ORIGINAL CONTRIBUTION

# Common Misdiagnosis of a Common Neurological Disorder

## *How Are We Misdiagnosing Essential Tremor?*

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**Background:** As a common neurological disorder, the diagnosis of essential tremor (ET) is considered routine. Despite this, previous work suggests that misdiagnoses may be common. Among other things, these misdiagnoses can lead to treatment errors.

**Objectives:** To estimate how often other tremor disorders are misdiagnosed as ET and to identify factors that increase the odds of misdiagnosing ET and to precisely quantify the extent to which they do so.

**Design:** Seventy-one consecutive patients underwent an evaluation at the Neurological Institute of New York, New York, between January 1, 2000, and December 31, 2005; these patients had a preevaluation diagnosis of ET. The criteria for ET were adapted from the consensus statement of the Movement Disorder Society.

**Results:** Twenty-six patients (37%) were misdiagnosed as having ET ("false ET"). Their true diagnoses were Parkinson disease (11 patients [15%]), dystonia (6 patients [8%]), Parkinson disease with ET (5 patients [7%]), and other disorders (4 patients [6%]). Factors associated with misdiagnosed ET included unilateral arm tremor (odds ratio, 10.5; 95% confidence interval, 1.2-95.4; $P$=.02), spooning of the hands and other dystonic postures (odds ratio, 16.3; 95% confidence interval, 4.0-66.4; $P$<.001), and other unusual features (isolated thumb tremor, isolated leg tremor, and nonrhythmic tremor) (odds ratio, 49.4; 95% confidence interval, 2.7-895.0; $P$<.001).

**Conclusions:** About 1 in 3 patients with tremor was misdiagnosed as having ET, with the most frequent false diagnoses being Parkinson disease and dystonia. Several factors that increased the odds of misdiagnosing ET were identified. These factors could be incorporated into improved diagnostic algorithms.

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DESPITE BEING ONE OF THE most common neurological disorders,[1] essential tremor (ET) can still be difficult to diagnose. This is due not only to its variable clinical presentation but also to a lack of agreement among movement disorder specialists as to how to define ET.[2] Indeed, multiple criteria have been proposed to more precisely define ET,[3,4] and it is still debated as to whether ET is a homogeneous or heterogeneous condition.[5,6] Distinguishing other conditions from ET is important for prognostication and treatment of the individual patient, and for clinical research.

Because ET is a common disorder, it is possible that other less common disorders are mistaken for ET. One previous study[7] reported that only 50% of patients who were diagnosed as having ET actually met the formal criteria for ET. However, that study used a narrower definition of the ET phenotype; patients with ET were required to have 3 or more generations of affected relatives. The 2 aims of the present study are (1) to estimate how often other tremor disorders are misdiagnosed as ET using the more widely applied criteria from the consensus statement of the Movement Disorder Society (MDS)[8] and (2) to identify factors in the neurological history and examination that increase the odds of misdiagnosing ET and to precisely quantify the extent to which they do so.

## METHODS

We identified 71 consecutive patients who fulfilled the following inclusion criteria: (1) initial outpatient evaluation by one of us (E.D.L.) at the Neurological Institute of New York, New York, between January 1, 2000, and December 31, 2005, and (2) preevaluation diagnosis of ET. Data were retrospectively abstracted from their clinical charts using standardized forms

**Table 1. Demographic and Clinical Characteristics of Patients With False vs True ET***

| Characteristic | Patients With False ET (n = 26) | Patients With True ET (n = 45) | Total Patients (N = 71) | *P* Value for True vs False ET |
|---|---|---|---|---|
| Age, y | | | | |
| At current evaluation | 57.3 (17.1) | 65.4 (19.8) | 62.4 (19.2) | .08 |
| At tremor onset | 43.5 (24.9) | 44.9 (21.9) | 44.4 (22.9) | .81 |
| Duration of tremor, y | 11.4 (13.9) | 21.3 (17.3) | 17.8 (16.8) | .02 |
| Female sex† | 17 (65) | 24 (53) | 41 (58) | .32 |

Abbreviation: ET, essential tremor.
*Data are given as mean (SD) unless otherwise indicated.
†Data are given as number (percentage) of each group.

