Validity of a Screening Question for Head Tremor: An Analysis of Four Essential Tremor Case Samples

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Key Words

Essential tremor · Epidemiology · Clinical · Screening · Validity · Head tremor

Abstract

Background: The goal of this study was to assess the validity of a screening question for head tremor in essential tremor (ET). There are no published data on this topic, and the knowledge will guide future epidemiological investigations of this disorder. **Methods:** These analyses utilized four distinct patient samples: a population-based study in northern Manhattan, a study of the environmental epidemiology of ET, a genetics study, and a brain repository. Sensitivity was the proportion of ET cases with head tremor on examination who self-reported head tremor. **Results:** The sensitivity of the screening question for head tremor was lowest in the population-based study (31.6%), and higher as well as somewhat similar across the remaining studies (46.7 to 62.2%). Higher sensitivity was associated with tremor of longer duration, presence of voice tremor on examination, female gender, and lower education. The use of the screening question would have increased case ascertainment during the screening phase of these four studies by 1.9, 4.1, 10.2, and 20.3%.

Conclusions: A screening question for head tremor had low-to-moderate sensitivity in ET. The use of such a screening questionnaire, however, has the potential to increase case ascertainment by as much as 20% in some screening settings.

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Introduction

The initial step in much of epidemiological research is case ascertainment. In prevalence and incidence studies, complete ascertainment of cases is of prime importance. Nevertheless, case identification is often fraught with difficulties. In essential tremor (ET) research, for example, spiral drawing is a commonly employed method to screen populations. Hand-drawn spirals may easily be collected by email, facsimile, postal service and other methods, none of which require the investigator to travel, thereby saving time and resources when screening large numbers of people. However, some ET cases may not exhibit tremor in their hand-drawn spiral. Indeed, population-based studies estimate that 34.5% of ET cases have tremor that is either minimal or absent when drawing a spiral with their dominant

arm [1]. Failure to detect one in three ET cases, when using this popular screening method, is highly problematic.

Head tremor is a common feature in ET, occurring in 10.9% to 18.0% of ET cases in population-based studies [2–4] and as many as 60.6% of cases in more selected samples such as brain repositories [5]. Therefore, screening for and identifying individuals with head tremor has the potential to boost case ascertainment in neuroepidemiological studies.

Thus, the question naturally arises, how valid are reports of head tremor among patients with ET? There are compelling reasons to expect that ET patients would not report head tremor even when it is present – ET patients are often completely unaware of their own head tremor. A proposed mechanism is that reduced sensitivity to head motion allows patients to achieve a sense of perceptual stability [6]. This type of perceptual cancelling occurs in patients with congenital nystagmus as well [7].

The primary aim of the current study was to assess the validity of a screening question for head tremor in ET. There are no published data on this topic, and the knowledge will guide future epidemiological investigations of this disorder. A second aim was to estimate the number of additional ET cases who would have been ascertained with the addition of a screening question for head tremor. In order to broadly assess this issue across a wide range of possible settings, these analyses utilized four distinct patient samples: a population-based study in northern Manhattan [8], a study of the environmental epidemiology of ET [9], a genetics study [10], and a brain repository [5]; in total, more than 800 ET patients were studied in these four parallel datasets.

Methods

Four ET case samples were used – cases all signed written informed consent as approved by our institutional ethics board.

Population-Based Study in Northern Manhattan

The Washington Heights-Inwood Genetic Study of Essential Tremor (WHIGET) was a family study of ET in the Washington Heights-Inwood community in northern Manhattan, New York. Enrollment was completed in 2000. There were 106 ET cases, including 59 probands with ET, 33 of their relatives with ET, and 14 affected relatives of control probands. The design of this population-based study has been described in detail [8, 11, 12]. All enrollees underwent a demographic and medical history and a videotaped tremor examination.

Study of the Environmental Epidemiology of ET

ET cases were enrolled in a study of the environmental epidemiology of ET, from 2000–2009 [9]. As described, cases were derived from two main sources: the Neurological Institute of New

York at Columbia University Medical Center (CUMC) and the membership of the International Essential Tremor Foundation (IETF). After enrollment, all 388 ET cases underwent a demographic and medical history and a videotaped tremor examination.

