

# World Parkinson Congress

Washington DC, USA, 22-26 February, 2006.

The first ever World Parkinson Congress gathered together over 3000 people in Washington in late February. The group attending consisted of scientists, clinicians, other medical therapists, patients and carers. As such, the meeting was a true mix of those with the disease and those interested in it at both the scientific and medical level. The four day meeting began each day with two exemplary lectures giving way to a range of parallel sessions that were broadly divided into science and community based presentations, totalling about 16 in a day. This was then followed by final sessions on hot topics selected from the poster presentations and a wrap up from all those chairing the majority of the parallel sessions. It is thus impossible to do justice to the meeting, but a number of common themes emerged.

## What is Parkinson's disease?

Fundamental to the whole four days was a growing frustration with our inability to define Parkinson's disease (PD). The long held view that PD is a movement disorder with nigrostriatal dopaminergic loss is not in doubt but the recent pathological staging by Braak et al has highlighted the extent to which pathology extends out of this pathway, and with this the growing realisation that clinical features are multiple and involve a large number of different domains. However, as many argued, if we are not to use the term Parkinson's disease because we don't know what it is, with what should it be replaced? Alternatives included the Parkinson's complex, Parkinsonian syndrome, the shaking palsy and Parkinson-Lewy disease. In addition there was a consensus that seemed to be emerging that the term Parkinson's disease or equivalent should only refer to conditions where there is no known aetiology, in which case the genetic causes of "PD" would lie outside the definition, which may help in clarifying an important distinction at this stage between genetic parkinsonism and sporadic Parkinson's disease.

## The genetics of Parkinson's disease

The genetics of Parkinson's disease continues to be a major research issue and during this meeting several issues emerged on a number of occasions. Firstly, the recent identification of families with duplication or triplication of alpha synuclein resulting in Parkinson's disease with dementia clearly shows that this protein expressed at high levels but in a normal form can induce widespread pathology, highlighting that protein load as much as abnormalities in protein structure and function can cause disease. In addition the recent interest in the LRRK2 gene as a relatively common cause of Parkinson's disease continues to gain consensus, with estimates of about 5% in familial cases and 1.5% in series of sporadic cases. However, there is clearly a great deal of variability depending on ethnic groups, with a particular emphasis in North Africans and Ashkenazi Jews. Finally, heterozygosity in autosomal recessive forms of Parkinson's disease continues to be a very active issue, in particular the extent to which carrying



Dr Stanley Fahn, Chair of the World Parkinson Congress (WPC), welcomed the attendees and gave a brief history of the WPC.



Mary Baker, President of the European Parkinson's Disease Association introduced the Global Declaration on PD which was launched in December 2003 in Mumbai, India.



Michael J Fox, actor and PD advocate, welcomed the attendees at the first-ever World Parkinson Congress in February 2006 in Washington DC, USA. He thanked the medical professionals who dedicated their lives to curing PD or improving the care and he thanked the patients and caregivers who took an active role in fighting PD.

one single abnormal gene predisposes people to developing the disease. It appears that in some cases this is true but the extent to which this happens requires further clarification.

## Is there a pre-Parkinson's disease state?

There was much discussion about detecting the presymptomatic phase of PD with several studies suggesting that this may be recognised as a state of constipation, REM sleep behavioural disorder and a loss of olfactory function. However, if you believe that such a state exists then questions arise as to the 'at-risk' group which should be screened, especially given that we don't have any effective neuroprotective treatments. Thus should we be screening relatives of patients with Parkinson's disease, elderly patients, or whole populations? Indeed such questions as this also arise in the genetic screening of patients, given the issues raised above.

## The non-motor features of Parkinson's disease

The non-motor features of Parkinson's disease continue to generate a great deal of interest. There is now a growing realisation that cognitive deficits are common in Parkinson's disease and that ultimately 30% of patients will develop a dementia with this condition. Identifying this subgroup of patients is a key issue and the risk factors that seem important and are emerging are increasing age of patient and disease duration, non tremor akinetic rigid forms of the disease and early hallucinations with behavioural abnormalities. The cause of this aspect of PD seems to be at the neurochemical level related to cholinergic deficits, whilst the pathological correlate appears to be Lewy body formation in the cortex. In terms of other non-motor features, the affective aspects of PD also seem common, with about 40% of patients having depression at some point in their disease course, although the aetiology and the optimal treatment of this remains controversial. Abnormalities of olfaction occur early in Parkinson's disease, as mentioned before, but it does not seem to necessarily progress over time, so whilst helping possibly in the diagnosis it may not be a good longitudinal biomarker - similar to the story with the REM behavioural sleep disorder in PD.

## The pathogenesis of Parkinson's disease

The pathogenesis of Parkinson's disease was discussed in the context of two particular models. The first model of disease uses known genetic abnormalities in transgenic animals, whilst the second uses established neurotoxin models. The former model using transgenic animals informed us once more on the role of protein aggregation and how this may lead to cell death, possibly through mitochondrial and proteosomal dysfunction. In the second approach using neurotoxic models there was a great deal of interest in the extent to which inflammation may be driving disease progression. I think it is fair to say that this remains controversial and unproven.

**Other issues**

Other issues that surfaced a number of times during the meeting were biomarkers, especially those relying on functional imaging and systems approaches. Many of these new techniques use complex statistical analysis, especially principal component analysis, a process where one identifies a series of abnormalities in patients with Parkinson's disease that forms a distinctive signature that can then be used to distinguish it from other conditions. At the moment these techniques remain in their infancy but nevertheless offer enormous potential and there were particularly powerful demonstrations of this using metabolic PET imaging and lymphocyte proteomic profiling.

