Personality in essential tremor: further evidence of non-motor manifestations of the disease

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Objective: To ascertain whether patients with essential tremor have distinct definable personality traits.

Methods: A case-control study of patients with essential tremor was carried out to look for differences in personality characteristics. The controls were derived from the same source population. Using the tridimensional personality questionnaire (TPQ), personality traits were assessed in three dimensions: harm avoidance (HA), novelty seeking (NS), and reward dependence (RD). Additional analyses were conducted to address the possibility of selection bias among the patients with essential tremor.

Results: There were 55 patients and 61 controls. There was a difference between patients and controls in HA subscale scores ($p=0.005$) but not in NS or RD scores. The difference remained significant in analyses that adjusted for age, sex, race, and education ($p=0.005$). HA subscale scores did not correlate with subjective or objective measures of disability or with indices of severity of tremor.

Conclusions: Patients with essential tremor scored higher on the harm avoidance subscale scores than control subjects. HA subscale scores did not correlate with the severity of tremor or with subjective and objective scales of disability, suggesting that the personality profile observed was not entirely related to functional disability caused by the tremor. Longitudinal studies of personality in essential tremor are needed to characterise the stability and evolution of these personality traits within the natural history of the disease process.

Research on essential tremor has focused almost exclusively on the motor aspects of the disorder, especially on action tremor and gait abnormality.^{1–3} Recently, however, cognitive deficits have been identified in several reports.^{4–8} The presence of such deficits is intriguing and raises the question of whether other non-motor domains may also be affected. For example, personality has never been studied in essential tremor, although characteristic personality traits have been associated with several other movement disorders including Huntington's disease⁹ and Parkinson's disease.^{10–11} A broader understanding of the clinical picture of essential tremor encompassing both motor and non-motor deficits would be beneficial, not just in understanding the pathophysiology of the disease but also as an aid to understanding patient motivations and perceptions during treatment. We conducted a case-control study of personality in essential tremor, using a commonly employed a self reported measure of personality, the tridimensional personality questionnaire (TPQ).^{12–13} The goal of the study was to determine whether patients with essential tremor differ from controls in any of the three main dimensions of personality.

METHODS

Epidemiological study

As part of an epidemiological study of essential tremor, 100 patients with this condition and 100 controls underwent the same evaluation. This case-control study design has been described in detail in previously published studies.^{14–18} Briefly, patients and controls were ascertained from the same source population in the New York tristate region (that is, controls were selected from the same set of zip codes in New York, New Jersey, and Connecticut as were the patients). The 100 patients with essential tremor, who all lived in the New York tristate region, were cared for at the Neurological Institute of New York, Columbia-Presbyterian Medical Center (CPMC), either at the Center for Parkinson's Disease and Other Movement Disorders (CPD) or by general neurologists.

Patients with diagnoses of other movement disorders (Parkinson's disease, dystonia) were excluded. The 100 control subjects were recruited from the same set of zip codes as the patients in the New York, New Jersey, and Connecticut region by random digit telephone dialling and were frequency matched to patients with essential tremor by age, sex, and race. As will be detailed below, the majority of these controls also received their health care at the same medical centre as the patients with essential tremor (CPMC). Before enrolment in the epidemiological study, patients and controls underwent the 10 minute telephone interview for cognitive status (TICS),¹⁹ and those with evidence of cognitive impairment (score $<30/41$) were not enrolled.

After enrolment, current demographic information was collected by an in-person interview with a trained tester, including data on age, sex, race (coded as "Caucasian" (white) v "non-Caucasian"), alcohol use (coded as yes (one or more alcoholic beverage a week) v no), years of education, marital status (married v unmarried/divorced), and family history of essential tremor (having a first degree relative with tremor v not having a first degree relative with tremor). Information on current drug treatment, including antidepressants, was collected. Computerised hospital records were searched to ascertain how many of the control subjects were outpatients at CPMC in departments other than neurology. This information was used to assess the comparability of our patients and the control subjects.

