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Review Article

Exercise Benefits for Progressive Supranuclear Palsy: A Narrative Review

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Abstract

Progressive Supranuclear Palsy (PSP) is a rare neurodegenerative disease characterized by the accumulation of 4R-tau protein aggregates in the cortex, brainstem and basal ganglia. The clinical ramifications are variable but often include a combination of vertical gaze palsy, axial rigidity, cognitive impairment and postural instability leading to frequent falls. Currently, PSP has no cure, and available pharmacological treatments offer limited benefit. Exercise-based therapy has emerged as a promising supportive approach for managing the functional decline in PSP. This narrative review summarizes the current evidence regarding the benefits of exercise interventions for individuals with PSP. A literature search was conducted using different medical databases to identify studies examining physiotherapy, rehabilitation, and structured exercise programs in PSP. The findings suggest that exercise interventions targeting balance, gait, and strength may improve motor performance, reduce fall risk, and enhance quality of life. However, evidence remains limited by small sample sizes, differing methodologies, and short follow-up. Despite these limitations, exercise appears to be a safe and valuable adjunct therapy for patients. Further research is needed to establish standardized exercise protocols and determine long-term outcomes.

Introduction

Progressive Supranuclear Palsy (PSP) is a rare neurodegenerative disorder characterized by 4R-tau accumulation in brain cells within the cerebral cortex, brainstem, and basal ganglia [1]. Patients typically present at an average age of 65 years and exhibit some symptoms similar to those of Parkinson's disease. However, unlike Parkinson's disease patients, PSP patients typically do not respond to dopaminergic medications and endure rapid disease progression, with a median survival of 6.8-8 years [2]. Each individual patient's symptoms can vary but most experience a combination of progressive vertical gaze palsy, axial rigidity, cognitive impairment, and gait imbalance leading to frequent falls [2]. The efficacy of pharmacological therapies for PSP is limited. Some patients may experience modest improvement in their axial rigidity from dopaminergic medications, but the effect, if present, is typically short-lived [3]. Other agents typically used in Parkinson's disease, including monoamine oxidase type B inhibitors, amantadine, or dopamine agonists, provide little to no benefit in PSP. Currently, there are no disease modifying agents, and deep brain stimulation has not demonstrated efficacy [4]. As a result, many multidisciplinary teams caring for patients with PSP mainly focus on the prevention of complications, including falls or aspiration. Additionally, they emphasize supportive and rehabilitative strategies aimed at preserving function and improving quality of life [5]. Exercise therapy has demonstrated benefits in preserving function and improving quality of life in a variety of neurodegenerative disorders, particularly Parkinson's disease, and may offer similar advantages in PSP [6]. This narrative review aims to evaluate current evidence regarding the efficacy of exercise interventions in PSP and to discuss clinical implications and future research directions.

Review Methodology

A narrative literature review was conducted using PubMed, Google Scholar, and Scopus databases. Search terms included "progressive supranuclear palsy," "exercise," "physiotherapy," "rehabilitation," "balance training," and "gait training." Peer-reviewed articles published in English were included and the references searched for additional relevant articles. Studies included randomized controlled trials, observational studies, case series, and relevant reviews. Given the rarity of PSP, exercise intervention studies for cohorts which combined PSP and related atypical parkinsonian disorders (multiple system atrophy and corticobasal degeneration) were included where relevant.

Pathophysiological Basis for Exercise in PSP

The neuropathology of PSP involves degeneration of brain regions critical for postural control (i.e., cerebellum), motor planning (i.e., basal ganglia), eye movement (i.e., brainstem) and cognition (i.e., cerebral cortex) [7]. Dysfunction of the Pedunculo Pontine Nucleus (PPN) and impaired vestibular integration also contributes to balance dysfunction and subsequent falls [8]. Therefore, therapies that can slow degeneration or aid in regeneration or neuroplasticity may be beneficial for patients with PSP. Exercise has been demonstrated in patients with Parkinson's disease and animal models of the disease to i) increase neuroplasticity, ii) be neuroprotective, and iii) improve overall brain health [9]. Although the literature on PSP and exercise is much smaller, the same principles may apply. In particular, increased neuroplasticity (e.g., synaptogenesis, neuronal sprouting, neurogenesis and potentiation of synaptic strength) could be beneficial for patients with PSP and may strengthen residual motor pathways. Additionally, neuroprotective effects of exercise could slow the rate of disease progression. One of the complications of PSP is muscle mass loss, which progresses more rapidly than in Parkinson's disease, likely due to more rapid loss of mobility [10]. Resistance and balance training may counteract this secondary deconditioning. Another disabling feature of PSP is its associated fatigue [11]. Aerobic exercise, designed to boost cardiovascular fitness, may reduce this symptom in PSP.



