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Posturographic abnormalities in ambulatory atypical parkinsonian disorders: Differentiating characteristics

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A R T I C L E I N F O

Keywords:
Postural instability
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A B S T R A C T

Background: Postural instability is a common complaint in patients with Parkinson's disease (PD), multiple system atrophy (MSA) and progressive supranuclear palsy (PSP). However, objective evaluation to identify posturographic characteristics to enable clinical differentiation is limited.
Method: Postural sway abnormalities in 35 atypical parkinsonian patients (19 PSP, 16 MSA), 35 matched PD patients, and healthy subjects were assessed under static posturography with eyes-open (EO) and eyes-closed (EC).
Results: With EO, MSA patients showed a significantly greater mean ML sway than PD patients ($p = 0.03$), but with EC even more parameters were significantly different, including mean sway in both ML ($p = 0.02$) and AP directions ($p = 0.01$), sway area ($p = 0.001$), and sway path length ($p = 0.003$). While differences between MSA and PD were seen in both ML and AP directions, significant differences between PD and PSP were limited to greater mean ML sway (p = 0.01) with EO, greater mean ($p = 0.002$) and maximal AP sway ($p = 0.02$) amongst PSP patient with EC. Moderate and significant correlation was demonstrated between HY stage and mean AP sway amongst APD patients (r = 0.56, $p < 0.01$) and in PSP patients (r = 0.62, $p < 0.01$).
Conclusion: Our study identifies a number of objective sway measures assessed with EC that are potentially useful for clinical differentiation between APDs and PD. In comparison to PD, MSA showed greater sway area and a mean sway distance in both AP and ML directions, while the difference was limited to AP in PSP. Significant correlation between HY stage and sway parameters further supports postural sway as a potential disease progression marker in APDs.

1. Introduction

Postural instability (PI) is a common complaint in patients with parkinsonian disorders. It is included as one of the cardinal signs in clinical diagnostic criteria of Parkinson's disease (PD), a core feature in the Movement Disorder Society criteria of progressive supranuclear palsy (PSP), and an additional feature in the consensus statement of multiple system atrophy (MSA) [1–3]. For clinical differentiation, neurologists usually rely on the onset of PI, within three years of motor onset, as an indicator for atypical parkinsonian disorders (APDs) [2,3]. Once falls occur, the information on fall circumstances as well as direction-specific PI can assist neurologists in clinical diagnosis. While PD patients tend to fall forwards as a result of freezing of gait, PSP patients are likely to fall backwards and drop-down falls are usually indicative of MSA [4]. However, identification of PI and falls by clinical interview or fall diaries is often inaccurate as those at higher falls-risk are less likely to return diaries, but more likely to report falls [5].

A number of clinical tests have been developed to determine the presence and severity of PI amongst parkinsonian patients. The most widely used test for PI is the pull test which, according to the method provided in the Unified Parkinson's Disease Rating Scale (UPDRS), requires the examiner to pull on the patient's shoulders while standing behind them in order to catch them, should they start to fall [6]. Other tests that have been shown to distinguish APDs from PD are the ability to perform tandem gait and the timed-up-and-go test [7]. However, the value of these tests as a sensitive measurement of PI has been raised as, for example, moderate correlation between pull test and dynamic posturography has been established in PD patients only during the ‘off’, but not the ‘on’ periods [8]. Moreover, these tests are only likely to detect PI when patients become symptomatic, precluding early

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detection of PI in these patients. Indeed, early stage PD patients without any symptoms of PI have been shown to have subclinical PI, when evaluated by objective assessments (e.g. posturography), which compensated for by patients to keep their balance in unstable conditions [9,10]. Therefore, this evidence suggests that subclinical PI exists in PD and probably also in APDs.

