole trihexylphenidil		Rehabilitation clinic	2
C	C	Palembang (0 km)	31,4	Once a month	N/A	L/B L/C/E Pramipexole trihexylphenidil		Rehabilitation clinic	2
D	C	Sekayu (120 km)	6,6	Once a week	61,5	L/B Pramipexole trihexylphenidil		Rehabilitation clinic	1
E	B	Muara Enim (220 km)	15,3	Once a week	62,2	L/B Pramipexole trihexylphenidil		Rehabilitation clinic	1

Note: L/B = levodopa/benserazide; L/C/E = Levodopa/carbidopa/entacapone

COMPREHENSIVE CARE: Daily life activities including working & driving

LBP.79

Inside the mind of a working mum with Parkinson's disease!

*Genna Douglas**
Loughborough, United Kingdom

When I was diagnosed with Parkinson's at the age of 34 years old I felt like my world had crumbled around me. I knew very little about the disease. I'd never 'knowingly' met anyone with the Parkinson's. I say knowingly as I've since learnt that everyone with Parkinson's disease presents there symptoms in different ways. I for instance don't have any obvious outward signs. I have no obvious tremor. Which is a blessing and a curse at the same time. I say that because it's nice that I can be seen as a 'normal 36 year old' by

strangers but at the same time people don't understand when I have slowness of movement, I'm struggling, tiered or stumbling.
Nearly three years on I think back to my diagnoses. That moment when the consultant said those three words 'you have Parkinson's all I could think about was my little girls. 'Is it hirredotory?', 'am I going to die from it?', the thought of leaving them was unbearable. I left the appointment bewildered, upset, shocked and with the task of telling my parents. Hundreds of questions running through my head but no idea of where to start to try and find the answers!
The most annoying thing about Parkinson's is the frustration I feel, my body doesn't do what it's supposed to do! Something which is so very hard to explain to anyone without PD.
Despite all the frustration, anger and why me's I'm determined to try and stay positive, live for now and, as with many parkinsons patients I've met I'll try not to think to far ahead. I keep myself stupidly busy. A distraction from all the questions going on inside my head!
Someone once told me that ladies of 36 are at the busiest time in there lives. Imagine that! Then imagine having Parkinson's disease to also deal with!
Despite all that this working mum of two will not let Parkinson's take her spirit!
My poster will aim to raise awareness for young onset Parkinson's and people just like me!

LBP.80

Characteristics and difficulties patients with Parkinson's disease have with going out
*Yumi Iwasa**
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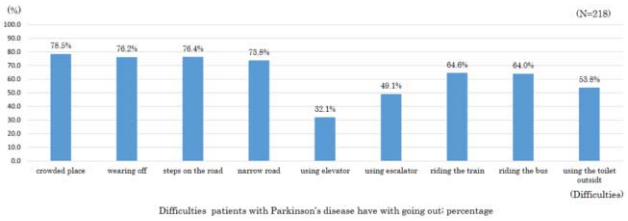
Getting out of the house is not only an opportunity for patients with Parkinson's disease to exercise, but it is also an opportunity to develop daily rhythms. It can be expected to have a good influence on their mental states.
We conducted a questionnaire survey with 436 members of the Hyogo branch of the Japan Parkinson's Association and obtained valid responses from 249 people (57.1%). In the five groups of each Yahr stage, from 1 to 5, the average outing days per week for patients were 5.1, 3.7, 3.3, 2.1, and 1.2, respectively. There was a negative correlation between the number of days going out and the Yahr stage (CC-0.358). The average number of outing days for men was 3.3, and 2.7 for women. Men tended to have significantly more days out (P<0.1). A total of 69.6% of people wanted to increase the number of days that they went out. People who desired such an increase were those without work or hobbies, who did not live alone, and who did not use the Internet. They were also people who were at a higher level than Yahr 3 (P<0.05). Of the total, 69.7% had difficulty going out alone. The reasons for such difficulties were crowds (78.5%), the wearing off (76.2%), using small coins (68.4%), and using the toilet (53.8%). It was more difficult for them to walk in the city if there were steps on the road (76.4%), the road was narrow (73.8%), than to ride the bus (64.0%).
Only 5.6% of people were able to get services to support their outings. Volunteer support should increase to meet this need. Results suggest that participants were able to increase the number of days that they went out by increasing work opportunities. In addition, environmental improvements in the city must be prioritized.



