

## Balance and Eye Movement Training to Improve Gait in People With Progressive Supranuclear Palsy: Quasi-Randomized Clinical Trial

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**Background and Purpose.** Although vertical gaze palsy and gait instability are cardinal features of progressive supranuclear palsy (PSP), little research has been done to address oculomotor and gait rehabilitation for PSP. The purpose of this study was to compare the benefits of a program of balance training complemented with eye movement and visual awareness training versus balance training alone to rehabilitate gait in people with PSP.

**Participants.** Nineteen people moderately affected by the disease were assigned to either a treatment group (balance plus eye movement exercises, n=10) or a comparison group (balance exercises only, n=9) in a quasi-random fashion.

**Methods.** The baseline characteristics assessed were diagnosis (possible versus probable), sex, age, time of symptom onset, dementia, and severity of symptoms. Within-group, between-group, and effect size analyses were performed on kinematic gait parameters (stance time, swing time, and step length) and clinical tests (8-ft [2.4-m] walk test and Timed “Up & Go” Test).

**Results.** The within-group analysis revealed significant improvements in stance time and walking speed for the treatment group, whereas the comparison group showed improvements in step length only. Moderate to large effects of the intervention were observed for the treatment group, and small effects were observed for the comparison group. The between-group analysis did not reveal significant changes for either group.

**Discussion and Conclusion.** These preliminary findings support the use of eye movement exercises as a complementary therapy for balance training in the rehabilitation of gait in people with PSP and moderate impairments. Additional studies powered at a higher level are needed to confirm these results.



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**P**rogressive supranuclear palsy (PSP) is the most frequently occurring form of atypical parkinsonism.<sup>1</sup> The average survival time is 7 years; however, there have been reports of neuropathologically confirmed cases of survival of up to 11 years<sup>2</sup> or 16 years.<sup>3</sup> Gait and mobility problems are among the most common early features of this disease,<sup>1</sup> and gait deficits progress rapidly.<sup>4</sup> Oculomotor problems, such as vertical gaze palsy, also known as “slowness of saccades,”<sup>3,5,6</sup> and deficits in vestibuloocular reflex suppression, are also symptoms of PSP.<sup>7-9</sup>

Gait problems in PSP are different from those in Parkinson disease (PD). Although freezing and festination are very common in PD,<sup>10</sup> these features are typically not observed in PSP, although there have been reports of freezing in a few cases in which the diagnosis was confirmed postmortem.<sup>11</sup> The typical gait in PSP is unstable, with frequent falls,<sup>1</sup> and is clinically described as clumsy, resembling the gait of a drunken sailor.<sup>11</sup>

There are several approaches to gait rehabilitation in PSP. There have been reports of balance training with a tiltboard,<sup>12</sup> eye-head movement strategies to improve awareness and safety during ambulation,<sup>12</sup> strength (force-generating capacity) training with resistive and isokinetic exercises,<sup>13</sup> coordination exercises,<sup>12,13</sup> gait training over ground,<sup>13</sup> and body-weight-supported treadmill training.<sup>14,15</sup> However, the outcomes were primarily qualitative, reflecting the opinions of therapists and patients. Improvement in standing balance<sup>12</sup> and safer ambulation were the main observations.<sup>12,13</sup> Quantitative measures were reported in only one study and included increases in walking speed, cadence, and step length.<sup>15</sup>

Rehabilitation of gait in PSP should also include oculomotor training because the ability to control eye movements is directly related to the control of gait and safe ambulation. Vision plays a critical role in the control of locomotion because it provides input for anticipatory reactions of the body in response to constraints of the environment.<sup>16</sup> Anticipatory saccades occur normally in situations that involve changing the direction of walking<sup>17</sup> or avoiding obstacles.<sup>18</sup> When downward saccades are not frequently generated during obstacle avoidance tasks, there is an increase in the risk for falling. Di Fabio et al<sup>19</sup> reported that elderly people at a high risk for falling generated fewer saccades than their low-risk counterparts during activities involving stepping over obstacles. In addition, foot clearance trajectories were asymmetric in the high-risk group, with the lag foot trajectory being significantly lower than the lead foot trajectory. Similar behavior has been observed in patients with PSP during stair-climbing activities. Di Fabio et al<sup>20</sup> recently reported that patients with severe oculomotor limitations had a lower lag foot trajectory than those with mild oculomotor limitations.

Aside from the influence of oculomotor control on stepping kinematics, deficits in cognition, especially attention and executive functions, also have been linked to an increased risk for falling in elderly people<sup>19,21</sup> and people with Alzheimer disease<sup>22</sup> and PD.<sup>23</sup> In PSP, in particular, a strong correlation has been found between the ability to suppress the vertical vestibuloocular reflex and certain domains of cognition: attention and visual awareness.<sup>9</sup>

Even though evidence has shown that gaze limitations have a strong impact on locomotion, the effects of eye movement training have never been investigated in a group of sub-

jects with PSP. The purpose of this study was to compare the benefits of a program of balance training supplemented with oculomotor and visual awareness training versus balance training alone for gait rehabilitation in PSP. We hypothesized that greater improvements in gait would be observed for subjects who received balance and eye movement exercises than for subjects who received balance training alone.

