Parkinson's disease: a multi-faceted disease

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The content of this supplement of the Journal of Neurology is the essence of lectures and workshops which were presented during the 11th German Parkinson Expert Meeting in Dresden in October 2010. Cutting-edge information on many major developments in the field of Parkinson's disease (PD) is provided.

The etiopathogenesis of PD is still unknown, although we have unraveled interplay between oxidative stress, genetic abnormalities, mitochondrial dysfunction, inflammation and apoptosis. In spite of these findings, the initial step in the development of PD is unknown. More and more important information is being gained from the study of patients with familial PD as their genetic abnormalities are elucidated, and, to a lesser degree, from non-familial PD patients.

A major focus of modern PD research is on the pre-motor phase of the disease. Many patients present first with hyposmia, REM sleep disorder, depression, constipation or other autonomic disturbances, before they develop motor signs. Thus, a better understanding of the pre-motor phase could lead to early treatment with potential neuroprotective agents. In the paper by Winkler et al., a Parkinson's disease risk score is presented which aims for the early diagnosis of PD.

The most recent findings in PD suggest that patients have a relatively bad drug adherence, maybe due to the complexity of the drug regimen or due to progressive cognitive impairment. For this reason, once daily formulations are preferable. In addition, long-lasting continuous dopamine replacement therapy prohibits the occurrence of dyskinesia. There is good evidence that extended release preparations such as ropinirole PR lead to equal efficacy with better tolerability when compared with immediate release preparations. Both de novo patients and those in advanced stages of the disease derive benefit from these preparations. It is of particular note that even advanced patients tolerate ropinirole PR and improve significantly with respect to motor function, especially with being "on". In a head to head comparison, the extended release preparation was even superior to the immediate release form.

Non-motor symptoms are becoming of particular interest, since they lead to a major impairment of the quality of life of our patients. A whole variety of non-motor symptoms is discussed in detail in this supplement, and special focus is placed on sleep impairment in PD. REM sleep disbehavior is one of the early signs of PD and should give rise to careful clinical examination. The use of modern extended release preparations of dopamine agonists, has led to an improvement in sleep, especially sleep quality and early morning akinesia. Nonetheless, there are still many patients who wake up too early or wake up due to nocturia. A detailed description is given for different specific sleep disturbances such as restless legs syndrome, rapid eye movement sleep behaviour disorder, periodic limb movements in sleep and obstructive sleep apnea.

Impulse control disorders have not previously played a major role in PD treatment. However, we now know that levodopa, and in particular, high doses of dopamine agonists, may cause hypersexuality, binge eating, gambling,

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compulsive buying and compulsive reckless driving. In addition, punding is a symptom of the dopamine dysregulation syndrome which also includes levodopa addiction. We describe in detail the classification, epidemiology, neurobiology and management of impulse control disorders which are to be found in 6–17% of patients treated with dopamine agonists and which are potentially not only embarrassing to the patient and the treating physician, but may also be harmful.

Dysautonomia is also a rather common, so far underdiagnosed problem in PD. Many if not most of our patients suffer from symptoms such as incontinence, orthostatic dysregulation, or profuse sweating. These symptoms are not always formally assessed and thus frequently overlooked or misdiagnosed, yet management of these autonomic disorders is rather important for the quality of life of

our patients. Treatment of cardiovascular, gastrointestinal, urogenital and sudomotor autonomic dysfunction is presented in one contribution to the supplement.

Many patients are asking for cell replacement therapy, i.e. stem cell therapy. Up to now it is certainly fair to say that there are several interesting options for how this can be achieved, but there are still many hurdles to be overcome.

For this reason the question arises whether basic science has a helpful impact on clinical practice. This question is discussed in detail and it is underlined that we need more appropriate models for Parkinson's disease. On the other hand, genetic findings in familiar PD have led to important conclusions in the more usual, sporadic form of PD too. They may even open new windows of opportunities in the treatment of PD in the future.