



Progressive Supranuclear Palsy-a Mirror Image of Parkinson's Disease, A Literature Review of Rehabilitation Strategies

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Progressive supranuclear palsy (PSP) is a rare neurodegenerative disease which mimic similar to Parkinsonism. PSP advances much quicker than in PD yet no effective medication or therapy to manage PSP available. This literature review aimed to discover the recent advances in the physical therapy treatment options for PSP. Databases such as PubMed, Elsevier and SAGE journal searched for both published and unpublished studies. Last 10-year studies were included in this review. Limited clinical trial conducted in this population due to which a structured protocol or rehabilitation strategies is missing for this condition. Balance exercise and gait training showed potential benefit and music-cued walking demonstrated participant's satisfaction.

Keywords: *Progressive supranuclear palsy; atypical parkinsonism; steele richardson-olszewski syndrome; rehabilitation; physiotherapy.*

1. INTRODUCTION

Progressive supranuclear palsy (PSP) or Steele Richardson-Olszewski syndrome, is a rare

neurodegenerative disease first described in 1963 by John Steele, J clivord Richardson and Jerzy Olszewski. [1,2] Which is earlier classified among atypical Parkinsonism, that is often

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misdiagnosed as Parkinson's disease due to its similar presentation. Supranuclear vertical gaze palsy, frequent falls, rapid deterioration in balance, greater axial rigidity than appendicular rigidity, speech disturbance, fatigue and cognitive impairment are the characteristic features of this fast-progressing condition. Restriction of vertical gaze with preserved oculocephalic reflexes is the most specific and characteristic feature of PSP. Based on the clinical presentation PSP clinical stages are divided into three, early stage, middle and late stage [3–6].

PSP Affecting around a million people worldwide of 5–6 cases per 100,000 [7]. Patients with PSP are typically 3 years from their first symptom before they get diagnosed. Based on one study in a southern Italian population, 7.1 year is the mean survival of PSP and a median survival of between 5.3 and 10.2 years since the onset of symptom according to 2017 meta-analysis [8,9].

Progressive supranuclear palsy is a *tau-opathy*. Tau, present in the central nervous system, is a Microtubule-associated protein (MAPS) as well as a cytosolic protein, primarily present in axons and participate in anterograde axonal transport. [11,12] Under normal physiological circumstances it facilitates microtubule assembly and stabilization of microtubule. Tau protein may get altered in certain pathological conditions, through phosphorylation, which results in the production of aberrant aggregates or a diverse expression of some of its isoforms that are toxic to neurons. This process is known as *tauopathies* which provoke pathological effects in PSP. [12-14].

The build-up of tau protein and neuropil threads is seen in PSP, mainly in the basal ganglia structures like pallidum, substantia nigra, subthalamic nucleus, red nucleus, etc., furthermore multiple subcortical and brain stem nuclei have been reported with marked neuronal degeneration and gliosis. [15,16] Evidence from MR imaging and Pathologic findings specify that the Atrophy of the midbrain and the superior cerebellar peduncles (SCPS) is the distinguishing pathologic finding PSP. Furthermore, mutations in MAPT have been pinpointed in both sporadic and familial PSP condition. MAPT gene found to be producing a type of familial frontotemporal lobar degeneration with tauopathy. [17-20].

1.1 The Diagnosis of PSP

The -primary indicators of PSP are postural instability that is early in onset and abnormal eye movement, remarkably vertical supranuclear ophthalmoplegia (SNO) or slow of downward saccades, [21-23].

However, Presently the most accepted criteria for the diagnosis of PSP are established by the Society for Progressive Supranuclear Palsy (SPSP) and National Institute of Neurological Disorders and Stroke (NINDS). The diagnosis is mainly depended on clinical findings and these criteria were redefined in 2003. The patients may be classified into three categories (possible, probable, or definite) PSP [24,25] (Table-1).