Difficulties patients with Parkinson's disease have with going out: percentage

COMPREHENSIVE CARE: Self-management, empowerment, coping strategies

LBP.81

Development of a structured psychosocial intervention programme for patients with Parkinson's disease and their families
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Background: Parkinson's disease (PD) is the second most common neurodegenerative disorder after Alzheimer's disease, affecting approximately 1 percent of the population older than 50 years. Caregiving of the patients with especially during the advanced stages can be quite a difficult task. A double impact of the illness is operative in PD; care is needed for physical limitations of the patient as well as the inevitable cognitive and psychiatric complications, which can begin early in the disease. Given the irreversible nature of the illness, the multiple dimensions of care and diverse needs must to be given due importance. In the social and cultural context that is unique to India, family has a major role to play in decision making as well as direct caregiving for the patient.
Methods: An exploratory qualitative study was conducted to derive the needs associated with care giving in Parkinson's disease through in- depth interviews with ten patients – caregiver dyads. The interviews were respondent driven and lasted about forty-five minutes to one hour with each dyad. The interviews were transcribed and analysed using constant comparison method (Strauss & Corbin 1988). Based on the themes derived from the analysis, the informational, emotional and practical daily life care needs emerged as major areas of concern. 'Getting on' was identified as the overarching theme that defined the help seeking process. Deriving from the needs and review of literature, a model for psychosocial care delivery was developed. Rolland's (1987) psychosocial typology of illness is presented as a feasible framework to understand and intervene in Parkinson's disease. Clinical Social Worker is an important member of the multidisciplinary team and work as a care manager, who would coordinate the functional rehabilitation process.
Conclusion: A conceptual framework for intervention based on Rolland's psychosocial typology of illness is a valuable tool in service delivery with Parkinson's disease. The Knowledge, skills, facilitators and challenging conditions for integration of psychosocial care into routine care will be discussed. The model needs to undergo rigorous validation process to establish its effectiveness.

LIVING WITH PARKINSON'S: Public education or awareness programs

LBP.82

Apple: the first website about Parkinson's disease for the patients in Japan

*Toshiko Atoda**
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Apple is the first website about Parkinson's disease (PD) for the patients in Japan. Currently Apple is not visible any longer. I write this in memory of Apple. Apple is really epoch- making and many loved. Not the patients but physicians and health care professionals visited there. Actually almost young onset patients could not continue the running or updates more than 10 years as being aged and advanced any longer. At the beginning Yoshiko Okada chose the English articles to translate in Japanese. One by one Apple grew up. Apple had various contents including the medical information, the news digest, the care & welfare, disabled pension Q&A, DBS information & reports, complimentary therapies, the communicational spaces and so on. Also we had two surveys one about the allowance for the incurable disease different by prefecture, inquiring all prefectural government the detail. Another survey is about the price of PD medicine by country. inquiring the prices to foreign friends with PD. And I translated the articles which I was interested in, including "Female and PD." And the articles of Difficulty in walking, Falls and Freezing, Depression and Visible Disorder in PD. As well, the book titled " The way to live the life with ON & OFF" by three co-authors was published in 2010. During these time, I found the pleasure of writing that is great gift for me. Since 2003, I have been writing the essays about PD, my life, my thoughts and others. Since I had PD in 1965, age of 17, my life was not only the life with PD. I didn't have any confidences in myself and any pride to live my life. Anyway, currently I always use a wheelchair because of falling easily and I have macular dystrophy for more than 15 years. However thanks to Apple, thanks to writing, my life came to be worthy. Now I can say my life is full of happiness and blessed.

