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# The role of the rehabilitation in subjects with PSP: a narrative review

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## Abstract

Progressive Supranuclear Palsy (PSP) is a progressive neurodegenerative disorder due to the deposition of abnormal proteins in neurons of the basal ganglia that limit motor ability producing disability and reduced quality of life. So far, no pharmacologic therapy has been developed and the treatment remains symptomatic. The aim of the present study was to investigate systematically literature, and to determine the types and effects of rehabilitative interventions. A search of all studies was conducted in MEDLINE/PubMed, the Cochrane Central Register of Controlled Trials, CINAHL and EMBASE. Twelve studies were individuated including 6 case reports, 3 case series, one case control, one quasi-RT crossover study and one RCT, with 88 patients investigated overall. Rehabilitative interventions varied in type, number, frequency and duration of sessions. The most commonly used clinical measures were Progressive Supranuclear Palsy-Rating Scale (PSP-RS) and Unified Parkinson's Disease Rating Scale (UPDRS). Physical exercises were the main rehabilitative strategy but were associated with other interventions and rehabilitative devices, in particular treadmill and robot-assisted gait training. All studies showed an improvement of balance and gait impairment with a reduction of falls after rehabilitation treatment. Due to poor methodological quality and the variability of rehabilitative approach with different and variable strategies, there was no evidence of the effectiveness of a specific rehabilitation intervention in PSP. Despite this finding, rehabilitation might improve balance and gait, thereby reducing falls in PSP subjects.



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**Keywords: Progressive supranuclear palsy; gait; balance; rehabilitation; review**

## Introduction

Progressive supranuclear palsy (PSP) is a neurodegenerative disorder that was described over 50 years ago by Steele, Richardson and Olszewsky [1]. The onset is after 60 years of age and the mean survival from diagnosis is reported from 5.3 to 10.2 years. The clinical hallmark of PSP is the vertical supranuclear gaze palsy, but the presence of Parkinsonism signs such as bradykinesia, resting tremor and muscular rigidity, led PSP to be considered an atypical Parkinsonism syndrome (APS) which also includes corticobasal degeneration (CBD), multiple system atrophy and dementia with Lewy bodies [2]. PSP is the most common APS, even if the incidence is typical of a rare disease, with a rate of 4-5/100,000 persons. Based on neuropathology features, PSP is defined as "taupathy", a neurodegenerative disorder due to the deposition of hyperphosphorylated tau proteins predominantly involving isoforms with four microtubule-binding repeats (4R-tau) in neurons of the basal ganglia, brain stem, dentate, and oculomotor nuclei [3-4]. The dysfunction of the involved cerebral regions produces typical clinical Parkinsonism features that can exhibit heterogeneous clinical pictures. Indeed, different phenotypes have been described that could be due to differences in the topographical distribution of tau pathology and/or differences in the density of tau deposition in the specific affected cerebral areas [5-6]. Among phenotypes, the most common is the classic PSP or Richardson's variant characterized by early gait instability, falls, supranuclear gaze palsy, axial rigidity, dysarthria, dysphagia and progressive dementia. Despite half a century from the first description, PSP diagnoses remain "probable" or "possible" based on the criteria of the National Institute of Neurological Disorders and Stroke/Society (NINDS) for PSP [7]. Recently, three levels of certainty: "probable", "possible", and "suggestive" PSP have been proposed on the basis of four functional domains including ocular motor dysfunction, postural instability, akinesia, and cognitive dysfunction, and by specific combinations of these clinical features [8], but a definite diagnosis is only possible post-mortem by neuropathological findings. PSP shares clinical features with PD, but it does not respond to L-dopa therapy. Despite new advances in neuropathology, neuroimaging [9] and prognosis, no pharmacologic therapy has been developed that modifies the pathophysiology of tau-associated neurodegeneration, preventing or improving neurological impairments and the treatment remains symptomatic. So far, experimental pharmacologic strategies by inhibitors of glycogen synthase kinase 3 (GSK-3) that has a key role in tau hyperphosphorylation, as well as substances stabilising microtubules (davunetide) have been ineffective [10-12]. A growing number of studies have reported the effectiveness of rehabilitation in Parkinson Disease (PD), in particular the effect of physical exercises [13-15], and weight support treadmill training [16] in improving gait parameters and balance. Little has been published about the rehabilitation interventions in PSP and whether rehabilitative interventions might produce benefit is unclear. The aim of the present study was to systematically review the overall rehabilitation studies in PSP, and to determine types of the rehabilitative interventions and the effect of rehabilitation on the functional outcome of subjects suffering from PSP.