Identification of PI in parkinsonian patients who are still ambulatory has several important implications. As PI and postural sway are associated with severity and progression in PD, early detection of these features, even though subclinical or mildly symptomatic, alerts physicians and enables early interventions to be put in place to reduce their impact [11,12]. In a recent meta-analysis in PD, early intervention of exercise training may improve balance, gait, and prevent falls in patients with PD [13]. For APDs, early benefits from specific rehabilitation programmes have been demonstrated in patients with PSP and MSA [14,15]. Also, identifying specific patterns of PI may provide additional clues to allow differential diagnosis. A lack of objective evaluation may be one of the reasons why APDs are undiagnosed by general neurologists, especially in the early stage when pertinent clinical signs are not evident on clinical examination [16]. As an objective and quantitative measure of balance and PI, posturography has been shown to enable differential diagnosis of parkinsonian disorders through the application of varying sensory inputs that may elicit significant abnormalities [17]. When early PD patients without PI were assessed by posturography during visual deprivation (eye closed), greater mean sway area compared to control subjects was demonstrated [9,10]. Although it seems to be common knowledge to most neurologists that PI affects most forms of APDs in the early stage, few studies have attempted to perform objective posturographic assessments to determine specific patterns of PI between PD and specific APDs, including MSA and PSP, or a combination of MSA and PSP as a group of APDs, for the purpose of early differential diagnosis when patients are still ambulatory [18–20]. Therefore, the aim of the present study is to objectively compare PI in ambulatory patients with PD and APDs with eyes open and eyes closed, to test whether quantitative posturographic analysis could be used for a differential diagnosis of PD and APDs, or even between specific APDs like PSP and MSA, and to stimulate scientific discussion on the underlying pathophysiology of PI in PD and APDs.

2. Methods

2.1. Subjects

35 patients with a clinical diagnosis of APDs (19 PSP, 16 MSA; 10 MSA-P and 6 MSA-C) and 35 PD patients who were matched for age (± 5 years), sex, weight (± 2 kg), height (± 5 cm), body mass index (BMI, ± 2), and Hoehn & Yahr (HY) were recruited from the outpatient clinic of the Chulalongkorn Centre of Excellence for Parkinson's Disease and Related Disorders (www.chulapd.org) between June 2017 and October 2018. 35 healthy controls with no sign of parkinsonism with a similar matched for the same parameters were also recruited. The diagnosis of probable PSP, probable MSA, and PD was based on the standard diagnostic criteria [1–3]. As defined in the previous literature, participants were categorised as MSA-P if they exhibited parkinsonism but no cerebellar features and if parkinsonism preceded cerebellar signs by at least 1 year. Patients with MSA-C were defined as having predominant cerebellar signs, but little or no parkinsonism and cerebellar signs that preceded parkinsonism by at least 1 year [21]. We excluded subjects if they were: 1) unable to ambulate independently as determined by HY stage 4–5; 2) diagnosed with secondary parkinsonism (e.g. vascular parkinsonism, normal pressure hydrocephalus); 3) examined to have comorbidities that may affect posture and balance, including neuropathy, impaired proprioception, vestibular disorders, visual disturbances, and tremor in the lower extremities that may interfere with posturographic evaluation; and 4) diagnosed with severe dementia, as determined by the Thai Mini-Mental Status Examination (TMSE) score of less than 21, and major depression as defined by the DSM-V criteria. All subjects were screened not to take sedatives and must have a negative Romberg's test. All subjects were assessed in the morning, and for PD and APD patients, at least 12 h after the last dose of anti-parkinsonian medications in order to reduce the effect of dopaminergic medications on posturographic findings.

Baseline clinical characteristics were recorded in all subjects. Scale-based assessments were performed in all PD and APD subjects, including the UPDRS total scores, UPDRS-III (motor) sub-scores, and UPDRS axial sub-score (sum of UPDRS items 18, 22, 27–30). Fall rates were obtained from a standardised fall diary, which was sent out to all subjects in three monthly batches with pre-paid return envelopes. Subjects were asked to send diaries back on a monthly basis. A fall was defined as an event which results in a person coming to rest inadvertently on the ground, floor, or other lower level [22]. The study was approved by the Human Subjects Ethics Committee of the Faculty of Medicine, Chulalongkorn University (297/58). All subjects gave their written informed consent before entering the study in accordance with the declaration of Helsinki.