LBP.83

YOPD: A rare opportunity (to rebrand for the better)

*Gaynor Edwards**
SpotlightYOPD, Playden, Rye, East Sussex, United Kingdom

There are many reasons why those diagnosed with PD at a younger age struggle to get the awareness, support and understanding needed. We believe there is a need to redress the balance and reinvent the image of Young Onset – effectively creating the global brand of YOPD. In this way we hope to erase the public perception that Parkinson's is exclusively a disease of the elderly and bring younger PwPs together. The WPC itself is a perfect example of how collaboration leads to change.
The wider PD community needs the young, newly diagnosed perhaps more than any other group because:

> Their medical history is probably easier to track.
> They are purer PwPs – with the many other age-related diseases yet to develop.
> They have the energy and voice to be effective advocates.
> They are rightly more invested in the future – as they will expect/hope to see it.
> They are well-connected – being the age of those in power and decision-makers, they have the time/life expectancy and influence required.

D is not for just for disease:
YOPD has rare disease status – but on diagnosis people don't feel just rare they feel alone.

- The diagnosis can take months or even years.
- That dialogue and how the three words 'you have Parkinson's' are conveyed make a lasting impression.
- Not all doctors have a full understanding of YOPD.
- There is a need for a dedicated pathway – based on international guidelines.
- For YOPD-diagnosed the images of older PwPs is detrimental and can cause some to turn away from engaging with the condition – missing out on the support from fellow younger positive proactive PwPs, better treatment and trials for the greater good.

SO… what's in the favour of Brand YOPD:
The automatic membership is young, media-friendly and web-savvy and has that initial energy and determination to make a difference. Attracted by a community of their own age, they feel they belong and rightly believe THIS TIME they can make a difference.
They are to be embraced and encouraged.
Log onto YOPD.info (TO COME)

LIVING WITH PARKINSON'S: Government advocacy/Campaigns/Public policy

LBP.84

The economic burden of Parkinson's disease (PD) in the United States

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Objective: To provide a comprehensive assessment of the direct and indirect medical costs of PD in the US
Background: In addition to the debilitating symptoms of PD itself, people with PD (PWP) also experience injuries from falls and other comorbidities. As a result, PWP have higher medical needs, often miss work, retire early and require caregiver assistance. PD prevalence is predicted to increase in coming decades. Comprehensive information on the economic burden of PD is needed.
Methods: Multiple data sources were used to estimate the different components of the cost of PD, including: The US Census population projections combined with Medicare Current Beneficiary Survey (MCBS) and the Medical Expenditure Panel Survey (MEPS) data; claims data from Medicare Standard Analytical File (SAF), non-acute care and prescription drug components from the MCBS, CDC Wonder data, average earnings data from Bureau of Labor Statistics, and one of the largest claims databases for the privately insured. Other indirect and non-medical cost components were estimated using a primary survey that was designed and implemented for this study. Costs were determined for an estimated 1 million Americans with PD using 2017 costs.

Results: The estimated total medical cost attributable to PD is just over $25 billion in the US. Nearly 90% of the total direct medical cost of PD are borne by Medicare and its beneficiaries with PD, with inpatient and non-acute institutional care representing the largest shares of the total direct cost. The average per-person direct cost was $22,671 for the privately insured PWP 65 years of age) with PD. The average indirect and non-medical cost per PWP is $18,229 for PWP alone and $24,149 for PWP combined with unpaid care partner burden. The estimated total indirect and non-medical cost of PD is $25.05 billion in 2017, with $18.9 billion attributed to PWP and another $6.1 billion to unpaid care partners.
Conclusions: This is the most comprehensive US study to-date in examining the overall economic burden of PD. Our findings underscore the significant burden of PD to society, payers, people with PD and their care partners.