Few of the recent literature identified probable differentiating features between PSP and Parkinson. Patients exhibit distinct gait patterns in early-stage PD and PSP, which indicating different underlying pathophysiological mechanisms. Patients with PSP revealed decreased cadence and velocity, reduced step and cycle length, and a long duration of gait cycle. Furthermore, few of the clinical presentations are opposite to the presentation of Parkinson disease [26,27]. PSP patients having symmetrical limb signs, no tremor, and axial rigidity which is exclusively seen in the trunk and neck, and less rigidity noted in the periphery. [28] In addition laboratory tests and imaging exams can be used rule out other pathologies to narrow down the diagnosis [29].

Since the preliminary clinical features appear like PD, [30,31] with the wrong diagnosis several patients are referred for rehabilitation services. PSP advances much faster than in PD yet no effective medication or cure to manage PSP available. Physical therapists must be aware of the peculiarity this condition to guarantee that the patients are diagnosed and rehabilitated appropriately however there is no strong existing literature evidence backing its effectiveness in spite of the demand for rehabilitation in this population. To address this existing fact, this literature review aimed to discover the recent advances in the physical therapy treatment options for PSP and to make proposals for the plan of exercise programmes.

Table 1. Inclusion criteria and diagnostic categories

Inclusion Criteria	Diagnostic Categories	
Gradually progressive disorder Age at onset at 40 or later	Possible	<ul style="list-style-type: none"> ○ Instability of Postural with falls < 1 year disease onset ○ Vertical supranuclear palsy OR ○ vertical saccades Slowing
	Probable	<ul style="list-style-type: none"> ○ Prominent postural instability with falls within first year of disease onset ○ Vertical supranuclear palsy
	Definite	<ul style="list-style-type: none"> ○ Histopathologic confirmation at autopsy confirming possible or probable diagnosis
Exclusion Criteria	<ul style="list-style-type: none"> ○ history of Recent encephalitis ○ Alien limb syndrome ○ Sensory deficits (Cortical) ○ Focal atrophy (frontal or temporoparietal) ○ Hallucinations or delusions unrelated to dopaminergic therapy ○ Alzheimer type Cortical dementia ○ Prominent early cerebellar symptoms or unexpected dysautonomia ○ Evidence of other diseases that could explain the clinical features 	

(Table-1) * [25] Litvan I, Bhatia KP, Burn DJ, et al. SIC task force appraisal of clinical diagnostic criteria for parkinsonian disorders. *Mov Disord.* 2003; 18:467– 486

2. METHODOLOGY

In order to gain a better insight into the effectiveness of exercise for the improvement of the patient with PSP, various previously published articles were studied thoroughly. The following databases were searched for both published and unpublished studies- PubMed, Elsevier and SAGE journal. Last 10-year studies were included.

2.1 Keywords Used

Progressive supranuclear palsy, atypical parkinsonism rehabilitation, physical therapy, exercise, physiotherapy.

2.2 Inclusion Criteria

Systematic review, metastatic analysis, clinical trial, randomized control trail, year 2011-2021.

2.3 Exclusion Criteria

Parkinson's Disease, review, Manuscript, Books and Documents

3. RESULTS

From a yield of numerous studies, finally only 7 studies were selected depending upon the inclusion and exclusion criteria.

4. DISCUSSION

Progressive supranuclear palsy is a neurological condition which is similar and misdiagnosed mostly as Parkinson's diseases. Even though many are affected because to this condition fewer research work is conducted in this field due to the misdiagnosis or obvious unawareness from the researchers. From the last 10-year search results we could barely find few articles which has done clinical trial in this population. Mostly we could find case report and case series during the search strategies.

From this literature review we could identify 7 articles, out of which 2 are systematic review and 6 were experimental study.