**Literature Search Strategy**

A search of all studies was conducted in MEDLINE/PubMed, the Cochrane Central Register of Controlled Trials, CINAHL and EMBASE. The search included studies published from January 1966 to May 2017. Furthermore, ongoing similar researches were ascertained through the PROSPERO database. No search on the present topic was detected. Search terms varied slightly across databases but included: “PSP”, “progressive supranuclear palsy”, “Parkinson plus”, “atypical parkinsonism”, and “gaze palsy” as either MeSH terms, keywords, or subject headings. Related terms were combined using the Boolean “OR” and “AND” with the terms “rehabilitation”, “gait”, “posture”, “balance”, and “gaze palsy”. An example of the search strategy applied in MEDLINE/PubMed can be viewed in the supplemental data (Appendix).

Given the incidence rate and limited therapeutic management of PSP, it was hypothesized that few studies were published concerning rehabilitation; therefore, all studies were considered including case reports, case series, case controls and randomized trials. Unpublished, non-peer-reviewed sources, such as conference abstracts, were not included. Studies were eligible only if they were published in English. Data related to study design, duration and frequency of the intervention program, type of the control, sample size, and outcome measures were extracted for qualitative analysis in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (PRISMA).

## Results

Thirteen studies were individuated, including 6 case reports [17, 18, 19, 20, 21, 22], 3 case series [23-25], one case control study [26], one randomized control trial (RCT) [27] and 2 quasi-RT crossover studies [28-29]. Both quasi-RTs described the same sample of subjects. Likewise, 2 case reports [20-21] described the same subject, since one of those reported the long-term follow-up, both studies were included leaving 12 studies in the analysis (Figure 1). Studies varied in size, rehabilitative interventions and outcome measures, and most had poor methodological quality. Overall, 88 participants were investigated. In case series studies, a number of patients ranging from 5 to 10 patients was enrolled. Likewise, small samples ranging from 16 to 24 patients were enrolled in quasi-RT and RCT.

### *Functional evaluation and measures*

Despite the small number of studies, a huge variety of clinical measures and instruments were used in evaluating the outcomes. The measures widely varied across studies as 16 tools (11 clinical and 5 instrumentals) were employed. Clinical measures in assessing the balance were: Berg Balance Scale (BBS) [19, 23, 20, 27, 22], activities-specific balance confidence (ABC), sharpened Romberg test [20-21], Functional Reach Test (FRT) [20-21], and 360° degree turns [19]. Likewise, several clinical measures were used in assessing the walk: “Timed Up & Go” test (TUG) [19, 23, 20, 28, 22], six-minute walking test (6-MWT) [20, 27 22, 29], ten-metre walk test (10-WMT) [22], 15.2-metre walk [19], 8-foot (2.4-metres) walk test [28], and five step test [19]. Furthermore, balance and gait parameters were assessed by variable instruments including audio-biofeedback (ABF) device [23], baropodometry static and dynamic [24], and computerized systems: GAITRite system [19], 3D-Gait analysis (3D-GA), [25], force platforms [25].

Global functionality and motor modification were assessed in 8 studies using only 2 scales: Progressive Supranuclear Palsy-Rating Scale (PSP-RS), which was used in 4 studies [28, 24, 26, 27], and Unified Parkinson's Disease Rating Scale (UPDRS), typical of PD evaluation that was used in 4 studies [19, 28, 23, 26]. Among the clinical measures, BBS and TUG were those which were mostly used: 5 [19, 23, 20, 27, 22] and 5 studies [19, 23, 20, 28, 22], respectively.

***Physical exercises***

The interventions consisted of physical exercises associated with different rehabilitative strategies and the use of machines or robotic devices by which subjects with PSP were trained.