LIVING WITH PARKINSON'S: Living well with PD

LBP.85

Wearable device use increases the quality of life in people with Parkinson's disease
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Walk With Path, Copenhagen, Denmark

The symptom of Freezing of Gait in Parkinson's disease affect approximately 50% of the Parkinsonian population. Freezing of Gait stops a person being able to initiate or continue walking independently due to the feeling of their feet being 'glued to the floor'.
Wearable, or assistive, devices in healthcare have the ability to improve a person's Quality of Life (QoL), independence and ability to manage symptoms.
Path Finder is an innovative wearable device using lasers as visual cues. Path Finder reduces FoG by 50% in people with this symptom. Path Finder has the ability to bring about change by improving people's QoL. This is evidenced through user interview by the Psychosocial Impact of Assistive Devices Scale (PIADS) on the specific user population. PIADS was developed specifically to assess the perceived impacts technologies and assistive devices have on the QoL of users. The users in the study were verified by the Parkinson's disease Questionnaire (PDQ39) and the Freezing of Gait (FOG). Video documentation from users shows an increase in their ability to access their community.
Path Finder increased the majority of users self-esteem, competence and adaptability, resulting in an overall increase in the QoL of the users. This indicates the ability for a wearable device to improve the daily life of a person with Parkinson's disease, and the need for further research in the use of wearable devices in allowing a person to maintain or improve their QoL.

LBP.86

Parky Life
*Matt Eagles**
Havas Lynx, Manchester, United Kingdom

"Travelling from London on the train one evening I saw a guy twitching and writhing about. The more he tried to hide it the worse it got. I said, "Don't worry, I know exactly how you feel. I do the same, I have Parkinson's."
Strangely his shakes began to subside – it was almost as if a huge weight had been lifted from his shoulders.
I smiled at him and said, "Parkinson's isn't the end of the world, you can turn potentially awkward situations to your advantage you know."
All the way back home I was thinking how terrible that moment of diagnosis must have been for him and how frightened he looked on the train. I wondered if we could help him and others see Parkinson's in a different light. And Parkylife was born."
Matt Eagles, Parkinson's Advocate and spokesperson.
Parkylife is a platform for Parky people, by Parky people. Co-created with real Parkinson's patients, it brings together stories, hacks, perks and spotlights the inspiring folk who have achieved great things despite their diagnosis. It's all about learning to adapt to life with Parkinson's by applying a healthy dose of positivity.
After gathering all of their insights, over 100 illustrators were briefed to give each one its own bespoke, bright, positive, visual.
So we created a website and started conversations on Instagram. We even made a t-shirt. Most importantly, to make diagnosis less terrifying, we created a simple pack of 52 cards, each showcasing our slices of positivity. The pack was carefully designed for patients to dip in and out of when they needed a boost. Even the box was designed for ease of use if hands were shaking too much.
It doesn't stop there. Lots of Parkinson's charities, including Parkinson's UK and The Cure Parkinson's Trust, as well as organisations and neuroscientists, love the idea of Parkylife so much they are happy to support the idea. So Parkylife will reach many more Parky people, helping them feel less isolated, overcome symptoms and ultimately feel happier.
Which, for people who lack dopamine, can only be a good thing.

LBP.87

How to maintain a good voice for people with PD: A fun vocal exercise
*Merrill Tanner**
Glenrose Rehabilitation Hospital, Edmonton, AB, Canada

As a speech language pathologist, voice therapist and singer who works with people with PD, I recommend this simple but effective home exercise at least 2 times per day to help you maintain a strong