Specific Exercise Interventions in PSP

Gait and balance training

Balance-focused physiotherapy is central to PSP rehabilitation since falls (particularly backwards) are common in the condition. Several non-controlled trials have shown improved balance in small cohorts of PSP patients using different balance training techniques [12-14]. This physiotherapy can also be used in combinations with other therapies, including eye movement training.

Treadmill training

Treadmill training, with or without body support for added safety, is a common therapeutic modality in PSP. Suteerawattananon et al. [15] were the first to report the benefit of supported treadmill training on balance in PSP. Clerici et al. [16] reported that balance, measured by the Berg Balance Scale, could be improved in patients with PSP following either treadmill training with visual cues and auditory feedback or robot-assisted walking. Steffen et al [17] reported a patient with PSP who had stable balance and no falls during a decade of treadmill training.

Strength training

Proximal muscle weakness is a prominent feature of PSP [10]. A systematic review of 13 randomized control trials studying strength training in Parkinson's disease showed improvements in quality of life and physical parameters [18]. No similar studies have been conducted in patients with PSP. Although it is possible that patients with PSP may also benefit from strength training, evidence is currently lacking.

Aerobic exercise

Aerobic exercise, including walking programs, stationary cycling, and elliptical trainers, may improve endurance and reduce fatigue in PSP [19]. Due to safety concerns, particularly fall risk and autonomic dysfunction, aerobic training should be individualized and closely monitored.

Other non-exercise interventions

Small, non-control, observational trials of robot assisted gait training [20], use of Xbox Kinect virtual gaming system [21] and transcranial magnetic stimulation [22] have reported benefits in balance for patients with PSP. Similar trials of music-cued movements [23] and auditory-biofeedback [24] have also reported benefits on balance and gait.

Discussion

A recurring theme appears in the literature on exercise for patients with PSP: individual studies offer promising results, but systematic reviews are less optimistic. Twelve individual studies discussed in a previous narrative review of this topic in 2018 all reported that rehabilitation for patients with PSP improved balance and gait with reduced falls [25]. In a later review in 2023, however, Dale et al. [26] found no robust evidence for rehabilitation in PSP. In the latest systematic review on this topic in 2020, Slade et al. [19] reviewed eleven studies and concluded that robust evidence was not found for exercise in patients with PSP. The nature of the illness makes it difficult to determine the effectiveness of exercises on the symptoms of PSP. The condition is rare and thus large trials with the power to demonstrate statistical evidence are unlikely without multicentre collaboration. Any multicentre trial would require a standardized exercise regime and yet no one protocol has emerged from the previous two decades of research in this field. Each patient can have different symptoms impacting their quality of life and many researchers have emphasized that therapy needs to be individualized not standardized, thus it would be difficult to construct one exercise protocol that would benefit all patients. The rapidity of neurological decline also makes the impact of any intervention temporary. Even with all these caveats, current evidence suggests that exercise interventions may confer modest but meaningful benefits in individuals with PSP. Exercise appears to be safe and well tolerated when appropriately supervised. The current literature on exercise in PSP is limited by small sample sizes, heterogeneous study designs, and lack of long-term follow-up. Variability

in exercise protocols and outcome measures complicates comparison between studies. Additionally, the progressive and heterogeneous clinical manifestations of PSP also make the assessment of outcomes for any exercise therapy difficult.

Future Directions

Current research in PSP is focused on both the early detection of the disorder and its pharmacological treatment. Early detection strategies include MRI, PET and biomarker analysis [1]. Pharmacological therapies include microtubule-stabilizing agents, tau-directed monoclonal antibodies and gene therapy [1]. Future research to evaluate the benefits of exercise in PSP will require multicenter randomized controlled trials [27] with standardized exercise protocols and clinically meaningful outcome measures. Long-term studies are also needed to assess sustainability of any benefits.

Conclusion

Progressive supranuclear palsy is a debilitating neurodegenerative disorder with limited pharmacological treatment options. Evidence from this narrative review suggests that exercise interventions may improve balance, gait and quality of life in individuals with PSP. Although current evidence is limited, exercise represents a valuable adjunct therapy within multidisciplinary care. Further research is required to establish best practices and optimize outcomes.

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