Novel treatment approaches were also discussed although surprisingly little was mentioned on GDNF and stem cells, at least within the sessions that I attended. There seemed to be more on viral gene therapies which are entering, or are about to enter, the clinic, including the AAV GAD delivery to the subthalamic nucleus and the planned neurturin growth factor study.



Dr Oliver Sacks, Honorary Chair of the Creativity & PD Subcommittee, greeted the audience and encouraged them to actively participate in the creative side of the WPC and to remember to keep a sense of humour.

Finally, there were sessions on a mass of other issues that affect patients with PD, including the value of alternative non-drug therapies such as music therapies, language therapy, as well as a great deal of time given to the importance of developing more effective inter-disciplinary teams to help patients, carers and families with

Parkinson's disease.

In conclusion, this meeting was a great success and a tribute to Stan Fahn, Howard Federoff and Elias Zerhouni who originally had the idea to put this event together. Of course with any new event of this scale there are teething problems and so there were issues of repetition, the number of parallel sessions and the absence of major gaps in the daily programme. Nevertheless, by virtue of being a one disease meeting and involving everyone involved with PD, including patients, it meant that many useful discussions and themes were developed which helped focus attention onto the key issues, and as such help set up the critical questions which will no doubt form the basis of the second World Parkinson Congress planned for Paris in 2009.

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## 4th World Congress for Neurorehabilitation

Hong Kong, China, 13-16 February, 2006.

**H**ong Kong, although now technically part of China, likes to market itself as the gateway to China where 'East meets West'. Although there was no formal theme to the conference (which was mentioned by a few delegates) the prevailing theme was very much 'East meets West' of Neurorehabilitation.

The congress got off to a good start with the opening ceremony thankfully short on speeches, followed by a wonderful performance of four two-person (traditional Chinese) costumed dragons who jumped between pedestals around the stage to the beat of Oriental drums. There were nearly 1500 delegates from all disciplines and all six continents represented, the Asians naturally being the most numerous. The programme included a wide variety of topics (from botulinum toxin to tai chi) covered in the plenary, parallel and free paper sessions with generous coffee/tea breaks and lunch of an hour and a half to allow for discussion, or a quick spot of shopping.

With the parallel sessions one was often in a dilemma to choose between some very promising talks on at the same time. As expected, this report reflects my own interests and attendance rather than a pick of the best talks.

The opening session on "Neuroplasticity and Recovery of Brain Function" was a look to the future of the science underlying rehabilitation, featuring two speakers from the US. The first speaker from the NIH outlined how recent studies using fMRI, PET, TMS and MEG demonstrated interhemispheric interactions as influential in motor recovery after stroke. Increased somatosensory feedback from the paretic and reduction from the intact arm (possibly the mechanism of constraint therapy) as well as pharmacological interventions have potential to improve motor performance of the paretic arm. The second talk was on the migration of neuro-

lasts from the subventricular zone to the peri-infarct cortex in the mouse model. So the adult mammal brain does have some potential for neuroregeneration after all. As the area around the infarct ('peri-infarct niche') exists in an area of altered blood-brain barrier the potential for systemic drugs to improve neural repair apparently beckons.

There was an excellent presentation by Prof. Delph from Stanford on the development of a computer model to simulate the biomechanical factors of human gait. He illustrated graphically with this model how altered postures can change the 'usual' action of a muscle and thus will impact on choice of target muscle for treatment. His models are subject-specific and thus allow for prediction of effect of interventions such as botulinum toxin in an individual. One hopes that the 2-3 years he predicts for a widely available and reasonably priced product on the market will be realised.

In other plenary sessions, there were two talks on robotics and the developments in this area of rehabilitation, although one of these had a bit too much technical emphasis. The last plenary session covered the role of genetics in recovery after brain injury and their potential roles in practice. The group from the University of Southampton presented data on apolipoprotein E gene association with poorer outcome in traumatic brain injury and other conditions. Future work may allow better prediction of individual outcome and also to identify targets for therapy.

There were interesting sessions on cognitive rehabilitation after traumatic brain injury and the use of new technology, especially internet-based telerehabilitation. The group from Hong Kong Polytechnic University paid a touching tribute to one of their colleagues, Professor Alan Tam (who died unexpectedly last year) and pre-

sented work he was involved with in "telestroke and telerehabilitation". Two centres from Italy also presented some of their work and research to allow more rehabilitation to occur in the home setting.

Mild Traumatic Brain Injury affects large numbers of individuals each year (100-300/100,000 population). Although no new findings were presented, the questions and answers did clarify some issues over the continuing lack of definition and that simple written information seems as effective as more complex intervention for routine follow-up.

Speaking to attendees, it was clear that the challenges faced by all countries were similar: competition for limited healthcare funding, continued need to demonstrate evidence for rehabilitation and innovations with new technologies and techniques. The congress provided an overview of current knowledge, with a look at what the future may hold, but also an opportunity to share and discuss ideas and experiences.

One of the best features of the conference was the 'technical visit' to a number of rehabilitation centres in Hong Kong. I was in the group to visit Kowloon rehabilitation and spinal unit. It was fascinating to see how they were so advanced technologically, yet staffing ratios, especially in nursing, raised a few eyebrows amongst the visitors. Not surprisingly, there was close integration of traditional and Western medicine.

Whatever the extra-curricular attractions of Hong Kong, the next congress in 2008 to be held in Rio de Janeiro had more than a few making plans to present their next research project there.

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