## Method

### Design Overview

A quasi-randomized 2-group pretest-posttest crossover design was used to study the effects of balance and eye movement (balance + eye) training and of balance training alone on gait. Twenty people were alternately assigned to either a treatment group (balance + eye training) or a comparison group (balance training only), except for allocation based on geographical distance from the testing center (several people who resided in distant locations and were unable to participate in the crossover component of the study were assigned to a treatment group that did not cross over). For validation of the allocation procedure, the equivalence of baseline characteristics in the comparison and treatment groups was evaluated (see discussion below). The crossover component of the larger study is not presented here. Only the pretest-posttest phase was analyzed for the present study. At the beginning of the study, there were 10 participants in each group; however, 1 individual dropped out because of a urinary tract infection, leaving the comparison group with 9 participants.

The baseline characteristics assessed were diagnosis (possible versus probable), sex (male versus female), age, time of symptom onset, dementia (with the Mini-Mental State Examination [MMSE] score),<sup>24</sup> severity of symptoms (with the Unified Parkin-

son's Disease Rating Scale motor component [UPDRSm] score),<sup>25</sup> and the PSP Rating Scale.<sup>26</sup> The UPDRSm, originally specific for PD, has been tested for PSP as well and has shown high internal consistency (Cronbach alpha=.90).<sup>25</sup> The PSP Rating Scale has good interrater reliability, with an intraclass correlation coefficient of .86.<sup>26</sup>

### Participants

Twenty people with PSP and living in the community were enrolled in this study. Participants were recruited through the University of Minnesota Movement Disorders Clinic, local PD clinics, and the PSP Society. Recruitment occurred over a period of 2 years. To be included, participants needed to have a possible or probable diagnosis of PSP according to the criteria established by the National Institute of Neurological Disorders and Stroke.<sup>27</sup> Other inclusion criteria were the ability to walk short distances independently (with an assistive device when necessary but no direct assistance from another person), an MMSE score of  $\geq 23$ ,<sup>24</sup> and a corrected far visual acuity of at least 20/80. No changes in medications were implemented for this investigation. All participants provided written informed consent prior to enrollment.

### Intervention

The intervention was performed by a trained group of researchers supervised by the investigators of this study. Researchers administering the intervention were aware of group assignments. A different group of researchers involved with baseline and postintervention data collection and analysis were unaware of group assignments. The intervention sessions were delivered to each participant individually. All treatment sessions took place in the Motion Analysis Laboratory, Department of Physical Medicine and Rehabilitation, University of Minnesota. The location of the

intervention sessions minimized sound and visual distractions. Participants in both groups received the intervention for 1 hour 3 times per week for 4 weeks. The duration of the intervention was chosen on the basis of literature reporting rehabilitation for PD<sup>28,29</sup> and on standard practice adopted by local rehabilitation clinics. Each group of participants received common and group-specific sets of exercises.

**Common exercises.** Both groups practiced a tandem stance with eyes open and closed, turning 360 degrees while marching in place, moving from a sitting position on a chair to a standing position (sit-to-stand), and moving from a standing position to a sitting position on a chair (stand-to-sit). These exercises were based on a fall prevention program for older women.<sup>30</sup> In addition, participants practiced corrective postural reactions to gentle perturbations backward. Trainers pulled on the participants' shoulders or hips with enough strength to evoke protective steps backward. A similar technique has been used to improve postural instability and gait in PD.<sup>29,31</sup> The common exercises were performed by both groups once per week for 1 hour each time. Appendix 1 describes the details of the common exercises. In addition, each group received a supplemental set of exercises 2 times per week for 1 hour each time. These activities are listed below.

**Group-specific exercises.** Participants in the treatment group received eye movement and visual awareness training as a supplemental activity. To develop this protocol, we gathered parts of protocols from different studies on the rehabilitation of people with similar problems. To improve the visual awareness of our participants, we developed a scanning exercise based on techniques used for visual neglect attributable to

stroke.<sup>32,33</sup> The practice consisted of scanning the environment to identify hidden objects. To improve saccadic eye movements, we used computer-assisted saccade exercises, in which participants had to respond with a key press to visual stimuli presented in random locations on the computer screen. For this practice, we used software developed by the Optometric Extension Program Foundation,\* which has been used mainly to improve reading skills in the general population. Another technique that we adopted to improve saccades was auditory feedback, in which participants practiced changing the direction of eye movements to produce different sounds.<sup>34</sup> This technique has been proven successful in the rehabilitation of congenital nystagmus.<sup>35</sup> Finally, our protocol also involved a stimulus-response compatibility paradigm with the objective of improving attention and enhancing eye-foot coordination. This paradigm was developed and tested in our laboratory<sup>18</sup> with elderly individuals. The supplemental exercises were performed 2 times per week for 1 hour each time. Appendix 2 describes the details of these exercises.

Supplemental activity for the comparison group consisted of additional supervised balance exercises that were also part of a fall prevention program.<sup>30</sup> These exercises were performed 2 times per week for 1 hour each time. Appendix 3 describes the details of these exercises. Appendix 4 shows an outline of the protocol.

### Outcome Measures

Outcome measures consisted of kinematic gait assessments and clinical tests. The kinematic gait measures were stance time (amount of time that the foot was in contact with the ground, in seconds), swing time

\* Vision Builder Software, Helga Blystadsvæi 8, 2316 Hamar, Norway.

