Over 350 neurologists from all over the world converged on Cannes, France in October for the 3rd International Scientific Symposium on Parkinson’s Disease and Restless Legs Syndrome. The two-day symposium was supported by an unrestricted educational grant from Boehringer Ingelheim and accredited by the European Federation of Neurological Societies (EFNS).

Welcoming delegates to the first day of the meeting, Oliver Rascol (Toulouse, France) pointed out that although effective treatments have deeply modified the clinical spectrum of Parkinson’s Disease (PD), the presence of multiple options make it a challenge in setting a consensus and a unified strategy for the optimal management of the individual patient.

Marie Vidalhét (Paris, France) highlighted the non-motor symptoms of PD. She said that although PD is typically defined as a syndrome consisting of tremor, bradykiniesia, rigidity and postural instability, the clinical spectrum was much more diverse. “Beyond these principally motor features”, she said, “there is increasing recognition of non-motor problems including cognitive impairment, mood disorders and autonomic failure”. And she stressed that it was these aspects of the illness rather than the motor symptoms that lead to the most profound disability, and impact on quality of life.

Anthony Schapira (London, UK) then took to the floor to discuss the dopaminergic and non-dopaminergic actions of dopamine agonists. He said that recently dopamine agonists have attracted attention as potential disease modifying agents, adding that they appear able to prevent cell death in a variety of cell culture and animal model systems. He also presented evidence showing that the D2/D3 agonist pramipexole has been shown to significantly reduce dopaminergic cell loss in the nigra of MPTP treated primates. He also presented data from the CALM-PD study that used imaging of the nigrostriatal system as a surrogate marker for disease progression in patients receiving pramipexole or levodopa. The results showed a significant reduction in the rate of loss of imaging marker over the four-year study period with pramipexole.

The focus then turned to the non-motor symptoms of PD. Paolo Barone (Naples, Italy) said that depression was a common complication of PD with a prevalence averaging 40% in patients attending outpatient clinics. He also highlighted that the quality of life of PD patients was significantly and inversely associated with depression. Yet he stressed: “There is little evidence for the efficacy and safety of antidepressant therapies in PD”. He went on to present findings from an open-label randomised study comparing the efficacy and tolerability of pramipexole versus the selective serotonin reuptake inhibitor sertraline in the treatment of depression in stable PD patients without fluctuations and under levodopa monotherapy. Pramipexole was found to have significant antidepressant effects in patients with PD. Less pramipexole patients discontinued as a result of side effects and in a secondary analysis of the intent-to-treat population, the percentage of patients recovering from depression was statistically significantly higher with pramipexole at 60.6% compared with sertraline (27.3%). Barone commented: “These findings suggest that there may be significant advantage for PD patients with depression to receive the dopamine agonist pramipexole in preference to a classic antidepressant.”

Werner Poewe (Innsbruck, Austria) then reviewed disorders of sleep in PD patients. He stressed that the management of sleep disorders in PD was complex and has to target underlying mechanisms. He said that dopamine agonists might be helpful with sleep fragmentation due to nocturnal motor disability due to either restless legs syndrome or periodic limb movements in sleep.

Andrew Lees (London, UK) highlighted that a small number of PD patients develop cognitive and neuropsychiatric disturbances that may be directly related to taking increasing doses of dopaminergic drugs well in excess of those needed to control motor symptoms. He said that such patients could be identified by a demand for escalating doses of dopamine replacement therapy often against medical advice. He said that treatment involved early identification for risk and stringent enforced restriction of medication with minimisation of short duration formulations.

Ken Marek (New Haven, USA) provided an update on imaging. He said that imaging continues to expand its role in translating clinical neuroscience into better understanding and more effective therapies for PD. One of the most exciting potential uses he spent some time elaborating on was preliminary work demonstrating that combining imaging with other potential PD screening tools may enable presymptomatic screening for PD in at risk groups.

Continuing on this theme, Christopher Goetz (Chicago, USA) highlighted the need for the development of new scales for the clinical assessment of PD. Goetz has been recruited by the MDS to organise a committee to provide a new UPDRS. The new scale retains the original structure of the UPDRS with four newly titled components: non-motor experience of daily living (part I and II), motor examination and motor complications. In addition, an official appendix recommends more in-depth assessment for several of the non-motor items including depression, cognitive deficits, insomnia and quality of life.

Concluding the first day, Warren Olanow, (New York, USA) outlined new and future therapies for the treatment of PD. These included cell based therapies; trophic factors; gene therapies and neuroprotective approaches.

