Rest Tremor in Patients With Essential Tremor

Prevalence, Clinical Correlates, and Electrophysiologic Characteristics

Oren Cohen, MD; Seth Pullman, MD; Eva Jurewicz, BA; Dryden Watner, MA; Elan D. Louis, MD, MS

Background: Isolated rest tremor, which is observed in some patients with essential tremor (ET), poses a diagnostic challenge. The phenomenon has been examined in few studies and is poorly understood.

Objectives: To determine the prevalence and study the clinical correlates of rest tremor in ET and to examine the electrophysiologic features in a subgroup of patients.

Methods: Sixty-four patients with ET cared for at a tertiary referral center underwent neurologic examination. Five of 12 patients with rest tremor also underwent quantitative computerized tremor analysis using accelerometry and handwritten spiral analysis.

Results: Twelve of 64 patients with ET had rest tremor (prevalence, 18.8%; 95% confidence interval, 9.2%-28.4%). Compared with the 52 patients with ET without rest tremor, these 12 had disease of longer duration and greater severity. Also, their ET was more widely disseminated, as evidenced by a larger proportion with head tremor. None had clinical signs of bradykinesia or rigidity. The 5 patients with rest tremor who underwent electrophysiologic study had electrophysiologic features consistent with parkinsonism (eg, slow spiral speed and increased decrement of spiral speed with radius).

Conclusions: In our sample, 1 in 5 patients with ET had rest tremor. The tremor was associated with disease that was more severe, more disseminated, and of longer duration. Some of these patients had electrophysiologic features consistent with parkinsonism. The basis for the rest tremor could be basal ganglia involvement, raising the possibility that the pathologic process responsible for ET may extend to these structures.

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Essential tremor (ET), the most common tremor disorder,1-3 usually is characterized by kinetic and postural tremors, whereas tremor at rest is considered to be more characteristic of parkinsonism. Rest tremor in the absence of bradykinesia, rigidity, or other clinically detectable features of parkinsonism is known to occur in ET, although only 18 of these cases have been reported.4-6 The precise prevalence of rest tremor in patients with ET is unknown, although it is probably more common than these few articles would suggest. In addition, the clinical correlates (ie, the nature and extent of the relationships between this rest tremor and other disease manifestations) have not been studied, and our understanding of the phenomenon remains limited. Finally, electrophysiologic study has been restricted to data on tremor amplitude and frequency.4

The aims of this study are to estimate the prevalence of rest tremor in patients with ET cared for at a tertiary referral center and to study the clinical correlates of this rest tremor. In addition, a subsample of patients with ET and rest tremor underwent detailed electrophysiologic studies.

Methods

Patients and Setting

A computerized database at the Center for Parkinson's Disease and Other Movement Disorders at Columbia-Presbyterian Medical Center, New York, lists 794 patients who were diagnosed as having ET by one of the Center's neurologists specializing in movement disorders. Patients are being selected, alphabeti-
cally, for enrollment in an ongoing epidemiologic study of ET. The goal is to enroll 300 patients. One of us (E.D.L.) reviews the clinical charts of potential participants, and those with diagnoses or physical signs of dystonia, Parkinson disease (PD), or spinocerebellar ataxia are excluded. Patients with rest tremor are included unless the neurologist equivocated about a diagnosis of PD. To date, 64 patients with ET have been enrolled.

STUDY PROCEDURE

All participants underwent a tremor interview and a videotaped neurologic examination. Tests for tremor included sustained arm extension, 3 tests for kinetic tremor, and 3 tests for rest tremor (arms in the lap, arms hanging at sides while standing, and arms while walking). The trained tester was specifically instructed to ensure that during the rest positions the patient’s arms were fully relaxed. Other features of parkinsonism were videotaped, including bradykinesia (10-15 finger taps each with the index finger and thumb, pronation-supination of each hand 10-15 times, and 10-15 taps with each foot), hypomimia (the face was filmed for 2 minutes), micrographia (2 spirals were drawn with each hand), hypophonia, and tachypnea (the patient was asked to speak freely and to read a 1- to 2-minute passage), and gait and posture (the patient walked 9-12 m, turned around, and returned, and this was repeated 3 times). Rigidity was assessed by the trained tester at each elbow and wrist and was commented on (present or absent) in the videotape. The examination was videotaped using a manually operated video camera recorder. Two studies11,12 have demonstrated the sensitivity of videotaped neurologic examinations in detecting PD.

