

SHORT REPORT

ABSTRACT: In previous studies, we developed a postural stiffness measure that is extracted from foot center-of-pressure (COP) trajectories from quietly standing individuals and is based on an analytical mechanical model of posture control. Here we apply this measure to patients with Parkinson's disease (PD). We correlated the postural stiffness measure with different clinical rating scales, obtained from patients. Kendall's rank correlation was highly significant between the stiffness measure and rigidity, bradykinesia, posture impairment, gait, and leg agility, respectively, as rated by the Unified Parkinson's Disease Rating Scale. These results provide further evidence that a higher intrinsic muscle stiffness may contribute to the aforementioned clinically defined symptoms. From a clinical standpoint, this work indicates that the proposed postural stiffness measure may be useful as an assessment tool for the evaluation of PD patients subsequent to pharmacological and surgical treatment.

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ASSESSING MUSCLE STIFFNESS FROM QUIET STANCE IN PARKINSON'S DISEASE

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In previous studies, we have shown that center-of-pressure (COP) trajectories collected with a force platform under the feet of quietly standing subjects can reveal many details about an individual's balance control capacity in both quasi-static and dynamic situations.^{7-9,18,19} We have also developed a mechanical model that well describes the COP dynamics and the associated dynamics of the postural control system.⁶

Our mechanical model assumes that the body

during quiet standing can be represented by a flexible string (polymer) with stiffness and damping.⁶ In addition, our model predicts the analytical form of the time-dependent correlations of the COP displacements, from which a set of physiologically relevant parameters can be extracted.⁶ From these parameters, a mechanical postural stiffness measure k can be constructed. Previous studies have demonstrated the validity of the model in predicting the correlations of COP displacements for healthy young subjects.^{6,18} Thus, using the mechanical model as a basis, we can extract parameters from the correlation function of the COP motion and use them to construct the measure k .^{6,18} In this study, we test the hypothesis that the postural stiffness measure k can be used to characterize quantitatively some of the major motor impairments associated with Parkin-

Abbreviations: COP, center of pressure; PD, Parkinson's disease; UPDRS, Unified Parkinson's Disease Rating Scale

Key words: measurement; muscle stiffness; Parkinson's disease; postural stiffness; posture control

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son's disease (PD). Parkinson's disease is characterized by a number of motor impairments, including bradykinesia, rigidity, postural instability, and tremor. These modifications to the motor control system typically result in diminished balance and locomotor function^{1,3,8,10,11,15,17,23} and predispose patients to falls,^{14,17,20} which are a common cause of morbidity and mortality among older persons. Most previous attempts to develop a method for quantifying the severity of motor disabilities in PD have focused on local measures of rigidity,^{5,13,16,22,27} i.e., measures estimated from data collected at a single, isolated joint. These techniques have had varying degrees of success, and, as of yet, they have not been widely adopted clinically. Parkinson's disease rigidity has been characterized quantitatively by mechanical limb impedance or stiffness,^{5,16,22} which is given by the relationship between force and displacement. This is obtained either by forcing the limb periodically and extracting an impedance measure from the measured force (torque) versus displacement curve, or by imposing a specific displacement and measuring the resultant force (torque). Certain ambiguities can arise when implementing these methods. First, the torque-displacement curves are nonlinear and frequency-dependent,^{5,16,22} requiring choices in how the limb should be forced (e.g., the frequency of forcing) and in how best to estimate the stiffness from the resulting data. Second, the rigidity can change depending on the state of the patient. For instance, if the unexamined limb is actively engaged in some standard motor task, the stiffness of the examined limb will increase via a mechanism known as activated rigidity.^{5,29} Third, the measurements are usually specific to a given limb,^{5,13,16,22,27} and stiffness may change from limb to limb.¹¹ Our method for characterizing overall (rather than focal) stiffness, using COP data, avoids these difficulties. We apply our postural stiffness measure k , calculated from quiet-standing COP data, to a population of 18 PD patients and compare the results with the Unified Parkinson's Disease Rating Scale (UPDRS) and its components.¹²

METHODS

Subjects. Eighteen subjects with PD were included in the study. Each PD subject had their diagnosis confirmed by an experienced neurologist. All subjects were able to stand independently. Informed consent was obtained from each subject prior to their participation. All subjects underwent a detailed clinical evaluation by a physician trained in geriatric medicine. This assessment included a complete history and medication review (with attention to medi-

cal conditions and drugs associated with increased risk of falls). A targeted physical examination included the evaluation of postural vital signs, height, weight, body mass index, cardiovascular function, and neurological signs. Subjects were excluded if they had debilitating rheumatological or orthopedic conditions, neurological diagnoses (other than PD), or cognitive impairment such that they could not understand the study protocol. Subjects were required to be able to stand safely without assistance. The disease duration ranged from 1.5 to 16.0 years [mean 8.6 ± 3.6 (SD) years].

