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Open-loop and closed-loop postural control mechanisms in Parkinson's disease: increased mediolateral activity during quiet standing

S.L. Mitchell[a,*], J.J. Collins[b], C.J. De Luca[b], A. Burrows[a], L.A. Lipsitz[a,b]

[a]*Hebrew Rehabilitation Center for Aged Research and Training Institute, Department of Medicine of Beth Israel Hospital, and Division on Aging, Harvard Medical School, Boston, MA, USA*

[b]*NeuroMuscular Research Center and Department of Biomedical Engineering, Boston University, Boston, MA, USA*

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Abstract

Stabilogram-diffusion analysis was used to gain insights into how idiopathic Parkinson's disease (IPD) affects the postural control mechanisms involved in maintaining erect stance. Twenty-two subjects with IPD and twenty-four healthy elderly subjects were studied under eyes-open, quiet-standing conditions. The postural control mechanisms in the parkinsonian subjects, compared to the healthy elderly, were characterized by an increase in the effective stochastic activity in the mediolateral direction. Mediolateral posturographic measures were also associated with a history of falls and poor performance on clinical measures of balance. It is hypothesized that the increase in mediolateral activity in subjects with IPD may reflect an attempt to maintain potentially stabilizing movements during quiet standing in the face of impaired movement in the anteroposterior direction. This study supports the notion that mediolateral instability is an important posturographic marker of functional balance impairment in the elderly.

Keywords: Posture; Balance; Aging; Elderly; Parkinsonism; Center of pressure; Sway; Falls

Idiopathic Parkinson's disease (IPD) is a common neurodegenerative disease of later life. The clinical hallmark of advanced IPD is postural instability, which can result in significant morbidity due to falls, associated injury and functional impairment. Despite the morbid consequences of this problem, the postural dyscontrol associated with IPD remains a poorly understood phenomenon.

Most previous investigations of postural control mechanisms in IPD have measured motor responses to various external perturbations and disturbances [7,13,15,16]. Studies of this sort, however, can be difficult to perform and often yield conflicting results. The few studies which have analyzed quiet-standing stability in IPD have been contradictory, with some reporting a decrease in postural sway compared to healthy subjects [13] and others reporting an increase in sway [16]. Furthermore, these investigations limited their analyses to singular responses (e.g. reaction times) of isolated systems and thus failed to provide meaningful insights into how the complex integration of the different components of the postural control system breaks down in advanced IPD.

Stabilogram diffusion analysis [4,5] is based on a random-walk approach to quiet-standing center-of-pressure (COP) trajectories. It has the advantage over traditional posturographic approaches in that it yields COP parameters which relate directly to the steady-state behavior and functional interaction of the neuromuscular mechanisms underlying the maintenance of erect stance. Stabilogram-diffusion analysis has recently been used to gain insight into how the natural aging process affects the operational characteristics of the postural control mechanisms involved in quiet standing [6]. Given the relative ease and safety with which this technique can be applied to older adults, we utilized stabilogram-diffusion analysis in the present study to yield physiologically meaningful insights into the postural dyscontrol associated with IPD.

Twenty-two subjects with IPD and twenty-four healthy elderly control subjects were included in this study. IPD subjects had their diagnosis previously confirmed by a neurologist. All subjects were able to stand independently. Informed consent was obtained from each subject prior to their participation.

* Corresponding author, Hebrew Rehabilitation Center for Aged, 1200 Center St., Boston, MA 02131, USA. Tel.: +1 617 3258000; Fax: +1 617 327 7639, E-mail: mitchell@hera.hrca.harvard.edu.

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In order to screen for clinical findings associated with impaired balance and gait, all subjects underwent a detailed clinical evaluation by one of two physicians trained in geriatric medicine (S.M. or A.B.). This assessment included a complete history and medication review (with attention to medical conditions and drugs associated with increased risk of falls). A history of falls over the previous 12 months was determined by subjects' self-report. A targeted physical examination included the evaluation of postural vital signs, height, weight, body mass index, cardiovascular function, neurological signs, the Mini-Mental Status Examination [10], and the Geriatric Depression Scale (short form) [18]. Subjects were excluded if they had debilitating rheumatological or orthopaedic conditions, neurological diagnoses (other than IPD), or cognitive impairment such that they could not understand the study protocol. Clinical measures of balance and gait included habitual gait speed, functional reach (the ability to reach as far as possible with an outstretched arm without taking a step) [8], and a clinical balance scale [2] (IPD group only).