A neurological examination was videotaped and reviewed by a neurologist (EDL), and a total tremor score (0–36) was

Abbreviations: CIRS, cumulative illness rating scale; CPMC, Columbia-Presbyterian Medical Center; DSM-SCID, structured clinical interview for DSM-IV dissociative disorders; DSM-IV, *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition; HA, harm avoidance; NS, novelty seeking; RD, reward dependence; TICS, telephone interview for cognitive status; TPQ, tridimensional personality questionnaire

Table 1 Personality dimensions measured by the tridimensional personality questionnaire (TPQ)

Temperament	High scorers	Low scorers
Harm avoidance subscore (range 0 to 34)	Worrying and pessimistic; fearful and doubtful; shy; fatigable	Relaxed and optimistic; bold and confident; outgoing; vigorous
Novelty seeking subscore (range 0 to 34)	Exploratory and curious; impulsive; extravagant and enthusiastic; disorderly	Indifferent; reflective; frugal and detached; orderly and regimented
Reward dependence subscore (range 0 to 30)	Sentimental and warm; dedicated and attached; dependent	Practical and cold; withdrawn and detached; independent

assigned based on a 0 to 3 rating of action tremor during 12 activities.²⁰

A tremor disability questionnaire²⁰ was used to assess subjective perceptions of disability (tremor disability score, range 0 to 31 (maximally impaired)) and a performance based test of function²⁰ was used to assess performance of several daily activities including eating, pouring, and writing (performance based test score, range 0 to 100 (maximally impaired)). Evaluation of medical illness burden was done using the cumulative illness rating scale (CIRS), which rates the severity of illness in 14 body systems using a 0 to 3 rating (range 0 to 42 (most severe)).²¹

Study of personality in essential tremor

The TPQ is a 98 item self administered true/false instrument.²² It has been used in assessing personality characteristics in neurological illnesses such as Parkinson's disease and migraine.^{23–24} The TPQ measures personality traits across three higher order dimensions. These dimensions are harm avoidance (HA, anxiety prone *v* risk taking), novelty seeking (NS, anger prone *v* docile), and reward dependence (RD, sentimental *v* aloof). Each dimension may be evaluated with a subscale score (HA, NS, RD subscale scores), which are summed to yield a TPQ score (table 1).²² The TPQ correlates well with other measures of personality in common use,²⁵ has been translated into several languages and used cross culturally with success,²⁶ and has been shown to be stable over time as an assessment of personality.²⁷

Sample size estimation and statistical analysis

To have 80% power to detect a 10% difference in the TPQ score between patients with essential tremor and controls, we required data on 57 of the 100 patients and 57 of the 100 controls who had been enrolled in the epidemiological study. These calculations used published TPQ data in normative population groups¹³ and assumed an $\alpha = 0.05$. We assumed a response rate of 75%, and mailed the TPQ to 76 randomly selected patients and 76 randomly selected controls in an attempt to obtain responses from 57 (75%) of each. Fifty five patients (72%) and 61 controls (80%) responded, returning their completed questionnaires by mail.

We used χ^2 tests for categorical variables, and Student's *t* test, analysis of variance (ANOVA), and Pearson's correlation coefficient (*r*) for continuous variables. In some analyses, the total tremor score, performance based test score, and disease duration were each divided into tertiles. To assess differences between patients and controls in HA subscale scores while adjusting for age, sex, race, and years of education, a linear regression analysis was done in which the outcome variable was the HA subscale score. As we had no *a priori* hypothesis as to which of the three subscale cores if any would be different between patients and controls, we used a Bonferroni correction to adjust for the three comparisons.

RESULTS

There were 116 responders (55 patients and 61 controls) and 36 non-responders (21 patients and 15 controls). Responders

were similar to non-responders with respect to age ($t = 1.59$, $p = 0.12$), sex ($\chi^2 = 0.86$, $p = 0.35$), race ($\chi^2 = 0.03$, $p = 0.86$), and years of education ($t = 0.68$, $p = 0.50$).

Patients with essential tremor were older than the controls but were similar in terms of sex, race, and education (table 2). CIRS scores were no different between patients and controls (mean (SD)): 4.1 (2.7) *v* 4.2 (3.4), $p = 0.89$).

The mean HA subscale score was higher in patients than in controls (15.5 (8.1) *v* 11.6 (7.2), $p = 0.005$) (table 3), a difference that remained significant after a Bonferroni correction. Mean RD and NS subscale scores did not differ between patients and controls (table 3).

