Clinical Correlates of Action Tremor in Parkinson Disease

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Background: Action tremor is often noted in patients with Parkinson disease (PD), yet the clinical correlates of this type of tremor have been the focus of few studies. It is not clear whether this action tremor is a manifestation of the underlying basal ganglia disease.

Objective: To determine whether the severity of action tremor in PD is associated with age, age at disease onset, disease duration, levodopa dose, severity of rest tremor, or other motor (ie, bradykinesia, rigidity) and nonmotor manifestations of PD.

Methods: Patients with PD (N=197) were ascertained as part of a familial aggregation study. All patients underwent a neurological examination. Rest tremor was rated with the Unified Parkinson Disease Rating Scale; and action tremor, with the Washington Heights–Inwood Genetic Study of Essential Tremor Rating Scale.

Results: Action tremor was present in 184 (93.4%) of 197 patients. Four patients (2%) met criteria for definite essential tremor. The action tremor score was not associated with age, age at onset, or disease duration. The action tremor score was associated with the rest tremor score (r=0.37; P<.001), and more strongly with the ipsilateral than contralateral rest tremor score. The association between the action tremor score and the rest tremor score was diminished but still significant (r=0.21, P=.02) even when we excluded these 63 patients with re-emergent tremor. Neither the action nor the rest tremor score was associated with the bradykinesia or rigidity scores, Hoehn and Yahr scale score, or modified Mini-Mental State Examination score.

Conclusions: Action tremor was associated with rest tremor in PD, suggesting that, at least in part, action tremor is a manifestation of the underlying basal ganglia disease. Neither tremor was associated with other motor and nonmotor manifestations of PD. This in turn suggests that tremor in PD may represent an underlying pathophysiological process different from these other manifestations.

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Action tremor often has been observed in Parkinson disease (PD).1,2 The prevalence may be as high as 92%.3 While some consider this tremor to be of minor importance, in clinical practice, a moderate action tremor is regarded to be more disabling than a severe rest tremor.3

The basis for the action tremor in PD is not clear. In some patients, the tremor has been reported to be more pronounced on the side of the body that is more affected by PD.4 Also, a significant reduction in action tremor amplitude has been reported with single-dose challenges of dopaminergic and anticholinergic agents,5 suggesting that, like rest tremor, action tremor may be a manifestation of the underlying basal ganglia disease. However, based on tremor recordings, others have suggested that the action tremor in PD may represent an exaggeration of normal physiological tremor.6,7

Although action tremor has been reported and its prevalence estimated,1,2,5-7 the clinical correlates of this tremor have received little attention, and a study focused on these could provide some insight into the basis for action tremor in PD. As part of a familial aggregation study, we examined several hundred patients with PD using standardized tremor rating scales. While action tremor was highly prevalent in this group, most did not meet diagnostic criteria for essential tremor (ET).8 We distinguished, based on clinical observation, between postural tremor that began after a latency period (ie, “re-emergent tremor”)9 and that which did not. The purpose of this study was to determine whether the severity of action tremor in PD correlated with age, age at onset, disease duration, dose of medica-
PATIENTS AND METHODS

PATIENTS

Patients with PD were enrolled in a study of the genetic epidemiology of the disease. They were ascertained from neurology clinics or neurologists’ offices at the Neurological Institute of New York, Columbia-Presbyterian Medical Center (New York, NY). Diagnoses were based on a standardized neurological evaluation. 11 Idiopathic PD, defined by clinical and research criteria, 12-14 did not include PD plus syndromes.

STUDY PROCEDURE

As part of the current evaluation, a neurologist examined each patient and administered and rated the motor portion of the Unified Parkinson Disease Rating Scale (UPDRS) 15 and assigned a Hoehn and Yahr scale score. 16 In addition, all patients were interviewed by a trained tester who collected demographic data, information on names and dosages of medications, age at onset of motor signs of PD, age at diagnosis of PD, and disease duration. The trained tester administered a modified Mini-Mental State Examination (range, 0-30 [high]). 17 The tester also administered and videotaped a detailed examination designed to elicit action tremor, in which the following 6 items were assessed: sustained arm extension (first with arms held in front of body and then in a wing-beat position), pouring water between 2 cups, drinking water from a cup, using a spoon to drink water, finger-to-nose movements, and drawing Archimedes spirals. 8,17 Each of these 6 items was performed both with the dominant and the nondominant arm (12 items total). A manually operated video camera recorder (Sony CCD-TR700; Sony Corp, Park Ridge, NJ) was used to videotape the examination.

The videotaped examination was reviewed by a neurologist (K.M.) who rated the 12 action tremor items using the Washington Heights–Inwood Genetic Study of Essential Tremor (WHIGET) Rating Scale. 8 Ratings were 0 (no visible tremor), 1 (low-amplitude or intermittent tremor), 2 (tremor of moderate amplitude, clearly oscillatory, and usually present), and 3 (large-amplitude tremor). This is a reliable and validated tremor rating scale. 8,17

As part of the videotaped examination, patients were asked to raise their arms from a position where they had been resting in their laps, to horizontal outstretched positions (first with arms held in front of body and then in a wing-beat position), and to maintain their arms in each of these positions for 10 seconds. Time, in seconds, minutes, and hours, was automatically displayed in the margin of the video recording. The shortest latency period, in seconds, between the newly achieved horizontal position and the onset of a clinically observable postural tremor was noted. The neurologist (K.M.) had been specifically instructed to observe this latency period.

