The fifth meeting of the Parkinson disease Non-Motor Group (PDKMG) was held at the Royal Society of Medicine, London. This year the international faculty sought to look deeper into issues surrounding treatment and quality of life in Parkinson’s disease (PD).

Professor K Ray Chaudhuri (UK), the PDKMG chairman and meeting organiser, welcomed the delegates by presenting an overview regarding the recognition and prevalence of non motor symptoms (NMS) of PD. Professor AHV Schapira (UK), formally began the meeting by shedding light on neuroprotection approaches for PD. He discussed recent evidence which encourages early initiation of treatment, highlighting the results from ADA-GO, TEMPO and DATATOP trials which suggest that PD patients who started on early treatment had better outcomes with more symptomatic relief. He postulated that drugs such as selegiline, rasagiline and levodopa are able to promote brain plasticity and compensation. Prof Schapira emphasised preclinical non-motor markers of PD, including olfaction and constipation. He concluded that the decision of starting treatment should be based upon weighing treatment side effects and effects on quality of life with symptom control and disease progression. However, with questions surrounding the conclusiveness of the data and the power of the studies, further robust trials are required to further understand the possible disease-modifying properties of PD drugs.

Next, Prof DJ Brooks (UK) discussed the role of neuroinflammation in PD. He explored the evidence suggesting a pathogenic role of microglia in PD. Microglia are most highly concentrated in the substantia nigra, and most highly active and clustered around dystrophic dopaminergic neurones. Cytokine release leads to microglial and macrophage activation and subsequent dopaminergic and cholinergic cell death and brain remodelling. Prof Brooks outlined the uses of FDG-PET, FP-SPECT, FDopa PET, acetylcholinesterase imaging and PET amyloid plaque imaging in PD. These neuroimaging strategies provide biomarkers of the ongoing disease activity. Finally, he examined the correlation between Braak staging of PD with clinical manifestations, imagining the substantia nigra and the non-motor symptoms including olfactory disturbances, autonomic symptoms and disorders in the cognitive domain.

Prof Chaudhuri provided a succinct review of pain in PD. As well as outlining a classification of pain in PD (symptomatically grouped into musculoskeletal, radicular/neuropathic, dystonic, central or primary pain, and akathisia) he highlighted that depression may contribute to the intractability of a chronic pain syndrome. Orofacial pain is a poorly understood NMS but highly detrimental to quality of life. It encompasses headaches, burning mouth syndrome, temporomandibular joint pain and compromised trigeminal reflexes. He emphasised that most painful symptoms could occur during ‘off periods’, particularly early in the morning. Prof Chaudhuri discussed the generic pain evaluation tool - McGill Pain Questionnaire (MPQ). The MPQ, used judiciously, is useful for defining the prevalence and characteristics of pain according to its location, intensity and temporal pattern, thus enabling a pain specialist to tailor management plans and monitor treatment response.

Professors P Martinez-Martin (Spain) and P Odin (Germany) discussed the impact of NMS in the PD population. They described epidemiology and evolution of NMS in the psychiatric domain which was most frequent, with apathy being most associated with reduced quality of life scores. NMS are closely associated with cognitive impairment, with the number of NMS per patient increasing with age and disease severity. Finally, the PRIAMO study highlighted the high prevalence of NMS in the PD population (38.6%). For the treatment of NMS, Prof Antonini went on to discuss pramipexole, which has negative effects on daytime sleepiness but may significantly alleviate depression. The clinical benefit of DBS in NMS is relatively much higher than that of apomorphine. However, while DBS may improve dyskinesias in late PD, it does not seem to have any effects on sexual aspect of NMS in PD. Lastly, intrajejunal infusion of levodopa is a more invasive treatment than apomorphine. Levodopa infusion not only replaces oral medication but also helps in avoiding swallowing problems.

