

## Editorial

---

# The Most Cited Parkinson's Disease Researchers – A Personal Perspective

Niall Quinn\*

*UCL Institute of Neurology, Honorary Consultant Neurologist, The National Hospital for Neurology and Neurosurgery, London, UK*

As the inaugural issue of *Journal of Parkinson's Disease* ([www.journalofparkinsonsdisease.com](http://www.journalofparkinsonsdisease.com)) features an article highlighting the most cited 100 Parkinson's disease researchers over the past 26 years and so many of them were based in or passed through the Maudsley and King's College Hospitals in Denmark Hill and the National Hospital, Queen Square, in London while I was there, the editors suggested that I write a short piece about the transformation of "Parkinsonology" from that perspective and the contributions of some of those individuals. Sadly there is not enough space to mention all of the many other people who passed through, or collaborated, and also made significant contributions.

Developments over the last 50 years or so have transformed the study of Parkinson's disease from a relatively obscure untreatable neurological disease of unknown aetiology into a thriving modern neuroscience discipline involving specialist clinics and nurses, sophisticated clinical trials, dedicated brain banks, structural and functional imaging, genetic discoveries, animal models, patient and professional societies, and specialist journals, now including this new addition. We now have a much greater understanding of underlying mechanisms that paves the way to developing a second generation of strategies and therapies designed to modify the disease itself, and hopefully even to prevent it. The most cited 100 researchers have played an important part in this transformation.

---

\*Correspondence to: Niall Quinn, Emeritus Professor of Clinical Neurology, UCL Institute of Neurology, Honorary Consultant Neurologist, The National Hospital for Neurology and Neurosurgery, Queen Square, London WC1N 3BG, UK. E-mail: [niallquinn@blueyonder.co.uk](mailto:niallquinn@blueyonder.co.uk).

It is impossible to write such an account without mentioning my mentor the late David Marsden (number 2 on the list). The fact that he remained number 2, 13 years after his death in 1998, so only lived through half of the period sampled, is testament to his huge productiveness, which was the basis of his enormous influence internationally in many of the major advances in Parkinson's disease. David was clearly exceptional, and also something of a paradox. He was a man of huge charisma who would effortlessly dominate any gathering by sheer force of personality and intellectual ability, yet he was quite shy in some ways. Physically he was quite short (a former England Schools rugby scrum half), but it was years before I noticed that. At a party ("symposium") he could drink everyone else under the table until the early hours but, much to everyone's amazement and envy, still get up and deliver a brilliant and inspiring talk the next morning. His key strengths were in being able to "see the wood for the trees" and in inspiring others to adopt this approach to scientific problems. He was meticulous, thorough, and well-organised, and no paper left his stable until it had gone through huge numbers of drafts until it was as near perfect as possible, so very few were bounced back or rejected. After thinking about what he would like to write, he would apparently sometimes dictate whole chapters or papers into a dictaphone without notes whilst walking about in his garden at home.

In his early days at Denmark Hill David was responsible for several major innovations in Parkinson's disease research. He established, with David Parkes, the second specialist Parkinson's disease clinic in the UK (the first was established in 1969 by Gerald Stern and Donald Calne (number 30) at University College

Hospital (UCLH), of which Queen Square is now part). These clinics brought Parkinson's patients together in significant numbers, which enabled both research and clinical trials. Building on this, David surrounded himself with many other talented people to set up other avenues of research.

With John Rothwell (number 55) and Brian Day, David set up a team, later joined by Philip Thompson and Peter Brown, to study the physiology of Parkinson's disease which most recently has pioneered much of the work on high frequency oscillations in basal ganglia. He also enlisted Richard Brown and Marjan Jahanshahi to explore the neuropsychology of Parkinson's disease.

He set up another team with Peter Jenner (number 7) to study the neurochemistry and neuropharmacology of Parkinson's disease. This unit worked with Brain Bank material to produce some of the pioneering work on the roles of iron and of oxidative stress. They also worked with animal models, initially the 6-hydroxydopamine-lesioned rat. However, more significant was the development of the MPTP-induced model of Parkinson's disease in marmosets. MPTP had previously been linked to parkinsonism by Bill Langston (number 26) in California, but it did not cause parkinsonism in rats. However, MPTP-treated primates showed akinesia and rigidity, often had tremor, had selective nigral cell loss, and also responded to L-dopa, and developed dyskinesias on chronic treatment. Several groups developed models on medium-size monkeys that were difficult and expensive to obtain, breed, house, and care for, but Peter developed a marmoset model that overcame many of these drawbacks, and which has been used as a testbed for potential therapies and for understanding drug-induced dyskinesias.