Family Study of Essential Tremor

ET cases (probands) and their first- and second-degree relatives were enrolled in the Family Study of Essential Tremor (FASET), a genetics study of ET at CUMC [13, 14]. The study was advertised on two ET society websites. Based upon a telephone interview with the proband, relatives with ET were identified. The final sample included 207 individuals (52 probands and 155 relatives), including 160 ET, 28 borderline ET, and 19 normal [13]. After enrollment, subjects underwent a demographic and medical history and a videotaped tremor examination.

Essential Tremor Centralized Brain Repository

The Essential Tremor Centralized Brain Repository (ETCBR) at Columbia University is a centralized repository for the prospective collection and study of ET brains [5, 15]. ET cases were recruited as future brain donors through the IETF and other sources. Once enrolled, they underwent a demographic and medical history and a videotaped tremor examination. Head tremor on videotaped examination was rated by a neurologist specializing in movement disorders (E.D.L.) as absent, mild and infrequent, mild or infrequent, moderate, or severe. These ET cases were highly selected because many were ascertained through a disease-specific organization and because they self-referred to the brain repository as future brain donors [5, 11]. The large majority of these cases have seen physicians who have diagnosed ET [15].

Medical History, Videotaped Tremor Examination and Diagnostic Confirmation

In all four studies, the medical history included questions on demographics, medications, and features of tremor, including the question, ‘Does your head sometimes shake?’ (in the Family Study of Essential Tremor) or ‘Does your head often shake uncontrollably?’ (in the remaining three studies). The videotaped tremor examination included assessments of postural and kinetic tremors in the arms, as well as head (neck), voice, and jaw tremors. This included one test for postural tremor and five for kinetic tremor (pouring, using spoon, drinking, finger-nose-finger, drawing spirals) performed with each arm (12 tests total). In each study, a neurologist specializing in movement disorders (E.D.L.) used a reliable [16] and valid [17] clinical rating scale, the WHIGET Tremor Rating Scale, to rate postural and kinetic tremor during each test: 0 (none), 1 (mild), 2 (moderate), 3 (severe). These ratings resulted in a total tremor score (range = 0–36), which is an assessment of postural and kinetic tremor in the arms [9].

In each study, the diagnosis of ET was re-assessed (E.D.L.) based on the history and videotaped examination. All of the cases included in these analyses met published criteria for ET (moderate or greater amplitude kinetic tremor of the arms during at least three tasks or head tremor, in the absence of Parkinson’s disease, dystonia or another neurological disorder) [12].

Statistical Analyses

Data on each of the four case samples were analyzed separately in SPSS (Version 21). Sensitivity was the proportion of ET cases with head tremor on examination who self-reported head

Table 1. Demographic and clinical features of ET cases in four ET case samples

	Population-Based Study in Northern Manhattan [8, 11, 12]	Study of the Environmental Epidemiology of ET [9]	Family Study of Essential Tremor [13, 14]	Essential Tremor Centralized Brain Repository [5, 15]
Sample size	106	388	160	177
Age in years	69.8±18.4	67.4±15.3	60.0±18.0	83.7±5.8
Female gender	63 (59.4)	201 (51.8)	82 (51.3)	108 (61.0)
Education in years	not available	15.1±3.8	16.4±3.5	14.9±3.2
Total tremor score	16.4±6.7	18.8±7.2	20.1±5.2	24.2±6.7
Tremor duration in years	15.4±18.8	22.8±18.7	32.8±19.3	41.3±22.3
Age of tremor onset in years	56.7±25.6	44.7±22.5	27.0±17.8	42.4±22.9
Currently taking medication for tremor	5 (4.7)	209 (53.9)	79 (49.4)	115 (65.0)
Family history of ET	106 (100)	119 (30.7)	160 (100)	48 (27.1)
Voice tremor on examination	16 (15.1)	118 (30.4)	26 (16.3)	71 (40.1)
Head tremor on examination	19 (17.9)	143 (36.9)	60 (37.5)	92 (52.0)
Self-reported head tremor	9 (8.5)	131 (33.8)	58 (36.3)	53 (29.9)
Moderate or greater tremor in one or both arms during spiral drawing	74 (69.8)	197 (50.8)	98 (61.3)	159 (89.8)
No tremor or mild tremor in both arms during spiral drawing but screened positive for head tremor and had head tremor on examination	3	40	10	3

All values are means ± standard deviations or numbers (percentages).

tremor. Specificity was the proportion of ET cases without head tremor on examination who did not self-report head tremor. False positives were ET cases who self-reported head tremor but had no head tremor on examination. Estimates of the sensitivity included point estimates and 95% confidence intervals (CI). In a logistic regression model, we assessed the association between the dependent variable (reported head tremor in the setting of head tremor on examination) and head tremor severity category (independent variable, coded as absent, mild and infrequent, mild or infrequent, moderate, or severe). We also present data on a range of demographic clinical features that were of *a priori* interest because we thought that sensitivity could co-vary with these.