The second day of the meeting was devoted to Restless Legs Syndrome (RLS). Karl Ekbom, son of Karl-Axel Ekbom who in 1945 published a doctoral thesis on restless legs, provided an introduction to the day highlighting the potential promise of dopamine agonists. Markku Partinen (Helsinki, Finland) reviewed the clinical presentation and diagnosis of RLS. He stressed that all symptoms of the RLS quartet must be present in order to make the diagnosis – an urge to move usually accompanied by unpleasant sensations in the legs; aggravation of symptoms at rest; relief of symptoms with activity and a circadian pattern with worse symptoms experienced in the evening or night.

Wayne Hening (New Brunswick, USA) then elaborated on the clinical importance of RLS. He highlighted findings from the recent REST study showing that 3% of the primary care population reported that they had RLS symptoms at least twice a week and that when the symptoms occurred they caused moderate to severe distress. Among these patients, 82% reported that they were bothered by the leg discomfort and more reported difficulties with sleep. Over half of RLS sufferers reported significant problems with functions the day after nocturnal symptoms – including fatigue and cognitive difficulties. Overall he stressed that RLS had a significant impact on quality of life, adding that treatment of RLS can both alleviate symptoms and improve quality of life.

Richard Allen (Baltimore, USA) then reviewed the pathophysiology of RLS highlighting the importance of dopamine abnormalities. He said that levodopa and all dopamine agonists provide dramatic and immediate relief of symptoms when used at doses much lower than those used for treatment of PD.

Luigi Ferini-Strambi (Milan, Italy) proposed that RLS was a poorly recognised and under-treated condition. Reviewing latest epidemiological studies he said that around one in ten of the adult population have RLS – a truly common disease and that women were twice as often affected as men.

Turning to treatment options, Diego Garcia-Borreguero (Madrid, Spain) reviewed the efficacy and safety of dopaminergic compounds. Although he said that several ergoline-derived dopamine receptor agonists have been investigated, due to the higher incidence of side effects research is now focused on the non-ergoline derivatives including pramipexole and ropinirole. He cited studies showing that pramipexole has been shown to be more effective than placebo at a dose of 0.125 mg per day and is currently being investigated in large, double blind randomised controlled trials. He also said that pramipexole had the advantage of having therapeutic efficacy at the initial dosage. This he said meant that if confirmed by future studies pramipexole could be used not only for as a continuous treatment but also for non-daily treatment of RLS.
European Committee for Treatment and Research in Multiple Sclerosis

October 6-9, 2004; Vienna, Austria.

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uperb weather for October and a fantastic venue, Vienna, Austria, witnessed the 20th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) and the 9th Annual Meeting on Rehabilitation of MS (RIMS). Delegates travelled from far afield to attend. The meeting comprised 33 lectures spread over four plenary and 12 parallel sessions and a total of 638 posters/abstracts. Fortunately, all the posters were displayed throughout the conference, allowing delegates time to view them at their leisure.

The teaching course titled “Symptom management and rehabilitation in MS” was divided into “Neurorehabilitation in MS” (G. Comin, Milan) and “Symptom Management in MS” (Keselring, Valens). It illustrated that functional MRI has the potential to provide information about cortical reorganisation following MS-related tissue damage. The key target for the management of MS is the enhancement of cortical adaptive plasticity by both cognitive and physical rehabilitation. “Assessment in MS” (J. Horbart, Plymouth) demonstrated the importance of using and relying on rating scales to measure the impact of MS symptoms to evaluate the endpoints of clinical trials, with emphasis on the patient's perspective.

The first plenary session “New insights in primary progressive MS (PPMS)” (J.S. Wolinsky, USA) illustrated that the phenotype of PPMS has an unrelenting course from the onset without discernible attacks. The PROMiSe study explored whether glatiramer acetate (GA) could slow the disease. It involved 41 MS patients (21 relapsing-remitting, 352 secondary progressive, 143 primary progressive). Mitoxantrone was generally well tolerated. Another study also suggested that the drug might have beneficial effects upon cognitive function in MS (Zephir, France). Recent National Institute for Clinical Excellence (NICE) guidelines for MS Management (2003) recommend that mitoxantrone is used only by an expert in the use of this drug after a full discussion and explanation of the risks to the patient. A poster (Porter, UK) described the complications encountered in the use of mitoxantrone, such as neutropenia, extravasation, infections, amenorrhoea, which were compounded by poor documentation, lack of advice on potential infertility problems and an absence of pregnancy screening. To address these issues they developed an integrated care pathway, including patient screening, informed consent, infusion protocol and long-term management monitoring.