These innovations enabled new translational research in Parkinson's disease. For the first time we could test a drug in an animal and take it right through to clinical trials. I recall giving the first human injection of levodopa methyl ester in the presence of David Cooper, one of Peter's team who had done the preceding animal work, and also supervising Richard Coleman doing clinical studies of PHNO, an early transdermally active dopamine agonist, the prior marmoset studies having been done by Hiro Nomoto in Peter's lab.

During David's time at Denmark Hill from 1970 to 1987, many fellows and visiting researchers were drawn by his growing reputation. The first one was Roger Duvoisin (number 47), followed by many others, including Wolfgang Oertel (number 45), Alberto Albanese (number 61), Tony Lang (number 4), and Jose

Obeso (number 22). I have particularly fond memories of the period 1980 to 1982, when Tony Lang, Jose Obeso and I were simultaneously fellows of David. This was the most exciting and rewarding time of my professional life: Tony and Jose were bright and keen and we all bounced ideas off each other. It was a truly formative and bonding experience and we remain great friends to this day.

Andrew Lees (number 1 on the list) was appointed as a consultant at Queen Square in 1982, and started to establish a movement disorder niche there (his mentor was Gerald Stern who worked at the nearby UCL and Middlesex Hospitals). Shortly after he co-founded, with David Marsden, what was originally called the UK Parkinson's Disease Society Brain Bank, at Denmark Hill, which moved with David to Queen Square in 1988, and has since become the Queen Square Brain Bank for Neurological Disorders. Andrew had a more hands-on role, and Susan Daniel (number 19) was the dedicated neuropathologist (succeeded by Tamas Revesz). This has really been a jewel in the crown of research into parkinsonian disorders, allowing David Dexter (number 36 on the list) and Peter Jenner to show an increased iron load in the substantia nigra in Parkinson's disease, and propose that it may contribute to neurodegeneration. David suggested to Tony Schapira (number 28) that in addition to studying mitochondria in muscle diseases he should study mitochondria in Parkinson's disease tissue from the brain bank, contributing to the discovery of mitochondrial defects in Parkinson's disease in the late 1980s.

Andrew and his colleagues were responsible for two of the most influential advances stemming from the Brain Bank which transformed the diagnosis of the disease. One was the establishment, with Bill Gibb, of the UK Brain Bank criteria for the diagnosis of Parkinson's disease, and the other, with Andrew Hughes (number 52) and Susan Daniel used clinicopathological correlation to show that in the preceding few years a clinical diagnosis of Parkinson's disease had a 24% error rate, which could be much improved by adoption of the brain bank criteria. A major clinical advance also pioneered by Andrew was to exhume apomorphine and give it a second lease of life as an extremely useful treatment for fluctuating Parkinson's disease patients.

Another milestone was achieved in a hotel room in Hamburg in 1985. A few months earlier Stan Fahn (number 9) and David had first mentioned to Gerald Stern in a hotel bar at a meeting in New York that they were thinking of starting a Movement Disorder Society and what did he think? Gerald claims the role of wet nurse rather than parent, and the idea was developed



Fig. 1. Meeting in a hotel room in Hamburg in 1985 when the MDS was established. From left to right (all looking rather young!): Eduardo Tolosa, Stan Fahn, Andrew Lees, Joe Jankovic and David Marsden.

at a founding meeting involving Stan, David, Andrew Lees, Eduardo Tolosa (number 78) and Joe Jankovic (number 18) three months later in a hotel room at the World Congress of Neurology in Hamburg (Fig. 1, courtesy of Joe Jankovic). The Society has since grown in strength so that it now has over 3,500 members, three regional sections, and since its first congress in Washington in 1990 (attendance 700) has moved to annual meetings with up to 5,000 attendees. Stan and then David were the first MDS Presidents, followed by Mark Hallett, Werner Poewe (number 35), Tony Lang, Andrew Lees and Philip Thompson, all people who had trained at King's or at Queen Square or UCLH. The other major legacy of this development was the founding in 1986 of the *Movement Disorders Journal* (2009 impact factor 4.014), with Stan and David as first co-chief editors for a decade, followed until 2003 by Tony Lang and Andrew Lees.