and healthy voice, in addition to LSVT LOUD® or Speak OUT® exercises.
You need a straw, a glass ¼ full with water.
Put your straw in and blow air into the water in the glass. Notice the bubbles that are produced.
Say “hello” in your normal voice (to see how your voice sounds and feels before the exercise).
1. Now blow into the glass through the straw and make sound at the same time. It might happen right away or you might have fiddle until you can do it.
2. Prolong a sound as long as you can. Repeat 5 times or more.
Check in and say “hello”. How does your voice feel? How does it sound?
3. Slide from low pitch to high pitch as smoothly as possible. Don’t skip notes.
4. Now slide down from high pitch to low pitch.
WHY DOES IT WORK SO WELL?
This exercise is a type of semi-occluded vocal tract (SOVT) exercise. SOVT exercises have been shown to reduce vocal fatigue and vocal cord swelling and train healthy breathing, better resonance and more efficient vocal fold vibration.
The lip seal you make with the straw helps your lips pucker which in turn helps to lower your larynx making it easier for the vocal cords to approach each other and vibrate together.
The puckered lips also encourage more forward resonance which makes your voice carry. It also keeps your facial muscles more active and may help reduce flat affect.
The straw extends the length of your vocal tube, causing more resistance and making your breathing muscles work harder than you would normally.
You also receive visual, auditory and kinesthetic feedback about your voice and breath.

LIVING WITH PARKINSON’S: Other

LBP.88

Living with Parkinson’s disease in Peru
*Christine Jeyachandran**
SIM, Arequipa, Peru

In Peru there are no official statistics but it is estimated that 30,000 people suffer with Parkinson’s. Every year 2000–3000 new people are diagnosed. People hide disabilities because of social embarrassment so the actual numbers are higher. People don’t tell others because of discrimination. I’ve also heard shocking stories of misdiagnosis, early surgery, common depression and prescription of Levodopa too early after diagnosis.
The treatment and lack of education about the disease is concerning. Parkinson’s disease is diagnosed by a neurologist but outside of Lima there are no Movement Specialist neurologists. Unfortunately ‘Levodopa’ is often prescribed from the diagnosis of the disease. Other drugs called Antagonists should be prescribed but they are expensive and may not be covered by health insurance in Peru (public or private).
The most important treatment that slows the diseases advancement is exercise but doctors here rarely mention this. Patient education is not a priority. Doctors don’t seem to know the great benefits of exercise therapy. Likewise physiotherapist lack training too.
What is needed is expansion of the Parkinson’s Association to regional areas to:
Educate patients/family members/multi disciplinary teams – speech/ diet/physio/psychological
Regular meetings and weekly exercise classes to motivate sufferers
Case study 1: One sufferer of 49 years of age has severe Parkinson’s. Levodopa has limited effect for her. Despite encouragement for her to do exercise, she was unmotivated, depressed and didn’t want to go out. But she came all the way to Lima (17 hours on a bus) to attend the Parkinson’s Association meeting and it encouraged her and empowered her. She still struggles with depression and discipline with exercise but her attitude has changed.
Case Study 2: A lady came to me depressed and unable to move forward. We talked, cried and exercised together and the change was phenomenal – “I have accepted it now” she said. She is confident again and proactive about helping others with a disease. She cannot go public as she is the CEO of a company and can’t risk her job as she is a single mum.

LBP.89

Impairment of static balance in patients with Parkinson’s disease using wearable device
Ho Won Lee, Pan Woo Ko, Kyunghun Kang, Yong-Hyun Lim*
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Background: Postural instability in patients with Idiopathic Parkinson’s disease (IPD) is one of main problems threaten the independence and activities of daily living. They are also closely related to the disease severity. Patients with IPD are usually evaluated by the Unified Parkinson’s Disease Rating Scale (UPDRS). Postural instability is also a part of them. However, the daily use of the tools is difficult due to its many assessments and they are not sufficiently sensitive for the assessment of short-term interval changes. Wearable sensors provide the affordable alternative for clinicians because of its convenience and accuracy. Therefore, we evaluated the usefulness of variables using a triaxial accelerometer in patients with IPD to assess their balance.
Methods: IPD subjects were selected in consecutive order form a prospectively enrolled ataxia registry. We also enrolled normal controls. All participants were instructed to maintain an upright position in front of a white wall. To measure postural stability, we used tri-axial gyro-based motion sensors attached to participants' upper body (vertex, 7th cervical, and 5th lumbar spine). 30-sec trials were performed consisting of two randomized, blocked repetition.
Results: This study involved 28 patients with IPD and 9 healthy controls. Various parameters including mean distance, mean velocity and mean acceleration were analyzed. The mean distance (IPD: controls, 1.303cm, : 0.799cm, $p<0.001$)) and mean velocity (IPD: Controls, 5.913cm/s : 4.939cm/s, $p<0.001$) of patients with IPD is significantly higher than control group.
Conclusions: Using mean distance and mean velocity to assess the balance of IPD patients is useful. And it is sensitive and objective markers for the assessment and follow-up of imbalance in patients with cerebellar ataxia. With further study with a larger scale, it may show an evidence to measure subtle changes of balance.

