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Depressive Traits in Essential Tremor: Impact on Disability, Quality of Life and Medication Adherence

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Abstract

Background—There is growing study of the psychiatric features of essential tremor. Depressive symptoms occur in a considerable number of patients. Yet their impact, as a primary factor, has received almost no attention. We assessed whether, independent of tremor severity, patients with more depressive symptoms have more perceived tremor-related disability, lower tremor-related quality of life, and poorer compliance with tremor medication.

Methods—Based on their Center for Epidemiological Studies Depression Scale score, we stratified 70 essential tremor patients into three groups: 41 with minimal depressive symptoms, 24 with moderate depressive symptoms, and 5 with severe depressive symptoms. Importantly, the three groups had similar tremor severity on neurological examination. We assessed: self-reported tremor-related disability, tremor-related quality of life (Quality of Life in Essential Tremor Questionnaire), and medication compliance.

Results—Cases with minimal depressive symptoms had the lowest quality of life scores, cases with moderate depressive symptoms had intermediate scores, and those with severe depressive symptoms had the highest scores ($p < 0.001$). Depressive symptoms were a stronger predictor of tremor-related quality of life than was the main motor feature of ET itself (tremor). Self-reported medication compliance was lowest in cases with severe depressive symptoms and highest in cases with minimal depressive symptoms.

Conclusions—The physical disability caused by the tremor of ET has traditionally been regarded as the most important feature of the disease that causes distress, and it has received the most attention in the management of patients with this disease. Our data indicate that this may not be the case.

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Keywords

essential tremor; psychiatric; depression; disability; quality of life; medication; treatment; clinical

Introduction

Essential tremor (ET) is among the most common disorders seen by general neurologists, and is the most common adult-onset movement disorder [1]. While it has canonically been viewed as a motor disorder, there is now a growing interest in non-motor features of ET [2, 3].

In particular, depressive symptoms may occur in a considerable proportion of patients with ET [4, 5]. These symptoms have traditionally been regarded as a psychiatric response to the neurological symptoms, which may be debilitating [6]. In this model, the flow of events is from tremor to its psychiatric byproduct, depressive symptoms.

This uni-directional model, though logical, is likely to be an oversimplification, and one which no longer completely encapsulates and serves the patient experience. Are there additional effects in the opposite direction? Can preexisting depressive traits, independent of the tremor, have an effect on how an ET patient perceives and copes with their tremor? Can these traits influence how ET patients interface with ET medications, their medication compliance and their willingness to follow through with a medical regimen? Are ET patients who are prone to negativity, a depressive outlook or depressive symptoms more prone to lower quality of life, greater perceived disability, and poorer compliance with medication regimens?

In this study, we stratified ET patients into three groups: those with minimal depressive symptoms, those with moderate depressive symptoms, and those with severe depressive symptoms. Importantly, the three groups did not differ with respect to the severity of tremor on neurological examination. We examined in each group the extent of perceived (i.e., self-reported) tremor-related disability, tremor-related quality of life, and medication compliance.

It is important for treating clinicians to identify depressed patients and the factors that determine their disease experience. Depressive symptoms could be a primary target for treatment, with the dual effect of improving those symptoms as well as ET-associated quality of life. Treatment of these symptoms might possibly improve patients' interface with their tremor medications.

Methods

ET cases were enrolled in a clinical-epidemiological research study at Columbia-University Medical Center (CUMC) [7, 8]. They were selected randomly from a computerized billing database at the Center for Parkinson's Disease and Other Movement Disorders (CPD), CUMC. Each case had been diagnosed with ET by a CPD neurologist. All clinical ET diagnoses were reconfirmed based on chart review and videotaped neurological examination by a senior movement disorder neurologist (E.D.L.) who used published diagnostic criteria (moderate or greater amplitude kinetic tremor during three activities or a head tremor in the absence of Parkinson's disease [PD], dystonia or another known cause) [9, 10].

ET cases signed informed written consent approved by the CUMC Institutional Review Board, and were evaluated in person by a trained tester who collected demographic and clinical data.