In recent years, dementia has been recognised as a common albeit highly variable feature of PD. Professor D Aarsland (Norway) outlined the clinical and neuropathological differences between PD dementia (PDD) and Alzheimer’s disease (AD) pathology with or...
without dementia. Old age, visual hallucinations, and more marked motor symptoms are established risk factors for PDD, with at least 75% of PD patients developing dementia within 10 years. Differentiating PDD with Alzheimer’s disease (AD) pathology remains difficult, since half of dementia patients have enough pathology to be diagnosed with AD while PDD can develop without any AD pathology at all. However, a shorter duration of PD symptoms before onset of dementia in an older patient may suggest PDD+AD pathology. Sufferers are prone to experience cognitive impairment, psychiatric fluctuations and sleep disturbances. There are a wide range of treatment approaches for dementia in PD. Prof. Aarsland reviewed cholinesterase inhibitors and memantine (specifically licensed for AD) as possible treatments for PDD. Statins, anti amyloid strategies, anti inflammatory treatments and anti psychotic therapies were also briefly discussed.

Dystonia is not classically regarded as one of the non motor symptoms of PD but it seems to share analogous features with NMS in PD. Like NMS, dystonia is under-recognised as well as undertreated. Prof. T. Warner (UK) discussed the multiple factors which may induce dystonia before reviewing the diverse treatment strategies for dystonia in PD. Purported links between dopa-responsive dystonia and exercise-induced dystonia with PD remain unclear. Dystonia in PD seems to have a genetic connection - autosomal recessive inheritance, involving mutations in PARK2 and PARK6 genes. He recommended anti-dyskinetic drugs like amantadine, continuous levodopa infusions, botulinum toxin to treat this troublesome, albeit rare, problem in PD.

Professor F. Stocchi (Italy) examined the correlation between gastrointestinal problems in PD and quality of life. Dribbling of saliva, swallowing abnormalities, nausea, vomiting and constipation are some of the most common NMS seen in PD. Prof. Stocchi outlined that constipation could precede the motor symptoms and be regarded as one of the pre-clinical markers of PD. There are many therapies that have been advocated for the treatment of gastrointestinal symptoms in PD, including botulinum toxin as a solution for dribbling of saliva and even constipation.

Dr Graeme MacPhee (UK) examined the aetiology prevalence and the various assessment tools and treatment strategies for depression in PD. Depression is a key neuropsychiatric NMS and can affect up to 45% of PD patients. Dysfunctions of dopaminergic, serotonergic and noradrenergic pathways in the limbic system of depressed PD patients have been implicated. He recommended the use of the Hamilton depression scale (HAD Scale) to identify depression. The treatment should be tailored to symptom severity. In addition, recent SIGN guidelines examining the treatment of depression in PD identified that tricyclic antidepressants showed the best efficacy but that these agents often came at the expense of adverse effects. SSRIs are often used in routine practice.

The meeting ended with video case presentations of PD patients facilitated by Prof. Chaudhuri, Prof. Stocchi and Professor G. MacPhee. The interactive session examined the sometimes puzzling and atypical presentation of parkinsonism and was buoyed by enthusiastic audience contribution.

Non motor symptoms have a significant impact on quality of life – more so than their motor counterparts. The search for a therapy that adequately addresses motor and non-motor symptoms continues. In the meantime, clinicians must adopt a holistic approach to their treatment, and place the patient’s individual perception of their symptoms at the core of any management strategy. On reflection, it is clear that since its genesis 6 years ago, the PDNMG has gone some way in achieving its initial mission statement. Thanks in part to the widespread use of the group’s internationally validated assessment tools, non motor symptoms are now a widely recognised feature of PD. It is likely that from 2011 onwards, meetings will take place under the banner of EUROPAR, a group dedicated to the advancement of non-motor research in PD.

The organisers acknowledge the support of the meeting’s sponsors, Boehringer Ingelheim Ltd, Solvay and Britannia Pharmaceuticals, Teva & Lundbeck Ltd and Ipsen Pharmaceuticals, without whom the meeting would not have been possible.

**Sixth World Congress for Neurorehabilitation 2010**


The 6th World Congress for Neurorehabilitation was held between the 21st and 25th March in Vienna. Over 1600 health professionals from 71 countries met in the historical Congress Centre in the Hofburg Vienna’s former imperial palace.