2.2. Experimental protocol

Postural assessment in terms of postural sway was analysed using a 50 × 50 cm force platform (Cosmogamma, Emildue, Cento, Italy) with three dynamometric load cells measuring the forces exerted by the subjects on the support surface at a sampling rate of 20 Hz. Changes in positions and the Centre of Pressure (CoP) trajectories were calculated by a software (BalancePlatform v. 8.0.1). Platform calibration was performed each day before testing.

All subjects were asked to maintain an upright standing position on the force platform, with arms at their sides, and bare feet externally rotated at an angle of 30° and heel-to-heel distance was standardised at 2 cm. All test conditions were conducted in a comfortable quiet environment. With eyes open (EO), subjects were asked to look straight at a fixed point on the wall which was 1 m away for 30 s. In order to remove visual input, all subjects were asked to repeat the same procedure with eyes closed (EC). Each trial was repeated three times and mean values for these trials were reported for all subjects. Rest periods of 2 min were permitted between each trial. Each subject was tested in a 1-day session.

Full details of the experimental set-up and its analysis have been previously published [10]. Five dependent variables were calculated from the raw data: 1) mean and maximal sway (mm); 2) sway path length (mm); 3) sway area (cm^2); and 4) the Romberg quotient. All variables were computed for its directional subcomponents: anteroposterior (AP) and mediolateral (ML). In addition, a 95% confidence ellipse for each trial was estimated and the area of the confidence ellipse and the direction of maximal sway were quantified.

2.3. Statistical analysis

Baseline characteristics and posturographic parameters were summarised using either means and standard deviations (SD), or frequencies and percentages as appropriate. Shapiro-Wilk test was performed to evaluate the normality of demographics and posturographic parameters in each group. Differences among atypical parkinsonian disorders (APDs), Parkinson's disease (PD) and healthy controls were evaluated using one-way analysis of variance (ANOVA) with two-sample t-tests or Kruskal-Wallis rank sum test with Mann-Whitney test for post-hoc pair-wise tests for continuous and ordinal variables. Bonferroni's adjustment was used for multiple comparison between groups. To compare between PSP, MSA, PD and healthy controls, one-way ANOVA or Kruskal-Wallis rank sum test was performed with two-sample t-tests or Mann-Whitney tests for post-hoc pair-wise comparisons. Correlations across the sway data, and between the sway data and the patient's demographics, were evaluated with the non-

Table 1
Clinical demographics of Parkinson's disease patients, atypical parkinsonian patients and control subjects.

	Controls (N = 35)	PD (N = 35)	APD (N = 35)	p-value[a]	PSP (N = 19)	MSA (N = 16)	p-value[a]
Age (years)	64.2 ± 10.9	64.7 ± 8.7	64.5 ± 9.5	0.97	69.1 ± 7.0	59.1 ± 9.4	0.02* (PSP > MSA)
Sex (% female)	18 (51%)	18 (51%)	18 (51%)	0.53	9 (47%)	9 (56%)	0.68
Body weight (kg)	62.2 ± 8.7	61.8 ± 13.4	60.8 ± 10.4	0.42	60.0 ± 9.3	61.7 ± 11.9	0.63
Height (cm)	162.5 ± 8.0	159.8 ± 9.3	160.7 ± 8.9	0.86	160.5 ± 9.5	161.1 ± 8.5	0.91
Body mass index	23.6 ± 3.0	24.1 ± 4.2	23.4 ± 2.7	0.67	23.2 ± 2.3	23.6 ± 3.2	0.81
HY stage	–	2.7 ± 0.3	2.8 ± 0.3	0.07	2.8 ± 0.3	2.7 ± 0.3	0.12
Disease duration (Years)	–	8.5 ± 5.2	4.4 ± 2.8	0.001*	4.3 ± 2.6	4.4 ± 3.3	0.004* (PD > PSP) (PD > MSA)
TMSE	28.4 ± 1.1	27.7 ± 1.9	27.0 ± 2.9	0.10	26.6 ± [3.3]	27.5 ± 2.5	0.22
UPDRS-III sub-score	–	25.5 ± 12.6	31.5 ± 11.5	0.09	31.2 ± 10.5	31.7 ± 13.2	0.25
UPDRS axial sub-score	–	7.7 ± 2.4	12.8 ± 2.9	0.003*	13.8 ± 1.9	10.7 ± 4.0	0.005* (PSP > PD)
LED (mg)	–	731 ± 392	657 ± 435	0.75	759 ± 441	525 ± 405	0.31
Fall rate	0	0.5 ± 0.8	5 ± 3.8	< 0.001* (APD > PD > C)	3.7 ± 1.3	6.7 ± 5.7	< 0.001* (PSP > PD=C) (MSA > PD=C)