The Quality of Life in Essential Tremor Questionnaire (QUEST) was administered [11]. In this questionnaire, 30 items can be rated on a five-point scale (score 0–4), corresponding to the frequency (never, rarely, sometimes, frequently, always) with which tremor is perceived to currently impact a function or to be associated with various feelings or attitudes [11]. Items have been grouped into five domains: physical (n = 9, e.g., tremor interferes with eating), psychosocial (n = 9, e.g., tremor interferes with relationships with others), communication (n = 3, e.g., tremor interferes with ability to communicate with others), hobbies/leisure (n = 3, e.g., I have quit hobbies because of my tremor), and work/finance (n = 6 items) [11]. Four items from the work/finance domain did not apply to the vast majority of our cases, who were elderly and past retirement, so that the final version of the QUEST we used included two of the six work/finance items (tremor resulted in early retirement, tremor lead to financial problems/concerns), for a total of 26 QUEST items. The psychometric attributes of the QUEST have been assessed and most are satisfactory [12].

Tremor-related motor disability was evaluated with a brief 10-item version of a 36-item, validated tremor disability questionnaire [13]; self-reported ability to perform a range of motor activities was assessed (signing name, carrying a cup, dialing a telephone, using a key), with the possible score range from 0 - 100 (maximum disability). The Voice Handicap Index is a validated 30-item voice handicap questionnaire, with each item rated from 0 (voice never affected) – 4 (voice always affected), with the total score ranging from 0–120 (maximum disability from voice tremor) [14].

A brief series of questions dealing with issues of medication adherence was also administered: Do you sometimes forget to take your ET medication? Over the last week, have you missed some doses of your ET medication? Over the past two weeks, were there days when you did not take your ET medications? Have you at times cut back or stopped taking your ET medication without telling your doctor?

The Folstein Mini-Mental State Exam (MMSE)[15] was administered (range = 0–30 [no impairment]), as was the Center for Epidemiological Studies Depression Scale (CESD-10), a self-report ten-item screening questionnaire for depressive symptoms (range = 0–30 [greater depressive symptoms]) [16]. The CESD-10 has been shown to have good reliability, and excellent sensitivity and specificity using a diagnosis of Major Depressive Disorder as diagnosed using the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised, as the gold standard [17, 18].

Each ET case underwent a videotaped neurological examination, which included a detailed assessment of postural tremor and five tests of kinetic tremor as well as voice tremor during sustained phonation and conversation [19]. A senior movement disorders neurologist (E.D.L.) reviewed all videotaped examinations, and the severity of postural and kinetic arm tremors were rated (0–3), resulting in a total tremor score (range = 0–36 [maximum]), a measure of the severity of action tremor [19]. Voice tremor was noted to be present or absent as well.

Statistical analyses were carried out using SPSS (version 18.0.2; Chicago, Illinois). Several CESD-10 cut-offs have been recommended for depression, including a score 10 [16], and a more conservative score 20 [20]. To incorporate both sets of recommendations, we divided subjects into three groups based on their CESD-10 score: 0–9 (minimal depressive symptoms), 10–19 (moderate depressive symptoms), 20 (severe depressive symptoms). Scores > 20 have high sensitivity and specificity for the diagnosis of Major Depressive Disorder as defined in the DSM [17, 18]. We also treated the CESD-10 as a continuous variable (range = 0–30) in some analyses in order to fully utilize the available range of scores. Parametric tests were used, including chi-square tests (X^2), analysis of variance

(ANOVA), and Pearson's correlation coefficients. When a test variable was not normally-distributed, non-parametric tests were used (Kruskal-Wallis test, Spearman's correlation coefficient). For several analyses, we supplemented the standard X^2 test with one that examined a trend across the three groups (i.e., linear-by-linear association). Also, in a series of linear regression models, we assessed the predictors of the QUEST score (i.e., the dependent variable). Independent variables that we analyzed included demographic and clinical variables (Tables 1 and 2). The final linear regression model was that which maximized the variance explained by the independent variables.