There was an extensive programme of workshops, lectures and symposia on clinical practice and research covering topics from basic science to practical applications. The breadth of content attracted neurorehabilitation clinicians and therapists from all disciplines. Just a few highlights follow.

In the Opening Ceremony, Heinrich Binder, President of the Austrian Society of Neurorehabilitation welcomed delegates to Vienna. The President of the World Federation for Neurorehabilitation (WFNR), Michael Selzer, then introduced the first Michael P Barnes Lecturer in Neurorehabilitation, given by the eminent Alberto Juan Aguayo. This Lecture will now be the highlight of each WFNR World Congress, in recognition of the visionary leadership of the WFNR’s founder, Michael P Barnes.

Alberto Aguayo gave an historical overview of axon regeneration in the central nervous sys-
tem (CNS), beginning with Santiago Ramón y Cajal's 'Degeneration and Regeneration of the Nervous System,' which was published in 1914 and anticipated many of the current ideas in the field. Beginning in the 1980s, Dr Aguayo and his colleagues at McGill University carried out pioneering studies that showed injured axons of the central nervous system were not intrinsically incapable of regenerating after injury, as had been assumed. Aguayo rediscovered an old finding by Cajal and his students that these axons could grow for long distances into grafts of peripheral nerve. In a long series of elegant experiments in the spinal cord, brain and optic nerve, Aguayo showed that the extracellular environment of the CNS is an important factor in limiting the regenerative ability of axons. These studies laid the groundwork for the subsequent discovery of molecules found in the CNS that are now inhibitory.

Later in the congress, Dr Selzer introduced two of the most prominent scientists in the field, who focused on the molecular mechanisms that underlie Aguayo's findings. Dr James Fawcett of Cambridge University described how perineuronal nets containing chondroitin sulphate proteoglycans and other inhibitory molecules suppress axon regeneration and sprouting, a form of plasticity in the brains and spinal cords of rats. Enzymatic digestion of chondroitin sulphate proteoglycans increased sprouting in the injured spinal cord, but this did not automatically result in functional improvement, unless the treatment was combined with behavioural reinforcement (physical therapy). This demonstrates what neurorehabilitation researchers have long suspected; that restored anatomical connections will have to be scuplted by physical therapy in order to achieve optimal restoration of function. Dr Marie Filbin of the City University of New York focused on another group of inhibitory molecules, those contained in CNS myelin. These molecules bind to the Nogo receptor, part of a receptor complex present in the membranes of axons that triggers inhibition of their growth. Dr Filbin has discovered many of the steps in the intra-neuronal Nogo cascade that leads from binding to the Nogo receptor to shut-down of axon growth. Clinical trials still ongoing are aimed at neutralising these inhibitory molecules in patients with spinal cord injury.

Although actual cures for serious nerve injuries have not yet been achieved and there are many challenges ahead, multiple strategies are now converging to manipulate the nervous system at many levels in order to promote axon sprouting and regeneration.

A session entitled Cell Therapies: Hope or Illusion? introduced by Dr Bruce Dobkin encapsulated the acceleration of neurological research in the field of stem cells for conditions such as stroke, multiple sclerosis, Parkinson's and Huntington's disease. The session began with an audience vote on whether they believed that cell therapy interventions would eventually improve life for the most severely impaired patients. The majority of the audience voted yes. However, Dr Dobkin cautioned against the selling of hope to vulnerable people and families by ‘forespint stem cell organisations’ and strongly advocated the conduct of prospective, randomised, multicentre controlled trials as ethically and scientifically necessary.

A very encouraging development was reported by Dr Wise Young, who has worked with research communities around the world, including the Peoples Republic of China, to adopt the use of standardised frameworks to guide future pre-clinical and clinical research. This session was attended by several disabled young people who asked the speakers and audience to encourage “partnerships with the spinal cord injury community” and ensure that patients understand the basics of this exciting science.