**Table 2. Factors From the Neurological History That Influenced the Odds of Having False vs True ET**

| Factor | Patients With False ET (n = 26)* | Patients With True ET (n = 45)* | OR (95% CI)† | *P* Value |
|---|---|---|---|---|
| Atypical distribution of tremor at onset‡ vs onset of tremor in both arms | 21 (81) | 20 (44) | 5.3 (1.7-16.7) | .003 |
| Current tremor distribution (by report) | | | | |
| Head only | 5 (19) | 0 | 10.5 (1.3-95.4)§ | .005 |
| Both arms, head, and voice | 8 (31) | 34 (76) | 0.1 (0.05-0.4) | <.001 |
| Current reported tremor type | | | | |
| Kinetic | 12 (46) | 39 (87) | 0.1 (0.04-0.4) | .001 |
| Postural | 2 (8) | 3 (7) | 1.2 (0.2-7.5) | >.99 |
| Rest | 5 (19) | 0 | 10.5 (1.3-95.4)§ | .005 |
| Tremor progression | 23 (88) | 38 (84) | 1.4 (0.3-6.0) | .74 |
| Family history of ET | 2 (8) | 13 (29) | 0.2 (0.04-0.99) | .04 |
| Ethanol responsiveness | 6 (23) | 15 (33) | 0.6 (0.2-1.8) | .43 |

Abbreviations: CI, confidence interval; ET, essential tremor; OR, odds ratio.
*Data are given as number (percentage) of patients.
†The odds of having false vs true ET.
‡Any of the following distributions: (1) unilateral arm; (2) unilateral leg; (3) isolated head, chin, or voice; (4) both legs; (5) both arms plus head or voice; or (6) all extremities.
§In instances in which a data cell contained no observations, the OR was conservatively estimated by placing the value 1 in that cell.

designed for the present study; these data included the diagnosis and details about the neurological history and neurological examination.

All patients had a preevaluation diagnosis of ET. The postevaluation diagnosis (assigned by E.D.L.) was also recorded; the diagnostic criteria used were those for classic ET (found in the MDS consensus statement).[8] These criteria stipulated the presence of bilateral, predominantly symmetric postural, or kinetic tremor in the upper extremities, with possible head tremor in the absence of abnormal posturing. The criteria did not have a stipulation regarding tremor duration. They excluded patients with known causes of enhanced physiologic tremor or with other abnormal neurological signs, especially dystonia. "False ET" was used to designate the situation in which the postevaluation diagnosis was not ET, whereas "true ET" was used when the postevaluation diagnosis was ET.

As previously noted, demographic and historical data were abstracted from the clinical charts (**Table 1** and **Table 2**). These included present age, sex, age at tremor onset, duration of tremor, tremor distribution at onset (ie, body parts affected), current tremor distribution, type of tremor (kinetic, postural, or rest), tremor progression (patient reports that tremor has worsened over time), family history of ET (presence by report of ≥1 first-degree relative with ET), ethanol responsiveness (patient reports a noticeable decrease in tremor severity after consuming ≥1 ethanol-containing beverage), whether the patient was self-referred or referred by the treating physician, and the time (in months) between the patient's last outside evaluation and the patient's evaluation at the Neurological Institute of New York.

Data on the neurological examination were also abstracted from the clinical charts (**Table 3**). These included data on tremor distribution, tremor type (postural, kinetic, rest, or reemergent [tremor that emerges after a variable latency while the patient maintains his or her arms extended against gravity][9,10]), relative severity of each type of tremor (eg, predominant rest tremor with mild postural or kinetic tremor), presence of dystonic features (dystonic postures like "spooning" of hands [ie, slight dystonic wrist flexion with hyperextension of the fingers when arms are outstretched]), presence of a null point or use of a sensory trick to diminish the tremor, tremor "directionality" (ie, tremor has a predominance of motion in 1 direction) and muscle hypertrophy, presence of parkinsonian features (slow rapid-alternating movements, reduced arm swing, hypomimia, axial rigidity, and hemibody tremor [ie, tremor confined to the right or left side of the body]), or other unusual features (eg, nonrhythmic tremor [tremor that is not regularly recurrent] or thumb tremor).