Physical exercises (PhyE) were used in 7 studies [17, 18, 28, 20, 21, 27, 22] to improve strength, coordination activities and gait and were always associated with other interventions or rehabilitative device training. Of these, 5 were case reports [17, 18, 20, 21, 22], one quasi-RT trial with crossover design [28], and one RCT [27]. In all case reports, an improvement of balance and walking was observed after rehabilitative treatment. Izzo et al. described two subjects who underwent PhyE plus eyes training. Both subjects achieved independence in transfers and most activities of daily living after rehabilitation [17]. Sosner et al. reported 2 subjects with PSP: one received PhyE combined with a biomechanical ankle platform system (BAPS) in order to improve coordination and balance, whereas gait training, generalized muscle strengthening, coordination and speech training were used in the other one. Both subjects showed functional improvement after rehabilitation [18]. Steffen et al. reported the case of a subject suffering from a combined form of PSP and CBD, who was followed for 10 years and described by 2 case reports. Rehabilitative interventions consisting of PhyE and body weight support treadmill training over 10-year period improved balance and reduced the rate of falls from an average of 1.9 falls per month to 0.3 per month. Interestingly, longitudinal quantitative brain measurements by MRI indicated that the subject after ten years of regular and stable rehabilitative interventions showed a slower rate of whole brain volume loss and ventricular expansion than subjects with autopsy-proven CBD or PSP (-0.79% vs. -1% and -2.3% for PSP and CBD group, respectively), [21]. Seamon et al. described a PSP female that performed 2 sessions a week for six weeks with PhyE plus Xbox Kinect virtual gaming system training. The subject reported an improvement in balance and a reduction in falls, and the authors suggested that common virtual games could be feasibly implemented for rehabilitative treatment in an out-patient setting [22].

Of the remaining 2 studies, one was a quasi-RT trial with cross-over design and one was an RCT. In the quasi-RT, 19 subjects with PSP were divided into 2 groups. The control group (n. 9 subjects) received PhyE alone, whereas the experimental group (n.10 subjects) was treated by PhyE plus eye movement and visual awareness training as supplemental activity based on techniques used for visual neglect. No statistically significant differences between the groups were observed after treatment. However, the experimental group showed an improvement in spatial gait parameters, gait speed, TUG scores and ability to shift gaze downward, whereas no changes was observed in subjects who received training balance only. The study had methodological limitations since several subjects in the experimental group did not crossover and eye exercises were laboratory-based that might differ from feasible clinical application [28].

The only RCT enrolled 24 PSP subjects who were randomized into 2 groups, each composed of 12 patients. The aim of the study was to ascertain whether a robot machine (Lokomat) was superior to a treadmill with visual cues and auditory feedbacks (treadmill plus) in the context of an aerobic, multidisciplinary, intensive, motor-cognitive and goal-based rehabilitation treatment that had been conceived for PD. In this study, PhyE was a component of standard multi-disciplinary interventions consisting of four daily sessions (table). The primary outcome was the PSP rating scale change and the scores obtained in the “limb” and “gait” sub-sections. Total PSPRS, PSPRS-gait, BBS, 6MWT and number of falls improved significantly by the end of the training in both groups. However, PSPRS-limb improved significantly only in the treadmill plus group (p = .0020, effect size = -0.7).

Furthermore, a significant difference was observed only for total PSPRS (p = .047), indicating a slightly better improvement for patients in the treadmill plus group [27]. The authors concluded that the use of robot device, compared to the treadmill-plus training, did not add any further benefit in the context of a multi-disciplinary rehabilitative treatment.

***Instrument training***

Several machines and devices were employed in rehabilitative training and included treadmill, robot-assisted gait machine, wearable audio-biofeedback device, biomechanical ankle platform system (BAPS), dynamic antigravity postural system (SPAD), vibration sound system (ViSS), and Xbox Kinect virtual gaming system. The machines were used in 9 studies [18-25, 27] and were either a component of combined rehabilitation training, generally associated with PhyE, as mentioned above, or employed alone representing the rehabilitative treatment [23-25]. Treadmill training associated with PhyE [19-21, 27] as well as part of multi-disciplinary treatment [27] was the most commonly used machine.

The use of instruments alone without the adjunct of other interventions was investigated in 3 studies [23-25]. Nicolai et al. investigated 6 PSP subjects (6 F, 2 M; mean age 66±6.1 years) to evaluate the effect of audio-feedback (ABF) device on the posture and dynamic balance. The device included a sensing unit based on a 3D accelerometer and gyroscope to measure trunk acceleration along the anterior-posterior and medio-lateral anatomical axes. Two types of feedback were found, consisting of different sounds: one to maintain corrected posture that started when leaving the predefined target and one to support the transfer that appeared only when the predefined goal was reached. For this cue, the patient had to bend forward as far as needed to reach the sound that gives the signal to stand up. Several clinical measures were used (Table 1). After training, PSP patients showed a significant improvement in BBS and ABC: median score 35 and 44, (p=.047); 13.8 and 6.9 (p=.047) at baseline and after training for BBS and ABC, respectively. No improvement was observed for UPDRS, TUG, and 5FC. Therefore, the authors suggested that audio-feedback training could be a promising rehabilitative strategy to improve balance [23].