DEFINITIONS

Action tremor consists of both kinetic and postural tremor. Kinetic tremor was defined as a tremor present during hand movement (eg, finger-to-nose maneuver or writing). Postural tremor was defined as a tremor present during sustained arm extension. Rest tremor was defined as a tremor present while the arms are resting in the lap or at the side. Re-emergent tremor was defined as a postural tremor occurring after any latency period (>0 seconds). 9

SCORES

The kinetic tremor score (range, 0-30) was the sum of the ratings of kinetic tremor on the WHIGET Tremor Rating Scale. Ten items (5 per arm) were rated from 0-3. The postural tremor score (range, 0-6) was the sum of the ratings of postural tremor on the WHIGET Tremor Rating Scale. Two items (1 per arm) were rated from 0-3. The action tremor score (range, 0-36) was the sum of the kinetic and postural tremor scores. The rest tremor score (range, 0-8) was the sum of the ratings of rest tremor in the arms on the UPDRS. Two items (1 per arm) were rated from 0 to 4. The rigidity score (range, 0-24) was the sum of the ratings of bradykinesia in the arms on the UPDRS. Six items (3 per arm) were rated from 0 to 4. The rigidity score (range, 0-8) was the sum of the ratings of rigidity in the arms on the UPDRS. Two items (1 per arm) were rated from 0 to 4.

STATISTICAL ANALYSES

To assess associations between categorical variables, χ2 tests were used, and for continuous variables, Pearson correlation coefficients were used. A t test was used to assess differences between continuous variables. Multiple linear regression analyses were performed, in which the dependent variable was the action tremor score, and the independent variables were the rest tremor score, patient sex, and smoking.

RESULTS

There were 197 patients with PD (Table 1). Action tremor, defined as having a WHIGET rating of 1 or greater (mild tremor) on 1 of the 12 action tremor items, was present in 184 patients (93.4%), and 102 patients (51.8%) had an action tremor rated 2 or greater (moderate tremor) on at least 1 of the 12 action tremor items. If patients had not had PD, then based on their action tremor, 4 (2.0%) would have met either our previously published diagnostic criteria for definite ET (postural tremor that received a rating of ≥2, and kinetic tremor that received a rating of ≥2 on at least 4 items) 9 or criteria for definite ET (visible and persistent bilateral postural tremor) formulated by the Tremor Research Investigation Group. 9 Mean tremor scores are presented in Table 2. The action tremor score was associated with age, age at onset of motor signs of PD, years since onset of motor signs of PD, or years since diagnosis of PD. Rest tremor score was associated with none of these variables. Patients who were currently taking levodopa had similar mean action tremor scores. 18


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scores compared with those who were not taking levodopa (7.33 vs 8.13; t=0.98, P=.33). The relationship between dose (milligrams) of levodopa and the action tremor score (r=−0.13) did not reach statistical significance (P=.07). Action tremor was not associated with the dose of any of the dopamine agonists (pergolide, bromocriptine, or pramipexole), amantadine, selegiline, or anticholinergic agents (trihexyphenidyl, procyclidine, biperiden, or benzotropine). By contrast, there was a negative association between dose of levodopa and severity of rest tremor (r=−0.24, P=.001) such that higher doses of levodopa were associated with less severe rest tremor.

The action tremor was much more likely to be more severe on the side of the body in which the rest tremor was predominant (χ²=21.1, P<.001). Moreover, the action tremor score was correlated with the rest tremor score (r=0.37, P<.001) (Table 3), even when controlling for dose of levodopa (r=0.34, P<.001). Because re-emergent tremor is considered to be a form of rest tremor, we removed 63 patients (32.0%) with re-emergent tremor. The association between the action tremor score and the rest tremor score was diminished but still significant (r=0.21, P=.02) even when we excluded these 63 patients with re-emergent tremor.

The association between the postural tremor score and the rest tremor score (r=0.53, P<.001) was greater than the association between the kinetic tremor score and the rest tremor score (r=0.30, P<.001); however, when we excluded the 63 patients with re-emergent tremor, the associations were more similar (r=0.27, P=.002 and r=0.17, P=.04, respectively).

The action tremor score was not associated with the bradykinesia or rigidity scores, Hoehn and Yahr scale score, or the modified Mini-Mental State Examination score. Neither was the rest tremor score associated with any of these items. By contrast, the rigidity and bradykinesia scores were associated with each other (r=0.60, P<.001) as well as with the Hoehn and Yahr scale score (r=0.40 and 0.61, respectively; P<.001 for both associations). There was an association between the bradykinesia score and modified Mini-Mental State Examination score (r=−0.32, P<.001; ie, greater bradykinesia was associated with more cognitive impairment). The association between the rigidity and modified Mini-Mental State Examination scores did not reach significance (r=−0.14, P=.07).

