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Exercise as a Supplementary Treatment for Parkinson's Disease

Sarah Cortese[1,*], Shamus Menard[1,*], Alexa Ranahan[1,*, †], Emma Reiter[1,*], Borislav Sinik[1,*], Kelly Oiyee To[1,*], Darren E. R. Warburton[1]

1 School of Kinesiology, Faculty of Education, University of British Columbia, Vancouver, BC, Canada V6T1Z4

***** ***These authors are co-first authors making equal contributions to the published work.***

† ***Corresponding author: ranahanalexa@gmail.com***

Abstract

Background: Parkinson's Disease (PD) is a common neurological disorder with debilitating motor and non-motor symptoms. **Purpose:** To explore and understand PD, establish exercise as a treatment option, and determine the optimal evidence-based prescription of exercise based on current evidence. **Methods:** A narrative review of PD literature was conducted and four categories of findings were established. **Results:** Based on the review of literature, established risk factors for PD include personal, genetic, and environmental factors. Clinical tests for postural sway and instability are used for diagnosis. PD is associated with fatigue and falls, leading to further adversities. Treatment options such as medication and surgical procedures can mitigate symptoms but have side effects and do not improve postural stability. Exercise as a co-treatment has been indicated as a potential solution to some limitations. Guidelines include a variety of exercises and a progressive increase in frequency. Optimal benefits arise from aerobic components, amplitude-specific training, and vigorous intensity. **Conclusion:** Exercise is a valid component of PD treatment. Prescription should be individualized and include a variety of exercises, including balance, flexibility, resistance, aerobic, and amplitude-specific exercises performed at a vigorous intensity whenever possible.

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Introduction

Currently, around 55,000 Canadians living in private households have been diagnosed with Parkinson's Disease (PD), and 79% of individuals living with PD are aged 65 or older (Wong, Gilmour, & Ramage-Morin, 2014). Additionally, around 12,500 residents living in long-term residential care facilities are reported with PD (Wong et al., 2014). According to Wooten, Currie, Bovbjery, Lee, & Patrie (2004), males are 1.5 times more likely to develop PD than females. In Canada, PD is the second most common age-related neurodegenerative disorder after Alzheimer's disease, making it a common and serious health concern for many Canadian citizens (Wong et al., 2014).

PD is a progressive disorder associated with the loss of dopamine-producing neurons in a section of the midbrain called the substantia nigra pars compacta (Dauer & Przedborski, 2003). Dopamine plays a pivotal role in controlling several brain functions including motor behaviour, motivation and working memory (Chinta &

Andersen, 2005). Patients with PD have shown degeneration of the nigrostriatal pathway in their brains which affects their ability to control voluntary motor movements (Chinta & Andersen, 2005). Severe dopamine depletion leads to the clinical characteristics of PD, including resting tremor, rigidity (body stiffness), bradykinesia (slowness of movement), akinesia (impairment of voluntary movement), and postural instability (Nussbaum & Ellis, 2003). Non-motor symptoms of PD include sleep disturbances, cognitive and sensory dysfunction, gastrointestinal dysfunction and fatigue, significantly impacting quality of life (Pfeiffer, 2016). Overall, the objective of this narrative review was to explore and understand the risk factors, clinical testing procedures, associated adversities, and current medical treatments associated with PD. Additionally, this review sought to establish if the health benefits associated with exercise can be a helpful co-treatment option for PD, and determine the optimal evidence-based prescription of exercise.

Methods

A literature review of PubMed and MedLine databases was conducted by 6 researchers. The search included articles published from 1996 to November 2019, with keywords "Parkinson's disease", "statistics", "risk factors", "clinical testing", "treatment", and "exercise". Sources were also identified from the reference list of relevant articles and current online resources such as Parkinson Canada and Parkinson's Society of British Columbia. The search was limited to English, peer-reviewed, and published articles only, and abstracts were examined and included if they met the previously listed review objectives. Those that were unrelated to PD were excluded and questionable articles were reviewed and settled through discussion. Based on results from the review, findings were categorized into four sections: risk factors, clinical testing, associated adversities, and treatment.