Di Pancrazio et al. [24] investigated the efficacy of a rehabilitative program combining a dynamic antigravity postural system (SPAD) and a vibration sound system (ViSS) on postural instability in 10 subjects with PSP. The SPAD is a machine with body weight support that permits the patient to be suspended through a mechanical antigravity vertical traction system. ViSS is a multi-frequency system which reaches 300 Hz and an amplitude of 200 mbar which uses focalized mechanic-acoustic vibrations. The patient body weight was alleviated by 20 to 30% and underwent SPAD and VISS treatments with a 3 sessions/week schedule for 2 months. PSP-RS, BBS and stabilimotery, baropodometry static and dynamic were used to evaluate balance and walking. After training, BBS score improved: 37.7±12.1 and 47.6±9.2 (p=.02), at the baseline and at the end of treatment, respectively. Stabilometry test showed a significant improvement in the distribution of load in percentage compared to pre-treatment conditions, as well as dynamic baropodometric dynamics. The patients showed an increase in walking speed, greater stability and a reduction in the risk of falling.

Sale et al. investigated whether an end-effector robotic rehabilitation locomotion training (G-EO system device) improved walking. Five PSP subjects were submitted to a rehabilitative program of robot-assisted walking sessions for 45 min, 5 times a week for 4 weeks. Gait velocity (T0: 0.54 ± 0.17 m/s and T1: 0.69 ± 0.15 m/s) and cadence (T0: 83.00 ± 9.61 and T1: 93.60 ± 15.43) improved by 15% and 23.8%, respectively. Participants also demonstrated an improvement of 11% in step length left and of 35% in step length right. However, no statistical significance was found in all the analyzed parameters. The patients clearly felt safe and comfortable with the robot at the end of the training [25].

## Discussion

Few studies have been reported concerning the rehabilitation of subjects with PSP and only one was an RCT. Due to the poor methodological quality and variability of rehabilitative approach with different and variable interventions, no evidence supports the effectiveness of rehabilitation in PSP according to evidence based medicine criteria [32-33]. The studies were predominantly case reports and the remaining varied in size, outcome measures, and type of interventions; therefore, it was not possible to compare and pool data for formal meta-analysis. However, all of the studies showed that PSP subjects achieved an improvement in balance and gait impairments with a reduction of falls after rehabilitation treatment. Given that most disabling disorders in PSP are due to balance deficit, walking impairment and falls with related injuries, all studies predominantly focused on these functional domains, in particular balance and gait impairment, apart from one study that addressed voice and speech phonation [26]. Indeed, recent studies have showed that postural instability with early falls, Richardson's type and dementia are the main predictive negative factors [32-33]. With regard to balance, all case reports showed an improvement of this functionality with a reduction of falls. Also, the study describing the effect of Xbox Kinect game system reported that balance measure remained stable and no decline below fall risk was observed [22] during the training. Likewise, a significant improvement of balance compared to pre-training was observed in case series [23-24] and in the only RCT [27]. Although, the primary end-point in this study was PSP-RS change, a significant improvement in PSP-RS gait, BBS 6MWT other than PSPRS-total was observed. Furthermore, a significant reduction of falls by the end of the training was observed in all treated subjects. Likewise, all studies showed an improvement of gait after rehabilitation treatment. Gait was evaluated by quantification of several spatiotemporal walk parameters including speed velocity, cadence, distribution of body load and step length. All studies showed an improvement of evaluated gait parameters, even if all investigations were case reports or case series [19-21, 24-25, 28].