*p-value < 0.05.
PD: Parkinson's disease; APD: Atypical parkinsonian disorders; PSP: Progressive supranuclear palsy; MSA: Multiple system atrophy; C: Controls; HY: Hoehn & Yahr; TMSE: Thai version of the Mini-Mental Status Examination; UPDRS: Unified Parkinson's Disease Rating Scale; LED: Levodopa equivalent dose.
[a] P-value from one-way analysis of variance (ANOVA) or Kruskal-Wallis rank sum test for continuous and ordinal variables.

parametric Spearman's rank test. Statistical analysis was performed using SPSS version 23.0 software (SPSS Inc., Chicago IL).

To determine the sample size, power analysis was performed based on the exploratory hypothesis if that the sway path between PD and APDs patients is different with references from previously published studies between MSA and PD (mean difference = 0.9 and SD = 0.6) [19] and PSP and PD (mean difference = 0.13 and SD = 0.13) [18]. A sample size of at least 15 subjects per group was identified to detect an effect size of 0.5 with power of 0.8 with one-way ANOVA.

3. Results

There were no significant differences between PD and APD groups on demographic and baseline characteristics except for a significant longer disease duration (8.5 ± 5.2 vs. 4.4 ± 2.8, $p = 0.001$) and higher fall rate (0.5 ± 0.8 vs. 5.0 ± 3.8, $p < 0.001$) in APD patients (Table 1). The mean HY stage in both PD and APD groups was comparable between 2.7 and 2.8, indicating mild-to-moderate bilateral disease with some postural instability, but still physically independent. While the UPDRS-III sub-score between PD and APD groups was not statistically different, the UPDRS-axial score was significantly higher in APD than PD patients (12.8 ± 2.9 vs. 7.7 ± 2.4, $p = 0.003$). All three groups were similar with respect to age, gender, height, weight, BMI and TMSE.

All participants were able to complete both tasks without any complications. With EO, APD patients showed significantly greater mean ML sway ($p = 0.003$), maximal ML sway ($p = 0.007$), maximal AP sway ($p = 0.03$), sway area ($p = 0.02$) than PD patients, while no significant differences were demonstrated in other posturographic parameters (Table 2). With EC, significant differences were observed in several posturographic parameters; APD patients exhibited greater sway area ($p = 0.001$), mean ML and AP sway (ML: $p = 0.005$; AP: $p < 0.001$), maximal ML and AP sway (ML: $p = 0.007$; AP: $p < 0.001$), and sway area ($p = 0.001$) than PD patients (Table 2). PD patients tended to exhibit larger sway area, mean and maximal ML sway, and sway path length than control subjects, however none of these parameters reach significance.

Subgroup analysis revealed several significant findings (Table 2). With EO, MSA patients only showed a significantly greater mean ML sway than PD patients ($p = 0.03$), but, with EC, several parameters became significantly different, including mean sway in both ML ($p = 0.02$) and AP directions ($p = 0.01$) as well as sway area ($p = 0.001$), and sway path length ($p = 0.003$). Similar differences were also observed between MSA-P and PD as well as MSA-C and PD with EC. Interestingly, while differences between MSA and PD were in both ML and AP directions, the only significant difference between PD and PSP was limited to greater mean ML sway ($p = 0.01$) with EO, mean ($p = 0.002$) and maximal AP sway ($p = 0.02$) for PSP patients with EC. MSA patients demonstrated significantly greater sway path length ($p = 0.04$) compared to PSP patients with EC. However, significant difference was limited to sway path length ($p = 0.04$) between MSA-P and PSP. No significant differences on posturographic parameters between patients with MSA-P and MSA-C were observed. The Romberg quotient was lowest in MSA patients, with a significantly difference from PD ($p = 0.02$). 95% confidence ellipse of mean sway representing a mean CoP displacement with EC of all three subject groups (PD, APD, control group) and subgroups is shown in Fig. 1. With EC, the CoP trajectory of APD patients covered a larger area than in the PD and control groups in both AP and ML directions. In comparison to PD, the area of CoP displacement with EC in MSA was larger in both ML and AP directions while the same observation was only observed in the AP direction in PSP patients. Amongst all parkinsonian syndromes, sway area was largest in MSA, followed by PSP, and smallest in PD. Full results with multiple comparison analysis are included in the supplementary data 1 (Supplementary Figs. 1 and 2).