Results

Risk Factors

PD is a multifaceted disorder and the risk factors vary considerably. Research indicates that PD is likely caused by a combination of genetic and environmental factors. Specifically, mutations of the SNCA, LRRK2, GBA and parkin genes are most commonly found in PD patients; however, the majority of diagnoses are idiopathic (Kalia & Lang, 2015; Koros, Simitsi, & Stefanis, 2017). Furthermore, environmental factors such as pesticide exposure, history of head injury and beta-blocker use have also been linked to the disease (Kalia & Lang, 2015; Noyce et al., 2012). Other risk factors include age, gender, and ethnicity, with age being the greatest risk factor overall (Kalia & Lang, 2015).

Clinical Testing

Three key clinical tests for PD were identified, and all examine postural sway or instability in patients. Retropulsion is considered the gold standard test for postural instability that can be performed within a clinical setting (Nonnekes, Goselink, Weerdesteyn, & Bloem, 2015). Static tests were found to comprise multiple postural stances such as single leg or tandem stance which can easily be performed in a clinic by a practitioner (Smithson, Morris, & Iansek, 1998). Furthermore, it was established that dynamic posturography is a better indicator for PD than static posturography (Ebersbach & Gunkel, 2010).

Associated Adversities

Three primary adversities were found to be associated with PD. Fatigue is the most common, affecting 50% of people with PD (Sicilano et al., 2018). Fatigue may decrease physical activity levels, further increasing the risk of a range of chronic diseases including cardiovascular disease and cancer (Sicilano et al., 2018; Warburton, Nicol, & Bredin, 2006). Fatigue, postural instability, and other symptoms increase the risk of falls three-fold compared to age-matched controls (Bloem, Hausdorff, Visser, & Giladi, 2004). Falls could result in fracture, brain injury, and decreased quality of life (Bloem et al., 2004). Stemming from fatigue and stiffness, people with PD have difficulty turning in bed which results in a supine sleeping position twice as often as healthy controls (Sommerauer et al., 2015). This decreases the quality of sleep and may contribute to overall disease burden (Oksenberg, Silverberg, Arons, & Radwan, 1999; Oksenberg, Khamaysi, & Silverberg, 2001).

Treatment Options

Medication is commonly used to treat motor symptoms of PD. Most medications, such as Levodopa and dopamine agonists, enhance intracerebral dopamine concentration or mimic dopamine action, and are generally successful in treating bradykinesia and rigidity (Kalia & Lang, 2015). Medications also have side effects including wearing off, dyskinesia, nausea, and uncontrolled behaviour (Sethi, 2008).