Given that PSP shares several symptoms and clinical phenotypes overlapping PD, rehabilitative interventions were borrowed from those applied in PD subjects in order to improve mainly balance and gait impairment. With regard to this aspect, a growing number of studies has reported that PhyE [34, 13-15], and treadmill training [16] are efficacious in the rehabilitation of subjects with PD. In particular, it has been reported that PhyE improves strength, posture and gait of PD patients [35-37, 15]. The suggested physiological mechanisms responsible of PhyE effect have been related to different factors including changes in brain connectivity comparable to medication, increased synaptic strength and functional circuitry, favouring brain-plasticity [38-39]. Likewise, a similar rehabilitative approach was also used in subjects with PSP. Indeed, PhyE was the main rehabilitative strategy to improve balance and gait disorders. Although PhyE was used in 7 studies, only one was an RCT. This study had low level of bias, but PyE was associated with variable interventions and rehabilitative tools with the aim of investigating the effect of a robot-assisted gait training compared to treadmill [27] training. Furthermore, PhyE was part of an intensive multi-disciplinary rehabilitative strategy, also including occupational therapy, speech therapy and machine training. Given that no data exist about the effect of solely PhyE on the recovery of PSP subjects, it not possible recommend the use of PhyE alone in PSP, even if this strategy associated with combined interventions might help to ameliorate the balance and gait in PSP. Indeed, combined rehabilitative interventions were generally employed, but it were variable and no study replicated same therapeutic approach and strategy. Well pre-specified multidisciplinary therapy was used in the only one RCT study [27], but further studies should be planned to confirm the benefit of proposed rehabilitative strategy. A multi-component rehabilitative approach is interesting and has been proposed in other rare neurodegenerative diseases such as Huntington disease (HD) [40-41] on the basis that multidisciplinary rehabilitation facilitates an adaptive stress response that decreases circulating glucocorticoids, thereby enhancing cerebral angiogenesis and brain-derived neurotrophic factor expression, encouraging neurogenesis and structural brain changes [42].

Another aspect emerging with the present review was the frequent use of machines in the PSP rehabilitation approach, in particular treadmill and robot-assisted devices. However, the employed instruments were borrowed from their use in different diseases such as spinal cord injury, stroke and PD. In subjects with PD, the treadmill might improve clinically relevant gait parameters such as gait speed and stride length [16]. In this line, treadmill with body weight support was the most commonly used machine in the rehabilitation of PSP subjects, either combined to PhyE [19-21, 27] and a component of multi-disciplinary treatment [27].

Currently, technology is rapidly spreading in the rehabilitation field. The robotic task-specific repetitive approach is regarded as the most promising to restore motor function in stroke [43-44] and in PD [45]; therefore, this approach was also investigated in PSP compared to treadmill training. Given that the use of robot machine or treadmill was part of the multi-disciplinary therapy and both treated groups improved after training [27], it was not possible to determine whether the improvement was due to one of used rehabilitative interventions or to the machines. However, in the studies that employed treadmills, robot systems or other devices, an improvement in balance and gait parameters was observed.

Severe methodological limitations characterized the studies and a large number of questions remain currently unsolved: i) number, frequency and duration of rehabilitative treatment; ii) whether PhyE alone or PhyE associated with other interventions produces benefits, and in this case what type of rehabilitative interventions should be adjunct; iii) whether multi-disciplinary rehabilitative strategy is superior to single rehabilitative interventions; iv) what type of interventions should be part of combined rehabilitative strategy; v) role and effect of machines and devices in rehabilitative training; and vi) whether device-assisted training is superior to conventional rehabilitation and whether the devices should be used alone or combined to other rehabilitative interventions.

**Conclusion**

Due to poor methodological quality and the variability of rehabilitative approaches with different and variable strategies, no evidence supports the effectiveness of specific rehabilitation intervention in PSP. Despite this finding, rehabilitation might improve balance and gait impairment with a reduction of falls in PSP subjects. Further extensive and well-designed investigations are required to establish whether rehabilitation is a valuable and efficacious approach, and if so, what interventions and devices should be used. Given the incidence rate of PSP, multi-centre, RCTs with larger samples addressing well-specified rehabilitative interventions and instruments might contribute to clear above mentioned issues.