Table 2. Literature reviews data set

Author/ Year	Aim/ Objective	Methodology	Conclusion	References
Anna D. Hohler (2012)	Movement disorders program effectiveness in a atypical parkinsonism patients who respond poorly to pharmacologic intervention	91 Atypical Parkinsonism (AP) ;(4-PSP) Inpatient movement disorders program: - Speech, Occupational and Physical therapy Daily3 hours, 5 to 7 days/week, Medications changes based on daily observation and data.	Improvements in total FIM, motor FIM, cognitive FIM, TMW, TUG, BBS, and left and right FT. Among patients who received rehabilitation only, without changes to their medication regimens, statistically significant improvement seen.	32
Tilley, E., et al, 2016 (Systematic review)	Symptomatic management of PSP using physical, occupational and speech therapy interventions and to find the efficacy of the same	Quantitative study designs Search duration-1996–2014 Participants- PSP patients Aged -over 40 years. Studies which examining any kind of therapy that addressed movement, visual system, swallowing, cognition and communication.	In people affected by PSP physiotherapy rehabilitation programs could improve gaze control balance & gait (velocity, cadence, step length and step width)	33
Clerici I, et al (2017)	To assess the use of the Lokomat(robotic device) in PSP patients	24 PSP patients. 12 subjects trained for 4-week using motor-cognitive and goal-based rehabilitation treatment (MIRT) with use of treadmill, the treadmill-plus (MIRT group). Another 12 subjects undertook training by replacing the treadmill-plus with Lokomat® (MIRT-Lokomat group) Outcome measure: PSP Rating Scale (PSPRS), PSPRS-gait, BBS and 6MWT	With specific aerobic, intensive, motor-cognitive, goal-based and multidisciplinary rehabilitation protocol the Total PSPRS, PSPRS-gait, BBS and 6MWT scores improved with decrease in the number of falls. Use of Lokomat, compared to the treadmill-plus training, does not add any further benefit	34
Wittwer, J. E. 2018	To assess the use and effectiveness of supervised, home-based, music-cued training to improve gait speed of gait and stability in PSP Patients	For four weeks, per week two training sessions, conducted by physiotherapists. Training were done at home, each session consisted of a range of activities such as standing or walking. Training was with and without auditory cues. Music played using a portable player which consisting of rhythmic auditory cues, by choosing available	with the provision of caregivers, gait training with music-cue can offer a feasible method to improving disorders of gait. Training with music is fetching and pleasurable which can help adherence to rehabilitation.	35

Author/ Year	Aim/ Objective	Methodology	Conclusion	References
Slade, S. et al 2019 Systematic review	To assess the efficacy of exercise and physical activity interventions in the PSP	commercial tracks. Spatiotemporal gait measures were recorded using an 8 m long GAITRite® mat. Cochrane, EMBASE, AMED, CINAHL, MEDLINE, PEDro, PsycINFO, PubMed and SportDiscus were searched until 18 August 2019. Cochrane guidelines informed review methods Studies included - on Progressive Supranuclear Palsy	11 studies included. (3 RCT,2 quasi-experimental studies, 4 case studies, 1 case series and 1 cohort study) None of the PSP studies sufficiently defined exercise rudiments that would allow exact imitation of the interventions In early PSP patients- Weight-supported treadmill training, music-cued movement rehabilitation and robotic-assisted gait training may be beneficial	36
Yamato et al (2019)	To elucidate the mid-term results of spinal fusion surgery in patients with Atypical Parkinsonism.	Patients who underwent extensive fusion surgery > 5 years prior were included. 22 patients (2 patients with PSP) ADL over time were assessed.	moderate short-term benefits were seen in the outcomes The patients' conditions deteriorated because of complications within 3 years and deteriorating of PD over 3 years post- surgery.	37
Valero-Cabré, A (2019)	To discover whether in patients with progressive supranuclear palsy (PSP) transcranial direct current stimulation (tDCS) over the dorsolateral prefrontal cortex (DLPFC) can improve language capacities	12 subjects diagnosed case of PSP. 3 sessions. Measured the capacity to enhance the left DLPFC via left-anodal (excitatory) and right-cathodal (inhibitory) tDCS. Comparison with sham tDCS Tasks_assessing letter fluency task & category judgment task taken instantly pre- and post-the tDCS sessions	tDCS-driven language improvement in PSP.	38