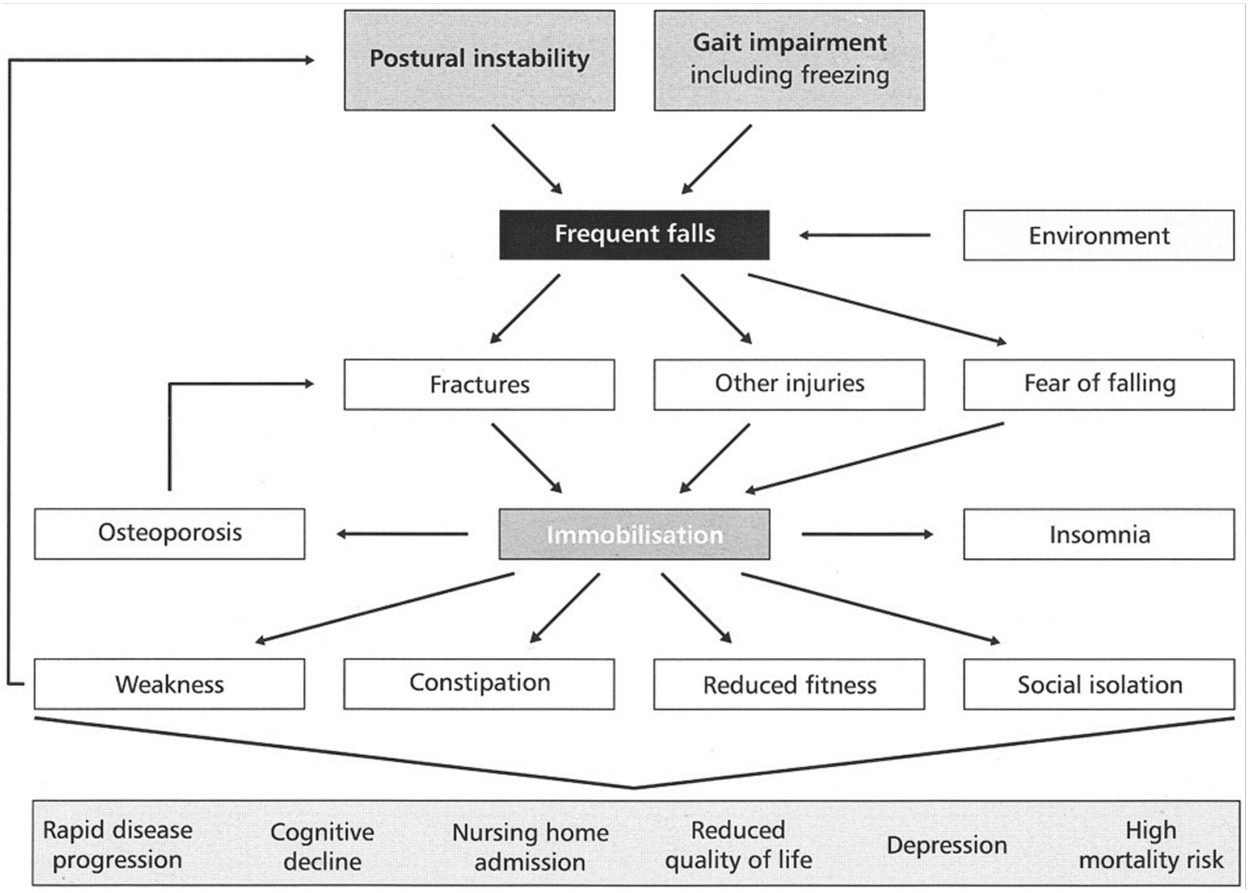
Deep brain stimulation (DBS) is another treatment often utilized in advanced PD, and it can be more effective than medication in improving motor function (Weaver et al., 2009). Commonly, electrodes are placed in the globus pallidus interna or subthalamic nucleus, benefitting tremor, bradykinesia, dyskinesia, rigidity, and quality of life (Ramirez-Zamora & Ostrem, 2018). Less common pedunculopontine nucleus placement potentially reduces gait freezing in some populations (Thevathasan et al., 2018).

It is important to note that postural instability and other comorbidities have minimal response to medical intervention, indicating that pathology extends beyond dopaminergic pathways (Bloem et al., 1996; Sethi, 2008). These symptoms are the most detrimental for injury and mortality (Bennett et al., 1996; Woodford & Walker, 2005), and can lead to a vicious cycle of symptoms (see Figure 1).

Exercise

Research is ongoing, but exercise has been identified as a possible solution to some of the limitations and side effects of medical treatment (Goodwin et al., 2011). For example, current research suggests that early exercise intervention may halt disease progression (Farley, Fox, Ramig, & McFarland, 2008). Additionally, six to thirty-six hours of physiotherapist-led flexibility, balance, and submaximal strength exercise per week has been found to reduce bradykinesia, lower the risk of mild cognitive impairment by increasing gray matter, and increase serum brain derived neurotrophic factor levels, which in turn enhances dopamine synthesis therefore improving dopaminergic transmission (Farley et al., 2008; Goodwin, Richards, Taylor, Taylor, & Campbell, 2008). Current guidelines incorporate a variety of exercises and stress the importance of gradually building to 30-60 min/day to ensure the person's current health-related physical fitness level is considered (Parkinson Canada, 2012).

Figure 1: Vicious cycle and clinical impact due to postural instability and gait impairment in PD. Reprinted from "Falls and freezing of gait in parkinson's disease: A review of two interconnected episodic phenomena," by Bloem, B.R., Hausdorff, J.M., Visser, J.E., & Giladi, N., 2004, *Movement Disorders*, 19(8), 871-884. Copyright 2004 "Movement Disorder Society". Reprinted with permission.