Results

Demographic and clinical features of ET cases are presented (table 1). As would be expected, the severity of arm tremor (total tremor score), the duration of tremor, and the prevalence of head tremor on examination was lowest in the population-based study in northern Manhattan and was highest in the Essential Tremor Centralized Brain Repository (table 1).

The sensitivity of the question on self-reported head tremor was lowest in the population-based study in northern Manhattan (31.6%), and higher as well as some-

what similar across the remaining three studies (46.7%, 56.7%, 62.2%, table 2).

In the Essential Tremor Centralized Brain Repository, the severity of head tremor on neurological examination was rated. With increasing head tremor severity, there was an increase in the sensitivity of the screening question (i.e., the proportion of ET cases with head tremor on examination who self-reported head tremor): 7 (28.0%) of 25 with mild and infrequent head tremor, 11 (39.3%) of 28 with mild or infrequent head tremor, 23 (62.2%) of 37 with moderate head tremor, and 2 (100%) of 2 with severe head tremor (odds ratio = 2.36, 95% confidence interval = 1.75–3.18, $p < 0.001$ in a logistic regression model).

The specificity of self-reported head tremor was 84/87 (96.6%) in the population-based study in northern Manhattan, 203/245 (82.9%) in the study of the environmental epidemiology of ET, 76/100 (76.0%) in the Family Study of Essential Tremor, and 76/85 (89.4%) in Essential Tremor Centralized Brain Repository; hence the proportion of false positives (ET cases who self-reported head tremor yet who did not have head tremor on examination) ranged from 3.4 to 24.0%.

We explored a wide range of clinical features that could be predictive of increased sensitivity (that is, subgroups of patients who might be better historians) (table 2). We

Table 2. Sensitivity of question on self-reported head tremor

	Population-Based Study in Northern Manhattan [8, 11, 12]	Study of the Environmental Epidemiology of ET [9]	Family Study of Essential Tremor [13, 14]	Essential Tremor Centralized Brain Repository [5, 15]
All cases*	6/19, 31.6% (15.4–54.0%)	89/143, 62.2% (54.1–69.8%)	34/60, 56.7% (44.1–68.4%)	43/92, 46.7% (36.9–56.9%)
<Median age	2/9, 22.2%	37/52, 71.2%	13/23, 56.5%	22/48, 45.8%
>Median age	4/10, 40.0%	52/91, 57.1%	21/37, 56.8%	21/44, 47.7%
Male	0/5, 0.0%	24/43, 55.8%	12/25, 48.0%	8/24, 33.3%
Female	6/14, 42.9%	65/100, 65.0%	22/35, 62.9%	35/68, 51.5%
≤Median education	information	50/74, 67.6%	15/22, 68.2%	27/45, 60.0%
>Median education	not available	39/68, 57.4%	19/38, 50.0%	15/46, 32.6%
<Median TTS	4/11, 36.4%	36/55, 65.5%	11/24, 45.8%	15/38, 39.5%
≥Median TTS	2/8, 25.0%	53/85, 62.4%	23/36, 63.9%	27/53, 50.9%
≤Median duration	1/5, 20.0%	34/63, 54.0%	8/22, 36.4%	13/43, 30.2%
>Median duration	5/8, 62.5%	55/79, 69.6%	25/37, 67.6%	30/48, 62.5%
+ET medication	2/3, 66.7%	48/78, 61.5%	21/31, 67.7%	34/73, 46.6%
–ET medication	4/16, 25.0%	41/65, 63.1%	13/29, 44.8%	9/19, 47.4%
+Family history	all cases had a family	30/44, 68.2%	all cases had a family	34/72, 47.2%
–Family history	history of ET	56/94, 59.6%	history of ET	9/20, 45.0%
Voice tremor (exam)	2/5, 40.0%	42/61, 68.9%	13/17, 76.5%	28/52, 53.9%
No voice tremor	4/13, 30.8%	44/79, 55.7%	21/43, 48.8%	15/38, 39.5%