(amount of time that the foot was not in contact with the ground, in seconds), and step length (distance from the heel strike of one foot to the heel strike of the opposite foot in the forward direction, in centimeters). The clinical assessments included the 8-ft (2.4-m) walk test,<sup>36</sup> a measurement of gait speed, and the Timed “Up & Go” Test (TUG),<sup>37</sup> a measurement of general mobility and risk for falling. Excellent reliability has been reported for the 8-ft walk test (intraclass correlation coefficient = .79) in frail elderly people<sup>38</sup> and for the TUG in people with PD,<sup>37</sup> with Pearson correlations of .79 and .99 in people on and off medications, respectively, and an intraclass correlation coefficient of .99.<sup>37</sup> The reported minimal clinically important difference (MCID) for comfortable gait speed in people with PD is about 0.18 m/s.<sup>39,40</sup> The MCID for the TUG in people with PD varies; there have been reports of 2 seconds,<sup>39</sup> 5 seconds,<sup>41</sup> and 11 seconds.<sup>40</sup>

**Gait analysis.** Tracking of foot motion was done with electromagnetic sensors with 6 degrees of freedom.<sup>†</sup> The sensors were fixed with electrode tape to the dorsum of each foot. Participants wore a headband apparatus that held an infrared oculography system (Series 1000 Binocular Infrared Recording System)<sup>‡,42</sup> and an eye-tracking camera<sup>§</sup> positioned laterally to avoid obstruction of vision. Analysis of eye movements was part of a larger study and is described elsewhere.<sup>43</sup> Kinematic data were collected at 100 Hz and exported to Matlab<sup>||</sup> for offline processing. Custom-designed software in the form of Matlab m-files was developed

to allow the researchers to view each trial and select relevant parts of the traces corresponding to the kinematic gait measures defined above. Participants were asked to walk at a comfortable speed on a 3-m walkway while guarded by a laboratory assistant to prevent falls. For each participant, 2 trials were analyzed and then averaged for data analysis.

**Clinical measures.** During the 8-ft walk test and the TUG, participants were asked to walk at a comfortable speed. Data were averaged from 2 trials.

### Data Analysis

Skewness, kurtosis, and omnibus normality were tested with NCSS statistical software.\* All hypotheses were nondirectional (no difference between means), and the critical alpha level was established at .05.

**Baseline comparisons.** To examine baseline differences between the treatment and the comparison groups, we used a chi-square test to compare categorical baseline measurements: diagnosis (possible versus probable) and sex (male versus female). A 2-sample *t* test was used to compare continuous baseline measurements: disease duration, UPDRSm,<sup>25</sup> PSP Rating Scale,<sup>26</sup> the gait section of the PSP Rating Scale, and MMSE baseline values.<sup>24</sup>

**Between-group comparisons.** Differences between groups were analyzed with a 2-sample *t* test, in which change scores for each group were compared for each variable (change score = posttest value – pretest value). When data did not conform to a normal distribution, a Mann-Whitney *U* test for the difference in means was used, and a *z* score was approximated with correction for continuity.

**Within-group comparisons.** To further explore improvements within groups separately, we used a matched-pairs *t* test to compare pretest and posttest scores within each group. When data did not conform to a normal distribution, a Wilcoxon signed rank test for the difference in medians was used, and a *z* score was approximated with correction for continuity.

**Effect sizes (ES).** To express the clinical meaningfulness of the data, we also calculated ES across groups by using change scores as the unit of measure. The formula used to calculate ES was as follows: (change score for treatment group – change score for comparison group)/SD of change score for comparison group. To interpret ES, we followed the criteria established by Cohen, in which an ES of .2 is considered small, an ES of .5 is considered moderate, and an ES of .8 is considered large.<sup>44</sup>

### Role of the Funding Source

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## Results

### Baseline Measurements

The baseline characteristics of each group are shown in Table 1. Measurements obtained for disease severity with the UPDRSm<sup>25</sup> and the PSP Rating Scale<sup>26</sup> indicated moderate stages of the disease. There were no significant differences between the groups for diagnosis (possible versus probable), sex, age, time of symptom onset, disease severity, or PSP Rating Scale scores. A significantly lower MMSE score was observed for the treatment group.

<sup>†</sup> Innovative Sports Training Inc, 3711 N Ravenswood, Suite 150, Chicago, IL 60613.

<sup>‡</sup> MicroGuide Inc, 1635 Plum Ct, Downers Grove, IL 60515.

<sup>§</sup> Arrington Research Inc, 27237 N 71st Pl, Scottsdale, AZ 85266.

<sup>||</sup> The Mathworks Inc, 3 Apple Hill Dr, Natick, MA 01760-2098.

\* NCSS Software, 329 North 1000 East, Kaysville, UT 84037.

## Balance and Eye Movement Training for Progressive Supranuclear Palsy

**Table 1.**  
Group Characteristics<sup>a</sup>

Variable	Treatment Group	Comparison Group	P
Diagnosis (no. of possible/probable)	2/8	4/5	.25
Sex (no. of men/women)	5/5	5/4	.80
Age (y)	71.20 (5.28)	67.55 (7.28)	.22
Symptom onset (mo since first symptom was noted)	40.6 (31.80)	53.0 (34.66)	.42
Mini-Mental State Examination score	25.7 (1.05)	27.44 (2.0)	.02 <sup>b</sup>
UPDRSm score	19.9 (6.74)	22.11 (7.33)	.50
PSP Rating Scale score	30.1 (10.34)	28.44 (8.38)	.70
PSPg score	7.7 (4.47)	9.55 (3.84)	.34

<sup>a</sup> Values are reported as means (SDs) for continuous variables. UPDRSm=motor component of the Unified Parkinson's Disease Rating Scale (maximum score=56), PSP=progressive supranuclear palsy, PSPg=gait section of the PSP Rating Scale (maximum score=20).

