Fatigue, mood disorders and sleep problems in patients with Parkinson's disease

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Summary

Parkinson's disease (PD) is a slowly progressive disease characterized by its motor and only recently recognized nonmotor features. This thesis focuses on fatigue, sleep problems and mood disorders, on the relationships between these nonmotor features and their impact on quality of life (QoL) of PD patients. QoL has become one of the most important measures and constructs for evaluating more comprehensively the outcomes of a chronic disease.

Previous research in this field has mostly been oriented on descriptive data showing that PD patients report worse QoL than the general population. Later determinants of worse QoL were studied, with an interest in typical motor problems and sociodemographic variables. For this reason the Global Parkinson's Disease Survey Committee was established in 2002. The results of this multinational cross-sectional study showed worse disease severity, a medication regime with only L-dopa and the presence of depression to significantly worsen QoL. This study was thus the first to evaluate the influence of nonmotor PD features on QoL. Recent research has also shown that the motor complications of L-dopa, pain or cognitive decline can worsen QoL.

This thesis tries to answer to following research questions: Is there a relationship between daytime and nighttime sleep disturbances and different QoL domains? How are different fatigue domains related to different QoL domains and is there a difference between physical and mental dimensions of QoL? Is there a relationship between nighttime or daytime sleep problems and fatigue, or are they independent from each other? Do mood disorders or comorbidities contribute to the development of fatigue? Is there a causal relation between disease severity and depression and fatigue; and between depression and fatigue?

The aim of Chapter 2 was to evaluate the impact of sleep disorders on QoL. Sleep problems are frequent in PD patients and they may occur during the nighttime as well as during the daytime. They may result from uncontrolled motor complications, medication side-effects, or as a result of the degeneration of the neuro-anatomical substrate responsible for the sleep-wake cycle. In our sample 73.1% of patients reported poor nighttime sleep and 23.7% reported excessive daytime sleepiness (ESS). We performed two separate linear regression analyses to evaluate the effect of poor night time sleep or excessive daytime sleepiness on quality of life, controlled for depression, anxiety and functional status. We found that poor nighttime sleep is a significant contributor to poor QoL,

but excessive daytime sleepiness is not. In addition, worse functional status and anxiety showed significant relationships with poor QoL, but depression was not significant in either model. Our results thus showed an important contribution of nighttime sleep disturbances and anxiety to poor QoL.

Chapter 3 examined the influence of fatigue on QoL. Fatigue is considered to be a multidimensional construct with mental and physical components which are independent from each other. It is considered to be one of the most disabling nonmotor symptoms of PD patients, being reported by one-third of PD patients. The presence of fatigue was associated with worse QoL in all domains – with Bodily Discomfort, Mobility and Emotional Well-being as the most affected. Looking closer at different fatigue components, the mental components (especially Mental fatigue) were associated with more psychological QoL domains (Emotional Well-being, Stigma, Social Support, Cognition, Communication), and the physical components (Reduced activity) were related to more physical QoL domains (Mobility, Activities of Daily Living and Stigma). Additionally, worse functional status was associated with worse QoL scores for all the domains except Social Support and Cognition; higher age was related with worse Cognition; longer disease duration with Emotional Well-being; and female gender with the Bodily Discomfort domains.

Chapter 4 deals with relationships between fatigue and sleep disturbances. We performed a series of linear regression analyses to evaluate the association of excessive daytime sleepiness or poor quality of sleep with different fatigue components. Our results showed that sleep disturbances (either daytime or nighttime) do not have significant relationships, thus indicating that these two problems – fatigue and sleep problems in PD patients – are independent from each other.

The aim of Chapter 5 was to evaluate factors associated with fatigue. Basic sociodemographic variables (age gender, disease duration, level of education), mood disorders (anxiety and depression), comorbidities (measured by Charlson index) and functional status were all entered into general linear model analysis. Our result showed worse disease severity and depression to have significant relationships with worse scores for all the fatigue components. Anxiety was associated with more serious General fatigue and Reduced motivation.

Chapter 6 evaluates the causal relationships between depression, functional status and fatigue. For this reason LISREL analysis was performed in order to examine how functional status explains depression, and how disease severity explains via depression the different fatigue components. We found that worse functional status and worse depression both lead to worse General fatigue, Reduced activity and Mental fatigue. Worse disease severity alone caused worse Physical fatigue, and worse depression alone caused more fatigue in the Reduced motivation

component.

A limitation, mentioned in the Discussion, is that our research was based on cross-sectional data. However, longitudinal data could provide us more satisfactory information for explaining the causal relationships between the variables. Future research could also be concentrated on the evaluation of the different PD population groups – patients with early PD and with advanced PD.

Nonmotor symptoms are universal features of idiopathic PD and involve dysfunction in the neuropsychiatric, sensory and autonomic domains. Together, they add significantly to the overall disability caused by PD and are critical determinants of health-related quality of life. In the era of effective symptomatic therapies for the motor symptoms of PD, non-motor dysfunction has developed into a major prognostic factor for overall disease burden and everyday function in PD.

We stress the importance of recognizing the different aspects of nonmotor features of Parkinson's disease. The recognition of possible treatable problems and their proper management is extremely important as they may lead to improvement of another nonmotor feature and may thus result in the improvement of the quality of life of PD patients.