* Values are number with self-reported head tremor/number with head tremor on examination, prevalence per 100 (95% confidence interval). TTS = Total tremor score. Some data points were missing for education, total tremor score, tremor duration, family history of ET, and voice tremor on examination.

found that higher sensitivity was associated with tremors of longer duration, presence of voice tremor on examination, female gender, and lower education (table 2).

A major goal of screening for head tremor is to enhance the ascertainment of ET cases in epidemiological studies. With this in mind, in each study, we assessed the number of additional ET cases who would have been ascertained by adding a screening question for head tremor to an assessment of the hand-drawn spiral. During the screening stage of the population-based study in northern Manhattan, 74 ET cases would have been ascertained based on spiral drawings; three additional ET cases (4.1% more) would have been ascertained by adding the screening question for head tremor (table 1). In the three other studies, this value was 20.3% (study of the environmental epidemiology of ET), 10.2% (Family Study of Essential Tremor) and 1.9% (Essential Tremor Centralized Brain Repository) (table 1).

Discussion

In the current study, we demonstrated that the sensitivity of a screening question for head tremor was very much dependent on the population being sampled, ranging from as low as 31.6% in a population-based study in northern Manhattan to as high as 62.2% in other studies. Hence, the sensitivity ranges from low to moderate. We also showed that the use of such a screening questionnaire has the potential to increase case ascertainment, in screening settings, by as much as 20% in some study settings.

The screening question had the lowest sensitivity in the population-based study in northern Manhattan. In general, the tremor observed in the population is milder than that in the other studies [2, 3]. Indeed, only 4.7% of patients in our population-based study in northern Manhattan were taking medication for tremor. The tremor in

our population-based study in northern Manhattan was also of relatively short duration. These factors may have contributed to a reduced awareness of head tremor in these cases.

We found a number of demographic and clinical features were associated with reports of greater validity: tremor of longer duration, presence of voice tremor on examination, female gender, and lower education. Having had tremor for longer duration might make patients more aware of or more in tune with their symptoms and signs. Additionally, the presence of other forms of cranial tremor (e.g., voice tremor) might increase the awareness of tremors in this general body region as well. Head tremor is more prevalent in women with ET than in men with ET [18], although this does not explain why women would be more likely to report tremor. One possible explanation is that published data indicate that women are better historians than men in a variety of medical settings ranging from self-reporting utilization of health services [19] to self-reporting stroke and acute myocardial infarction [20]. Moreover, head tremor is particularly noticeable and difficult to conceal. Given a greater susceptibility to body dissatisfaction [21], women might be more aware of and more likely to report head tremor than men.

The question we used to elicit tremor in three of the four studies was ‘Does your head often shake uncontrollably?’ In the Family Study of Essential Tremor, we encouraged the self-reporting of milder forms of head tremor (‘Does your head sometimes shake?’) Despite this difference, the sensitivity of self-reported tremor was similar in the Family Study of Essential Tremor and two of the three other studies.

The strengths of the study were that we utilized data on ET cases spanning a broad range of settings, from a population-based study to a highly-selected sample of brain donors, with our total sample size being in excess of

800. All cases underwent a detailed videotaped tremor examination, which was carefully assessed by a senior neurologist specializing in movement disorders. In three of the studies, the screening question was identical; in a fourth, we used a less restrictive question, allowing us to assess validity in this situation as well.

In summary, a screening question for head tremor had low-to-moderate sensitivity in ET. The use of such a screening questionnaire, however, has the potential to increase case ascertainment by as much as 20% in some screening settings.

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Disclosure Statement

The authors declare that there are no conflicts of interest and no competing financial interests.

Contributions

Elan D. Louis MD MSc: study conception and design, analysis and interpretation of data, study supervision, initial draft and critical revision of manuscript for important intellectual content.

Monika Michalec MPH: study design, critical revision of manuscript for important intellectual content.

Statistical Analyses

The statistical analyses were conducted by Dr. Louis.

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