

# Fifth Meeting of the UK PD Non Motor Group: Non Motor Symptoms of PD: Treatment & Quality of Life

**Conference details:** 20 March 2010, Royal Society of Medicine, London, UK. **Reviewed by:** Miss Chandni Chandiramani, Kings College and Institute of Psychiatry, London, UK and Mr Kartik Logishetty, Kings College, London, UK.

The fifth meeting of the Parkinson disease Non-Motor Group (PDNMG) 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 PDNMG 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 Schaipra (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 ADAGIO, 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, F-Dopa 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, imaging 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



Standing: Graham Macphee, Pablo Martinez-Martin, Peter Fletcher, Per Odin, Kieran Breen  
Seated: Alison Forbes, Fabrizio Stocchi, K Ray Chaudhuri, Cristian Falup-Precariu.



Per Odin, Alexandra Rizos, K Ray Chaudhuri, Dag Aarsland, Pablo Martinez-Martin.

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 on quality of life, and non-declaration of NMS in PD, respectively. Particular NMS including depression and autonomic, sexual and gastrointestinal dysfunction are under-reported by patients and as a result under-treated by health care professionals. This could be attributed to patients' lack of awareness between their NMS and PD or perhaps a reluctance to reveal embarrassing problems to a stranger. The recently published study recommends the

use of the patient-completed 'Non-Motor Symptom Questionnaire' (NMSQuest) to provide an early screen of NMS.

Professor A Antonini (Italy) offered an appraisal of drug therapy for motor and non-motor symptoms. He began with reviewing results from the recent PRIAMO study – a large Italian cross-sectional observational study which described epidemiology and evolution of NMS. NMS in the psychiatric domain were 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 (98.6%). 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 that may be commonly experienced in PD.

In recent years, dementia has been recognized 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 under-treated. Professor 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 inheri-

tance, 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 (UK). 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.

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