Computerized Posturography Analysis of Progressive Supranuclear Palsy

A Case-Control Comparison With Parkinson’s Disease and Healthy Controls

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Background: Progressive supranuclear palsy (PSP) is a neurodegenerative disorder that is frequently mistaken for Parkinson’s disease (PD) in its early stages.

Objective: To compare balance measures using computerized posturography in patients with early PSP and early PD.

Methods: We performed computerized posturography (SMART Balance Master; NeuroCom International, Inc, Clackamas, Ore) in 20 patients with clinically diagnosed mild to moderate PSP (ambulatory) and compared results with those from 20 patients with PD of similar age and disease duration who were not receiving medications, and from 20 healthy age- and sex-matched controls. Sensory organization testing (SOT), limits of stability (LOS), and toes-up perturbations (4° at 50° per second) were tested while receiving and not receiving a combination of oral carbidopa (25 mg) and levodopa (250 mg) in the PSP group. Clinical assessment included Unified Parkinson’s Disease Rating Scale, Performance-oriented assessments, and functional reach.

Results: When compared with the PD and control groups, total LOS time ($P_{.001}$) and path sway ($P_{.001}$) were significantly prolonged in PSP. Total SOT showed significantly worse scores in PSP compared with PD and control groups ($F_{2,37}=29.6; P_{<.001}$). Univariate follow-up tests comparing PSP and PD showed differences in the following conditions: eyes open and visual sway ($P_{.003}$), eyes open and platform sway ($P_{.003}$), eyes closed and platform sway ($P_{<.001}$), and eyes open and platform and visual sway ($P_{<.001}$). Medium- and long-latency responses to perturbation were similar, but a larger number in the PSP group lacked short-latency responses ($\chi^2=11.3; P_{.002}$). Levodopa administration did not significantly improve any aspect of posturography testing in PSP. In differentiating PSP from PD, LOS time and SOT condition of eyes open and platform and visual sway were nearly 100% sensitive and 100% specific (canonical correlation, 0.91).

Conclusions: Computerized posturography testing reliably differentiated early PSP from early PD and age-matched controls. The PSP group demonstrated severely contracted limits of stability with probable deficits in motor programming. Results of SOT in PSP suggested a vestibular pattern and overreliance on visual cues, even when incorrect. The absence of short-latency responses (monosynaptic reflex arch) suggests an additional disturbance in the spinal cord or peripheral nervous system.

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SUBJECTS AND METHODS

Twenty patients meeting clinical diagnostic criteria for PSP (still ambulatory),16 and 20 patients with a clinical diagnosis of PD (Hoehn and Yahr 1-2.5) were recruited from the Parkinson's Disease Center and Movement Disorders Clinic, Baylor College of Medicine, Houston, Tex. Patients with PD all demonstrated rigidity, bradykinesia, and rest tremor. Controls were recruited through the School of Physical Therapy, Texas Women's University, Denton. The protocol was approved by the Baylor College of Medicine institutional review board and all subjects signed an informed consent. Controls were matched to the PSP group for age; the PD group was matched to the PSP group for disease duration. Fifteen (75%) of the PSP group met all optimal criteria for PSP, whereas 5 patients did not have clear down-gaze abnormalities but met all other inclusion criteria.26 At the time of posturography testing, both patient groups underwent physical examination, Unified Parkinson's Disease Rating Scale (UPDRS) rating,27 the performance-oriented assessment (POA) (a validated measure of balance that correlates with falls),27 and functional reach (FR) assessment, the distance in inches that a patient can lean forward before losing balance.21 No specific PSP scale was available at the beginning of data acquisition. Clinical assessments and standardized CP assessments in the PSP group were performed without any medications (12-hour washout) and 45 minutes after taking a combination of oral carbidopa (25 mg) and levodopa (250 mg). Computerized posturography testing in the PD group was performed after a 12-hour medication washout period.

The posturography testing used a balance platform (SMART Balance Master; Neurocom International, Inc, Clackamas, Ore) and was performed at the Texas Women's University School of Physical Therapy.23 This device records vertical and horizontal shear forces at different points on the platform on which the patient stands (Table 1). Center of gravity calculations over time are then calculated. The main areas of interest included sensory organization test (SOT), limits of stability (LOS), center target (CT), and EMG, which was used to determine tibialis anterior and gastrocnemius response to rotary perturbation.

The SOT is a static test that measures stability, where sway and center-of-gravity measurements are obtained in different scenarios. Specific sensory organization conditions included the following: eyes open and fixed platform (EOF); eyes closed and fixed platform (ECF); eyes open and visual sway (EOVs); eyes open and platform sway (EOPS); eyes closed and platform sway (EOSS); eyes open and platform and visual sway (VSSS). The average of 3 consecutive trials was used in data analysis.