<sup>b</sup> Significant value.

### Between-Group Comparisons and ES

Change scores for the treatment and comparison groups for each variable are shown in Table 2. Negative values indicated that posttest values were lower than pretest values. For stance duration, swing time, and the TUG, a negative value meant improvement. For the other variables, a positive value indicated improvement. No statistically significant differences between the groups were observed. Although there was an improvement on the 8-ft walk test for the treatment group, this change did not reach significance.

Table 3 shows the ES for each dependent measure across groups. A large

intervention effect was observed for stance duration and the 8-ft walk test, and a moderate intervention effect was observed for the TUG, indicating substantially more improvement in the treatment group than in the comparison group. In contrast, the negative ES for swing time and step length indicated that the treatment group showed less change in these variables. In this case, the comparison group improved more than the treatment group, even though the effects were small.

### Within-Group Comparisons

The Figure (graphs A, B, and C) show pretest and posttest values for gait kinematics for each group. A statistically significant decrease in stance

time was observed in the treatment group (pretest:  $\bar{X}=0.94$ ,  $SE=0.09$ ; posttest:  $\bar{X}=0.79$ ,  $SE=0.03$ ; Wilcoxon  $P=.01$ ) but not in the comparison group (pretest:  $\bar{X}=1.12$ ,  $SE=0.25$ ; posttest:  $\bar{X}=1.08$ ,  $SE=0.21$ ; Wilcoxon  $P=.40$ ). Swing time did not show significant changes in the treatment group (pretest:  $\bar{X}=0.61$ ,  $SE=0.03$ ; posttest:  $\bar{X}=0.61$ ,  $SE=0.03$ ;  $P=.90$ ) or the comparison group (pretest:  $\bar{X}=0.71$ ,  $SE=0.04$ ; posttest:  $\bar{X}=0.76$ ,  $SE=0.07$ ;  $P=.20$ ). Step length increased significantly in the comparison group (pretest:  $\bar{X}=61.85$ ,  $SE=5.07$ ; posttest:  $\bar{X}=68.57$ ,  $SE=3.89$ ;  $P=.01$ ) but not in the treatment group (pretest:  $\bar{X}=58.26$ ,  $SE=4.45$ ; posttest:  $\bar{X}=61.86$ ,  $SE=4.79$ ;  $P=.08$ ).

**Table 2.**  
Between-Group Comparisons

Variable	Change Score, <sup>a</sup> $\bar{X}$ (SD), for:		P
	Treatment Group (n=10)	Comparison Group (n=9)	
Kinematic gait			
Stance duration (s)	-0.14 (0.22)	-0.04 (0.11)	.13
Swing time (s)	0 (6.35)	0.05 (0.11)	.21
Step length (cm)	3.60 (5.93)	6.71 (6.74)	.29
Clinical			
8-ft (2.4-m) walk test (cm/s)	10.85 (11.23)	0 (13.73)	.07
Timed "Up & Go" Test (s)	-3.90 (10.33)	-1.56 (3.18)	.52

<sup>a</sup> Change score = posttest value - pretest value.

**Table 3.**  
Effect Sizes and Clinical Significance

Variable	Effect Size	Intervention Effect <sup>a</sup>
Stance duration (s)	.90	Large
Swing time (s)	-.45	Small
Step length (cm)	-.46	Small
8-ft (2.4-m) walk test (cm/s)	.79	Large
Timed "Up & Go" Test (s)	.73	Moderate

<sup>a</sup> The intervention effect was based on the criteria established by Cohen.<sup>44</sup> A positive effect size means better performance for the treatment group. A negative effect size means better performance for the comparison group. Typically, large effects were observed for the treatment group, and small effects were observed for the comparison group. The formula used to calculate the effect size was as follows: (change score for treatment group – change score for comparison group)/SD of change score for comparison group.

The Figure (graphs D and E) show pretest and posttest values for clinical measurements for each group. There was a significant improvement in walking speed on the 8-ft walk test in the treatment group (pretest:  $\bar{X}$ =61.54, SE=5.89; posttest:  $\bar{X}$ =72.39, SE=6.12;  $P$ =.01) but not in the comparison group (pretest:  $\bar{X}$ =77.48, SE=7.54; posttest:  $\bar{X}$ =77.48, SE=6.01;  $P$ =1.00). The TUG score decreased more in the treatment group (pretest:  $\bar{X}$ =24.32, SE=3.34; posttest:  $\bar{X}$ =20.42, SE=3.19; Wilcoxon  $P$ =.08) than in the comparison group (pretest:  $\bar{X}$ =23.41, SE=3.93; posttest:  $\bar{X}$ =21.84, SE=3.24;  $P$ =.17), but the decrease did not reach significance.

## Discussion

In the present study, we investigated the benefits of balance training complemented with eye movement exercises versus balance training alone for improving gait in participants with PSP. Our within-group comparisons and ES analysis indicated that the subjects receiving balance + eye training showed more improvements than those receiving balance training only. We believe that these preliminary results support the use of balance + eye exercises to improve gait in people who have PSP and are still ambulatory.