The Unified Parkinson's Disease Rating Scale (UPDRS) [9] and the Hoehn and Yahr Scale [12] were used to quantify the severity of IPD. The distribution of subjects at each Hoehn and Yahr stage were as follows: stage 1.5 ($N = 1$), stage 2 ($N = 7$), stage 2.5 ($N = 7$), stage 3 ($N = 6$) and stage 4 ($N = 1$). The disease duration ranged from 1.5 to 16.0 years (mean 8.6 ± 3.6 (SD) years). The group mean score on the UPDRS motor subscale was 25 ± 14 (range 4–49).

Postural sway was evaluated using a Kistler multicomponent force platform to measure the time-varying displacements of the COP under each subject's feet. During the testing, each subject stood barefoot on the platform (feet abducted 10° and heels separated by 6 cm), with their arms relaxed at their sides and their eyes fixed on a point in front of them. A series of ten 30-s trials was conducted for each subject with their eyes open. The data were sampled at a frequency of 100 Hz. Rest periods of 60 s were permitted between each trial. IPD subjects were tested on their usual regimen of antiparkinsonian drugs, and those with symptom fluctuations were tested during an 'on period'. Each subject was tested in a 1-day session.

The COP trajectories were studied as one-dimensional and two-dimensional random walks according to stabilogram-diffusion analysis. This technique is described in detail in previous work [4,5]. With this approach, stabilogram-diffusion plots are generated for each subject by plotting the mean square COP displacement versus increasing time intervals. Stabilogram-diffusion plots have two regions, one over short-term time intervals and the other over long-term time intervals. These regions are separated by a critical period over which the slope of the plot changes considerably. Three sets of posturographic parameters are extracted from these plots: effective diffusion coefficients, scaling exponents, and critical point coordinates. Effective diffusion coefficients reflect the level of effective stochastic activity of the postural control system along the mediolateral (ML) and anteroposterior (AP) axes and about the plane of support. Scaling exponents assess the likelihood that the COP will move away from or toward a relative equilibrium point. Earlier studies using stabilogram-diffusion analysis [4–6] revealed that over short-term time intervals during undisturbed stance the COP behaves as a positively correlated random walk, i.e. one which tends to move or drift away from a relative equilibrium point, whereas over long-term time intervals it resembles a negatively correlated random walk, i.e. one which tends to return to a relative equilibrium point. We interpreted this finding as an indication that during quiet standing the postural control system utilizes open-loop and closed loop control schemes over short-term and long-term time intervals, respectively. (An open-loop control system is one which operates without feedback, whereas a closed-loop control system is one which operates with feedback.) The open-loop postural control mechanisms are characterized by relatively large effective diffusion coefficients (i.e. relatively large effective stochastic activity). The closed-loop postural control mechanisms, on the other hand, are characterized by smaller effective diffusion coefficients (i.e. less effective stochastic activity). The critical point coordinates (the critical time interval and critical mean square displacement) approximate the transition region separating the short-term and long-term regions, thus quantifying the temporal and spatial characteristics of the region over which the postural control system switches from open-loop control to closed-loop control.

The following commonly-used COP parameters were also calculated from the stabilogram time series: maximal AP displacement, maximal ML displacement, root mean square (RMS) displacement, and radial area [11]. These parameters were computed for each subject trial, and then averaged for each set of 10 trials to obtain a resultant measure for each parameter for each subject.