The LOS is a dynamic test that measures path sway, time, and distance traveled by the patient's center of gravity from an initial starting point to 8 different points set at 75% of the theoretic limit of stability (forward, backward, left, right, forward right, forward left, backward right, and backward left). Subjects obtain visual feedback from a computer screen while they lean until they reach the determined point on the computer screen. The average of 3 trials was used in data analysis.

Central target measures the ability to align the body with a centered visual target and assesses the ability of visual feedback to achieve the CT. The average of 3 trials was used.

Measurement of EMG latency and durations was performed to upward toe tilt (+4° at 50° per second, 20 random repetitions) with surface electrodes attached to the gastrocnemius and tibialis anterior muscles. Alcohol and abrasive rubbing were used to reduce impedance. The onset and integral (function of amplitude and duration) of EMG response for the short- (SL, gastrocnemius), medium- (ML, gastrocnemius), and long-latency (LL, anterior tibialis) responses were calculated for individual legs.

The patients were harnessed from above to prevent falls. Their bare feet were placed on the force platform as a function of patient height. Each part of the study was explained and patients were given a practice trial. The PD group (while not receiving medication) and controls underwent similar CP testing. Specific characteristics such as Mini-Mental State Examination (MMSE), magnetic resonance imaging findings, oculomotor findings, gait, width of walking base, and subjective balance complaints were also assessed in the PSP group.

Variables were grouped in separate construct categories. These categories represented variables for functional balance, sensory aspects of balance, motor aspects of balance, and automatic postural responses. Each construct was analyzed at the level of α = 0.05. A Bonferroni adjustment for multiple comparisons was performed for variables within a construct. Functional reach (FR) and the gait (POAG) and balance (POAB) sections of the POA comprised the functional balance variables. Sensory aspects of balance were represented by the 6 conditions of the SOT and the overall stability score from the SOT. Motor control aspects of balance were represented by the average time to reach 8 targets, the combined path deviation or sway of the trajectory toward those 8 targets (LOS test), and sway from the CT test. The last construct category included the presence of the SL and ML responses, and the latency and integral of all the automatic postural responses.

To determine if the PD and PSP groups differed from controls as well as from each other among several measures of balance, a 3-group multivariate analysis was conducted for the posturography variables and clinical measures of balance. Additional analyses were then performed to differentiate only the PD and PSP groups. These included multivariate analysis for the 6 conditions of SOT and χ2 test to determine the frequencies of occurrence for the SL, ML, and LL EMG responses between groups. Discriminant function tests were conducted with all the balance variables to determine which best predict membership in the PSP vs the PD group. Receiver operating characteristic curves were developed to determine optimal cutoff points for each of the discriminating variables based on highest sensitivity and specificity values.

Comparisons within the PSP group for differences between medication states were performed using the Wilcoxon signed rank test for ordinal data and the Sign test for SL, ML, and LL response frequencies. Repeated-measures analysis of variance (ANOVA) tests using the multivariate approach were used for the analysis of multiple dependent variables. A paired-samples t test was used for the FR. Unless otherwise indicated, data are given as means ± SD.
were no group differences in age, duration of symptoms, or age at onset. The presenting symptoms in the PSP group included gait and/or balance (n=13), bulbar (n=4), ocular (n=2), and appendicular abnormalities (n=1). Associated neurologic conditions included only restless legs syndrome (n=2) and essential tremor (n=1). In the 17 patients with PSP who underwent magnetic resonance imaging, interpretation of findings was completely normal (n=5) or minimal (n=4), mild (n=7), or moderate (n=1) age-related subcortical white matter changes. No patient had any distinct focal ischemia. Subjective levodopa response was no effect (n=9), mild or transient (n=6), and moderate (n=5). No patient reported a good or excellent response. Mean MMSE scores in PSP were 27.0±3.8 (range, 12-30). The single low outlier spoke English as a second language.

The PSP group underwent detailed subsequent assessments for a mean of 12.9±9.1 months (range, 0-32 months) without a change in diagnosis. The PD group was actively followed up for a mean of 17.1±14.3 months (range, 0-41 months) without a change in diagnosis.