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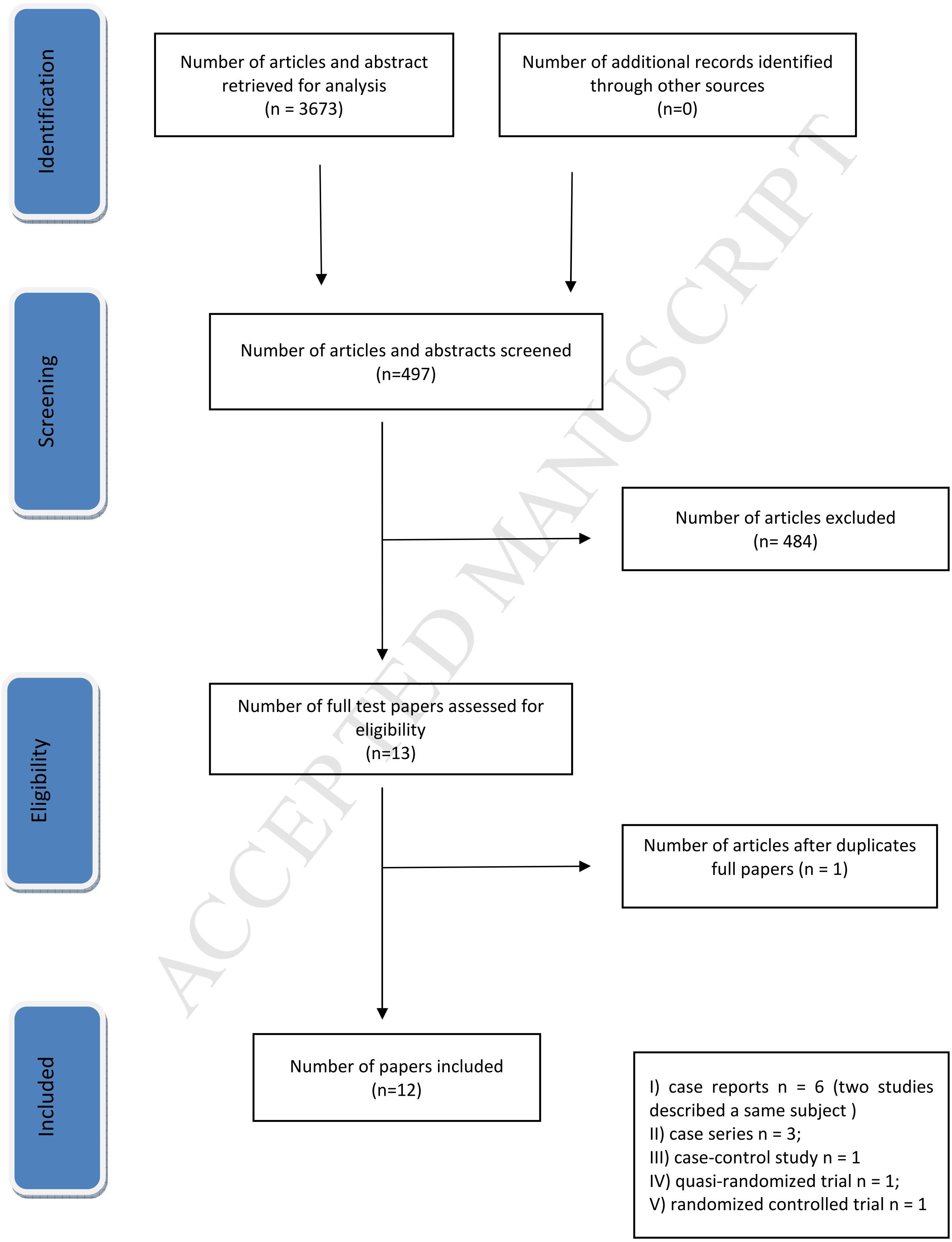
Table 1. Studies of rehabilitation treatment in subjects with PSP.