## Mechanisms Underlying Improvement

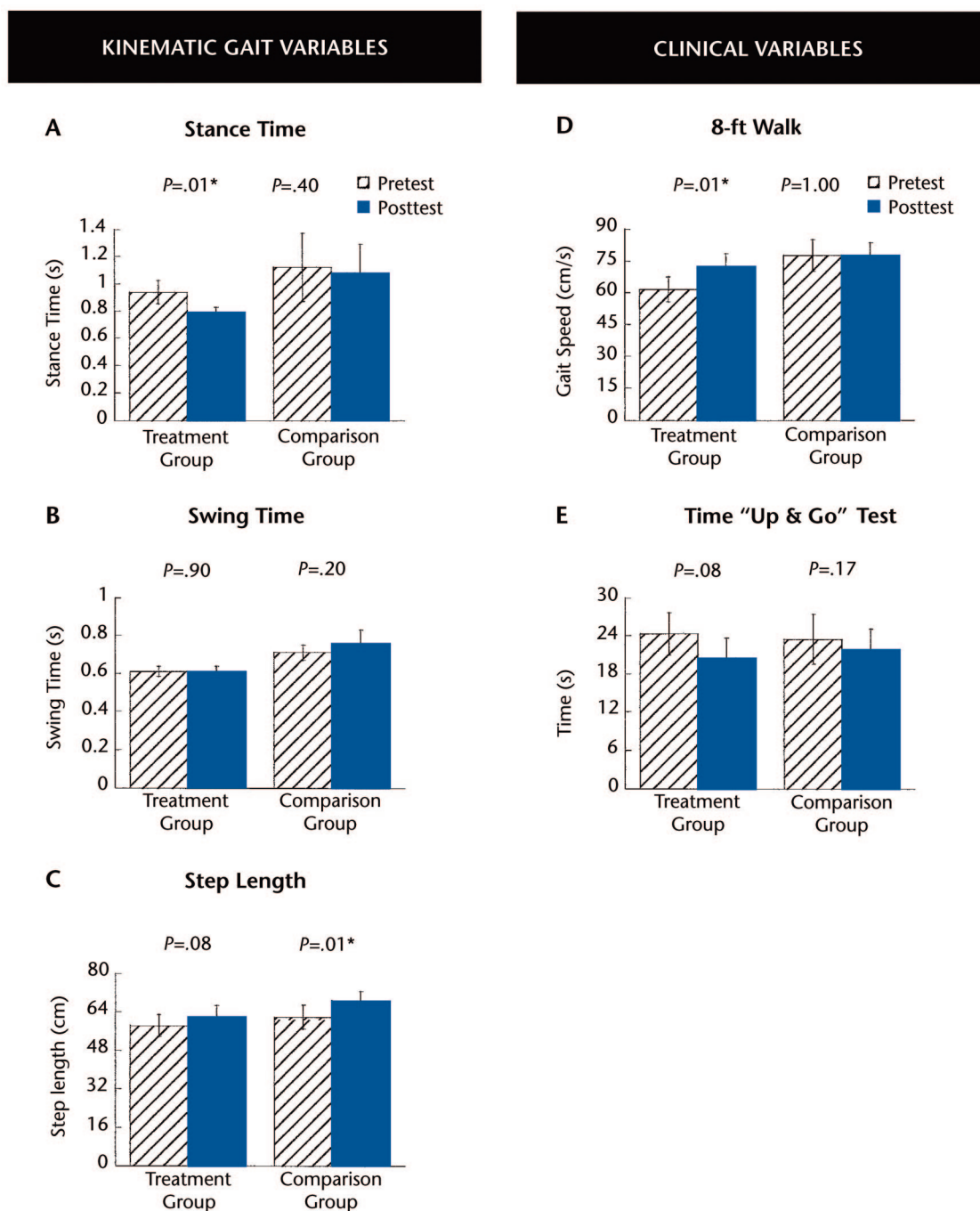
At baseline, the MMSE score was lower in the treatment group than in the comparison group (Tab. 1). This difference was not considered important because the score was used as a screening tool to ensure that participants were able to follow instructions, and participants in both groups reached the cutoff score of 23. In addition, because participants in the group with the lower MMSE score showed greater improvements, we do not believe that the MMSE score considerably affected our results.

In previous work, eye movement training was used to improve gait in people with cerebellar ataxia.<sup>45</sup> The exercises consisted of eye movement rehearsal to fixate objects on the floor (displayed in a random stepping pattern). After eye movement rehearsal, the participants showed improved temporal aspects of gait, such as stance time, double-support time, and swing time variability (reduced). When participants attempted repetitive walking without eye movement training, they did not show any improvement. Our findings agree with those of Crowdy et al<sup>45</sup> in that visual awareness can help improve temporal aspects of gait.

Like cerebellar ataxia, PSP also affects areas of the brain related to the cerebellum, such as the dentate nucleus, cerebellar peduncle, and mid-brain tectum.<sup>46</sup> Both diseases also have common deficits in balance, gait, and ocular movements. Both our findings and those of Crowdy et al show that oculomotor and gait control systems have the potential for rehabilitation even in progressive neurodegenerative disorders.