For each posturographic parameter and continuous clinical measure, analysis of variance (ANOVA) was used to compare group means between the healthy elderly and IPD subjects. Chi-squared tests were used to compare the frequency of the categorical clinical measures between each group. Since a significantly greater proportion of IPD subjects took antidepressant medications, separate covariance analyses (ANCOVA) were performed for all balance measures while controlling for the use of antidepressants. Pearson correlation coefficients were used to compare functional measures of balance (functional reach, gait speed, and the clinical balance scale) with posturographic parameters. ANOVA was used to compare balance measures between subjects with and without falls in the previous year. Because of the large number of analyses performed, the criterion level of significance was set

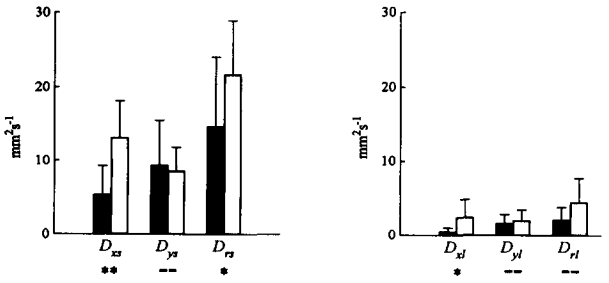

Fig. 1. Group means and standard deviations for the healthy elderly ($N = 24$) and subjects with IPD ($N = 22$) for: (a) short-term and (b) long-term effective diffusion coefficients. The symbols D_{xs}, D_{ys} and D_{rs} represent the short-term effective diffusion coefficients in the mediolateral, anteroposterior and planar directions, respectively. D_{xl}, D_{yl} and D_{rl} represent the long-term effective diffusion coefficients in the mediolateral, anteroposterior and planar directions, respectively. The symbols * and ** denote statistically significant differences at $P < 0.01$ and $P < 0.001$ levels, respectively, after controlling for the use of antidepressant medications (ANCOVA). The symbol -- denotes statistical comparisons that were not significant.

at $\alpha = 0.01$ to reduce the chance of type 1 (false positive) statistical errors.

The healthy elderly and IPD subjects were similar with respect to age (75 ± 2 versus 72 ± 10 years; NS), gender (10% versus 9% male; NS), height (1.6 ± 0.1 versus 1.6 ± 0.1 m; NS), weight (66.4 ± 13.9 versus 63.3 ± 14.8 kg; NS) and body mass index (26.5 ± 5.4 versus 25.5 ± 4.6 kg/m^2; NS). The two groups did not differ significantly in the number of comorbid medical conditions such as cardiovascular disease, diabetes, stroke or arthritis. Antidepressants were the only class of medications (other than antiparkinsonian drugs) used significantly more often in the IPD group (27.8% versus 0%; $P = 0.006$). Subjects with IPD had slower gait speeds (0.9 ± 0.3 versus 1.4 ± 0.3 m/s; $P < 0.0001$), smaller functional reach (10.6 ± 3.5 versus 13.9 ± 2.0 inches; $P = 0.0003$), and higher scores on the geriatric depression scale (0–15) (2.9 ± 2.9 versus 1.2 ± 2.5; $P = 0.04$) than the healthy elderly subjects. A greater percentage of subjects in the IPD group had at least one fall over the previous 12 months compared to the control group (50% versus 16.7%, $P = 0.02$). The groups did not differ significantly in their scores on the Mini-Mental State Exam.

A number of posturographic measures distinguished the IPD group from the healthy elderly subjects even after controlling for the use of anti-depressant drugs (ANCOVA). The ML ($P < 0.0001$) and planar ($P < 0.01$) effective diffusion coefficients were significantly greater in the IPD subjects over short-term time intervals. Over long-term time intervals, the effective diffusion coefficients for the IPD subjects were significantly greater in the ML direction only ($P = 0.002$) (Fig. 1). In addition, the ratio of the ML/AP short-term effective diffusion coefficients was significantly greater in the IPD group [1.7 ± 1.0 (SD) versus 0.6 ± 0.3 (SD); $P < 0.0001$]. There were no significant differences between the scaling exponents and critical time intervals for the two groups, but as expected from the aforementioned results for the effective diffusion coefficients, the ML ($P < 0.0001$) and planar ($P < 0.0001$) critical mean square displacements were greater in the IPD group. This finding reflects the fact that because the effective stochastic activity of the IPD subjects increased over short-term time intervals (along the ML axis and about the plane of support) without a change in the critical time intervals, the IPD subjects on average drifted a greater distance before switching from open-loop control to closed-loop control.

