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Intention Tremor in Essential Tremor: Prevalence and Association with Disease Duration

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Keywords

Essential tremor; intention tremor; duration; clinical; epidemiological; neurodegeneration; cerebellum

Scholarly attention only recently has been focused on intention tremor (IT) in essential tremor (ET).^{1, 2} Therefore, little has been written on its prevalence or clinical correlates. The association between IT and disease duration also remains unsettled. This question has pathophysiological implications. Studies have indicated metabolic and structural changes in the ET cerebellum.^{3, 4} If ET were a disease of progressive cerebellar dysregulation, one would expect more IT in patients with disease of longer duration. We assessed the prevalence and clinical correlates of IT and determined whether there was an association between IT and disease duration.

As documented previously,^{5, 6} ET cases were recruited for an epidemiological study at Columbia University. The protocol was approved by the University Human Ethics Committee. Signed informed consent was obtained and a medical questionnaire was administered. Tremor duration (current age - reported age of kinetic tremor onset) was used as a proxy for disease duration. A videotaped examination included detailed assessment of kinetic, postural, and resting arm tremors, and head, jaw, and voice tremors. Videotaped examinations were reviewed by a senior neurologist (E.D.L) and a total arm action tremor score (range = 0 – 36) was assigned. The finger-nose-finger maneuver included 10 repetitions per arm. IT was defined as present when tremor amplitude increased during visually guided movements towards the target.

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Statistical Analyses: The statistical analyses were conducted by Dr. Louis.

Author Contributions:

Elan D. Louis: Research project conception, organization and execution; statistical analyses design and execution; manuscript writing (writing the first draft and making subsequent revisions).

Steven J. Frucht: Research project execution; manuscript writing (making subsequent revisions).

Eileen Rios: Research project execution; manuscript writing (making subsequent revisions).

Videotape legend:

Cases 1 and 2. Mild postural tremor is noted in each case. IT, defined as present when tremor amplitude increased during visually guided movements towards the target, is present in each case in both hands during the finger-nose-finger maneuver.

¹ We excluded position-specific tremor or postural tremor at the end of movement. Similar to Deuschl et al.,¹ IT was rated (E.D.L.) in the terminal period of the finger-nose-finger test: 0 (no IT); 0.5 (probable IT); 1 (definite IT); 2 (incapacitating IT), although no cases received ratings of 2. The IT score (both arms combined) ranged from 0 – 2. Cases with definite IT in at least one arm or probable IT in both arms were labeled as ET with IT.¹ The IT score was not normally distributed and included zero values. Therefore, in linear regression analyses, the value $\log_{10}(\text{IT score} + 1)$ was used as the dependent variable.

Forty-five (38.5%) of 117 were ET with IT (Table, videotape). When compared to 72 without IT, these 45 had a similar age but a younger age of kinetic tremor onset and longer disease duration. Their total arm action tremor score was higher and a larger proportion had voice and rest tremors.

The IT score was correlated with disease duration (Spearman's $r = 0.41$, $p < 0.001$) but not age (Spearman's $r = 0.08$, $p = 0.37$). In an unadjusted linear regression model, disease duration (beta = 0.004, $p < 0.001$) but not age (beta = 0.000, $p = 0.65$) was associated with log-transformed IT score. Adjusting for gender, education, family history of ET, and daily medication for ET did not change the results (for duration, beta = 0.004 and $p < 0.001$; for age, beta = 0.001 and $p = 0.63$).

We divided disease duration into quartiles. IT scores in each quartile were: 0.28 ± 0.54 (duration ≤ 8 years), 0.42 ± 0.56 (duration > 8 and < 20 years), 0.79 ± 0.70 (duration ≥ 20 and ≤ 39 years), and 0.88 ± 0.72 (duration > 39 years). In a test for trend (log IT score = dependent variable, and duration quartile = independent variable), beta = 0.06, $p < 0.01$, indicating that increasing duration quartile was associated with increasing IT score.

Among the few studies to have estimated the prevalence of IT in ET, estimates varied considerably (9.6% – 51.9%).^{1, 2, 7} Combining our data with the two studies that used a similar definition of IT,^{1, 2} the overall prevalence would be 101 of 228 (44.3%).

In the two previous studies,^{1, 2} the association between IT and disease duration was not completely resolved. In the first study,¹ disease duration in ET patients with vs. without IT was similar. In the second,² disease duration was non-significantly greater in the former. Our sample size was larger, providing additional study power. Furthermore, the participants were older, thereby providing an expanded range of tremor durations.

There are a number of physiological studies demonstrating that tremor in ET may result from errors during the cerebellar processing of motor commands (i.e., dysregulation of the cerebellar system).^{8, 9} Indeed, in this study, IT occurred in approximately one-in-three ET cases. Furthermore, we showed that IT was robustly associated with disease duration. This suggests that dysregulation of the cerebellar system in ET might worsen with increasing disease duration.

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Table
Demographic and clinical characteristics of ET cases

Demographic and clinical characteristic	All ET cases (N = 117)	ET With IT (N = 45)	ET Without IT (N = 72)
Age (years)	66.2 ± 15.1 (70.0, 21 – 89)	67.7 ± 15.7 (71.0, 27 – 89)	65.3 ± 14.8 (69.5, 21 – 89)
Female gender	50 (42.7)	17 (37.8)	33 (45.8)
Education (years)	15.7 ± 2.9 (16.0, 4 – 20)	16.0 ± 2.8 (16.0, 12 – 20)	15.5 ± 2.9 (16.0, 4 – 20)
Age of kinetic tremor onset (years)	41.7 ± 23.3 (45.0, 5 – 86)	35.0 ± 23.7 (38.0, 6 – 77)*	45.8 ± 22.3 (50.0, 5 – 86)
Disease duration (years)	24.8 ± 19.7 (20.0, 1 – 81)	32.6 ± 21.5 (29.0, 3 – 81)**	20.0 ± 16.9 (14.0, 1 – 59)
Family history of ET	72 (61.5)	31 (68.9)	41 (56.9)
Takes daily medication for ET	44 (37.6)	18 (40.0)	26 (36.1)
Total arm action tremor score	17.9 ± 6.2 (17.0, 3 – 34)	21.7 ± 5.9 (21.0, 13 – 34)***	15.6 ± 5.1 (15.0, 3 – 27)
Head tremor on examination	38 (32.5)	18 (40.0)	20 (27.8)
Voice tremor on examination	38 (32.5)	21 (46.7)*	17 (23.6)
Jaw tremor on examination	11 (9.4)	6 (13.3)	5 (6.9)
Rest tremor in either arm on examination	15 (12.8)	10 (22.2)*	5 (6.9)
IT score	0.6 ± 0.7 (0.5, 0 – 2)	1.4 ± 0.4 (1.5, 1 – 2)***	0.1 ± 0.2 (0.0, 0 – 0.5)

Cases with definite IT in at least one arm or probable IT in both arms were labeled as ET with IT.¹

Data are expressed as mean ± SD (median, minimum – maximum) or number (%).

Age of kinetic tremor onset and disease duration were not known in 4 ET cases.

Age, age of kinetic tremor onset, disease duration, and IT score were not normally distributed and nonparametric tests (Mann Whitney test) were used for these analyses.

* p < 0.05 when comparing ET with IT to ET without IT.

** p < 0.01 when comparing ET with IT to ET without IT.

*** p < 0.001 when comparing ET with IT to ET without IT.