| Authors and year | Study and population | Training and sessions | Follow-up | Functional measures | Other measures | Techniques and Instrumental | Outcome |
|---|---|---|---|---|---|---|---|
| Izzo KL et al.[17] 1986 | case report n.1 | nr | nr | nr | - | Limb coordination activities, fine motor activities, tilt board balancing, ambulation training | Improvement of balance. The patient became independent in transfers and most activities of daily living |
| Sosner J. et al.[18] 1993 | case report n.2 | daily treatment; duration nr | nr | nr | - | Exercises to improve strength and coordination; static and dynamic balance; resistive and isokinetic exercises; BAPS | Improvement of ambulation |
| Suteerawattananon M et al.[19] 2002 | case report n.1 | 8 weeks 3 days/wk | 12 weeks | UPDRS; FRT; BBS; 15.2-m walk; 360° degree turns; TUG; 5-step test | - | Physical exercises; modified body weight support treadmill (15% of body weight) | Balance improvement and reduction of falls. The gait speed increased and reaction time for 7 directions improved after the treadmill training. |
| Zampieri C. and Di Fabio R.[28] 2008 | quasi-RT crossover design ; n. 19 pts n. 9 control group; n. 10 experimental group | 4 weeks; 3 sessions/wk 1 hour for session | 5 weeks | PSR-RS; UPDRS; TUG; gait parameters by electromagnetic sensors with 6 degrees of freedom; 8-ft (2.4-m) walk test | MMSE | Both groups performed physical exercises. Experimental group received eye movement and visual awareness training as supplemental activity based on techniques used for visual neglect | Improvements in spatial gait parameters, gait speed, and TUG scores were observed for participants who received balance plus eye training, but no statistically significant differences between the groups were observed. |
| Nicolai S et al.[23] 2010 | case series n.8 (6 F, 2 M; mean age 66±6.1 yrs) | 6 weeks 3 times/wk 45 minutes for session | 6 weeks | UPDRS; BBS; TUG; Five Chair Rise Test (5FR); ABC | BMI, MMSE; GDS; PDQ-39 | wearable audio-biofeedback (ABF device) | Significant improvement of balance at 4 weeks (p=.008); no improvement to UPDRS, TUG, 5FR |
| Di Pancrazio L et al.[24] 2013 | case series n. 10 (7 M, 3 F) | 8 weeks 3 sessions/wk | 4 weeks | PSR-RS; BBS; baropodometry static and dynamic; gait parameters | DBIS; PDQ-39 | SPAD; ViSS | Improvement of the distribution of body load on the right and left foot. Improvement of gait speed |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | | | | and step length. PSP RS showed improvement of the motor score posture item (p = .01) as well as BBS (p= .02) and PDQ-39 (p = .03) |
| Steffen MT et al.[20] 2007 | case report n.1 (subject with PSP and CBD) | over a 2.5-year period; 1 hour, twice weekly | 2.5 years | BBS; TUG; FFR; BFR; RFR; LFR; SRT; 6-MWT; comfortable and fast gait speeds | - | exercise program of stretching and strengthening; treadmill with and without body-weight support | fall frequency declined over the 3 years from 2 falls per month to 1 fall per month; tests of functional balance showed improved limits of stability and maintained balance function |
| Steffen MT et al.[21] 2014 | case report (same subjects) | 3 sessions/wk 6 weeks of intervention | 10 years | BBS; TUG; FFR; BFR; RFR; LFR; SRT; 6-MWT; comfortable and fast gait speeds | - | same rehabilitative strategy | slower rate of whole brain volume loss and ventricular expansion than subjects with autopsy-proven CBD or PSP |
| Sale P et al.[25] 2014 | case series n. 5 (3 M, 2 F, median age was 67.80 ± 11.71 years) | 4 weeks ; 5 days/wk | 4 weeks | gait parameters by 3D-Gait analysis (3D-GA) by ELITE system and 2 force platforms | - | robot assisted gait training, using the end effector system machines G-EO system device | significant improvement of gait parameters: velocity and cadence improved respectively by 15 and 23.8%. Increased right and left length step was also observed |
| Sale P et al.[26] 2015 | case control 16 pts with PSP and 23 with PD | 4 weeks 4 days/wk | 4 weeks | PSPRS; UPDRS; | digital sound level meter SM4 | speech therapy by Lee Silverman Voice Treatment (LSVT) | increase of maximum phonation duration and volume of voice in reading in both groups |
| Clerici I et al.[27] 2017 | RCT; 24 pts; 12 pts mean age 72.5±6.1 (control goup), 12 pts mean age 69.9±5.2 (experimental group) | 4 weeks; treadmill + MIRT (control); lokomat + MIRT (experimental) 5 days/wk | 4 weeks | PSP-RS total and gait sub-sections; BBS; 6MWT | MMSE; number of falls, Visual Analogical Scale | MIRT. Four daily sessions: 1$^{th}$ cardiovascular warm-up activities, relaxation, muscle-stretching exercises; 2$^{th}$ treadmill or robot assisted gait training; 3$^{th}$ occupational therapy; 4$^{th}$ one hour of speech therapy | total PSPRS, PSPRS-gait, BBS, 6MWT and number of falls improved significantly by the end of the training programs in both groups. A slightly better improvement for patients in the MIRT group was observed. |
| Seamon B et al.[22] | case report | 6 weeks; | 18 weeks | BBS; TUG; FGA; | number of | Physical therapy | balance measure remained |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 2017 | 65 years old woman | 2 days/wk | | 10MWT | falls; PDQ-39; FFABQ; | exercises and Xbox Kinect virtual gaming system | stable and no decline below fall risk, however a decline in PDQ-39 and in FFABQ was observed |