Data Recordings. Postural sway was evaluated using a Kistler multicomponent force platform to measure the time-varying displacements of the COP under each subject's feet (Fig. 1). A series of 10 30-s trials was conducted for each subject with the eyes open. Rest periods of 60 s were permitted between each trial. Parkinson's disease 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.

Data Analysis. The estimation of our postural stiffness measure k from the COP data involves a para-

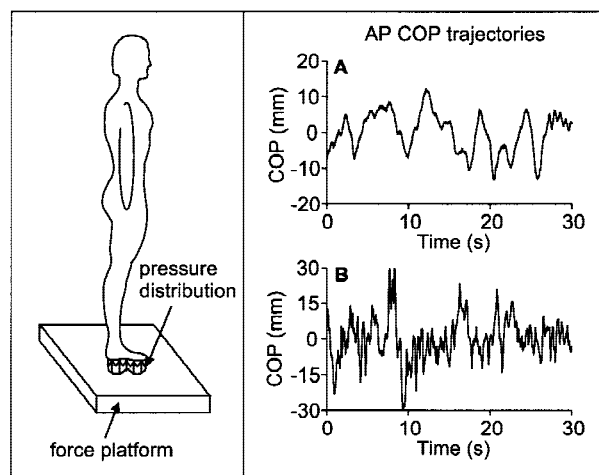


FIGURE 1. The left panel shows a schematic diagram of the experimental set-up. Each subject stood barefoot on the platform (feet abducted 10° and heels 6 cm apart), with arms relaxed at their sides and eyes fixed on a point in front of them. The data were sampled at a frequency of 100 Hz and stored on a computer for off-line analysis. **(A)** and **(B)** include two examples of the obtained anteroposterior (AP) COP time series. Shown are data from one patient with minimal symptoms **(A)** and data from a patient with severe rigidity, bradykinesia, and a postural disorder **(B)**. The sway amplitudes in the two cases do not differ substantially, but it can be seen that the curve in **(A)** is smoother than that in **(B)**.

metric fit of the analytical function of our mechanical posture model⁶ to the derivative of the correlation function of the COP time series in the anteroposterior direction. This procedure is described in detail elsewhere.¹⁸ In brief, the procedure involves computing the correlation function (mean-square time-dependent deviation) of the COP time series for each of the quiet-standing trials.⁴ Then for each single trial, the derivative of the correlation function is estimated by applying a simple two-point difference filter to the estimated correlations. The resulting single-trial estimations are then averaged, taking the time of the maximal amplitude as a trigger point. Each trial is normalized by its trigger-point amplitude prior to averaging. Therefore, the resulting curve is unit-free and covers only the dynamics. Figure 2 displays two examples of the single-trial averages of the derivative of the COP correlation function. The averaged derivative of the correlation function as calculated from the mechanical model^{6,18} has the form

$$e^{-t/2\beta} J_0\left(\frac{\sqrt{4\alpha\beta - 1}}{2\beta} t\right),$$

where $J_0(x)$ is the zero-order Bessel function. The parameters α and β are determined by a Levenberg-Marquardt fit²¹ of the data to this equation. The postural stiffness measure k is then given by $k = \alpha/\beta$. The standard error of the mean of the single trials is taken as an estimator for the error. This procedure, in addition to yielding an estimate for k , provides an estimate of the goodness of the fit and, therefore, a validation of the mechanical model.¹⁸ To test the reliability of the measure, we separated randomly the 10 trials for each subject into two groups of five trials each. We then estimated k for each of the two groups of trials for each subject. The Pearson correlation coefficient between the two estimates for k across the 18 subjects was as high as 0.9. We obtained similar results in 17 of the 18 patients tested, indicating that the measure k has high reliability.

Statistical Analysis. Correlation tests were performed between the postural stiffness measure k and the total UPDRS motor subscale and its components. The tests were conducted based on Kendall's rank correlation coefficient (the so-called Kendall's τ), which makes no assumptions on the underlying distribution.^{21,25} A significant positive value for Kendall's τ indicates that the two tested variables exhibit a rank correlation. In our case, this indicates that the "rank" of severity of the clinical measures correlates with the rank of k . From a clinical standpoint, this would suggest that our postural stiffness measure k increases with increasing severity of the respective motor system disabilities associated with PD. All p values given in Table 1 display the two-sided significance of a non-zero value of τ . Note that the absolute τ values should not be confused with Pearson's correlation coefficients. For discrete scales containing only a few whole numbers (e.g., the bradykinesia component of the UPDRS), Kendall's τ is always less than one, because it is not possible to rank all values (i.e., some of the values are always equal). Nevertheless, for such variables, Kendall's τ still provides a reliable test to decide whether two variables are correlated.

RESULTS

Figure 1 displays representative COP time series for two patients exhibiting different severities of parkinsonian symptoms: one with minimal symptoms (Fig. 1A) and one with severe symptoms (Fig. 1B). Figure 2 shows examples of the estimated derivatives of the COP correlation functions for the same two patients.