Although studies on gait in PSP are lacking, the literature supports the rehabilitation of gait in PD.<sup>47,48</sup> It is possible to improve gait cadence and speed with the use of external cues, such as visual stimuli, in PD.<sup>47</sup> The focus of interventions for PD, however, differs from that for PSP because freezing of gait is not the main problem in PSP. In our group of participants, only 2 of 20 reported freezing episodes. The main gait problem in PSP is instability, with frequent falls. Nevertheless, the concepts behind the effectiveness of eye movement training for PSP and visual cues for PD might be the same: Enhancing a person's attention and visual awareness, thereby enhancing cortical activity, could compensate for defective basal ganglion circuitry.

Blin et al<sup>49</sup> showed that some aspects of gait, primarily temporal parameters, such as stance time and swing time, are controlled by areas of the brain outside the basal ganglia (BG). In contrast, spatial parameters, such as step length, are probably controlled by dopa-sensitive areas of the brain.<sup>49</sup> Our results show that balance + eye training had a positive effect on the temporal aspects of gait (Tab. 3 and graphs A and D of the Figure). On the other hand, balance training alone had a positive effect on step length, which is a spatial parameter (Tab. 3 and graph C of the Figure). These findings support the idea that the "eye" exercise portion of the intervention might have had a



**Figure.**

Pretest and posttest values for the treatment and comparison groups for the following variables: stance time (A), swing time (B), step length (C), gait speed measured with the 8-ft (2.4-m) walk test (D), and time to complete the Timed "Up & Go" Test (E). Values are reported as means (SEs). Asterisk indicates significant difference.

specific effect on areas of the brain outside the BG, whereas the "balance" portion of the intervention might have elicited activity in the BG. Although there is a generalized

neuronal loss in the BG<sup>49</sup> of people with PSP, in the substantia nigra (pars reticulata and pars compacta), striatum, globus pallidus, and subtha-

lamic nucleus<sup>50-52</sup> there seems to be some potential for rehabilitation.

We speculate that, outside the BG, the brain stem and frontal cortex

might be recruited by balance + eye training. Many areas of the brain stem responsible for the control of eye movements are affected in PSP: the rostral interstitial nucleus of the medial longitudinal fasciculus, pontomesencephalic tegmentum, pontomedullary reticular formation, superior colliculus,<sup>50,53</sup> and pedunculo-pontine nucleus (PPN).<sup>54</sup> Most of these structures are restricted to the control of eye movements, but the PPN is known to integrate the systems controlling eye movements and locomotion<sup>55</sup>; therefore, it is the key target of balance + eye training. The PPN, located in the rostral portion of the midbrain, projects to the frontal eye field,<sup>56</sup> which is known to be an area of overlap for the control of eye movements and attention.<sup>57</sup> It also projects to the spinal cord through BG<sup>58</sup> and plays a role in the control of posture and gait.<sup>58</sup> The problems with postural instability and cognitive impairment in PSP have been attributed to neuronal loss involving cholinergic pathways,<sup>56</sup> including the PPN, which exhibits 60% neuronal loss in the presence of the disease.<sup>54</sup> Because the PPN has an integrative role and is not completely degenerated in PSP, we speculate that this structure and its neural circuitry remain responsive to balance + eye training.

### General Mobility, Gait Speed, Step Length, and Risk for Falling

Our results based on ES analysis showed that the balance + eye intervention had a moderate effect on general mobility, as measured with the TUG (Tab. 3). These results suggest that the eye exercise component of the therapy is the main factor causing the improvement in general mobility. The TUG involves a combination of tasks besides walking (turning, sit-to-stand, and stand-to-sit). It would be interesting to find the specific component of the test that improved with the exercises. It is possible that only the gait component

improved and that this improvement alone accounted for the decrease in time. In contrast, it is possible that visual awareness helped improve the other components of the test. We were unable to access that information because no motion analysis was done during the TUG.

The TUG not only is a measure of mobility but also helps evaluate the risk for falling. Scores of higher than 13.5 seconds indicate a higher risk in elderly people.<sup>59</sup> Participants who received the balance + eye intervention decreased their time by 3.90 seconds (Tab. 2). This change was not statistically significant, nor did it fall below the cutoff point of 13.5 seconds; these results indicate that, despite being faster after intervention, our participants were still at risk for falling. Still, an improvement of 3.90 seconds may have clinical relevance because it is greater than the MCID of 2 seconds reported in the literature.<sup>39</sup> Even though other authors have reported higher TUG MCID scores,<sup>40,41</sup> our participants likely were more functionally involved than the individuals with PD and, therefore, lower MCID scores were expected.

Gait speed values increased by 10.85 cm/s in participants receiving balance + eye training (Tab. 2). This improvement reflected a large effect of the intervention (Tab. 3). In addition, the change of 0.10 m/s was very close to the MCID of 0.18 m/s reported in the literature for PD.<sup>39</sup> We still consider these results to be clinically relevant given the severity of disease in our participants compared with that in the literature.

Regarding step length, the comparison group showed statistically significant improvements, as indicated by the within-group analysis and a small effect of the intervention (Tab. 3 and graph C of the Figure). The reason why the comparison group showed

improved step length whereas the treatment group did not may be a difference in the intervention protocols. Participants receiving balance training alone practiced more standing and stepping activities and, therefore, had more chances to improve stepping than participants receiving balance + eye training, who were seated for most of the “eye training” part of the intervention.