Among the traditional parameters, IPD subjects had significantly larger maximal displacements in the ML direction ($P < 0.0001$), but no significant difference in maximal AP displacements compared to the healthy elderly. Similarly, the ratio of the maximal ML/AP displacement was greater ($P < 0.0001$) in the IPD group. Radial area ($P < 0.0001$) and RMS displacement ($P < 0.001$) were also significantly larger in the IPD patients.

The ratio of ML/AP short-term effective diffusion coefficients for the subject population as a whole (i.e. healthy elderly and IPD subjects) was inversely correlated with functional reach ($R = -0.55$, $P < 0.0001$) and habitual gait speed ($R = -0.54$, $P < 0.0001$). Among the IPD subjects, this ratio was inversely correlated with their performance on the clinical balance scale (lower scores indicate poorer balance) ($R = -0.63$, $P = 0.001$) and directly correlated with the degree of difficulty they had standing up from a chair ($R = 0.65$, $P = 0.001$). The only posturographic measures which were significantly greater in the subjects who had fallen in the previous 12 months compared to 'non-fallers' were the ML short-term effective diffusion coefficient ($P = 0.01$) and the maximal ML displacement ($P = 0.01$). The ML long-term effective diffusion coefficient also had a tendency ($P = 0.03$) to be associated with a history of falls.

Thus, the postural control mechanisms in IPD during quiet standing are characterized by an increase in effective stochastic activity in the ML direction. These altered dynamics were present when the motor control system was operating both without (open-loop control) and with (closed-loop control) feedback, as the ML effective diffusion coefficients were greater for both short-term and long-term time intervals, respectively. In addition, ML posturographic measures were associated with a history of falls and poor performance on clinical measures of balance, suggesting that these measures may be related to postural instability.

Increased postural sway in the ML direction during quiet stance in subjects with IPD has not been previously reported. Compared to healthy elderly subjects, parkinsonian subjects have been found to have less sway in the AP direction during undisturbed stance [13] and on extreme forward or backward inclinations from a standing position [15]. It has been suggested that some amount of sway is needed to maintain balance during quiet stance

[15]. Accordingly, the observed reduced AP sway in patients with IPD has been hypothesized to be a sign of postural 'inflexibility', which in turn has been related to postural instability [13,15]. From the perspective of this hypothesis, the increase in ML activity we observed in subjects with IPD may reflect an attempt on their part to maintain these potentially stabilizing movements in the face of impaired movement in the AP direction. More specifically, the predominance of ML activity observed in the present study may be due to a compensatory strategy wherein subjects with IPD utilize their open-loop and closed-loop postural control mechanisms to introduce slight shifts and adjustments, respectively, in the ML direction to counteract the effects of restricted movement in the AP direction.

Perturbation experiments have revealed slower ankle joint displacement trajectories in parkinsonian patients compared to age-matched healthy subjects [7]. Bloem et al. [3] hypothesized that this difference is due primarily to increased ankle muscle stiffness in patients with IPD. It is reasonable to assume that this functional change in muscle characteristics would also affect the postural control system during undisturbed stance. Thus, the aforementioned hypothesized compensatory quiet-standing movements associated with IPD may be introduced at the hip, as opposed to the ankle. This speculative point is consistent with the finding of Beckley et al. [1] that parkinsonian subjects tend to select a proximal-distal ('hip strategy') activation sequence of long-latency responses to toe-up platform perturbations, which is a reversal of the normal distal-proximal ('ankle-strategy') activation sequence observed in healthy elderly subjects. This issue requires further study.

Maki et al. recently reported [14] that posturographic measures of ML sway are the best predictors of falling risk in an elderly population. We also found that the parameters which were most strongly associated with a history of falls and most highly correlated with clinical measures of balance, were those representing ML postural control activity. Thus, lateral instability may be an important posturographic marker of functional balance impairment. Given that measures of ML postural control activity are increased to such a significant degree in IPD, elderly fallers who display this behavior may have subtle parkinsonian features (which are often seen clinically in aging), or possibly early disease. Further work is needed to determine if this is a disease-specific finding or a non-specific indicator of advanced postural instability in the elderly.

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