LBP.90

α-synuclein-induced synaptic changes in Parkinson’s disease
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Intraneuronal inclusions consisting of aggregated α-synuclein are the pathological hallmark of Parkinson’s disease (PD) and dementia with Lewy bodies (DLB). A majority of α-synuclein aggregates can be found at the presynapse and have been linked to synaptic dysfunction. Physiological forms of α-synuclein are normally found

at the presynapse and can promote the formation of the soluble N-ethylmaleimide sensitive factor attachment protein receptor (SNARE) complex, which regulates neurotransmitter release. The aim of the study was to investigate the mechanistic link between synaptic α-synuclein aggregates and the functionality of the SNARE complex in PD, DLB and α-synuclein transgenic (tg) mouse brain and in cultured primary neurons.
Synaptosomal fractions from brain tissue from PD, DLB, healthy controls, and from 11 and 17 mo old (Thy-1)-h[A30P] α-synuclein tg and age-matched non-tg mice, were enriched by ultracentrifugation. Synaptic α-synuclein aggregates were quantified by proteinase K immunoassays. Quantitative western blot was used to measure individual SNARE proteins and intact SNARE complexes. The distribution of SNARE proteins in brain tissue sections will be assessed by proximity ligation assay (PLA). Primary neurons were isolated from mouse embryonic cortical tissue at E14 and were cultured for 21 d. Murine α-synuclein preformed fibrils will be used to induce aggregation of endogenous α-synuclein. The interaction between synaptic α-synuclein aggregates and the SNARE complex, and the interaction between individual SNARE proteins, will be measured by PLA.
The levels of synaptic α-synuclein aggregates isolated from tg α-synuclein mouse brain increased with age. No differences could be found in the total levels of SNARE (SNAP-25, syntaxin-1 and VAMP-2) or SNARE-associated proteins (Munc-18 and complexin-1/2) between tg α-synuclein and control mice by quantitative western blot. However, at 17 mo of age, tg α-synuclein mice had lower levels of intact SNARE complexes compared to age-matched controls. Ongoing analyses will determine levels of synaptic α-synuclein and intact SNARE complexes in PD and DLB brain tissue and in cultured primary neurons with induced α-synuclein pathology. The current study will increase the knowledge of how presynaptic α-synuclein aggregates may affect the functionality of the SNARE complex.

LBP.91

Development of gut and brain synucleinopathy in a mouse model of inflammatory bowel disease

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Synucleinopathies are characterized by the accumulation of alpha-synuclein (αSyn) aggregates and the degeneration of dopamine neurons in the substantia nigra. The αSyn aggregates in PD patients are suggested to accumulate first in the enteric nerves of the gut, and later propagate to the brain. However, the major factors facilitating the intestinal αSyn accumulation and subsequent propagation remains to be established. Using mice that over-express αSyn (i.e. Thy1-αSyn A30P mice), we report that inducing colon inflammation using dextran sodium sulphate elevates αSyn aggregation in the myenteric and submucosal plexuses of the colon, together with other peripheral organs such as the kidney, liver, and the heart. In addition, we report increased αSyn aggregation in the submucosal plexus of ulcerative colitis patients. The intestinal αSyn aggregates in our mice model colocalized with the peripheral neuronal marker peripherin. Further evaluation also revealed elevated mRNA levels of inflammatory cytokines including IL1-beta, IL-6 and CCL2 in the colon. Remarkably, chronic systemic DSS-induced inflammation exacerbated αSyn aggregation in the brain, with the pathology being rather prominent in the vagal and caudal mid-brain areas and more moderate pathology existing in brain areas such as the amygdala, ventral tegmental area and the substantia nigra. DSS treatment also elevated the degeneration of tyrosine hydroxylase-positive neurons in the substantia nigra. Together, these findings reveal that intestinal inflammation may be key in driving intestinal and brain αSyn accumulation and the degeneration of dopamine neurons.