Clinical motor assessments of the PSP, PD, and control groups are summarized in Table 3. Kruskal-Wallis tests showed significant differences in clinical balance assessments among the 3 groups (POAG, χ²₂=46.2 [P<.001]; POAB, χ²₂=46.2 [P<.001]). Follow-up Mann-Whitney tests showed that the PSP group was significantly worse than both other groups (POAG, z=−5.13 [P<.001]; POAB, z=−5.02 [P<.001]). The FR measures showed significant differences among the groups (F₂=48.2, P<.001, univariate ANOVA). Follow-up contrast analysis found that the PSP group scores were significantly lower than those of both other groups (P<.001), and that PD group scores were significantly lower than those of controls (P=.003). When comparing UPDRS data between PD and PSP groups, the PSP group had worse total scores, bulbar subscores, posture/balance subscores, and axial rigidity, whereas the PD group had worse

### RESULTS

Patient demographics are summarized in Table 2. There were no group differences in age, duration of symp-

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### Table 1. Abbreviations and Definitions

<table>
<thead>
<tr>
<th>Expansion</th>
<th>Definition</th>
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<tbody>
<tr>
<td>CP</td>
<td>Computerized posturography</td>
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<tr>
<td>SOT</td>
<td>Sensory organization test</td>
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<tr>
<td>EOF</td>
<td>Eyes open, platform fixed</td>
</tr>
<tr>
<td>ECF</td>
<td>Eyes closed, platform fixed</td>
</tr>
<tr>
<td>EDVS</td>
<td>Eyes open, visual sway</td>
</tr>
<tr>
<td>EDSS</td>
<td>Eyes open, platform sway</td>
</tr>
<tr>
<td>ECSV</td>
<td>Eyes closed, platform sway</td>
</tr>
<tr>
<td>VSSS</td>
<td>Eyes open, platform and vision sway</td>
</tr>
<tr>
<td>LOS</td>
<td>Limits of stability testing</td>
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<tr>
<td>CT</td>
<td>Center target</td>
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<td>SLR</td>
<td>Short latency response</td>
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<td>MLR</td>
<td>Medium latency response</td>
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<tr>
<td>LLR</td>
<td>Long latency response</td>
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<tr>
<td>PQA</td>
<td>Performance-oriented assessment</td>
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<td>FR</td>
<td>Functional reach</td>
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Combined SOT, LOS, and perturbation testing Measures patient sway while patient stands on a platform in 6 different scenarios Normal standing Normal standing with eyes closed Walls around the person move, thus altering visual input Platform floor moves, thus altering proprioception Platform floor moves and eyes are closed Eyes open but walls and platform floor both move Shows patient's center of gravity on a computer screen and tracks it as patient leans toward 8 other designated points on the same screen Starting point of the LOS test, which shows the patient's center of gravity and compares it with where it should be After the platform on which patient stands moves quickly, this is the first compensatory muscle response to regain balance; measured by electromyographic sensors on the gastrocnemius Second compensatory muscle response to regain balance; measured by electromyographic sensors on the gastrocnemius Third response seen, which actually counters the initial compensatory gastrocnemius contractions; measured on the anterior tibialis Validated clinical assessment of balance (B) and gait (G) Measures the farthest that someone can lean forward without falling

### Table 2. Patient Demographics*

<table>
<thead>
<tr>
<th></th>
<th>PSP Group (n = 20)</th>
<th>PD Group (n = 20)</th>
<th>Healthy Controls (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>68.0 ± 5.4</td>
<td>65.4 ± 5.3</td>
<td>69.0 ± 3.0</td>
</tr>
<tr>
<td>No. male-female</td>
<td>8:12</td>
<td>13:7</td>
<td>8:12</td>
</tr>
<tr>
<td>Disease duration, y</td>
<td>3.5 ± 1.5</td>
<td>4.4 ± 1.5</td>
<td>...</td>
</tr>
<tr>
<td>Age at onset, y</td>
<td>64.7 ± 5.0</td>
<td>61.0 ± 5.8</td>
<td>...</td>
</tr>
</tbody>
</table>

*PSP indicates progressive supranuclear palsy; PD, Parkinson's disease. Unless otherwise indicated, data are given as mean ± SD.
The PSP group tended to have significantly prolonged swaying in the anterior/posterior movements compared with the PD group (F6,108 = 14.16; P < .001). Multivariate analysis demonstrated the following: (1) CT sway was greater in the PSP than in the PD or control groups (P < .001) and muscle coactivation was marked; (2) total LOS measures of path sway to target (P < .001) and path sway from a straight line to target (P < .001) were significantly prolonged in the PSP compared with the PD and control groups. The PSP group tended to have better performance with lateral movement and worse with anterior/posterior movements (Figure). Total LOS correlated fairly well with total POA scores (Pearson correlation, 0.67).