Results

The 70 ET cases included 41 (58.6%) with minimal depressive symptoms, 24 (34.3%) with moderate depressive symptoms and 5 (7.1%) with severe depressive symptoms. Three of 41 (7.3%) ET cases with minimal depressive symptoms were taking an antidepressant medication, compared with 1 of 24 (4.2%) with moderate depressive symptoms, and none of the 5 (0.0%) ET cases with severe depressive symptoms ($X^2 = 0.61$, $p = 0.74$).

The three ET groups were similar with respect to demographic features (age, gender, education, race, marital status) and medical features (e.g., mental state test score, medical co-morbidities, number of prescription medications) (Table 1). Importantly, the total tremor score was similar in all three groups ($p = 0.45$, Table 1), as was tremor duration ($p = 0.36$, Table 1) and the proportion taking medication for tremor ($p = 0.64$, Table 1).

The CESD score was marginally associated with the tremor disability questionnaire score (Pearson's $r = 0.22$, $p = 0.06$), and markedly associated with the QUEST score (Pearson's $r = 0.48$, $p < 0.001$), and each QUEST subscore (Spearman's $r = 0.33$, $p = 0.005$ [physical], Spearman's $r = 0.63$, $p < 0.001$ [psychosocial], Spearman's $r = 0.32$, $p = 0.007$ [communication], Spearman's $r = 0.26$, $p = 0.029$ [hobbies/leisure], and Spearman's $r = 0.30$, $p = 0.01$ [work/finance]). Interestingly, the CESD score was not associated with the total tremor score (Spearman's $r = -0.14$, $p = 0.24$).

ET cases with minimal depressive symptoms had the lowest QUEST scores and QUEST subscores; cases with moderate depressive symptoms had intermediate QUEST scores and subscores, and those with severe depressive symptoms had the highest QUEST scores and subscores (Table 2). The Voice Handicap Index scores followed a similar pattern across the three groups, with patients with severe depressive symptoms having the highest scores ($p = 0.01$, Table 2) despite the observations that only 1 of these cases had any voice tremor on neurological examination (Table 1). Medication compliance, as assessed by four questions (Table 2), was lowest in the ET cases with severe depressive symptoms and highest in the ET cases with mild depressive symptoms.

In a series of linear regression models, we assessed the predictors of tremor-related quality of life (i.e., the QUEST score). In the final model, which explained 74.1% of the variance, the CESD score was the strongest predictor of QUEST score ($\beta = 1.14$, $p < 0.001$), followed by the tremor disability score ($\beta = 0.40$, $p < 0.001$), age ($\beta = -0.33$, $p = 0.01$) and marginally, the total tremor score ($\beta = 0.57$, $p = 0.09$).

Discussion

In the present study, ET patients were divided into three groups based on their depressive symptomatology (minimal, moderate, severe). Patients in each group had similar tremor severity and tremor duration. Across these groups, we observed a stepwise increase in perceived tremor-related disability, and a decrease in both health-related quality of life and

medication compliance. Indeed, depressive symptoms were a stronger predictor of tremor-related quality of life than was the main motor feature of ET itself (action tremor).

The physical disability caused by the tremor of ET has traditionally been regarded as the most important feature of the disease that causes distress, and it has received the most attention in the management of patients with this disease. Our data indicate that this may not be the case. In another study in England, a smaller group of ET patients ($n = 45$) underwent a series of neuropsychological evaluations, which included a more general set of self-reported measures of physical and psychosocial health status (the Sickness Impact Profile) and neuropsychiatric distress (the Profile of Mood States) than the tremor-specific measures (e.g., QUEST and tremor disability questionnaire) that we used [4]. That sample also differed from ours in the sense that all of their cases were candidates for thalamic deep brain stimulation surgery [4]. However, through a series of multiple regression analyses, that study was the first to demonstrate the possible independent contribution of neuropsychiatric symptoms to lower perceived health status among ET patients [4].