Exploratory correlation analysis was performed, indicating moderate and significant correlation with EC between HY stage and mean AP sway amongst APD patients (r = 0.56, $p < 0.01$) and in PSP patients for the subgroup analysis (r = 0.62, $p < 0.01$) (Fig. 2). Full details of correlation analysis were included in the supplementary data 2.

4. Discussion

Our study demonstrates objective evidence of PI in APD, and reveals significant posturographic differences when compared to PD and heathy controls with EO, and more distinctly with EC. Several clinical implications could be developed from observations made from this study. For example, increased ML sway, as observed amongst APD patients, could potentially contribute to poor performance on a 10-step tandem walk as demonstrated in a prospective clinical trial where, only 18% of APD patients could achieve this test compared to 92% of PD patients with the same disease duration, making this test a potential red flag for APD [23]. When visual input is withdrawn by simple eye closure, patients rely more on their proprioceptive function to maintain an upright posture, thus specific abnormalities become evident depending upon the deficits in sensorimotor integration of individual parkinsonian disorders. While sway area was increased only in the ML direction in APD patients with EO, sway area became larger in both ML and AP directions with EC. Larger sway area in both AP and ML directions were also observed between MSA and PD, but the differences were limited to

Table 2
Comparison of posturographic parameters between Parkinson's disease and atypical parkinsonian patients with subgroup analysis, including progressive supranuclear palsy and multiple system atrophy.

	Control (N = 35)	PD (N = 35)	APD (N = 35)	p-value[a]	PSP (N = 19)	MSA (N = 16)	p-value[a]
Eye open							
Maximum ML sway	7.36 ± 2.99	8.99 ± 6.09	12.8 ± 7.49	0.001* (APD > PD=C)	12.15 ± 6.25	13.56 ± 8.88	0.002* (PSP > C, MSA > C)
Maximum AP sway	9.16 ± 2.71	10.87 ± 6.55	14.29 ± 7.6	0.004* (APD > PD=C)	13.91 ± 7.46	14.74 ± 7.98	0.01*
Mean ML sway	2.28 ± 0.88	3.03 ± 2.15	4.54 ± 2.71	< 0.001* (APD > PD=C)	4.23 ± 1.88	4.9 ± 3.48	< 0.001* (PSP > PD=C, MSA > PD=C)
Mean AP sway	3.14 ± 0.98	3.77 ± 1.97	4.30 ± 2.00	0.05	4.46 ± 2.12	4.1 ± 1.88	0.11
Sway area	2.39 ± 1.07	4.06 ± 5.93	7.42 ± 10	0.001* (APD > PD=C)	6.23 ± 7.23	8.45 ± 12.69	0.002* (PSP > C, MSA > C)
Sway path length	315.2 ± 95.3	375.8 ± 203.5	479.3 ± 301.9	0.03* (APD > C)	435.1 ± 203	531.7 ± 375	0.06
Eye closed							
Maximum ML sway	9.46 ± 3.68	10.87 ± 6.15	16.01 ± 9.89	0.001* (APD > PD=C)	13.51 ± 5.84	18.98 ± 12.8	0.001* (MSA > PD=C)
Maximum AP sway	12.1 ± 3.59	12.49 ± 6.06	20.09 ± 9.56	< 0.001* (APD > PD=C)	18.76 ± 8.58	21.67 ± 10.7	0.001* (PSP > PD= C, MSA > PD=C)
Mean ML sway	2.81 ± 1.13	3.46 ± 2.12	5.15 ± 3.18	< 0.001* (APD > PD=C)	4.29 ± 1.7	6.18 ± 4.18	0.001* (MSA > PD=C, PSP > C)
Mean AP sway	4.17 ± 1.13	3.03 ± 1.84	5.98 ± 2.33	< 0.001* (APD > PD=C)	6.04 ± 2.37	5.9 ± 2.36	< 0.001* (PSP > PD= C, MSA > PD=C)
Sway area	4.34 ± 2.54	5.68 ± 5.31	11.89 ± 14.75	< 0.001* (APD > PD=C)	7.89 ± 6.11	16.6 ± 20.11	< 0.001* (MSA > PD=C)
Sway path length	441.9 ± 170	507.9 ± 295.5	704.6 ± 431.2	0.01* (APD > C)	561.8 ± 323	874.2 ± 489	0.001* (MSA > PD=C, MSA > PSP)
Romberg's quotient	0.75 ± 0.28	0.8 ± 0.22	0.79 ± 0.57	0.26	0.79 ± 0.17	0.6. ± 0.15	0.02* (PD=PSP > MSA)