The PSP and PD groups had similar onset and integral of SL, ML, and LL EMG responses to perturbations, but more patients in the PSP group lacked SL responses (26/40 vs 11/40 legs, χ² = 11.3; P = .002). Although difficult to quantify, the most impressive EMG characteristic in PSP was severe disorganization in all latencies. Frequently, subjects in the PSP group demonstrated multiple peaks, inconsistent temporal patterns, and muscle coactivation.

Levodopa administration did not significantly improve any aspect of functional assessment or CP assessment in the PSP group (Table 6).

Overall, LOS time to target and SOT condition 6 (SVSSF) best discriminated PSP from PD (canonical correlation of 0.91, 95% correctly classified). An LOS average time of greater than 5.0 seconds was 100% sensitive and 95% specific for a correct diagnosis of PSP compared with PD. An SOT VSSS score of less than 36 was 95% sensitive and 85% specific for a correct diagnosis of PSP compared with PD.

Our results demonstrate significant abnormalities of postural control in patients with PSP that were markedly worse than those seen in a PD group matched for age and disease duration, and in age-matched healthy controls.
Although clinical assessments also showed significant differences among the groups, CP was able to more accurately discriminate early PSP from early PD.

The dramatic reduction in LOS suggests that patients with PSP have a very narrow cone of stability. Weight distribution outside of this cone usually resulted in a fall. The SOT results (marked worsening after concurrent alteration of visual and proprioceptive input) are most consistent with a vestibular pattern of dysfunction. When both inputs were removed or confused, the PSP group was unable to compensate. The PSP group also relied more on visual than on somatosensory input, even when visual input was incorrect. This combination is seen in patients with central rather than peripheral vestibular dysfunction. Posturography is not able to further localize neuroanatomy within the vestibular pathways of the central nervous system.

The EMG responses were of normal onset, but often lacked the SL and were very disorganized. This suggests that although righting reflexes arrive quickly enough to compensate, they are inadequate in force, resulting in incomplete and stuttering muscle activity. The SL response abnormalities are believed to represent an impaired monosynaptic reflex arch, whereas ML responses represent polysynaptic responses mitigated by subcortical areas, and LL responses are affected by higher centers. This suggests that some abnormalities in PSP balance may occur within the spinal cord. Several pathologic reports have demonstrated motor neuron degeneration and neurofibrillary tangles throughout the spinal cord of patients with PSP; however, the absence of SL responses is the first physiological demonstration of this abnormality.

The lack of any balance improvement after dopaminergic therapy in PSP is not surprising, given the poor clinical response to dopaminergics in this population. Central vestibular dysfunction typically is not modified by dopaminergic treatment. This is in contrast to PD, where levodopa treatment modestly improves posturography results. The most consistent perturbation abnormality in PD is increased ML response amplitude. Delayed onset and reduced amplitude of LL response are less consistent findings. Early PD shows only minimal abnormalities in LOS and SOT, similar to those of healthy controls.

Despite some clinical similarities, the pathologic changes seen in PSP are quite different from those seen in PD. Brains with PSP show neurofibrillary fibers and neuropil threads throughout the basal ganglia and brainstem. These are present within the cell body and contain abnormally phosphorylated tau protein. Neuron loss in the substantia nigra occurs uniformly throughout the structure rather than just in the lateral pars compacta, as is seen in PD. There is also significant loss of striatal neurons and postsynaptic dopaminergic receptors. This may account for the poor response to levodopa treatment. Numerous other neurotransmitters including the γ-aminobutyric acid, cholinergic, and the adrenergic systems are also involved.

The major weakness of our study is the lack of any gold standard of diagnosis for PD or PSP. However, their diagnosis has not changed in any patient in the subsequent follow-up after posturography testing. Furthermore, down-gaze abnormalities have developed in 3 of the 5 patients who lacked that sign. One died and one was unavailable for follow-up. Their posturography results did not differ from those with down-gaze palsy. Matching 2 different diseases for severity is always problematic. It could be argued that the practical necessity of performing testing in patients with PSP while “off” levodopa and then while “on” levodopa could bias the results in favor of (learning effect) or against (fatigue effect) demonstrating improvement with levodopa. We do not believe that either of these had a significant impact on the results, since practice rounds were performed to counteract any learning effect and a 45-minute rest period was mandatory. Finally, a 12-hour medication washout for patients is standard for treatment trials; however, a long-duration levodopa response could mildly affect the “off” posturography. Despite these weaknesses, we believe that posturography testing objectively differentiates between early PD and PSP and can improve our physiological understanding of balance disorders in parkinsonian diseases.

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REFERENCES