The HA subscale score did not correlate with age ($r = 0.11$, $p = 0.26$) or years of education ($r = 0.11$, $p = 0.23$). HA subscale scores were similar in white and non-white subjects (13.3 (7.9) *v* 14.7 (6.9), $p = 0.59$), married and unmarried (or divorced) subjects (13.7 (7.8) *v* 13.2 (8.2), $p = 0.7$), women and men (13.8 (8.1) *v* 13.0 (7.7), $p = 0.59$), and subjects who used alcohol and those who did not (13.9 (8.1) *v* 13.5 (8.4), $p = 0.8$). HA subscale scores were not different in patients grouped by whether they were seen at the Neurological Institute by a general neurologist ($n = 8$) or by a movement disorder specialist ($n = 45$; two were seeing both) (17.1 (10.4) *v* 16.1 (7.7), $p = 0.74$) or by whether they had a family history of essential tremor ($n = 13$) or not ($n = 44$, one unknown) (16.3 (9.7) *v* 15.4 (7.9), $p = 0.75$). In patients, there was no correlation between the HA subscale score and the total tremor score ($r = 0.07$, $p = 0.61$), disease duration ($r = -0.15$, $p = 0.28$), tremor disability score ($r = 0.13$, $p = 0.36$), performance based test score ($r = 0.17$, $p = 0.24$), or CIRS score ($r = 0.13$, $p = 0.33$). To account for the possibility of a non-linear correlation between the HA subscale score and these variables, the total tremor score, performance based test score, and disease duration were each divided into tertiles. Mean HA subscale scores did not differ between total tremor score tertiles (15.2 (8.6) *v* 14.5 (9.5) *v* 17.0 (6.2), $F = 0.4$, $p = 0.6$), performance based test score tertiles (16.2 (9.6) *v* 13.7 (7.0) *v* 17.0 (7.1), $F = 0.7$, $p = 0.5$), or disease duration tertiles (16.5 (8.7) *v* 16.2 (6.7) *v* 13.6 (8.9), $F = 0.7$, $p = 0.6$).

Table 2 Characteristics of patients with essential tremor *v* controls

Variable	ET	Controls	p Value
Number of patients	55	61	–
Sex (male)	28 (50.9%)	28 (45.9%)	0.76
Race (white)	51 (92.7%)	57 (93.4%)	0.99
Education (years)	15.3 (2.9)	15.4 (3.3)	0.91
Age (years)	71.0 (11.6)	65.6 (11.2)	0.01
Disease duration (years)	21.9 (17.4)	–	–
Total tremor score	19.7 (7.7)	3.9 (3.3)	0.0001
Currently taking drugs to treat tremor	34 (61.8%)	0	0.0001

Values are mean (SD) or n (%).
ET, essential tremor.

Table 3 Tridimensional personality questionnaire (TPQ) subscale scores, essential tremor v control

TPQ subscale scores	ET	Control	t Value (p)
HA	15.5 (8.1)	11.6 (7.2)	2.85 (0.005)
RD	11.4 (3.1)	11.3 (3.7)	0.16 (0.87)
NS	13.1 (5.0)	14.5 (4.9)	1.38 (0.17)

Values are mean (SD).

ET, essential tremor; HA, harm avoidance; NS, novelty seeking; RD, reward dependence.

In a linear regression analysis that adjusted for age, the diagnosis (patient v control) remained significantly associated with the HA subscale score (dependent variable) ($\beta = 3.9$, $p = 0.009$). When the model was expanded to include age, sex, race, and years of education, the diagnosis (control v essential tremor) continued to be associated with the HA subscale score ($\beta = 4.6$, $p = 0.005$).

Seventeen of 55 patients were taking drugs that could alter mood (including antidepressants, anxiolytics, β blockers, barbiturates, or other mood stabilisers). HA scores were not significantly different between patients taking these drugs and those who were not (16.1 (5.5) v 15.5 (9.1), $p = 0.81$). After removing these 17 patients from the analysis, the HA scores remained different between patients with essential tremor and controls (15.6 (9.1) v 11.3 (7.3), $p = 0.016$). Three of 55 patients were taking an antidepressant drug. When these were removed from the analyses, the difference between patients and controls in HA scores remained ($p = 0.009$). As a part of a separate study, patients seen at the CPD ($n = 20$) also underwent a structured clinical interview for the DSM (SCID) to evaluate current dysthymia and depression. One was depressed (HA subscale score = 32). When this patient was removed from analyses, the difference between patients and controls in HA subscale score remained ($p = 0.009$).

An important issue is whether patients and controls were comparable and whether there was selection bias because patients were ascertained through a treatment setting whereas controls were living in the community. We evaluated this possibility by carrying out additional analyses. First, we determined the proportion of control subjects who were patients at the same medical centre as the patients with essential tremor. More than two thirds (41 of 61 (67.2%)) of the controls were outpatients at CPMC in departments other than neurology. Mean HA subscale scores were similar between controls who were outpatients at CPMC and those who were not (11.2 (6.8) v 12.0 (8.0), $p = 0.6$). Mean HA subscale scores were higher in the patients than in the 41 controls who were outpatients at CPMC ($t = 2.82$, $p = 0.007$). Second, we determined that three of our essential tremor cases were living in the Washington Heights-Inwood community. Their HA subscale scores were all uniformly high: 15, 20, and 24 (mean 19.6 (4.5); median 20). When we compared these three with the control group, the HA subscale score was higher in the community based essential tremor cases ($p = 0.05$).