*p value < 0.05.
PD: Parkinson's disease; APD: Atypical parkinsonian disorders; PSP: Progressive supranuclear palsy; MSA: Multiple system atrophy; C: Controls; ML: Mediolateral direction; AP: Anteroposterior direction.
[a] P-value from one-way analysis of variance (ANOVA) or Kruskal-Wallis rank sum test for normal distributed and non-normal distributed variables.

the AP direction between PSP and PD. That MSA had the lowest Romberg's quotient also indicates that sway area heavily depends on visual input. As previous studies have identified, low illumination or a lack of visual inputs is a potential exacerbator of PI in both older people and PD patients [10,24]. However, our study has provided an additional finding that the effect of visual deprivation on PI seems to be strongest in APD patients. This information could be useful when planning environmental adaptations for parkinsonian patients to ensure adequate lighting is maintained during ambulation where postural stability is essential.

In addition to visual input, PI could be influenced by the intrinsic disease itself, and manifested differently in individual parkinsonian disorders. Due to a more widespread degeneration in APDs, involving the basal ganglia and its efferent connections, it is expected that the severity of postural sway should be worse in APDs than PD [25]. Indeed, our study findings are consistent with existing literature in demonstrating significantly different spontaneous sway abnormalities amongst APD patients when compared to PD patients and healthy controls [26]. MSA effects multiple systems, including the cerebellum and brainstem, which explains why MSA patients exhibited increased sway in both AP and ML directions when compared to PD. However, significant differences were not observed between MSA-P and MSA-C patients, which may be related to insufficient statistical power or the inability of posturography to differentiate between MSA subtypes, particularly during the early disease stage. However, MSA-P patients have a significantly increased sway area and maximal sway in both AP and ML directions when compared to PD patients. This finding may allow the early differentiation between MSA-P and PD when clinical signs often overlap and levodopa responsiveness may still be present in both disorders. In contrast, sway area is not significantly different between PSP and PD, consistent with a prior study showing that spontaneous sway was smaller and slower in PSP patients [20]. However, a new finding from our study is the direction specific nature of the changes. In PSP, the maximum and mean sway was significantly increased in the AP direction, possibly owing to a predominant axial involvement amongst PSP patients. In PD, sway abnormalities are predominantly ML, so this AP sway predilection in PSP could be another useful clue when differentiating PSP from PD [11,27]. From this finding, the provision of specific early intervention to improve PI in PSP patients, such as goal-based rehabilitation that focuses on the coordination of motor and cognitive function can be applied to improve gait and balance parameters as well as a reduction of falls [28]. In addition, another important finding from our study is the significant correlation between HY stage and sway parameters (sway velocity in MSA and mean AP sway in PSP) indicating that postural sway is likely to be a marker of disease progression in APDs, as well as PD [11,29].