LBP.92

Characterization of arm swing asymmetry in Parkinson's disease patients using portable accelerometers

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Objective: To describe the differences in arm swing asymmetry between patients with Parkinson Disease (PD) and a healthy subjects group.
Background: Changes in gait kinematics are hallmarks for the diagnosis and follow up of patients with PD. Although motor changes mainly affect the lower limbs, recent studies showed that changes in arm movement are common and frequently reported, even in the early stages of the disease. These changes are generally characterized by a bilateral and asymmetric reduction of arm swing. This asymmetry can be assessed and described qualitatively using clinical strategies such as the MDS-UPDRS scale. However, there is a high variability in intra- and inter-observer assessment, which makes evaluation difficult. New technologies, like accelerometers, could help to objectify these motor variables, even out of the clinical context.
Methods: 10 PD patients and 10 healthy participants were recruited for the study. All subjects participated in a single gait-analysis session, to determine the motion of the arms. Wrist segments were tracked using a wristband with two triaxial accelerometers in each arm. Each subject was instructed to start at the beginning of a corridor (10 by 1.5 meters) and walk at normal pace wearing the device. Using digital signal processing techniques, arm swing RMS (Root Mean Square) and RMS asymmetry were obtained from angular acceleration. Mann-Whitney test was used for the comparison between groups. Statistically-significant difference was considered if the p-value was <0.05.
Results: Median duration of the disease from onset was 5 years (IQR 4-5). Hoehn and Yahr stage classification was 1 (10%), 1.5 (20%) and 2 (70%). MDS-UPDRS mean was 25.8 (± 10.27). Arm swing analysis: Patient group exhibited significantly lower RMS (PD: 4.06, Control group: 5.16; p: 0.003) and greater RMS asymmetry compared to the control group (PD: 19.44, Control group: 8.65; p: <0.001).
Conclusion: Arm RMS and arm swing RMS asymmetry measured using wristbands with triaxial accelerometers can differentiate quantitatively patients with Parkinson's disease from healthy subjects. Given their portability and low cost, these devices could be useful for obtaining objective gait measurements in real time during medical consultation or outside the hospital, in the patient's home.

LBP.93

Effects of virtual reality exercise therapy on balance function and quality of life among patients with Parkinson's disease

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Purpose: The purposes of this study were to evaluate the effectiveness of an 8-week virtual reality exercise program designed around the Nintendo Wii(Wii), in improving balance and quality of life among patients with Parkinson's disease(PD).
Methods: The subjects were 30 individuals with PD. 15 patients were assigned to experimental group to engage an in three 40-minute Wii balance-training sessions per week, for 12 weeks, and 15 to control group. They were asked to complete questionnaires including Berg Balance Scale(BBS), activities-specific balancing confidence scale (ABC), Parkinson's Disease Quality of Life (PDQ39) Scale, and fall index assessment before and after the intervention. Quantification of improvement was conducted utilizing Sensory Organization Test (SOT) of Computerized Dynamic Posturography (CDP). Statistical significance was tested in between the patients before and after treatment by ANOVA.
Results: There was a statistically significant improvement in scores of BBS, ABC, PDQ39, and fall index assessment results within the experimental group. SOT showed significant difference on condition 5, 6, and vestibular ratios within the experimental group from baseline to post-intervention.
Conclusion: Virtual reality exercise program can be an effective intervention method improving balance, balance confidence, and qualities of life among individuals with PD.

WPC 2019 Abstracts
Author Index