Changes in step length can also be related to a risk for falling. Kerrigan et al<sup>60</sup> showed that elderly people at a higher risk for falling have reduced hip extension, which is reflected by reduced step length. The authors suggested that falls are likely to occur in situations requiring a larger step to quickly adjust the base of support to maintain balance, such as a change in ground surfaces or obstacle avoidance. Therefore, an increase in step length can be viewed as a positive effect. However, the extent to which it translates into practical situations in which people are required to take larger steps quickly is not known, because we were unable to track episodes of falling in our participants. Participants were constantly monitored by their caretakers, making tracking of falling episodes an unreliable and biased measure.

### Limitations

One limitation of the present study was the fact that each group contained a small number of participants, limiting the statistical power to detect changes. However, given that PSP is a rare disease<sup>6,61</sup> and is often misdiagnosed as PD, it is very difficult to recruit large numbers of participants. We consider the number of participants recruited for the present study to be adequate for a preliminary investigation. In addition, given the lack of published rehabilitation studies for PSP, we believe that the present investigation makes an important contribution to the literature in this area.

Statistically, the most appropriate analysis for this kind of study is between-group analysis rather than within-group analysis. Our between-group analysis, however, lacked power to detect the effects of the intervention because of the low prevalence of PSP in the population<sup>6,61</sup> and, hence, a small number of participants in each group. In contrast, ES are not affected by the number of participants. Our descriptive analysis of between-group ES extended the findings of the other tests by illustrating the direction and magnitude of changes among the groups (Tab. 3). Our ES were normalized to the control group standard deviation rather than a pooled standard deviation (see Glass et al<sup>62</sup> for a discussion justifying this technique). Effect sizes calculated in this way highlighted some effects not found with the 2-sample *t* tests.

Other limitations included the lack of full research masking and the use of a short walkway (3 m) to collect kinematic gait data (usually, gait parameters are measured on longer walkways, but we were limited by physical space in the laboratory).

## Future Studies

The present study was a preliminary investigation with a limited number of participants. Additional studies powered at a higher level are needed to confirm these results. Furthermore, the treatment duration of 4 weeks might have been insufficient to promote an optimal response to the intervention in our participants. It remains unknown whether additional benefits can be obtained with a longer treatment period. In addition, we investigated the immediate effects of rehabilitation in PSP. Future studies should be done to investigate possible carryover effects of the therapy. It also would be interesting to learn how therapy involving balance + eye training can help people with other daily activities, such as negotiating obstacles or steps in the

walking path. In addition, more research is needed to investigate the effects of balance + eye training on populations with similar problems, such as cerebellar ataxia and corticobasal degeneration.

## Conclusion

The present study has provided preliminary evidence that balance exercises coupled with eye movement exercises may improve gait in people with PSP. Improvements in spatial gait parameters, gait speed, and TUG scores were observed for participants who received balance + eye training. Future research is needed to confirm these results on a larger scale, to explore the possible retention of improvements, to determine how balance + eye exercises may influence the ability to negotiate obstacles in the walking path, and to test the benefits of this intervention in other populations.

Both authors provided concept/idea/research design, writing, data collection and analysis, project management, and consultation (including review of manuscript before submission). Dr Di Fabio provided fund procurement, facilities/equipment, and institutional liaisons.

The protocol used in this study was approved by the University of Minnesota Human Subjects Research Committee.

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### Appendix 1.

#### Common Exercises for Balance Training

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1. Romberg (holding balance on the following positions for 20 seconds):
  - Standing with feet together and eyes open and eyes closed
  - Standing in tandem position with eyes open and eyes closed
2. Turning in place (5 times per side):
  - Turning to the left, transferring weight from side to side, and lifting up feet to avoid shuffling
  - Turning to the right, transferring weight from side to side, and lifting up feet to avoid shuffling
3. Backward perturbation training (10 times per leg):
  - Taking voluntary step back while trying to increase pace and amplitude of steps
  - Stepping back after an expected pull from shoulders and hips
  - Stepping back after an unexpected pull from shoulders and hips
4. Sit-to-stand practice (10 times):
  - Rocking back and forth on a chair in preparation for standing up (arms crossed)
  - Standing up from a chair using the arms of the chair and support from the therapist
  - Standing up from a chair with arms crossed and support from the therapist when necessary
  - Sitting down on a chair while controlling the descent (eccentric quadriceps femoris muscle contraction)

## Appendix 2.

### Specific Exercises for the Treatment Group

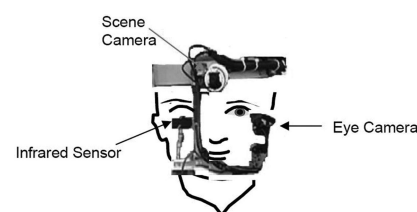
#### Visual Awareness Training

Participants stood in the middle of a room, and therapists presented objects (eg, tennis balls) to them and asked them to point out tennis balls hidden in the room. Participants had to turn in place and move their eyes and head in all directions to look for the hidden objects in the room. The therapists timed how long it took for the objects to be found. Participants were verbally encouraged to beat their own times and be faster on the next round (the number of rounds varied, depending on how fast the participants were). This exercise was done for 8 to 10 minutes.