It is difficult to place these findings in context, as there are few data. While on the one hand, the prevalence of severe depression (7.1%) seems higher than that seen in the elderly living in a community sample (estimated at 1–3%) [21], scores on the CESD are similar to that in elderly patients presenting to a primary care clinic (11%) [18] and less than the previously reported proportion of PD and dystonia patients with severe depression (31% and 30% respectively, as defined by the CESD)[20].

We do not have data on the patients' depressive symptoms prior to their development of tremor. The fact that the prevalence of depressive symptoms was similar to that in elderly patients presenting to a primary care clinic [18], though, suggests that the depressive symptoms we observed in our ET patients, or some portion of them, may be representative of their pre-existing mood symptoms (i.e., a trait) rather than an increase in depressive symptoms triggered by their tremor or directly by the neurological processes of their ET (a state). These mood traits appear to have a significant effect on how ET patients are prone to perceive and cope with their tremor and interface with medications, their medication compliance and their willingness to follow through with a medical regimen.

Depressive symptoms likely play a sizable role in disorders aside from ET. Thus, a study in patients with PD similarly reported that depressive symptoms greatly impact upon health-related quality of life [22]. Depressive symptoms were among the list of variables that had the most detrimental effect on overall quality of life [22]. In PD, depressive symptoms are increased out of proportion to disability and can occur prior to the development of motor symptoms, suggesting that there is an association between PD and depression that is independent of disability, i.e., the neurological process of PD can result in depressive symptoms [23, 24].

It behooves treating neurologists to identify factors that might be influencing their patients' disease experience and to identify subgroups of depressed patients. Our data indicate that depressive symptoms are undertreated in ET cases. Nearly none of the patients we identified with moderate or severe depressive symptoms were receiving treatment for depression. Depressive symptoms, in addition to being a target for treatment themselves, if treated, might have the added effect of improving quality of life, reducing distress, and increasing medication compliance.

This study had limitations. The number of ET cases in the highest depressive symptom group was small. Despite this, our sample had adequate power to detect a sizable number of significant associations. We only looked at depressive symptoms and not at other clusters of psychiatric symptoms such as anxiety, and depressive symptoms were assessed with a brief,

validated screening instrument; it is possible that more in-depth psychiatric assessments could uncover additional associations of interest. Finally, we did not collect data on past history of depression in these cases; such information would have supplemented the data we collected on current depressive symptoms and antidepressant medication use.

In summary, mood traits seem to greatly affect how ET patients are prone to perceive and cope with their tremor, and may furthermore influence how ET patients interface with medications, medication compliance and willingness to follow through with a medical regimen. Indeed, these traits were a stronger predictor of tremor-related quality of life than was the main motor feature of ET itself (action tremor). This makes these traits an important target point for further therapeutic evaluation and intervention.

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Table 1

Demographic and Clinical Characteristics of 70 ET Cases

	Minimal Depressive Symptoms (N = 41)	Moderate Depressive Symptoms (N = 24)	Severe Depressive Symptoms (N = 5)	Significance
Age (years)	73.1 ± 11.1	66.8 ± 16.1	75.0 ± 10.1	ANOVA F = 2.10, p = 0.13
Female Gender	22 (53.7)	12 (50.0)	3 (60.0)	X ² = 0.19, p = 0.91
Education (years)	16.5 ± 2.5	15.6 ± 2.3	15.6 ± 3.6	ANOVA F = 1.12, p = 0.33
White Race	39 (95.1)	24 (100)	4 (80.0)	X ² = 4.12, p = 0.13
Marital Status (currently married)	25 (61.0)	11 (45.8)	3 (60.0)	X ² = 1.45, p = 0.49
Folstein Mini-Mental State Exam score	28.9 ± 1.3 Median = 29	29.1 ± 1.6 Median = 30	28.4 ± 1.8 Median = 29	Kruskal-Wallis = 1.95, p = 0.38
Arthritis ^A	21 (51.2)	11 (45.8)	2 (40.0)	X ² = 0.34, p = 0.85
Diabetes mellitus ^A	6 (14.6)	2 (8.3)	0 (0.0)	X ² = 1.29, p = 0.53
Hip replacement ^A	1 (2.4)	0 (0.0)	0 (0.0)	X ² = 0.72, p = 0.70
Total current number of prescription medications	5.5 ± 3.3	4.9 ± 3.1	7.8 ± 3.6	ANOVA F = 1.69, p = 0.19
Total Tremor Score on neurological examination	21.9 ± 6.0	20.7 ± 5.3	18.8 ± 3.8	ANOVA F = 0.82, p = 0.45
Voice tremor on neurological examination	11 (26.8)	7 (29.2)	1 (20.0)	X ² = 0.18, p = 0.01
Currently takes medication to treat ET	23 (56.1)	15 (62.5)	2 (40.0)	X ² = 0.90, p = 0.64
Duration of tremor (years)	30.6 ± 17.6	36.0 ± 18.2	25.2 ± 11.1	ANOVA F = 1.04, p = 0.36