Breaking news included the first study to demonstrate a clear association between N-acetylaspartate (NAA) levels in cerebrospinal fluid (CSF) and MRI measures of brain atrophy in MS patients. It involved 41 MS patients (21 relapsing/remitting MS, 12 secondary progressive MS and 8 primary progressive MS). The last presentation of the symposium was a historical presentation by Mrs Aileen M. Burn, City Hospitals, Sunderland. She shared an account of a patient whose condition improved dramatically following treatment with interferon beta in the 1980s.

John Winkelman (Massachusetts, USA) reviewed the long-term experience to date with dopaminergic agents. He said that dopamine agonists have replaced levodopa as first-line treatment for RLS given the requirement for increased doses of levodopa due to loss of efficacy, re-emergence of symptoms in the second half of the night or worsening of symptoms during the day (augmentation). Although pergolide demonstrated persistent benefit for the majority of RLS responders when followed for 12 months, concerns regarding pleuropulmonary fibrosis and multivascular disease have recently been raised with long-term use of this dopamine agonist. Long-term experience with pramipexole was assessed in three large retrospective consecutive case studies. In two of the studies follow-up information was available for a mean of 21 – 27 months of continuous pramipexole administration. Long-term efficacy was confirmed and augmentation was found in only a third of patients and was generally easily managed by earlier administration of medication.

Wolfgang Oertel (Marburg, Germany) presented new data from the European Flexible dose study of pramipexole in RLS patients. In total 37 sites in 5 European countries participated in the study, which involved nearly 350 patients. Pramipexole was significantly superior to placebo in regard to change from baseline to week 6 on the IRLS scale and CGI- Improvement after six weeks and showed an excellent tolerability profile.

The last presentation of the symposium was given by Jacques Montplasir (Montreal, Canada) widely regarded as one of the main pioneers in this field. He confirmed that dopamine agonists should be considered as the first line therapy treatment of choice for RLS. He also called for more publicity about RLS saying that well-informed patients could present themselves for treatment, and drawing an analogy with public health campaigns in relation to sleep apnoea.

Helen Reilly, Freelance Medical Journalist, London.
Sino-British Joint Conference on Neurology
November 15-17, 2004; Beijing, China.

This two day meeting was organised by the Association of British Neurologists (ABN) in conjunction with the Chinese Society of Neurology, Chinese Medical Association and Hong Kong Neurological Society. A contingent of over 60 delegates from the UK made the long journey to Beijing, although many also took the opportunity to extend their stay for sight seeing. There was some trepidation from ABN members about the effect of potential language and cultural barriers on the smooth running of the scientific programme, but these fears were soon allayed. The use of dual projection, with many UK talks pre-translated into mandarin assisted the Chinese delegates, while joint chairs for all sessions kept the meeting to time. Plenary sessions ran in the morning (beginning at 0815), while parallel scientific sessions ran in the afternoon (finishing at 1800, for the hardy attendees). Apologies to colleagues not featured below, therefore, as it was impossible to sit in on all talks.

Professor Will (Edinburgh) gave a masterly overview of Creutzfeldt-Jakob disease, with emphasis on vCJD. This included very recent data, including description of a “preclinical” CJD case, as evidenced by PrPsc in the lymphoreticular system of a male patient dying from a ruptured aortic aneurysm who had previously received a blood transfusion from another CJD victim. Tonsillar biopsies have been positive in all 18 vCJD cases to date. Triphasic EEG complexes, not typically found in vCJD, have been recently described in the late stages of diseases in an Italian patient. One hundred cases of sporadic CJD have been reported in China since 1980, 56 of these pathologically confirmed (Lin). A single case of vCJD had worked in the UK for many years. Professor Colchester (Kent) advanced the hypothesis that BSE in the UK may have originated from Far Eastern mammal-derived imports, in association with a “spontaneous event”, inducing PrPsc formation in cattle, rather than species to species transfer. Dr Murray (Edinburgh) gave a comprehensive overview of MRI in CJD. Signal changes on FLAIR sequences and diffusion-weighted imaging, in particular, may be sensitive for cortical, thalamic and basal ganglia changes in sporadic and vCJD, although the exact pathological correlate is not yet known. Intriguing preliminary data was presented (Guo, Beijing) to suggest that tetracycline may reduce protease-resistance in PrP (a feature of PrPsc), while inoculation of scrapie material treated with tetracycline into mice prolonged the incubation time for disease by several days. The authors had not, however, administered tetracycline orally to the mice prior to scrapie inoculation. Such an approach would not, however, administered tetracycline orally to the mice prior to scrapie inoculation. Such an approach would not, however, be possible to sit in on all talks.

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