- 1) A study done by Anna D Hohler in patients with AP to find the effectiveness of an inpatient movement disorders program in 2012. 91 patients with AP were participated in the study in which 4 were PSP patients. The program consisted of speech, occupational and physical therapy for 3 hours per day, per week 5 to 7 days. Pharmacologic modifications were also done based on daily observation and data. Functional Independence Measure (FIM), motor FIM, cognitive FIM, timed up and go (TUG), Berg Balance Scale (BBS) were used as outcome measures. The found positive results in total FIM, motor FIM, cognitive FIM, TUG, BBS, and left and right ft.
- 2) Erica Tilley done a systematic review in 2016 on the effectiveness of physical, occupational and speech therapy interventions in the symptomatic management of PSP. From the time of development of the NINDS and the sPSP criteria in 1996–2014, all types of quantitative study designs published were included. Study added in which participants with PSP, aged over 40 years, who tested the effect of allied health therapy on vision, swallowing, mobility and other difficulties.

6 studies were included in the review. All six studies utilized different physiotherapy interventions such as a dynamic antigavity postural system (SPAD) and a vibration sound system (VISS) rehabilitation program, audio feedback during posture and balance training, balance and eye movement training, walking with robotic assistance and treadmill training with body weight support. Total of 4 case series, case study with single participant. One study examined a non-invasive brain stimulation therapy using rTMS. Five studies used interventions currently considered within the scope of practice for physiotherapy. The program consist SPAD and VISS treatments was conducted for 2 months, three sessions per week with each session of 20 minutes. Patients encouraged to walk by suspending the patient weights using mechanical vertical traction system and made to walk on a treadmill.

In another case series conducted in 2010, the intervention was done for three times in a week with 45 minutes in each session. A total duration of 6 weeks to improve balance by balance and

posture exercises with the help of audio-biofeedback. A sensor with audio biofeedback system, worn near the center of mass intended to measure acceleration of trunk along the sagittal axis and frontal axes.

Sale et al done a case series in five PSP patients underwent 45 minutes rehabilitation using robot-assisted walking device, weekly five times for 1 month, in comparison with baseline measurements. The participants trained floor walking (5–30 minutes) followed by repetitive simulated stair climbing (5–10 min) up and down.

Effectiveness of repetitive transcranial magnetic stimulation in improving gait/midline symptoms was the objective of the study done by Santens et al in 2009. The rTMS procedure comprised of 10hz stimulation for 5 s, with 55 s rest was given after that. A repetition of 20 times per session, 5 consecutive days undertaken by 6 participants. Baseline measurements was the comparator.

- 3) In 2017 Ilaria Clerici done a study in 24 PSP patients to assess the effect robotic device lokomat training in comparison with treadmill training through visual cues and auditory feedbacks. They enrolled a total of 24 PSP patients, out of which twelve subjects underwent a 1-month multidisciplinary intensive rehabilitation treatment (MIRT) exploiting the use of the treadmill-plus and the remaining 12 participants underwent the same treatment, however replacing the treadmill-plus with lokomat.

PSP rating scale (PSPRs) were used as primary outcome in addition berg balance scale (BBS), six minutes walking test (6mwt) and the number of falls were also taken as a secondary outcome measure. Total of 24 patients assigned into two group of 12 each. Both groups underwent 4 weeks training. Group 1 was MIRT group they underwent a treadmill training combined with visual cues and auditory feedbacks (treadmill-plus). On the other hand group 2, the MIRT-lokomat group, underwent MIRT replacing the treadmill-plus with lokomat. MIRT includes aerobic, multidisciplinary, intensive, motor-cognitive and goal-based rehabilitation treatment. It 4 sessions/ day for 5 days/week. MIRT group underwent 20-minutes treadmill-plus training /day 5 times a week. Using gait trainer 3 biodex, speed of treadmill increased maximum of 2.5 km/h from an initial 1.0±1.5 km/h. Visual cues and auditory feedbacks were used during the

training. Lokomat1, a gait robot, is a driven-gait orthosis that permits gait on a treadmill by simulating physiological stride pattern of the human. The study concluded with the following findings. Improvement of BBS score along with reduction in the fall incidences. Indicating both MIRT and the MIRT-lokomat improves balance dysfunction. In addition, 6mwt and PSPrs-gait score improved, suggesting that in PSP patient's treadmill-plus and lokomat, used in the context of MIRT, provided benefits. MIRT-lokomat group achieved remarkable functional improvements. Since it provides proprioceptive and exteroceptive feedbacks which allow patients walk repetitively. Furthermore, the MIRT group shown better PSPrs-limb score with trunk muscles active involvement. Author concluded that lokomat does not add additional benefits within a protocol like MIRT.

