

## **DO MOTOR SYMPTOMS REMAIN THE MAJOR COMPONENT OF PD? NO**

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Parkinson's disease (PD) is a neurodegenerative disorder characterized, from the clinical point of view, by motor manifestations as bradykinesia, rigidity, and rest tremor. In fact, the criteria for diagnosis of PD are still based on the identification of these signs. Also, the Hoehn and Yahr disease staging is based on motor impairment and disability. Nonetheless, the motor impairment is frequently preceded, even in years, by non-motor symptoms (NMS) such as loss of olfaction, constipation, depression, and REM sleep behavior disorder. Over time, and with progression of the disease, a variety of other non-motor manifestations may be evident and tend to accumulate in the same patient. Using an instrument for screening of 30 NMS, the Non-Motor Symptoms Questionnaire, several studies carried out in departments of Neurology have found a mean of 10 to 12 NMS per patient (Martinez-Martin et al. *Mov Disord* 2007; 22: 1623–1629; Chaudhuri et al. *Mov Disord* 2010; 25: 704–709; Rodriguez-Violante et al. *Clin Neurol Neurosurg* 2010; 112: 883–885), although this number may be lower in community surveys. Anyway, observational studies on patients surviving 15 or 20 years with the disease demonstrate that NMS have a leading role on disability at long-term (Hely et al. *Mov Disord* 2008; 23: 837–844). Dementia, urinary incontinence, severe sleep disturbances, hallucinations, delusions, apathy, orthostatism, choking and limitations for verbal expression involve a great deal of problems in daily living for patients and caregivers. As previously mentioned, these disorders tend to accumulate in the same patient (11 or more NMS were present in 50% of 951 patients evaluated with the Non-Motor Symptoms Scale; EUROPAR files), increasing the suffering and disability caused by the motor impairment and complications.

How the relative importance of the motor versus non-motor symptoms, as a whole, could be compared in PD?. Probably, the best approach is measuring the impact of these different manifestations on the patients' health-related quality of life, which is defined as "the perception and evaluation, by patients themselves, of the impact caused on their lives by the disease and its consequences" (Martinez-Martin, 1998). Using unified rating scales and specific patient-reported outcomes, and applying comparative and multiple regression techniques, researchers have found that NMS have a significantly greater impact than motor disturbances on patients quality of life (Barone et al. *Mov Disord* 2009; 24: 1641–1649; Qin et al. *Parkinsonism Relat Disord* 2009; 15: 767–771; Li et al. *Mov Disord* 2010; 25: 2740–2746; Martinez-Martin et al. *Mov Disord* 2011; 26: 399–406; Santos-Garcia et al. *Rev Neurol* 2011; 52: 385–393). This differential effect of the NMS on the quality of life is present both in early (Martinez-Martin et al. *Mov Disord* 2010; 25 [Suppl 2]: S424) and advanced stages of the disease (Martinez-Martin et al. *Mov Disord* 2010; 25 [Suppl 2]: S426). Some NMS are recognized determinant factors of quality of life; that is to say, they influence the patients' quality of life. Depression, anxiety, sleep disorders, and pain, for instance, belong to this group of factors causing quality of life deterioration (Rahman et al. *Mov Disord* 2008; 23: 1428–1434; Soh et al. *Parkinsonism Relat Disord* 2011; 17: 1–9; Martinez-Martin P. *J Neurol Sci* 2011; 310: 12–16; Shearer et al. *J Neurol* 2011. DOI: 10.1007/s00415-011-6202-y). Disability is also a determinant of quality of life, but it results from motor impairment and non-motor manifestations (*Mov Disord* 2003; 18: 985–992; Raggi et al. *Int J Rehabil Res* 2011; 34: 316–320).

From the patients' point of view, therefore, NMS are relevant and potentially more important than the motor disorder. In fact, most of symptoms centering the daily life of the PD patient are non-motor (Lee et al. *Parkinsonism Relat Disord* 2007; 13: 284–289). Considering the accumulation and severity of the NMS, the relative lack of effective therapies for their treatment, and the impact on the health state of patients, it is evident that motor symptoms are not the main component of PD.