Males had higher mean action tremor scores than did females (8.53 vs 6.60; t=2.59, P=.01). Disease duration did not differ by sex. Other factors (eg, smoking) may have contributed to enhanced tremor among males. Data on smoking was collected on some of these individuals participating in another study of risk factors for PD. These data were available on 76 patients. Patients who reported ever smoking had higher total tremor scores than those who did not (8.86 vs 6.13; t=2.06, P=.04). When smoking and sex were both included as independent variables in a multiple linear regression analysis with the outcome variable being the total tremor score, only smoking (P=.04) was associated with the total tremor score.

**COMMENT**

The presence of action tremor has been noted in cohorts of 30 to 80 patients with PD.1,2,5,7 However, the clinical correlates of this action tremor (ie, the nature and extent of the relationships between this action tremor and other disease manifestations) have received little attention. In addition, few studies have distinguished between re-emergent tremor (a form of rest tremor) and tremor that does not occur after a latency period. Examination of clinical correlates could provide additional insight into the basis for the action tremor in PD. As part of a familial aggregation study of PD, approximately 200 patients with PD were examined, providing an opportunity to study associations between the severity of action tremor and age, age at onset, disease duration, dosage of levodopa, and severity of rest tremor and other motor and nonmotor features of PD using a standardized assessment of action tremor.
The severity of action tremor was associated with the severity of rest tremor, particularly ipsilateral rest tremor. This provides support for the notion that the action tremor in PD is at least partly a manifestation of the underlying basal ganglia disease. There may be other support for this notion. In a study of PD kindreds, several of the relatives who had isolated mild postural tremor demonstrated reduced fluoro-dopa uptake in the putamen.  

Although the association between the rest tremor and action tremor scores was highly significant, the rest tremor score explained only 13.7% of the variance in the action tremor score ($r = 0.37, r^2 = 0.137, P < .001$), and the bradykinesia and rigidity scores were not associated with the action tremor score. The dose of levodopa only explained 1.7% of the variance in the action tremor score ($r = -0.13, r^2 = 0.017$). Even when combined, rest tremor score, dose of levodopa, disease duration, sex, and age only explained 18.6% of the variance in the action tremor score ($r = 0.43, r^2 = 0.186, P < .001$). This suggests that other factors contribute to the severity of the action tremor in PD, and that the severity of the action tremor in PD is probably not exclusively a manifestation of the underlying basal ganglia disease. As previously suggested,  a component of physiological or enhanced physiological tremor could be contributing to the severity of the action tremor in PD.

We reported that there were no relationships between the severity of action tremor and other manifestations of PD. The severity of action tremor was not associated with the severity of bradykinesia, rigidity, the Hoehn and Yahr scale score, the Mini-Mental State Examination score or the disease duration. This observation, that action tremor is associated with some manifestations of PD (eg, rest tremor) but not with other manifestations (eg, bradykinesia and rigidity) suggests that different mechanisms may underlie tremor (rest and action) and bradykinesia or rigidity. Further support for this comes with the observation that there was no association between the rest tremor score and bradykinesia and rigidity scores. There is evidence in the literature that the tremor in PD may represent a different underlying pathophysiological process than the rigidity and bradykinesia. First, factor analysis of signs in PD showed that rest tremor was relatively independent of the other cardinal signs of PD.  Second, we previously reported that while bradykinesia and rigidity worsened at similar annual rates in PD, rest tremor did not clearly worsen with time. Finally, there was no correlation between rest tremor and striatal $^{18}$F-dopa uptake in patients with PD.

One previous study examined the association between action and rest tremor in PD. An association was reported between postural and rest tremor, but not between kinetic and rest tremor. In a larger sample, we found that rest tremor was associated with both postural and kinetic tremor. As in the previous study, the association between rest tremor and postural tremor was particularly robust. However, when we excluded individuals with a reemergent tremor, the associations (rest tremor-postural tremor and rest tremor-kinetic tremor) were similar. This supports the previously suggested view that reemergent tremor in PD is a form of rest tremor. It also underscores the importance of distinguishing between different types of postural tremor in PD. Clinicians who use the UPDRS to rate action tremor should distinguish re-emergent tremors from tremor not occurring after a latency period. Those that occur after a latency are usually an expression of the patient’s rest tremor.

We realize that this study had limitations. Quantitative computerized tremor analysis was not performed in our patients, and this would have provided more precise quantification of tremor amplitudes. Despite this, significant associations were detected between action tremor and postural tremor.

In summary, action tremor was associated with rest tremor in PD, suggesting that, at least in part, action tremor is a manifestation of the underlying basal ganglia disease. Neither tremor was associated with other motor and nonmotor manifestations of PD, suggesting that tremor in PD may represent a different underlying pathophysiological process than these other manifestations.

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