Three key findings related to exercise type and intensity for PD repeatedly arose in the research. The first emphasized the importance of aerobic exercise in comparison to a strength-focused prescription. Silveria, Roy, Intzandt, & Almeida (2018) found aerobic exercise was more effective in improving cognitive domains of people with PD, activating and increasing the volume of brain areas involved in inhibitory control. This was also confirmed in a review by Ahlskog (2011) who noted cardiovascular fitness was often neglected in the current physical therapy treatment for PD, overlooking the benefits of this modality.

Current research highlights the importance of a moderate-to-vigorous level of intensity in relation to patient fitness level. This intensity level varies depending on the type of activity pursued, but generally refers to 50-85% of the individual's maximum heart rate (Riebe et al., 2018). For example, a cycling study found exercise benefits were rate dependent; reductions in PD symptoms were only seen when participants pedalled 35% faster than their voluntary speeds (Shah et. al, 2016). This was supported by

evidence demonstrating motor benefits of exercise were only generalizable to new environments when done at a moderate-to-vigorous intensity (Hirsch, Iyer, & Sanjak, 2016). In addition, Goodwin et al. (2008) suggested higher intensity activity was shown to maximize neuroplasticity, resulting in greater structural adaptations in the brain.

Intensive amplitude-specific training describes the use of exaggerated mannerisms to carry out prescribed movements. This training targets sensory mismatch in PD, where normal movements kinaesthetically feel larger, so patients must utilize intensive amplitude to relearn the required effort for normal movements (Farley et al., 2008). Furthermore, this reduces bradykinesia and improves movement speed and size in daily activities (Farley & Koshland, 2005).

Discussion

This narrative review aimed to explore the prevalence, symptoms, risk factors, associated adversities, and overall treatment options for PD. The results from current literature clearly demonstrate that PD is a common disease affecting many Canadians, and a majority of these individuals are older adults aged 65+ (Wong et al., 2014). PD is a major health concern with serious symptoms and associated adversities that increase the risk of mortality and decrease the quality of life of these individuals (Pfeiffer, 2016; Bloem, Hausdorff, Visser, & Giladi, 2004). These findings highlight the importance of treatment options, which can be stratified into medications, surgical procedures, and co-treatments such as exercise. Current medical interventions, including LevaDopa and DBS, control many symptoms, but side-effects are substantial and postural instability is not solved (Bloem et al., 1996; Sethi, 2008). Exercise has been found to address some of these side effects and limitations, such as improved control of movement, balance, dopamine, and cognitive scores (Goodwin et al., 2011; Farley & Koshland, 2005).

This review aimed to address the lack of usage of exercise as a prescribed co-treatment by providing support for its efficacy and presenting one cumulative prescription based on current findings. According to the research we have compiled, evidence-based, personally prescribed exercise is recommended and should include enjoyable balance, stretching, and strengthening exercises. For the most beneficial results, exercise prescription should include vigorous aerobic exercise, paired with intensive amplitude-specific training. This means individuals with PD should gradually work toward exercise at 50-70% of their maximum heart rate, and large exaggerated movements should be incorporated into exercise prescription. Overall, the extensive benefits that exercise can offer for people with PD make exercise a necessary addition to current medical treatments.

Conclusion

PD is a common disease associated with serious symptoms and comorbidities that affects a large proportion of the older Canadian population. While current medications and surgeries can help, exercise is a promising co-treatment to reduce side-effects and unresolved symptoms such as postural instability. The optimal prescription of exercise should be specific to the individual's current fitness levels and involve a variety of enjoyable activities performed at a moderate-to-vigorous intensity with large, exaggerated movements.

Authors' Qualifications

The authors' qualifications are as follows: Sarah Cortese, BKin; Shamus Menard, BKin; Alexa Ranahan, BKin; Emma Reiter, BKin; Borislav Sinik, BKin (C); Kelly Oiyee To, BKin (C); Darren E. R. Warburton MSc, PhD, HFFC CEP

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