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Effects of Exercise on Non-Motor Symptoms in Parkinson's Disease

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ABSTRACT

Patients with Parkinson's disease experience disabling non-motor symptoms, including autonomic dysfunction, cognitive decline, and sleep disorders. Pharmacologic treatments for these symptoms are often ineffective or have intolerable side effects. Therefore, non-pharmacologic interventions are an attractive alternative. Exercise in particular has the potential to alleviate the progressive impairment related to these non-motor symptoms. In this commentary, we explore available research that addresses the impact of exercise and physical activity on autonomic dysfunction, cognitive impairment, and sleep disorders in Parkinson's disease and suggest areas in need of further study. Many gaps remain in our understanding of the most effective exercise intervention for these symptoms, the mechanisms underlying exercise-induced changes, and the best way to monitor response to therapy. However, available research suggests that exercise is a promising approach to improve non-motor symptoms in patients with Parkinson's disease. (*Clin Ther*. 2017;∎:∎∎∎–∎∎∎)

Key words: autonomic function, cognition, exercise, non-motor symptoms, Parkinson's disease, sleep.

INTRODUCTION

Parkinson's disease (PD) is a progressive neurodegenerative disease diagnosed by its motor symptoms of bradykinesia, rest tremor, rigidity, and postural instability. In addition to these motor symptoms, patients with PD experience non-motor symptoms, including autonomic dysfunction (AutD), cognitive decline, sleep disorders, and neuropsychiatric symptoms such as depression, anxiety, and psychosis.[1] These non-motor symptoms adversely affect quality of life (QoL) and can be even more disabling than the motor symptoms.[2] Medications used to treat these symptoms are often inadequately effective and can cause intolerable side effects.[3,4] Therefore, patients, physicians, and researchers have developed increased interest in the potential of non-pharmacologic therapies to treat non-motor symptoms in PD.[5] For example, surgical therapies, such as deep brain stimulation (DBS), have been investigated for their influence on non-motor symptoms. An excellent review summarizes available evidence, which suggests that, in general, DBS can worsen performance within some cognitive domains and can improve other non-motor symptoms.[6]

Another non-pharmacologic therapy that has promise for improving non-motor symptoms is exercise. Exercise interventions have established efficacy for treating the motor symptoms of PD, with many different types of exercise activity, including stretching, walking, dance, tai chi, aerobic, resistance, and multimodal exercises showing beneficial effects on motor symptoms in PD.[7] From research in the general population, exercise also has the potential to improve autonomic function, attenuate cognitive decline, and improve sleep and daytime sleepiness. In this commentary, we discuss the available evidence that supports the use of exercise for treatment of AutD, cognitive decline, and sleep disorders in patients with PD and suggest areas for future research.

AUTONOMIC DYSFUNCTION

AutD in PD

AutD is common in PD, with reported prevalence ranging from 14% to 80%.[8] It may include dysregulation of cardiovascular, gastrointestinal (GI), urinary, pupillary, and thermoregulatory systems.[9] AutD can occur at any stage of the disease, with GI, urinary, and orthostatic symptoms increasing over

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time but notable in early and even premotor stages.[10] As the disease progresses, AutD significantly impairs QoL in patients with PD.[1]

Cardiovascular AutD and Exercise

Sympathetic dysfunction is the major cause of cardiovascular dysregulation in PD, which occurs in at least 50% of patients.[8] Cardiovascular AutD includes orthostatic hypotension (OH), supine hypertension, and increased resting heart rate.[8,11] These symptoms can be exacerbated by medications used to treat PD. Interestingly, the severity of OH does not necessarily increase with the duration of disease.[11] In addition to negatively affecting QoL, OH increases fall risk, hospitalizations, and cost of care in PD.[12]

Pharmacologic therapies for OH have limited efficacy and can be associated with serious side effects, including exacerbation of supine hypertension and ventricular hypertrophy.[8] Therefore, it is important to explore tolerable and effective non-pharmacologic strategies for treatment of AutD. Exercise has potential to enhance autonomic regulation, and this has been investigated in healthy adults. For example, a study of 17 healthy adults showed that regular exercise increases orthostatic tachycardia and cardiovagal baroreceptor sensitivity, which alleviates OH in the early phase after exercise.[13] Further, an aerobic training (stationary bike or treadmill) intervention over 1 year improved orthostatic tolerance in elderly participants in a small study ($n = 8$).[14] In addition, brief exercises can be used to control symptoms of OH. For example, a controlled study, which included 42 older patients, showed that participants who performed leg extension exercises against a resistance band had significantly less reduction in systolic blood pressure compared with a bed rest control group, when given an orthostatic challenge.[15] Despite these results, there are also potential risks of exercise on OH. For example, one study of older adults with OH due to various comorbidities failed to show improvement in orthostatic blood pressure in an 8-week home-based resistance training program group,[16] and another study of patients with long-term autonomic failure had exacerbation of OH with short-term exercise.[17] Therefore, studies of the influence of exercise on AutD in patients with PD are needed to determine whether this might be a meaningful treatment option for this patient group.

Only one randomized controlled trial (RCT) has been published that addressed the effects of exercise on cardiovascular AutD in PD. This study assigned 30 patients with PD to either resistance training or a control group for 12 weeks. PD participants in the training group had improved cardiac sympathetic modulation, as measured by heart rate variability and blood pressure response.[18] No change in parasympathetic modulation was seen. The improvement in sympathetic modulation has potential to help reduce symptoms and rates of cardiovascular morbidity and mortality in patients with PD.[18] Additional studies about the role of exercise in patients with PD are needed to better understand the underlying mechanisms involved in autonomic modulation.

Urinary Dysfunction and Exercise

Bladder dysfunction, including nocturia and increased urgency and frequency of micturition, is one of the most commonly reported symptoms of AutD in PD, affecting up to 93% of patients.[8] These symptoms can inhibit social activity, disrupt sleep, and impair QoL.[8] To our knowledge, no studies to date have investigated the influence of traditional exercise on bladder dysfunction in PD. However, bladder training exercises have been investigated and shown to reduce urinary incontinence in PD.[19] Therefore, more studies are required to establish any role of exercise in treating urinary dysfunction in patients with PD.

GI Dysfunction and Exercise

In patients with PD, autonomic impairment can occur along the entire length of the GI tract, resulting in sialorrhea, dysphagia, impaired gastric motility, constipation, and bowel incontinence.[20] These individual symptoms affect up to 70% of patients with PD.[20] In healthy adults, exercise is thought to improve constipation,[21] but questions remain about effects of exercise on constipation in PD. One randomized, controlled pilot study evaluated the effects of Qigong mediation movement exercises on constipation as a secondary outcome and found persistent benefit of the exercise over time in patients with PD.[22]. Other autonomic symptoms, including urinary and sexual dysfunction, remained unchanged in both groups over time. To our knowledge, no other studies have yet evaluated the influence of exercise or increased physical activity on constipation in patients