As with any meeting about neurorehabilitation, the use of technology provided lively discussion and debate. There is no doubt that rehabilitation robotics is a highly promising technology that has demonstrated benefit in several disabling neurological illnesses. Dr Hermanno Igo Krebs reported results of a prospective, randomised, multicentre controlled trial of robotic-assisted physical therapy for upper limb recovery after stroke, carried out in the US Department of Veterans Affairs. While conventional physical therapy resulted in almost as good recovery, this was only true if the intensity of therapy was equal. It is possible that robotics will allow a greater intensity of therapy.

The key problem faced by this technology is our uncertainty about the appropriate way to use these devices and their potential limitations. Maybe, as Dr William Rymer said “the problem is not with robotics but with us and our way of using them”. The key to successful use of robotics may be their simplification and adaptation to home use.

Another symposium focused on the potential use of brain-computer interfaces to permit totally paralysed patients to control assistive devices and even their own paralysed muscles. Dr John Donoghue explained that evidence from multielectrode microchips implanted in paralysed human patients shows that command neurons in the cerebral cortex survive despite the neurodegenerative nature of amyotrophic lateral sclerosis and trauma to axons in spinal cord injury.

But with all the high-technology advances in regenerative medicine and robotics, perhaps the most interesting theme of the congress related to the notion of simplicity in research design. A poster by Dr Bruce Dobkin and colleagues presented the results of a clinical trial designed to allow participation by investigators who have no access to specialised equipment. In the SIRROWS study, providing patients recovering from stroke with feedback on how quickly they walked improved their ultimate walking speed over ten metres and how far they could walk in three minutes. The improvement persisted at least as long as a three-month follow-up.

Three sessions addressed evidence-based neurorehabilitation, an area that has been slow to progress, partly due to the constraints of randomised controlled trials. Matching the right intervention for a patient's deficits can prove to be extremely difficult with a lack of treatment protocols available. An overview of guideline preparation was presented by Dr Lynne Turner-Stokes and Dr Thomas Platz who outlined guidelines for arm treatment after stroke.

Recent neuroscience research suggests that the neural systems underlying music also serve non-musical functions, such as linguistic processings, spatial control, memory and other functions. Dr Michael Thaut postulated that music can affect general cognitive and motor functions subserved by these brain systems via mechanisms of neural plasticity. There is now a new treatment model of Neurologic Music Therapy with considerable evidence of its effectiveness in treating disorders of the human nervous system.

When do you start neurorehabilitation? This key question was discussed by Dr Heinrich Binder and followed by Dr Anthony Ward who showed that the outcomes of brain injured patients were improved by interventions that took place in the intensive care rather than waiting until the patient has been transferred onto a rehabilitation ward. But perhaps the most impressive example of the application of simplicity to research design was given by Dr Gert Kwakkel of the Netherlands. Using multivariate analysis he showed that within a few days after a stroke, recovery of hand and arm coordination could be almost perfectly predicted by two findings on very simple bedside tests, a small amount of finger extension, and a small amount of shoulder abduction. Similarly recovery of walking could be predicted by whether the patient could sit up over the side of the bed.

There were over 400 interesting and diverse poster presentations throughout the week. The prize for the best poster by a student or fellow went to Dr Johan Gaverth of Sweden for developing a biomechanical model that can quantify spasticity and distinguish it from contrac-ture. The prize for the overall best poster went to Dr D Cinteza of Romania for a study that showed the superiority of training to step over obstacles during treadmill training for recovery of gait after stroke.

The meeting ended with a special lecture by Dr Henry Markram of Lausanne, Switzerland. He gave a spectacular demonstration of the Blue Brain Project, a combina-tion of experimental work and computer modelling that is developing an accurate representation of the cerebral cortex down to the finest details of synaptic connectivity and molecular mechanisms.
The third Positive Steps in Parkinson’s Disease meeting, sponsored by Teva Pharmaceuticals Ltd and Lundbeck Ltd, was held on March 5th-6th in London. The presentations and discussions covered both cutting-edge clinical research and aspects of daily practice that, although sometimes overlooked, have significant impact on patient quality of life. Although the presentations were varied in content, it was striking that a common theme was the recognition that Parkinson’s disease (PD) is no longer considered solely a motor disorder: physicians must now be able to interpret data and recognize that treatments that address motor symptoms often change in recognition of this.