All analyses were performed using a commercially available software program (SPSS, version 13.0; SPSS Inc, Chicago, Ill). For group comparisons of continuous variables, *t* tests or analyses of variance were used; and for comparisons of categorical variables, $\chi^2$ or Fisher exact tests were used. Logistic regression analyses were performed to identify specific features that were associated with the outcome variable, misdi-

**Table 3. Factors From the Neurological Examination That Influenced the Odds of Having False vs True ET**

| Factor | Patients With False ET (n = 26)* | Patients With True ET (n = 45)* | OR (95% CI) | *P* Value |
|---|---|---|---|---|
| Tremor distribution | | | | |
| Unilateral arm | 5 (19) | 1 (2) | 10.5 (1.2-95.4) | .02 |
| Head only | 4 (15) | 1 (2) | 8.0 (0.8-75.9) | .06 |
| Both arms, head, and voice | 5 (19) | 23 (51) | 0.2 (0.07-0.7) | .01 |
| Tremor type | | | | |
| Postural | 16 (62) | 41 (91) | 0.2 (0.04-0.6) | .004 |
| Kinetic | 15 (58) | 45 (100) | 0.3 (0.2-0.4) | <.001 |
| Rest | 13 (50) | 1 (2) | 44.0 (5.3-368.8) | <.001 |
| Reemergent | 3 (12) | 0 | 5.7 (0.3-58.3)† | .05 |
| Predominant rest tremor with mild postural or kinetic tremor | 10 (38) | 0 | 57.9 (3.2-1044.5)† | <.001 |
| Features of dystonia | | | | |
| Dystonic postures | 14 (54) | 3 (7) | 16.3 (4.0-66.4) | <.001 |
| Isolated head tremor | 2 (8) | 0 | 3.7 (0.3-42.6)† | .13 |
| Null point or sensory trick | 3 (12) | 0 | 5.7 (0.3-58.3)† | .05 |
| Tremor directionality | 4 (15) | 0 | 8.0 (0.8-75.9) | .02 |
| Muscle hypertrophy | 3 (12) | 1 (2) | 5.7 (0.6-58.3) | .10 |
| Features of parkinsonism | | | | |
| Slow RAMs | 14 (54) | 2 (4) | 25.1 (5.0-126.0) | <.001 |
| Reduced arm swing | 14 (54) | 6 (13) | 7.6 (2.4-24.1) | .001 |
| Hypomimia | 8 (31) | 0 | 19.6 (2.3-167.9)† | <.001 |
| Thumb tremor | 1 (4) | 0 | 1.8 (0.1-29.4)† | .37 |
| Axial rigidity | 3 (12) | 1 (2) | 5.7 (0.6-58.3) | .10 |
| Hemibody tremor | 2 (8) | 0 | 3.7 (0.3-42.6)† | .13 |
| Other unusual features (isolated thumb tremor, isolated leg tremor, or nonrhythmic tremor) | 9 (35) | 0 | 49.4 (2.7-895.0)† | <.001 |

Abbreviations: CI, confidence interval; ET, essential tremor; OR, odds ratio; RAM, rapid-alternating movement.
*Data are given as number (percentage) of patients.
†In instances in which a data cell contained no observations, the OR was conservatively estimated by placing the value 1 in that cell.

agnosed ET (false ET). These analyses resulted in odds ratios with 95% confidence intervals that reflected the odds of having false rather than true ET. In instances in which a data cell contained no observations, the odds ratio was conservatively estimated by placing the value 1 in that cell.

## RESULTS

### SAMPLE CHARACTERISTICS

Of the 71 patients, 66 (93%) had undergone an evaluation by another physician (56 [79%] by a neurologist and 10 [14%] by an internist, general practitioner, or another type of physician); 35 (49%) had been evaluated by 2 or more physicians before their evaluation at the Neurological Institute of New York. Of the 71 patients, 5 (7%) had not had a prior evaluation by another physician; 3 were self-diagnosed, and 2 were diagnosed by a family member. All 71 patients were diagnosed as having ET, with the median interval between the last preevaluation diagnosis by another physician and the postevaluation diagnosis being 4 months (mean, 10.4 months). Of the 71 patients, 63 (89%) were self-referred, whereas 8 (11%) were referred by their treating physician; these 8 patients included 4 with true ET (ie, the preevaluation and postevaluation diagnoses were ET) and 4 with false ET (ie, the preevaluation diagnosis was ET but the postevaluation diagnosis was not ET). Patients had experienced symptoms for a mean (SD) of 17.8 (16.8) years.

