Nonmotor Symptoms in Parkinson's Disease

Expanding the View of Parkinson's Disease Beyond a Pure Motor, Pure Dopaminergic Problem

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KEYWORDS

• Parkinson's disease • Nonmotor symptoms • Motor symptoms • Dopaminergic

KEY POINTS

- The pathology of Parkinson's disease (PD) extends far beyond the nigrostriatal dopamine pathway and results in nonmotor symptoms (NMS) in addition to the commonly accepted motor symptoms.
- NMS have a great impact on quality of life, but nonrecognition of NMS is an all too common problem, requiring a systematic approach to both recognizing and treating NMS.
- There are many useful questionnaires that might be used to detect and guide management of NMS.
- The number of evidence-based treatments for these problems remains limited.
- More work needs to be done in therapeutics, and it seems that future therapies for NMS should be developed specifically based on the pathogenesis of PD.
- Therapeutic strategies that use serotonin-based and noradrenaline-based approaches, in addition to dopamine therapy, may provide a more comprehensive control of the multitude of symptoms seen in most patients with PD.

INTRODUCTION

Ever since it was first recognized,[1] Parkinson's disease (PD) has been primarily identified by its cardinal motor symptoms: tremor, bradykinesia, muscle rigidity, and gait instability.[2] Current therapies act mainly on the dopaminergic system,[3] with the overall

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goal of improving motor symptoms and preserving independent function by enhancing dopamine tone.[2] However, intrinsic nonmotor symptoms (NMS) of PD are increasingly recognized as being critical to identify and treat because of their impact on quality of life in PD,[4–11] perhaps having an even greater impact than motor symptoms.[12] Despite increasing evidence of the importance of NMS on quality of life, studies clearly show that there are gaps in treatment of these issues.[11] Although physicians may be aware that NMS are common in PD, these gaps in treatment may be attributable to a need for increased information about and understanding of specific NMS, and clinical approaches for their assessment and management in the context of PD as a whole. This article discusses NMS of PD, how they may be related to the pathologic basis of PD, and how NMS can be best managed.

OVERVIEW OF NMS

The most commonly described primary NMS of PD (summarized in **Table 1**) are autonomic dysfunction, cognitive abnormalities, sleep disorders, mood disorders, pain, and sensory disorders.[7,9,10,13] These NMS are common in patients with PD, with the most common being autonomic dysfunction, mood disorders, and sleep problems.[13–15] There are also NMS in PD that are secondary to pharmacotherapy treatment, such as impulse control disorders and psychosis. In addition to being common, NMS have been reported by patient surveys to be more disabling than the motor symptoms of tremor and bradykinesia.[5]

Autonomic Dysfunction

Autonomic dysfunction associated with PD primarily consists of gastrointestinal (GI) dysfunction, genitourinary dysfunction, and cardiovascular dysfunction with orthostatic hypotension. Although it is a key feature of multiple system atrophy, autonomic dysfunction also commonly occurs in PD and is considered to be the most prevalent category of NMS, affecting more than 70% of patients in all stages of PD.[16]

Dysautonomia manifested as GI dysfunction, particularly constipation, is one of the most common NMS, with prevalence in the 50% to 70% range.[16,17] GI dysfunction was even described in James Parkinson's original monograph on PD[1] and often precedes the development of motor symptoms.[17] Another GI symptom includes drooling/sialorrhea, which is believed to be as much caused by decreased involuntary swallowing as it is to increased saliva production, and is believed to have a prevalence greater than 40%.[17] Incomplete bowel evacuation and bowel incontinence may also occur, but these are less common (30% and 8%, respectively) than constipation or drooling/sialorrhea.[17]

Genitourinary dysfunction is a frequent manifestation of dysautonomia in PD, mostly consisting of urinary urgency, frequency, and incontinence, and includes sexual dysfunction. Urinary dysfunction can be objectively assessed with urodynamic studies and is estimated to have a prevalence of 25% to 40%.[17–19] Sexual dysfunction in men with PD manifests primarily as erectile dysfunction; however, decreases in drive and orgasm have also been reported.[20]

One of the most debilitating NMS is the subcategory of dysautonomia categorized as cardiovascular dysfunction. Cardiac sympathetic denervation is known to occur in PD and is at least partially responsible for contributing to an array of symptoms ranging from orthostatic lightheadedness and hypotension to dyspnea on exertion and fatigue.[21] Although generally occurring later in the disease course and less severe than in multiple system atrophy, orthostatic hypotension can be particularly problematic, resulting in cerebral hypoperfusion, which may impair cognition. When severe,