The problems of dementia were reviewed in more detail by Professor David Burn who highlighted the high cumulative incidence of PD dementia (PDD) and its significant neuropsychiatric burden (including psychotic features and mood disturbances). The typical elderly patient with PD is no longer just the patient who suffers from mobility problems, but also from a multitude of non-motor symptoms, particularly autonomic dysfunction, sleep disorders, dementia and depression – often with considerable impact on caregivers and family.

Another problem associated with PD is poor oral health, and Dr Helen Roberts surprised the audience by giving one of the first talks on this topic at a national meeting. Although physicians who treat PD are very familiar with the problems of drooling and dysphagia, most are less aware of the problems of xerostomia (dry mouth), burning mouth hypersexuality are not uncommon. A recent large observational study conducted in the United States found that 13.6% of patients with PD had at least one ICD and 36% of these had more than one disorder. ICDs are often associated with dopamine agonists, but patients receiving both levodopa and a dopamine agonist appear to be at highest risk.

Dr Macphee suggested that non-physiological stimulation of dopamine receptors in the ventral striatum might underlie the development of ICDs, and the analogy later suggested by the panel was that ICDs may be regarded as a form of ‘limbic dyskinesia’.

Dr Peter Fletcher continued the theme, looking at non-motor problems in elderly patients with PD. People in the western world are now fitter and living longer, so more people are surviving other diseases to achieve older age, when PD becomes more prevalent. Added to this, improvements in the care of patients with PD mean that they are now surviving longer and this brings a new aspect to care; the elderly PD patient is no longer just the patient who developed PD in later life, but also includes patients who have lived with PD for a long time. In addition to the core motor symptoms of PD, patients receiving both levodopa and a dopamine agonist appear to be at highest risk.

Dr Macphee suggested that non-physiological stimulation of dopamine receptors in the ventral striatum might underlie the development of ICDs. The early signs being the emergence of atypical behaviours that the patients often try to hide. Notably, there is often a lack of pleasure associated with the behaviours, the patient needing rather than liking the feelings associated with the activities. Pathologically, it appears that degeneration in the ventral striatum and nucleus accumbens is more closely associated with these types of control than degeneration in the dorsal striatum.

Dr Macphee highlighted that recent research has tended to focus on the recognition and treatment of early disease in the hope of a treatment that will slow or halt the inexorable progression of PD. The recognition that non-motor symptoms (such as hypomimia and constipation) can often emerge before motor symptoms, or signs have given rise to the notion of diagnosing prodromal PD. Dr MacMahon stressed that the early recognition of PD becomes more crucial as we begin to review the role of early treatment. Last year saw the publication or release of several drugs that may help maintain patient function for longer.

Positive Steps in Parkinson’s Disease

Conference details: 5-6 March 2010, London UK. Reviewed by: David Burn, Professor in Movement Disorder Neurology, Newcastle University and Dr Doug MacMahon, Consultant Physician, Camborne-Redruth Hospital, Cornwall.
Review of the Third Biennial Meeting of the UK Swallowing Research Group

Conference details: 4-5 February 2010, London, UK. Reviewed by: Sophie Punzi CT, Medicine, University Hospital of Wales and Tom Hughes Consultant Neurologist, University Hospital of Wales.

The UK Swallowing Research Group held a conference on Thursday 4th & Friday 5th February 2010 in UCL Institute of Child Health, London. This was the third meeting of the group following its first meeting in Manchester four years ago. The attendees were from a range of backgrounds but speech therapy was the best represented profession. Although it may seem anomalous to some to arrange a conference around a single profession, it has opened up. A highly specialist field had been covered, I (SP) certainly felt that my knowledge of the swallowing mechanism and related pathology had increased. The importance of the multidisciplinary team was emphasized as levodopa can affect up to 55% of the PD patient remains stable and delay the onset of motor complications. Professor Jenner ended the meeting by stressing that in order to meet the developing needs of people with PD, physiologists should take a long-term strategic approach to treatment.