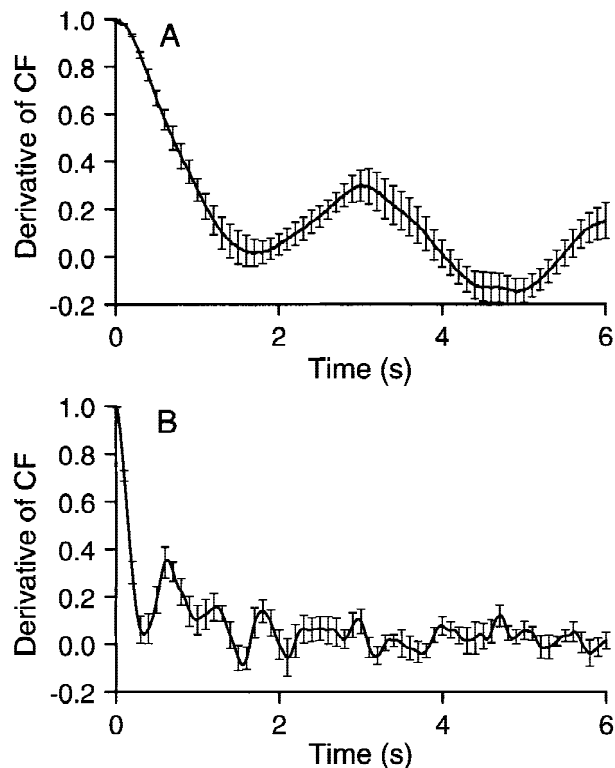


FIGURE 2. Derivative of the COP correlation function (CF) for the two patients of Figure 1. The curve for the patient with severe symptoms (**B**) decays faster from its highest point at time zero than does the curve for the patient with minimal symptoms (**A**). The frequency of the apparent decaying oscillations is higher in (**B**) than in (**A**), which corresponds to a higher postural-stiffness measure k in the patient with severe symptoms (**B**).

The dominant, decaying oscillation in the mildly affected patient (Fig. 2A) has a lower frequency than does the oscillation in the patient with severe symptoms (Fig. 2B). Furthermore, the derivative of the correlation function in Figure 2B decays faster to an equilibrium than that in Figure 2A. Kendall's rank correlation test indicated that the postural stiffness measure k correlated significantly with the rigidity component ($P < 0.006$), the bradykinesia component ($P < 0.008$), the posture component ($P < 0.0005$), the leg-agility component ($P < 0.003$), the retropulsion test score ($P < 0.05$), and gait ($P < 0.022$). The measure k was not significantly correlated with resting-tremor severity, postural-tremor severity, or the UPDRS component that quantifies a patient's ability to rise from a chair. The significant correlation coefficients are summarized in Table 1.

DISCUSSION

In this study, we showed that the postural-stiffness measure k is correlated with different clinical measures of motor impairment in PD patients. This finding indicates that the measure k well quantifies the severity of the aforementioned disabilities in the extrapyramidal motor system and thus can be used to distinguish between varying degrees of disability among PD patients. Whereas the sway variance appears to be in a normal range in patients with PD,^{15,24,26} the proposed new method is able to extract differences in the dynamics of quiet-standing COP data.

From a physiological standpoint, these results indicate that the increased intrinsic muscle stiffness in PD found in earlier studies^{2,3,11,15,28} might contribute to various clinically defined symptoms of the disease and not only to rigidity. Interestingly, Koller et

al.¹⁷ found that falling in PD patients correlates with rigidity, bradykinesia, gait and postural stability but not with tremor. In addition, Beckley et al.¹ found a correlation between a clinical score of bradykinesia and quantitative assessment of postural instability. We obtained similar correlation results for the postural stiffness measure k . The methods for obtaining measure k are objective, noninvasive, and easy to implement. The technique is applicable to all patients who are able to maintain an unsupported upright stance for approximately 30 s. Our proposed measure needs to be tested for its ability to distinguish extrapyramidal from pyramidal causes of increased muscle tone. Future studies are also needed to investigate the utility of the measure to assess response to pharmacological and surgical treatment and predict outcomes in populations of patients with PD.

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Table 1. Correlation coefficients obtained for the correlations between different clinical scales and the postural stiffness measure k .

Clinical scale	Average value (range; SD)*	Kendall's τ (p)†
Rigidity	3.11 (0-9; 3.22)	0.48 (<0.006)
Bradykinesia	1.29 (0-3; 0.98)	0.46 (<0.008)
Posture	0.9 (0-3; 0.85)	0.6 (<0.0005)
Gait	0.8 (0-3; 0.81)	0.40 (<0.021)
Retropulsion test	0.8 (0-2; 0.76)	0.34 (<0.05)
Leg agility	2.4 (1-5; 1.1)	0.52 (<0.0023)
UPDRS motor subscale	21.5 (4-48; 12.72)	0.49 (<0.005)

*Average values for the clinical scales, with their range and standard deviation (SD) in parentheses.

†Kendall's correlation coefficients τ between k and the respective clinical scales; values in parentheses are the significance levels, p . Absolute values of τ should not be confused with Pearson's correlation coefficient; they correspond to a different quantity²².

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