### HOW OFTEN OTHER TREMOR DISORDERS ARE MISDIAGNOSED AS ET

Of the 71 patients, 45 (63%) had true ET and 26 (37%) had false ET. Hence, approximately 1 in 3 patients were misdiagnosed as having ET (ie, they had false ET). Of the 26 patients with false ET, 23 (88%) had previously been evaluated by a neurologist, whereas 3 (12%) had been evaluated by an internist, general practitioner, or another type of physician. Of the 56 patients evaluated by neurologists, 23 (41%) had false ET; and of the 10 patients evaluated by an internist, general practitioner, or another type of physician, 3 (30%) had false ET. The most common postevaluation diagnoses in the 26 patients with false ET were Parkinson disease (PD) (11 patients [15% of 71]), focal dystonia with an accompanying dystonic tremor (6 patients [8% of 71]), and PD with concurrent ET (5 patients [7% of 71]). Other diagnoses (4 patients [6% of 71]) were myoclonus dystonia, primary writing tremor, and enhanced physiologic tremor. All of the 11 patients with PD last had been seen by their treating physician within the past year; 8 (73%) had been seen within the past 4 months and 3 (27%) within the past 1 month. Each of the 6 patients with focal dystonia had torticollis, and 3 had accompanying arm dystonia. The tremor in these patients was nonrhythmic and restricted to the body region(s) affected by focal dystonia.

## FACTORS THAT INCREASE THE ODDS OF DIAGNOSTIC ERROR IN PATIENTS WITH ET

Patients with false ET had a shorter duration of tremor and were marginally younger than patients with true ET (Table 1).

Several factors that increased the odds of having false vs true ET emerged from the neurological history (Table 2). The onset of tremor in an atypical distribution (eg, unilateral arm or unilateral leg) increased the odds of false ET by a factor of about 5. A history of current isolated head tremor increased the odds of false ET 10-fold, whereas a history of current tremor in the arms, head, and voice was associated with a decreased odds of false ET (Table 2). The presence, by report, of rest tremor was associated with a 10-fold increased odds of false ET, whereas reported kinetic tremor was associated with a decreased odds of false ET. Having a first-degree relative with ET was associated with a 5-fold decreased odds of having false ET (Table 2).

Numerous factors that increased the odds of having false vs true ET emerged from the neurological examination (Table 3). These factors included tremor distribution (eg, unilateral arm tremor and isolated head tremor), tremor type (rest tremor and reemergent tremor), several features of dystonia (dystonic postures, such as spooning of the hands, presence of a null point or sensory trick, and tremor directionality), features of parkinsonism (slow rapid-alternating movements, reduced arm swing, and hypomimia), and a collection of other unusual features (isolated thumb tremor, isolated leg tremor, or nonrhythmic tremor) (Table 3). More specifically, the odds of having false ET increased more than 10-fold for each of several factors: unilateral arm tremor, rest tremor, predominant rest tremor with mild postural or kinetic tremor, dystonic postures, slow rapid-alternating movements, hypomimia, and other unusual features (Table 3). The odds of false ET was increased by a factor of 5- to 10-fold by the presence on examination of several other factors (isolated head tremor, reemergent tremor, presence of a null point or sensory trick, tremor directionality, and reduced arm swing) (Table 3).