Towards the end of the morning, we heard about swallowing problems in two very different populations of patients; those with neuromuscular disorders such as Duchenne muscular dystrophy and patients who have suffered a stroke (Dr. Anita Wallace, Manchester, Ms. Sophie Frey, Germany). It became apparent that a number of different approaches are required to reduce morbidity and mortality. The relationship between swallowing and breathing was explored (Dr. Katie Ward, London), offering a further opportunity to consider dysphagia in a different context.

During the lunch break, while we all checked the integrity of our ICDs) are increasingly being considered. The benefits of deep brain stimulation (DBS) can be dramatic and studies have shown that the effects are relatively long lasting, but the ‘fitness’ of the patient should always be considered, as surgery is not without risk. Aside from the immediate risks of an invasive procedure (the overall rate of surgical complications is 3%), patients should be cognitively intact and have good speech as DBS can affect verbal fluency. Weight gain can also be a problem for some patients. Advances in the technology include changes in the electrode, for flexibility in targeting, and rechargeable batteries. There is also evidence that although earlier rather than later DBS treatment may optimise its benefits, there are logistical and financial obstacles to adopting this theoretical approach.

Following on seamlessly from this opening was a series of talks demonstrating the effect of dysphagia research on clinical practice, including the use of fibreoptic endoscopic evaluation of swallowing (FEES) in adult and paediatric patients (Ms Sarah Wallace, Manchester, Ms. Sophie Frey, Germany). Ms Rebecca Harris and Ms Martina Ryan, London.)

Towards the end of the morning, we heard about swallowing problems in two very different populations of patients; those with neuromuscular disorders such as Duchenne muscular dys trophy and patients who have suffered a stroke (Dr. Anita Wallace, Manchester). It became apparent that a number of different approaches are required to reduce morbidity and mortality. The relationship between swallowing and breathing was explored (Dr. Katie Ward, London), offering a further opportunity to consider dysphagia in a different context. During the lunch break, while we all checked the integrity of our ICDs, some of which are also platform presentations during the afternoons. Some of the notable presentations included Promoting the recovery of swallowing after stroke by stimulation of the motor cortex (Dr. Andrew Barratt, Kent), Reduction in rates of aspiration pneumonia after stroke (Dr. Somke Stanschus, Germany); and a pilot study into the effectiveness of thickened fluids in preventing pneumonia (Dr. Sue Wells, Sheffield), which won the prize for the best free paper.

The following day, there was an emphasis on assessment tools and rating scales, starting with an in-depth five-year research project carried out in the USA (Prof. Bonnie Martin Harris) using the modified barium swallowing study. We were also introduced to the pitfalls of rating scales (Dr. Stefan Cano, Plymouth), many of which, although commonly used, are based on weak scientific theory and questionable arithmetic.

Later in the afternoon, we had our focus brought back to patients with an overview of the holistic approach to swallowing problems and a reminder to view dysphagia in context, as an ‘oral feeding’ problem (Dr. Tom Hughes, Cardiff). The conference was closed with two talks concerning the regeneration of voice and swallowing using various methods including tissue replacement and neuromuscular electrical stimulation (Prof. Martin Birch, UCL; Ms Emilia Michou, Salford).

After such a variety of topics within this highly specialised field has been covered, I certainly felt that my knowledge of the swallowing mechanism and related pathology had increased. The importance of the multidisciplinary team was made more apparent to me: complex problems require input from several different sources. I was also amazed by the volume of new research into neuroprotective and neurorestorative therapies have yet to produce any real candidates for treatment. However, the introduction of new delivery systems for older drugs (including levodopa and a number of dopamine agonists) and revised treatment algorithms have already made a significant impact on patient care. For example, evidence is now accumulating that early intervention may increase the amount of time that the patient remains stable and delay the onset of motor complications. Professor Jenner ended the meeting by stressing that in order to meet the developing needs of people with PD, physiologists should take a long-term strategic approach to treatment.

The lively discussions and debate were all supplemented with workshops and interactive sessions and participants left eagerly looking forward to the next meeting planned for 4-5 March 2011 in Newcastle upon Tyne.