VIDEOTAPE REVIEW AND CONFIRMATION OF DIAGNOSIS

A neurologist (E.D.L.) specializing in movement disorders reviewed the videotaped examination, rated the postural and kinetic tremor using a scale from 0 to 3, and confirmed the diagnosis using published diagnostic criteria.3,9,10 Rest tremor was rated as present or absent; it was not coded as present if the limb did not seem to be fully at rest. In addition bradykinesia, hypomimia, micrographia, hypophonia, tachypnea, flexed posture, and reduced arm swing were noted as present or absent. Bradykinesia was considered present when there was loss of amplitude, pausing, or early fatiguing but not breakdown of alternate motion due to the intrusion of tremor. If 2 of the cardinal features of PD were present, then this diagnosis was made as well.

QUANTITATIVE COMPUTERIZED TREMOR ANALYSIS

Five of 12 patients with ET and rest tremor and 20 of 52 patients without rest tremor agreed to visit the Motor Neurophysiology Laboratory at Columbia-Presbyterian Medical Center for a tremor analysis. Those who agreed did not differ from those who did not in terms of age, sex, disease duration, and severity of action tremor. Tremor analysis and spiral analysis were performed with the patient’s arms flexed at 90°, fully supported against gravity, and kept stationary at the elbow to prevent transmitted upper arm movements to the forearm and hand. Findings from EMG confirmed that the tested limb was fully at rest. Posture and action movements were performed with the arms extended and the patient freely able to touch finger to nose as previously described.13,14 Tremor amplitudes were derived offline by double integration of wrist accelerometric data, filtering out low-frequency drift (<2 Hz) and averaging. Tremor frequencies were calculated using a fast Fourier transform algorithm to generate autocorrelation spectra. The EMG was full-wave rectified, integrated, and processed with the accelerometric data.13,14 In addition, a spiral analysis was performed by asking the patients to draw 10 archimedian spirals on a digitizing tablet. This tablet has a resolution of 2540 points per inch with an accuracy of 0.005 inch, an output rate of 200 points per second, and 256 levels of measurable pressure.15 The data were collected from 10 spirals from each hand and averaged in a virtual triaxial setup (X, Y, and Z pressure), and spiral tightness, spiral speed, and decrement of spiral speed were calculated as described in the following subsection.

DEFINITIONS

Rest tremor, defined as tremor that occurs when voluntary muscle activity is absent10 and unintended, was assessed in 3 positions as noted herein. Postural tremor was defined as tremor that occurs in an attempt to hold a body part motionless against the force of gravity, and kinetic tremor is tremor that occurs during a voluntary movement.

The kinetic tremor score was the sum of all clinical ratings (on a scale from 0-3) of kinetic tremor (range, 0-30). The postural tremor score was the sum of the clinical rating (on a scale from 0-3) of postural tremor in each hand (range, 0-6). The total tremor score (range, 0-36), a clinical score, was the sum of the kinetic and postural tremor scores. The rest–finger-to-nose tremor amplitude ratio was calculated by dividing rest tremor amplitude by finger-to-nose tremor amplitude, both of which were assessed during quantitative computerized tremor analysis.

During spiral analysis, patients were asked to draw a spiral in a 10×10-cm square. Spiral tightness is a kinematic equivalent of micrographia, and, as previously published,13 increased tightness may be seen in patients with PD. The tightness of a spiral was a ratio of the number of turns in a spiral drawn in a 10×10-cm square to a standard of 7 turns. For example, 14 turns would have a tightness of 2 (no units). Slow spiral speed may be evident in patients with PD and in these patients is a kinematic equivalent of bradykinesia. Decrement of spiral speed with radius, which also may be evident in patients with PD, is a kinematic equivalent of decreasing amplitude of repetitive movements. It is expressed as a ratio of the slope of the velocity (in centimeters per second) from the last 30% of the spiral to the first 30% of the spiral. As a ratio, it is without units. Large negative values indicate marked deceleration in the last 30% of the spiral, which can occur in severe clinical motor decrement. Large positive values indicate minimal change in velocity between the last and first 30% of the spiral, which typically occurs in severe bradykinesia. Because large positive and negative values occur in severe motor dysfunction, absolute values were used to illustrate this point.
STATISTICAL ANALYSES

A 2-tailed t test was used to assess continuous variables, and a χ² test was used to assess categorical variables. 95% Confidence intervals were calculated. A logistic regression analysis was performed to determine the independent effects of age and disease duration (covariates) on the presence or absence of rest tremor (dependent variable). Linear regression analyses were performed to determine whether spiral speed or decrementing speed with radius (dependent variables in different models) were associated with diagnostic group or age (independent variables).

RESULTS

PREVALENCE OF REST TREMOR

The 64 patients with ET had a mean±SD age of 68.0±14.3 years and a mean±SD disease duration of 21.9±18.9 years. Twelve patients had rest tremor (prevalence, 18.8%; 95% confidence interval, 9.2%-28.4%).