A strength of our study is the careful selection of subjects who fulfill not only the standard diagnostic criteria, but also stringent matched-criteria between three subject groups to avoid potential confounding factors. In contrast to prior studies, we intentionally matched HY stage in all three subject groups as the classification of HY stage relies on the presence of axial manifestations and PI [18,20]. Since the purpose of our study is to determine differentiating characteristics of posturographic abnormalities in those patients who are still ambulatory, matching by HY stage is probably a more appropriate method than by using disease duration as we can ensure the recruitment of all those subjects who are ambulatory, but, at the same time, exclude those who require assistance with their ambulation. Moreover, HY stage is an objective measure that can be verified by a trained investigator, in contrast to disease duration, which could be prone to recall bias. When HY is matched, disease duration is observed to be significantly longer in PD than APDs groups. As both UPDRS-III and HY scales have been validated not only in PD, but also in MSA and PSP, they can be used as common scales for assessment, for the purpose of comparison, of the severity and disability in PD, MSA, PSP patients respectively [30–33]. However, we need to bear in mind the limitations of implementing a set

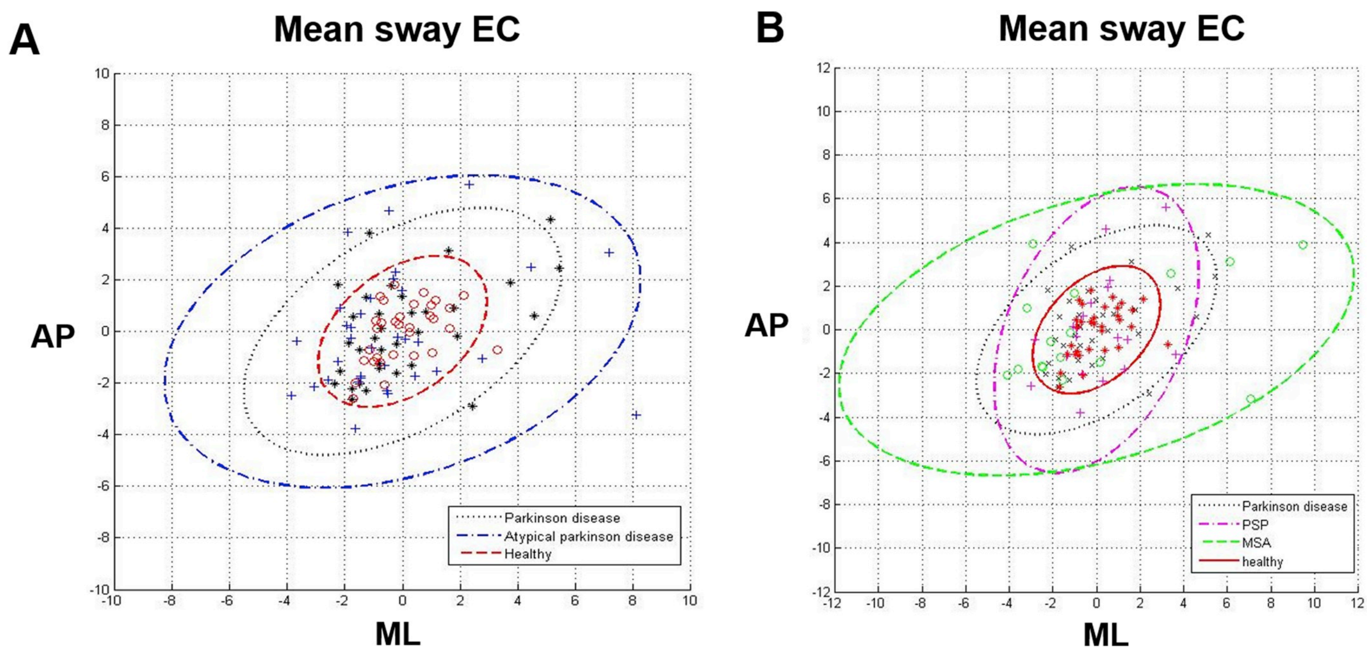

Fig. 1. 95% confidence eclipse of mean sway (mm) of Parkinson's disease, atypical parkinsonian disorder and healthy control subjects under eye closed condition. PSP: progressive supranuclear palsy; MSA: Multiple system atrophy.