4) Wittwer, j. E. et al done a study to improve gait speed and stability in PSP patients using supervised, home-based, music-cued training to improve gait speed and stability in PSP patients. Experienced physiotherapists over 4 weeks conducted one-hour training two times in a week, with and without auditory cues which included standing or walking activities. Using an 8m long gaitrite® mat spatiotemporal gait measures were documented. At self-selected comfortable pace participants walked without cues. The study results exhibited that out of five PSP patients two patients walked with normal speed and low gait unevenness. The author concluded that with the support of caregiver, home program with music cued gait training can improve gait issues.

5) In 2019, Susan C. et al Published a systematic review in PSP to evaluate the effect of exercise and physical activity interventions. All the study until 2018 was added. 11 studies were included with a total number of 99 patients. Treadmill training with harness support, robot-assisted gait rehabilitation and auditory-cued motor training found to have primary evidence as a useful rehabilitation in the early stages.

Total of 3 RCT were included in the systematic review. One was using locomote for gait training for 4weeks. Other two was exercises training which has sit-to-stand and stand-to-sit practice on a chair, tandem stance practice with eyes open and closed, marching in place while turning 360° for 1hour every day for 3 days in a week in a 4 weeks program. Most of the other studies were cohort and case study which included training such as posture improvement strategies

using weighted vest, robot-assisted walking for 4 weeks, weight relieving harness for walking (SPAD) plus vibration sensory stimulation (VISS) and dynamic exercises such as sitting, standing, transfers, sway, reaching or stepping one direction and multi direction stepping for 6 weeks. Different complex equipment's was used for the intervention however, strength training and physical activity having positive benefits in older adults and they are well established for general health also.

6) Yamato et al done a clinical trial in 2019 in patients with Parkinson's disease (PD) or atypical parkinsonism, to clarify the mid-term results of extensive spinal fusion surgery. Out of 22 Parkinson patients 2 were PSP patients. Patients who underwent extensive fusion surgery more than 5 years prior were included. Criteria assessed was perioperative and mechanical complications, surgical and radiographic parameters and indoor ADL over time. Short term outcome was good; yet, the patients' conditions worsened due to complications within 3 years and due to the disease progression.

7) To discover whether in PSP patient's language capacities can be improved by transcranial direct current stimulation (tDCS) over the dorsolateral prefrontal cortex (DLPFC) Valero-cabré, et al did a study in 2019. 12 patients were participated in the study. Compared to sham tDCS the capacity to boost the left DLPFC via left-anodal (excitatory) and right-cathodal (inhibitory) tDCS was higher. Before and after the tDCS, Letter fluency task and category judgment task were tested immediately. Contrasting poststimulation vs pre-stimulation performance across tDCS conditions revealed language improvement in the category judgment task.

5. CONCLUSION

PSP is a progressive neurological disorder, which misdiagnosed mostly as Parkinson disease. We could find there is limited clinical trial happening in this population due to which a structured protocol or rehabilitation strategies is missing in this population. From the article we analysed the systematic review available on this condition are based on the Cohort and case studies only. Very minimal RCT are conducted due to which drawing a conclusion is meaningless. However, Balance exercise and gait training showed potential benefit and music-cued walking demonstrated participant's

satisfaction. walking speed and quality were associated with music-cued movement rehabilitation, weight-supported treadmill training and robotic gait training.

6. FUTURE IMPLICATION

- Clinical trials with large sample size in the population must be conducted to throw light upon the effects of physical therapy on PSP patients.
- Should also try the rehabilitation benefits in different stages of PSP

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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