Legend: PSP = Progressive Supranuclear Palsy; CBD = Corticobasal Degeneration; RT = randomized trial; BAPS = Biomechanical Ankle Platform System; UPSP-RS = Unified Progressive Supranuclear Palsy Rating Scale; UPDRS = Unified Parkinson's Disease Rating Scale; FRT= Functional Reach Test ; BBS = Berg balance scale; 6-MWT = 6-minutes walking test; TUG = timed “Up & Go” Test ; FFR = forward functional reach; BFR = backward functional reach (BFR); RFR = right functional reach; LFR = left functional reach (LFR); SRT = sharpened Romberg Test; ABC = activities specific balance confidence; BMI = body mass index; MMSE = mini mental status exam; GDS = geriatric depression scale; PDQ39 = Parkinson’s Disease summary index of Parkinson’s disease questionnaire; DBIS = Digital Biometry Images Scanning; SPAD = dynamic antigravity postural system; ViSS = vibration sound system; MIRT = multiple disciplinary intensive rehabilitation treatment. FGA = functional gait analysis; FFABQ = fear of falling avoidance belief questionnaire; 10 MWT = 10 meter walk test


Identification
Number of articles and abstract retrieved for analysis (n = 3673)
Number of additional records identified through other sources (n=0)
Screening
Number of articles and abstracts screened (n=497)
Number of articles excluded (n= 484)
Eligibility
Number of full test papers assessed for eligibility (n=13)
Number of articles after duplicates full papers (n = 1)
Included
Number of papers included (n=12)
I) case reports n = 6 (two studies described a same subject )
II) case series n = 3;
III) case-control study n = 1
IV) quasi-randomized trial n = 1;
V) randomized controlled trial n = 1

Supplementary material

Search terms in MEDLINE

1. exp Progressive supranuclear palsy [mh] 3673
2. exp atypical Parkinson syndrome [mh] 222
3. exp Parkinson plus [mh] 817
4. exp Parkinson plus syndrome [mh]123
5. exp Steele Richardson Olszewski [mh] 144
6. exp Atypical parkinsonism [1544]
7. exp gaze palsy [mh] 1704
8. gaze palsy [mh] AND PSP [mh] 177
9. gaze palsy [mh] OR PSP [mh] 6696
10. progressive supranuclear palsy [mh] AND rehabilitation [mh] 98
11. progressive supranuclear palsy [mh] OR rehabilitation [mh] 520163
12. atypical Parkinson syndrome [mh] AND rehabilitation [mh] 2
13. atypical Parkinson syndrome [mh] OR rehabilitation [mh] 516808
14. Parkinson plus [mh] AND rehabilitation [mh] 58
15. Parkinson plus syndrome [mh] AND rehabilitation [mh] 3
16. Parkinson plus syndrome [mh] OR rehabilitation [mh] 516708
17. Steele Richardson Olszewski [mh] AND rehabilitation [mh] 1
18. Steele Richardson Olszewski [mh] OR rehabilitation [mh] 516731
19. Steele Richardson Olszewski [mh] AND gait [mh] 14
20. Steele Richardson Olszewski [mh] OR gait [mh] 48959
21. Progressive supranuclear palsy [mh] AND gait [mh] 251
22. Progressive supranuclear palsy [mh] OR gait [mh] 52251
23. atypical Parkinson syndrome [mh] AND gait [mh] 10
24. atypical Parkinson syndrome [mh] OR gait [mh] 49041
25. Parkinson plus [mh] AND gait [mh] 48
26. Parkinson plus [mh] OR gait [mh] 49598
27. Gaze palsy [mh]AND gait [mh] 123
28. Gaze palsy [mh] OR gait [mh] 50410
29. Progressive supranuclear palsy [mh]AND balance [mh] 89
30. Progressive supranuclear palsy [mh] OR balance [mh] 217398
31. atypical Parkinson syndrome[mh] AND balance [m] 8
32. atypical Parkinson syndrome [mh] OR balance [mh] 214008
33. Parkinson plus [mh]AND balance [mh] 28
34. Parkinson plus [mh]OR balance [mh] 214589
35. Gaze palsy [mh] AND balance [mh] 35
36. Gaze palsy [mh] OR balance [mh] 215473