A team in Lund, Sweden, comprising Olle Lindvall (number 66), Anders Björklund (number 23), Patrik Brundin (number 59), Stig Rehnström (number 78) and Håkan Widner (number 86) had started work on fetal nigral transplantation in Parkinson's disease in the early 1980s. They collaborated with David, myself and John Rothwell at Queen Square, and Richard Frackowiak (number 68) and his successor David Brooks (number 6) at the Hammersmith Cyclotron Unit in London. We contributed five patients of our own (of a total of 18 grafted in Lund in an open study), and did physiology and PET scanning on all the grafted subjects. Other PET people from the Hammersmith collaborating with David were Klaus (Nico) Leenders (number 91) and Guy Sawle (number 84). The Lund

collaboration lasted two decades and new insights are still emerging in relation to the mechanism of graft-induced dyskinesias, and the finding of Lewy bodies in grafted neurons at autopsy many years after the grafting procedure. Double-blind studies in the US, one involving Stan Fahn and the other Warren Olanow (number 5) failed to show group benefit from grafting but, like us, found some individuals who clearly derived major benefit. By studying the many variables it may be possible to optimise this approach to produce better results in future, and Stan is involved in a new multinational study headed by Roger Barker at Cambridge, who had been our registrar at Queen Square.

Deep brain stimulation as a therapy for Parkinson's disease also had its roots in the 1980s, when the neurosurgeon Alim-Louis Benabid (number 10) and the neurologist Pierre Pollak (number 13) in Grenoble, soon joined by Patricia Limousin (number 58), pioneered the approach and moved the preferred target from thalamus to pallidum and then to STN. Patricia later moved to Queen Square, and shortly after David died a dedicated functional stereotactic neurosurgery unit was established with the appointment of Marwan Hariz as the surgical lead.

Before we moved to Queen Square in the late 1980s, David Marsden had already collaborated with Anita Harding, who was then leading the neurogenetics unit, but died tragically of cancer early in 1995, at the age of 42. Anita was succeeded by Nick Wood (number 33), whose team was involved in identifying causative mutations in *PINK1* and *LRRK2*, and who was more recently joined by John Hardy (number 56). David himself did not live to see these discoveries as he died in 1998 at the age of 60, although he did live to see the discovery of alpha-synuclein by Roger Duvoisin's team, and *Parkin* by Yoshi Mizuno (number 8) and colleagues, and would have been pleasantly delighted and amazed at the advances in understanding Parkinson's disease genetics that we have made since his death, with clues from rare genetic forms identifying new disease mechanisms and possible neuroprotective avenues.

Other top 100 researchers passing through David's hands at Queen Square or UCLH have included Demetrius (Jim) Maraganore (number 41) and Jay Nutt (number 31), and Werner Poewe as fellow to Andrew.

Of course, recent fellows are a generation behind their mentors, and more likely to feature in the 2001-2010 top 100, which includes Dan Healy and Patrick Abou-Sleiman (working on genetics with Nick Wood), Fabrizio Stocchi, and Christine Klein who, whilst never

a fellow, managed to co-author three papers with me during her 4-month student elective at Queen Square.

Other notable past fellows of David include Dan Tarsy, Mark Hallett, Paul Bedard, Eldad Melamed, Reiner Benecke, Alfredo Berardelli and Giovanni Abbruzzese at King's, and Marie Vidailhet and Madhuri Behari at Queen Square, and in particular Kailash Bhatia, who was the first Indian national to be appointed a consultant (now Professor) at Queen Square. Other recent notable fellows of myself and Kailash have included Francois Tison, Bas Bloem, Mark Edwards and a remarkable quartet of young Germans - Gregor Wenning, Alex Munchau, Anette Schrag and Susanne Schneider. Other notable fellows of Andrew Lees have included the Aussie quartet of Peter Kempster, Andrew Hughes, Andrew Evans and David Williams, and Jan Ziljman, Huw Morris, Carlo Colosimo, Marcello Merello and Regina Katzen-schlager.

Other Consultants at Queen Square whose skills have enabled research on autonomic aspects of parkinsonian disorders have been Chris Mathias (successor to Sir Roger Bannister, of sub-4-minute mile fame) and Clare Fowler, the UK's first Professor of UroNeurology.

Finally, one should not forget our other movement disorder forebears at Queen Square: Sir William Gowers; Samuel Kinnear Wilson, who also was consultant at King's; Sir Gordon Holmes; Derek Denny-Brown; James Purdon Martin, who wrote a celebrated monograph on the Basal Ganglia and Posture; and McDonald Critchley, who wrote a paper in *Brain* in 1929 entitled "Arteriosclerotic parkinsonism" and lived long enough to partially recant in a chapter published 52 years later entitled "Arteriosclerotic pseudoparkinsonism".

Finally, on a personal note, I also have the most wonderful memories of a year working for and learning from Yves Agid (number 3) at the Salpêtrière Hospital in Paris in 1978-9.

It has been a fantastic few decades for Parkinson's disease research and the field owes a great debt to the people I have mentioned, and many more who I have not. There are now many promising lines of translational research and if the advances of the next 25 years of research are anything like as impressive the progress will be amazing indeed.

Niall Quinn (number 12)