CLINICAL CORRELATES

The 12 patients with rest tremor all had postural and kinetic tremors; none complained of rest tremor. Eleven patients with rest tremor (92%) had ET for more than 10 years, 8 (67%) for more than 20 years, and 3 (25%) for more than 60 years. None of these patients had signs of parkinsonism in their clinical chart from the Center for Parkinson’s Disease and Other Movement Disorders; bradykinesia, hypomimia, micrographia, hypophonia, tachyphemia, flexed posture, or reduced arm swing on the videotaped examination; or rigidity according to the trained tester.

Rest tremor was limited to the arms in all 12 patients with rest tremor and was bilateral in 8 (67%). The tremor was present while standing or walking in 3 patients (25%), while seated in 2 (17%), and during both activities in 7 (58%). Eight patients had asymmetrical rest tremor: in 2 patients the rest tremor was more severe in the hand that had the more severe kinetic tremor; in 5, more severe in the opposite hand; and in 1, the kinetic tremor was symmetrical.

Patients with rest tremor had disease of longer duration, had more severe postural and kinetic tremor, and were more likely to have head tremor than those without rest tremor (Table 1). In a logistic regression analysis, in which rest tremor (present vs absent) was the dependent variable and age and disease duration were the independent variables, only disease duration was significantly associated with rest tremor (P = .05).

ELECTROPHYSIOLOGIC CHARACTERISTICS OF PATIENTS WITH REST TREMOR

Five patients with ET and rest tremor agreed to undergo electrophysiologic study (Table 2). Each patient had asymmetrical rest tremor, with the mean amplitude on one side 2.3 to 29.4 times greater than that on the other side. In 3 patients, the frequency of the rest tremor was equal in both hands, and in the other 2 it was higher in the hand with higher rest tremor amplitude.

Three patients had a rest tremor frequency that was within the range of the classic parkinsonian tremor (3-5 Hz). The rest–finger-to-nose tremor amplitude ratio was below 1.0 in 3 patients, revealing that kinetic tremor in those patients was more severe than rest tremor. In the other 2 patients, the ratio was less than 1.0 in one hand but 1.01 and 2.78 in the other hand (Table 2). Spiral analysis revealed normal values for tightness in 4 of 5 patients; 1 patient had increased tightness. Spiral drawing speed was slow bilaterally in 3 patients. Increased decrement in spiral speed with radius was evident in both hands in 3 patients. Overall, abnormal spiral analysis data were evident in all 5 patients (Table 2).

COMPARISON OF ELECTROPHYSIOLOGIC DATA IN ALL PATIENT GROUPS

Controls had the fastest spiral speed, followed by patients with ET without rest tremor, patients with ET and rest tremor, and then patients with PD (P = .004).
Results were similar after adjusting for age (P = .006). Although it is possible that severe action tremor could have resulted in a compensatory slow spiral in patients with ET struggling to draw a spiral, our data did not support this. In our sample, 10 patients with ET without rest tremor had moderate to severe action tremor (total tremor score range, 20–32). The mean ± SD spiral speed in these 10 patients (11.72 ± 3.71 cm/s) was similar to that of their counterparts with mild action tremor and no rest tremor (12.15 ± 5.51 cm/s). Moreover, removing these 10 patients from the analyses did not significantly alter the results.

The lowest decrementing speed with radius was noted in controls, which was similar to that of patients

### Table 3. Comparison of Electrophysiologic Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patient No.</th>
<th>Age, y</th>
<th>Spiral Speed, cm/s</th>
<th>Spiral Tightness</th>
<th>Decrementing Speed With Radius</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD</td>
<td>8</td>
<td>66.8 ± 12.8</td>
<td>7.14 ± 4.82</td>
<td>1.74 ± 1.04</td>
<td>0.41 ± 0.276</td>
</tr>
<tr>
<td>ET with rest tremor</td>
<td>5</td>
<td>73.6 ± 10.0</td>
<td>9.36 ± 6.84†</td>
<td>1.25 ± 0.30</td>
<td>0.14 ± 0.204†</td>
</tr>
<tr>
<td>ET without rest tremor</td>
<td>21</td>
<td>68.8 ± 9.5</td>
<td>12.06 ± 4.54</td>
<td>1.24 ± 0.40</td>
<td>0.03 ± 0.022†</td>
</tr>
<tr>
<td>Controls</td>
<td>12</td>
<td>63.1 ± 12.7</td>
<td>13.20 ± 4.33</td>
<td>1.37 ± 0.35</td>
<td>0.02 ± 0.025</td>
</tr>
</tbody>
</table>

Abbreviations: ET, essential tremor; PD, Parkinson disease.