#### Biofeedback Training

The therapist and the participant were seated facing each other. The participant was wearing an infrared oculography device, as shown in the illustration (inset). Another therapist, behind the participant, was holding a bite bar to stabilize the participant's head. On the command of the therapist, the participant practiced the following eye movements:

- Maximum horizontal and vertical voluntary saccades, focusing on amplitude; no target was used
- Vertical downward saccades to a target (tip of a pen held by the therapist), focusing on speed



Binocular Infrared Recording System

Each exercise was repeated about 10 times with and without auditory feedback. Participants would hear a beat that changed in frequency according to the direction and speed of the eye movements. For example, when the eyes moved down, the beat would slow down until it was totally silent at maximum amplitudes. Participants were encouraged to reach the maximum amplitude of eye movements to silence the beat or speed it up, depending on the direction of movement.

#### Computer Training

Saccades were practiced in front of a computer screen. The computer program randomly presented arrows pointing either to the right or to the left at different locations on the computer screen. Participants practiced making rapid eye movements toward the arrow and clicking on the corresponding arrow on the keyboard. This activity enhanced eye movements in all directions because the arrows could appear randomly anywhere on the screen. The numbers of correct and incorrect answers and the average reaction times were obtained at the end of the practice. Participants performed 4 or 5 trains of stimuli in which each train of stimuli lasted 2 minutes.

#### Platform Limb Cue Training

Participants stood in front of a wooden platform (17.5 cm high, 57 cm wide, and 48 cm deep) facing a projector screen positioned 2.5 m ahead of the platform. A stimulus-response paradigm was used to integrate attention and stepping. Arrows were projected on the screen (one at a time) for 2 seconds, and the participants had to step on the platform after seeing the arrows. Along with the arrows, a high-pitch tone or a low-pitch tone was played. The cognitive challenge was to follow rules to decide which foot to use. When a high-pitch tone was played, the participants were supposed to step with the same foot as the arrow. When a low-pitch tone was played, the participants were supposed to step with the foot opposite the arrow. For each arrow, one step was supposed to be taken. On weeks 3 and 4 of therapy (sessions 9 and 12), a perturbation backward was introduced at random times to increase the balance challenge of the activity. This practice lasted 50 minutes.

### Appendix 3.

Specific Exercises for the Comparison Group

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#### Supplemental Balance Exercises

1. Alternating knee touches: Standing with feet shoulder level apart and arms abducted at 90 degrees, participants alternated reaching down and touching the opposite knee (10 repetitions per side).
2. Side stepping: Starting with feet together, participants practiced stepping to the right and to the left and shifting their weight to the same side (10 repetitions per side).
3. Walking heel to toe: Participants walked on a line of a 3-m walkway, with heels and toes almost touching, holding onto a railing when necessary (5 times).
4. Toe lifts: Standing with feet shoulder level apart, participants lifted up toes, one foot at a time, holding the position for 5 seconds; support from a railing was allowed when necessary (10 repetitions per foot).
5. Heel lifts: Standing with feet together, participants pushed down on toes and lifted up heels as high as possible, holding the position for 5 seconds; support from a railing was allowed when necessary (10 repetitions).
6. Single-leg standing: Participants stood on one foot, holding the position for 10 seconds (10 repetitions per leg).
7. Leg lifts: Standing facing a railing, participants practiced hip abduction with support when necessary (10 repetitions per leg).
8. Leg swings: Participants practiced swinging one leg at a time, forward then backward, as far as possible; support from a railing was allowed when necessary (10 repetitions per leg).
9. Step-ups: Participants practiced stepping up and down on a wooden platform; support from a railing was allowed when necessary (10 repetitions per leg).

## Appendix 4.

### Protocols for the Treatment and Comparison Groups

#### Protocol for the Treatment Group

Week 1	Session 1: treatment A ● Balance training 60 min	Session 2: treatment B ● Biofeedback training 45 min ● Computer training 15 min	Session 3: treatment C ● Visual awareness training 10 min ● Platform limb cue training (with no perturbation) 50 min
Week 2	Session 4: treatment A ● Balance training 60 min	Session 5: treatment B ● Biofeedback training 45 min ● Computer training 15 min	Session 6: treatment C ● Visual awareness training 10 min ● Platform limb cue training (with no perturbation) 50 min
Week 3	Session 7: treatment A ● Balance training 60 min	Session 8: treatment B ● Biofeedback training 45 min ● Computer training 15 min	Session 9: treatment C ● Visual awareness training 10 min ● Platform limb cue training (with perturbation) 50 min
Week 4	Session 10: treatment A ● Balance training 60 min	Session 11: treatment B ● Biofeedback training 45 min ● Computer training 15 min	Session 12: treatment C ● Visual awareness training 10 min ● Platform limb cue training (with perturbation) 50 min

#### Protocol for the Comparison Group

Week 1	Session 1: treatment A ● Balance training 60 min	Session 2: treatment B ● Supplemental balance exercises 60 min	Session 3 ● Treatment B continues 60 min
Week 2	Session 4: treatment A ● Balance training 60 min	Session 5: treatment B ● Supplemental balance exercises 60 min	Session 6 ● Treatment B continues 60 min
Week 3	Session 7: treatment A ● Balance training 60 min	Session 8: treatment B ● Supplemental balance exercises 60 min	Session 9 ● Treatment B continues 60 min
Week 4	Session 10: treatment A ● Balance training 60 min	Session 11: treatment B ● Supplemental balance exercises 60 min	Session 12 ● Treatment B continues 60 min