## COMMENT

We evaluated the diagnoses of patients who came to our tertiary referral center with a prior diagnosis of ET. More than 90% had been seen by another physician, with nearly half having seen 2 or more physicians before their evaluation with us. More than 1 in 3 such patients (37%) had atypical features that excluded the diagnosis of ET (using the diagnostic criteria for classic ET from the MDS consensus statement).[8] This proportion was slightly less than that reported by Schrag and colleagues,[7] who found that 50% of patients with previously diagnosed ET had false ET. However, that study used a defined phenotype that required ET to affect family members in at least 3 generations. We used the MDS criteria for diagnosing ET, which did not require a family history.[8]

Parkinson disease was the most common diagnosis among the patients with false ET. Indeed, nearly 1 in 4 "ET" patients had either PD or both diagnoses (ET and PD). Often, the parkinsonian signs were subtle (eg, a slight unilateral decrease in arm swing or mild hypomimia). At what time point these patients developed clinically evident parkinsonism is not known, but the presence of such patients highlights the importance of looking for subtle signs of parkinsonism in a patient referred with a diagnosis of ET. Not only does this lessen the chance of overdiagnosing ET but the possibility of PD allows for additional therapeutic options. The second most common diagnosis among the patients with false ET was dystonia. Although it is possible for dystonia and ET to coexist in the same individual,[6] all 6 patients with dystonia had nonrhythmic tremor that was restricted to the body region affected by dystonia. These patients were diagnosed as having focal dystonia with accompanying dystonic tremor rather than diagnosed as having ET and dystonia.

Previous literature[7] has not attempted to identify and quantify the impact of factors in the neurological history and examination that increase the odds of misdiagnosing ET. We found several characteristics that, if present by history or on neurological examination, should make clinicians question the diagnosis of ET. While several of these features may seem relatively self-evident (eg, features of dystonia like dystonic postures and the presence of a null point or sensory trick and features of parkinsonism like slow rapid-alternating movements, reduced arm swing, or hypomimia), the high proportion of misdiagnosed ET cases demonstrates that these characteristics may not always be fully appreciated. Furthermore, while the MDS criteria exclude a diagnosis of ET in the presence of other abnormal neurological signs, our study goes further and specifies several of these signs. We not only describe these features but also quantify the extent to which each affects the odds of having false ET. More widespread recognition of these symptoms and signs may reduce the overdiagnoses of ET. These features included unilateral arm tremor, isolated head tremor, and several other unusual features (tremor directionality, isolated thumb or isolated leg tremor, and nonrhythmic tremor). Each of these features increased the odds of false ET considerably.

There are several limitations to the interpretations of our findings. First, data were retrospectively abstracted; this approach can be problematic when individual data fields are not routinely coded. This, however, is likely to have resulted in more conservative estimates of the associations between individual factors and false diagnoses. Second, we sampled cases from one of us (E.D.L.), who evaluated patients at a tertiary referral center and, as a result, may have seen more complex and less common presentations of ET. Although this is a possibility, all of these patients had been diagnosed as having ET, rather than "unknown" or "complex tremor," by their initial treating physicians. Furthermore, most (89%) of these patients were self-referred rather than being referred by a treating physician in the setting of a diagnostic dilemma. Third, physical findings (eg, parkinsonism) may not have been as apparent during prior evaluations and disease progression can make the diagnosis more obvious. This is possible, although the median interval between the last preevaluation diagnosis and

the postevaluation diagnosis was only 4 months. Furthermore, historical features could have been recognized during prior evaluations to improve diagnostic accuracy. Fourth, while we suspect that physicians used a variety of criteria to assign preevaluation diagnoses of ET, we do not know which criteria they used, how certain they were of these diagnoses (eg, possible vs definite cases of ET), and what methods they used to assess signs of parkinsonism and dystonia. Despite these limitations, there are few data on the accuracy of the ET diagnosis, and, to our knowledge, no prior studies have attempted to precisely quantify the extent to which each of a variety of separate factors increased the odds of a false diagnosis of ET.

Essential tremor is a common neurological condition that can be variable in presentation,[11] and it is imprecisely diagnosed. These data suggest that diagnostic errors are common in this common neurological disorder. Specific findings in the neurological history and examination may serve as signs that one is not likely to be dealing with a patient with ET, and these may be used to reduce overdiagnosis of this common disorder. Greater awareness of some of the features we have identified may prevent overdiagnosis. Moreover, these factors could be incorporated into improved diagnostic algorithms.

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