*Values are given as mean ± SD and represent the means of the right and left hands.
†Value represents the hand that was more parkinsonian.
with ET without rest tremor. Patients with ET and rest tremor had higher decrementing speeds, and the highest was found in patients with PD (P < .001). The 10 patients with ET without rest tremor who had moderate to severe action tremor had a mean ± SD decrementing speed with radius (0.031 ± 0.013) that was similar to that of their counterparts with mild action tremor and no rest tremor (0.029 ± 0.031). Mean spiral tightness did not differ among ET groups and controls.

We sampled patients with ET from the Center for Parkinson’s Disease and Other Movement Disorders. Mean patient age and disease duration were comparable with those of patients described from other tertiary referral centers. Rest tremor was present in approximately 1 in 5 patients with ET, and in more than half of these, it was present during at least 2 activities (standing or walking and while seated). That the tremulous limb was fully at rest was evidenced by the absence of EMG activity in patients who were studied electrophysiologically. Rest tremor was associated with ET that was more prolonged, more severe, and more disseminated.

None of the patients had clinical signs of parkinsonism other than rest tremor by either neurologist examination or videotaped neurologic examination findings. However, electrophysiologic study results, which included spiral analysis, revealed features that are evident in patients with parkinsonism and, therefore, possibly consistent with basal ganglia dysfunction. In addition to the presence of rest tremor, there was a reduction in spiral speed and a change in slope over time. These features could not be attributed to severe action tremor because patients with ET and severe action tremor in the absence of rest tremor did not exhibit these features.

The basis for rest tremor in ET is not clear, although there are several possibilities. First, in patients with severe, long-standing, and disseminated disease, the pathologic process responsible for their ET may have spread into motor systems outside of the cerebellum-cerebellar outflow connections. The basal ganglia and/or their connections could be involved. There is evidence in the literature that ET may involve systems outside of the cerebellum. Results of recent studies of cognitive (especially executive function) abnormalities in ET suggest that in some cases there may be more widespread involvement. In a fluorodopa positron emission tomography study, uptake in the basal ganglia in patients with ET was 10% to 13% below that of controls, but the difference was not significant.

Idiopathic PD with rest tremor, bradykinesia, and rigidity may develop in some patients with ET, and a second possibility is that rest tremor may be the only clinically detectable sign of coexisting Lewy body PD that has developed in our patients. Against this possibility is the observation by Rajput et al that pathologic findings compatible with idiopathic PD were absent in 3 patients with ET and isolated rest tremor. Also, in the positron emission tomography study, although fluorodopa uptake in the basal ganglia was 10% to 13% below normal, it was well above the range seen in patients with idiopathic PD.

A third possibility is that the rest tremor in our patients is not a true rest tremor but a breakthrough postural tremor. The absence of EMG activity in patients who were studied electrophysiologically makes this possibility less likely. Also, in most patients with asymmetrical rest tremor, the hand with the more severe rest tremor was contralateral to the hand with the more severe kinetic tremor.

This study has limitations. We estimated the prevalence of rest tremor in ET at one medical center. The disease duration and age of our patients were similar to those reported in other series, suggesting that we did not select patients whose characteristics were atypical of ET. However, it is possible that the prevalence of rest tremor in ET could be lower in primary care settings. Second, only a portion of participants with rest tremor agreed to undergo electrophysiologic study. We do not think there was selection bias because individuals who underwent tremor analysis were similar to those who did not. Finally, it is possible that the trained tester did not correctly note the presence of rigidity and that some of the patients with rest tremor also had rigidity. Although this is possible, all patients were also routinely examined by neurologists specializing in movement disorders and were excluded from this study if rigidity was noted in the clinical chart.

In summary, in this study, 1 in 5 patients with ET had rest tremor. This tremor was associated with disease that was more long-standing, more severe, and more disseminated. Patients with ET and isolated rest tremor may have subtle signs of bradykinesia and decrementing amplitude that are not present on clinical examination but that are detectable during electrophysiologic study. The basis for the rest tremor could be basal ganglia involvement, raising the possibility that the pathologic process responsible for ET may extend to these structures.

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Author contributions: Study concept and design (Dr Louis); acquisition of data (Drs Pullman and Louis, Ms Jurewicz, and Ms Watner); analysis and interpretation of data (Drs Cohen, Pullman, and Louis); drafting of the manuscript (Drs Cohen and Louis); critical revision of the manuscript for important intellectual content (Drs Pullman and Louis, Ms Jurewicz, and Ms Watner); statistical expertise (Dr Louis); obtained funding (Dr Louis); administrative, technical, and material support (Drs Cohen, Pullman, and Louis, Ms Jurewicz, and Ms Watner); study supervision (Dr Louis).

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Corresponding author and reprints: Elan D. Louis, MD, MS, Neurological Institute, 710 W 168th St, Unit 198, New York, NY 10032 (e-mail: EDL2@Columbia.edu).
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