All values are mean ± standard deviation or number (%), unless otherwise specified.

ANOVA (analysis of variance with 2 degrees of freedom).

X² (Chi-square with 2 degrees of freedom).

KW (Kruskal-Wallis test with 2 degrees of freedom).

^AMedical history by self-report.

Table 2

Perceived Disability, Quality of Life, and Medication Compliance in 70 ET Cases

	Minimal Depressive Symptoms(N = 41)	Moderate Depressive Symptoms(N = 24)	Severe Depressive Symptoms(N = 5)	Significance
QUEST score	22.1 ± 16.5	37.1 ± 17.3	48.4 ± 24.2	ANOVA F = 9.10, p < 0.001
QUEST subscores				
Physical	13.10 ± 8.75, [11]	18.50 ± 8.18, [16.5]	19.20 ± 12.10, [25]	KW = 7.88, p = 0.019
Psychosocial	5.44 ± 5.74, [5]	12.00 ± 6.51, [12]	18.0 ± 10.1, [19]	KW = 20.05, p < 0.001
Communication	0.81 ± 1.72, [0]	2.29 ± 2.37, [2]	2.00 ± 2.55, [1]	KW = 9.95, p = 0.007
Hobbies/leisure	2.05 ± 3.99, [0]	3.63 ± 4.20, [1]	4.20 ± 4.38, [4]	KW = 5.11, p = 0.078
Work/finance	0.37 ± 1.26, [0]	0.42 ± 1.06, [0]	4.20 ± 3.77, [4]	KW = 16.75, p < 0.001
Voice Handicap Index Score	8.7 ± 19.0	20.6 ± 19.0	34.8 ± 47.7	ANOVA F = 4.53, p = 0.01
I sometimes forget to take my ET medication. ^A	5 (21.7)	6 (40.0)	2 (100)	X ² = 5.75, p = 0.056 LLA = 4.65, p = 0.03
Over the last week, I missed some doses of my ET medication. ^A	2 (8.7)	4 (26.7)	1 (50.0)	X ² = 3.57, p = 0.17 LLA = 3.46, p = 0.06
Over the past two weeks, there were days when I did not take my ET medications. ^A	3 (13.0)	2 (13.3)	2 (100)	X ² = 9.93, p = 0.007 LLA = 3.46, p = 0.06
I have at times cut back or stopped taking my ET medication without telling my doctor. ^A	1 (4.3)	1 (6.7)	1 (50.0)	X ² = 5.55, p = 0.06 LLA = 2.50, p = 0.11

All values are mean ± standard deviation, [median] or number (%) unless otherwise specified.

ANOVA (analysis of variance with 2 degrees of freedom).

X² (Chi-square with 2 degrees of freedom).

KW (Kruskal-Wallis test with 2 degrees of freedom).

LLA (Chi-square test with 2 degrees of freedom assessing linear-by-linear association).

^AForty of seventy cases who were currently taking medication for ET.