of common scales on a group of heterogenous disorders as they are not specifically designed to capture particular aspects of individual disorders. For example, the HY scale may not necessarily reflect the pattern of motor progression in PSP and MSA-C patients because these two disorders frequently begin with postural disturbances. In future studies, dedicated scales for individual disorders, including the Unified Multiple System Atrophy Rating Scale (UMSARS) for MSA and Progressive Supranuclear Palsy Rating Scale (PSPRS) for PSP should be used to determine the correlations with posturographic parameters [34,35]. The number of subjects in each group is comparable to previously published studies and we focused our study on those who are still ambulatory in order to identify posturographic characteristics that could supplement clinical evaluation in early differentiation of APDs [10,11,20,26]. Statistically insignificant posturographic findings between MSA subtypes could be related to a small number of MSA-P and MSA-C patients. It is also possible that static posturography alone is insensitive in differentiating between MSA-P and MSA-C patients, particularly during the early stage. Further studies involving a larger number of MSA-P and MSA-C subtypes with combined posturographic and gait assessments are required to determine their diagnostic utility. The effect of levodopa was also diminished in all subjects by performing the test of at least 12 h after the last dose of anti-parkinsonian medications [36]. Limitations of our study include a lack of postural reaction and adaptation evaluation, which is commonly performed by dynamic posturography, however, our study aimed to employ simple procedures or devices that could be implemented in non-laboratory clinical practice. Also, a lack of randomisation between EO and EC could potentially have caused a systematic bias. However, we followed an established protocol, as published in previous literature [10,18,37], where the learning effect is unlikely or minimal when the number of attempts in each trial is fewer than 4, optimal test retest reliability is achieved when the trial duration is 30-s, and no prior instruction is given to subjects on which paradigm (EO or EC) to perform [38,39]. A lack of subtype evaluation (e.g. PSP subtypes) could also limit further identification of posturographic features of each subtype.

In conclusion, our study has identified a number of objective sway measures with EC that are potentially useful for clinical differentiation between APDs and PD. In comparison to PD, MSA showed greater sway area and a mean sway distance in both AP and ML directions while the difference was limited to AP in PSP. Significant correlation between HY stage and sway parameters in APDs further supports postural sway as a potential marker of disease progression. Early identification of postural abnormalities in APDs does not only assist neurologists in the clinical differentiation, but also enable specific early intervention for goal-based rehabilitation.

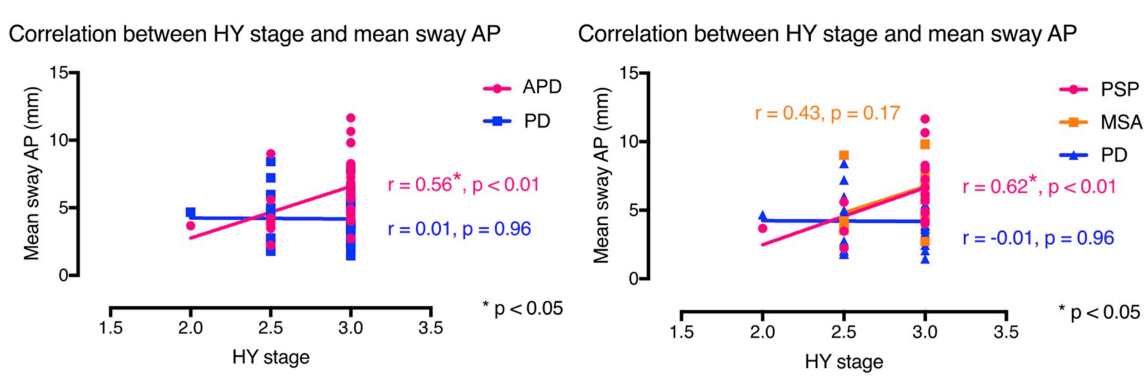

Fig. 2. Correlation analysis between the Hoehn & Yahr stage and sway area in the anteroposterior direction under eye closed condition. PD: Parkinson's disease; APD: Atypical parkinsonian disorders; PSP: Progressive supranuclear palsy; MSA: Multiple system atrophy.

Conflicts of interest

The authors have no conflict of interest.

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Appendix A. Supplementary data

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