DISCUSSION

To our knowledge, personality has not been studied in patients with essential tremor. We studied personality in patients with essential tremor compared with controls and showed that the patients had higher scores on the HA subscale of the TPQ. A high HA score defines a person who is pessimistic, fearful, shy, anxious, and easily fatigued.²² While the difference in HA subscale scores could reflect a lower score among our controls (rather than a higher score among

our patients), our control group had a mean HA subscale score that was similar to that of normative controls in published reports,¹² indicating that the difference between our patients and controls was not likely to reflect an unusually low HA subscale score in our control group.

Our patient sample was significantly older than our control group, and age may arguably be a confounding factor in our analyses. However, the results remained significant after controlling for age, indicating that age does not explain the differences observed.

We also assessed other potential confounding variables. Concomitant burden of medical illness was assessed through the CIRS and was no different between patients and controls. Availability of social support systems such as being married or not also did not affect the HA subscale scores significantly.

Our patients and controls, by design, were derived from the same source population (and the same set of zip codes) in the New York tristate region. We also undertook additional analyses to address the potential biases that might occur because our patients were recruited from a tertiary care medical centre while our controls were from the community. First, we determined that nearly 70% of our control subjects were also outpatients at the same medical centre as the patients with essential tremor, probably because they had been derived from the same source population. HA subscale score differences were thus unlikely to represent simply an unwillingness on the part of controls to seek medical care. The mean HA subscale scores of the essential tremor group remained higher than the controls who were outpatients in the same hospital. Second, we looked at the three patients in our essential tremor group who were community based and found that the mean HA subscale scores of these three cases were similar to the rest of the patient sample and significantly different from the control subjects, suggesting that community status did not affect the HA subscale scores.

It is unclear whether the higher HA subscale score in patients with essential tremor reflects functional disability caused by the tremor or whether it is a manifestation of disease pathology. This is a limitation of the cross sectional design of our study. HA scores did not correlate with the patients' own assessment of disability, the total tremor score, or performance based test scores, suggesting that the personality profile we observed was not entirely the result of tremor related disability, although longitudinal studies are needed to examine this issue fully.

Depression and anxiety may increase HA subscale scores.^{13, 28} Although we did not assess depression and anxiety systematically in all our patients and controls, a subset of our patients who were also enrolled in a study of functional disability in essential tremor was assessed for dysthymia, anxiety, and depression. Excluding patients with these diagnoses did not change our results. Furthermore, current use of antidepressants was assessed in all subjects, and excluding those on antidepressant drugs also did not change the results. Finally, excluding all patients who were on drug treatment that might alter mood (tricyclic antidepressants, selective serotonin reuptake inhibitors, barbiturates, β blockers, benzodiazepines, buspirone, valproate, or lithium) also did not affect the results.

Although we had some information about subjects who did not respond to our mailed questionnaire—and on these demographics the responding subjects were no different from those who did not respond—we cannot be certain that the non-responders were not different in terms of personality from those who chose to respond. If this difference in personality were differential by category (that is, different in some way between the essential tremor group and the controls), this would bias our results in unforeseeable ways.²⁹ This is a potential limitation of our study.

Little is known about putative neurotransmitter defects in essential tremor. Harmaline produces action tremor similar to essential tremor in laboratory animals and humans.³⁰ Serotonin (5-HT) may be involved in mediating the effect of harmaline.³⁰ The personality dimensions of the TPQ have been associated with changes in neurotransmitter activity. Patients with high HA scores have increased 5-HT release from presynaptic neurones after the administration of serotonergic agonists.³¹ Although this relation between the neurotransmitters and the dimensions of personality is still under investigation, it is of some interest that our patients with essential tremor had higher HA scores than the controls—a finding that would not be inconsistent with the possible role of serotonin in tremor genesis.

Neurodegenerative diseases such as Parkinson's disease and Huntington's disease have several prominent non-motor manifestations including personality changes, and these manifestations are likely to result from pathology in multiple brain regions. Essential tremor itself may be a neurodegenerative disease,¹⁷ and there is evidence of involvement of multiple brain regions, including the cerebellum,¹⁷ frontal-cerebellar connections,⁴ and possibly the peripheral nerves.³²

To our knowledge this is the first report on personality in patients with essential tremor. The emerging picture of essential tremor—which encompasses cognition, personality, and affect—may result in a better understanding of the pathological manifestations of this disorder. Longitudinal studies of personality in essential tremor are needed to characterise the stability and evolution of these personality traits within the natural history of the disease process.

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