



ORIGINAL RESEARCH

# Neuropsychiatric Approaches to Essential and Functional Tremor: A Comparative Study

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**Purpose:** Differentiating essential tremor (ET) from functional tremor (FT) remains a challenge due to their overlapping clinical presentations. This study aimed to elucidate the demographic and psychometric differences between the aforementioned tremor types to enhance diagnostic accuracy and therapeutic strategies.

**Patients and Methods:** This prospective study included 96 patients diagnosed with ET or FT and analysed their related demographic data, clinical symptoms, and psychometric evaluation scores. The statistical analysis involved Pearson's chi-square tests, Fisher's exact tests, and logistic regression to determine how the different variables impact tremor diagnosis.

**Results:** Our study demonstrated a higher prevalence of ET in males (p = 0.015). Furthermore, we demonstrated that patients with ET displayed a significantly lower body mass index and a lower age of onset compared to those with FT (p = 0.050 and p = 0.023, respectively). Psychometric assessments revealed higher cognitive and body image scores in patients with ET, whereas those with FT scored higher on the depression and anxiety scales. The misdiagnosis rate was 14.5%, emphasising the requirement for improved diagnostic criteria.

**Conclusion:** We established specific demographic and psychometric distinctions between ET and FT, which could potentially benefit clinicians in making accurate diagnoses and tailoring treatment approaches. These findings support the inclusion of comprehensive psychometric evaluations into standard diagnostic procedures to better differentiate tremor types.

Plain Language Summary: Essential Tremor (ET) and Functional Tremor (FT) can be more accurately identified. Functional and Essential tremor are frequently misdiagnosed. Due to misdiagnosis of both diseases, treatment is often delayed and treatment costs increase. This study distinguishes between Essential and Functional Tremor by exploring gender, age, and psychometric variables, highlighting crucial differences and the significant issue of misdiagnosis, aiming to refine diagnostic criteria and treatment approaches. We identified distinct profiles for ET and FT, particularly in psychometric assessments where FT patients showed significantly higher anxiety and depression scores. Our study brings to light the importance of incorporating psychological evaluations in routine assessments, marking a significant advancement in tremor diagnosis and treatment. In addition, psychiatry and neurology emphasize that they need to cooperate more by following this patient group together. The expected future implications in clinical settings include improved diagnostic accuracy, personalized treatment plans based on detailed patient profiles, and a decrease in the misdiagnosis rates currently seen in tremor disorders.

Keywords: essential tremor, functional tremor, neuropsychiatric evaluation, tremor diagnosis

## Introduction

Functional movement disorders (FMDs) are a group of movement disorders without any organic cause. The incidence of FMD is 2–20% of all movement disorders. These patients constitute a significant portion of the movement disease practice. FMDs are more common in women and are often associated with psychiatric disorders. The diagnosis of FMD is based on positive symptoms that are inconsistent with a neurological disorder, not on the exclusion of a neurological disorder. The motor subtypes include positive findings of tremor, dystonia, myoclonus, chorea and parkinsonism, and the

same patient may have more than one motor disorder.<sup>1</sup> In addition to motor disorders, patients may have non-motor symptoms and complaints. The diversity of clinical symptoms makes diagnosis difficult. Misdiagnosis delays treatment and also increases the cost of treatment. In addition, musculoskeletal disorders may be associated with movement disorders. This makes diagnosis and treatment even more difficult. Functional tremor (FT) is the most common subtype of FMD it is characterised by a sudden onset, and changes in frequency and amplitude, with a cognitive effort or improvement in tremor, and recovery periods lasting days or months are important in the diagnosis of FT.<sup>2,3</sup> Electrophysiology, accelerometry and neuroimaging are important in the differential diagnosis. FT can be a significant cause of disability. It can be refractory to treatment and requires a multidisciplinary approach. These patients are often followed in psychiatric clinics after diagnosis. However, they should be managed jointly by neurology and psychiatry with a holistic approach. In addition, some people with FT are diagnosed with Parkinson's disease or essential tremor and are treated incorrectly for a long time. Tremor caused by medications used in patients with psychiatric disorders is another aspect of the problem. In order to distinguish these patients from those with ET and FT, the onset of the disease and the drugs used should be examined in detail.

Essential tremor (ET) is the most common movement disorder and is a symmetrical tremor of the hand and forearm that occurs with posture and movement. Although hand tremor is most common, tremor of the tongue, jaw, head, trunk and legs can also be observed.<sup>4</sup> Half of patients have a positive family history, and the worldwide prevalence of ET is reported to be between 0.41 and 3.92%.<sup>5,6</sup> In contrast to the FT, the proportion of men and women with ET is similar. Pathophysiological studies of ET have suggested cerebellar involvement. In addition, although ET was previously considered to be a motor disorder only, recent studies have shown that this disorder also has cognitive and psychiatric features. In addition, social phobia, anxiety and depression are common in patients with ET.<sup>7–9</sup> On the other hand, comorbid psychiatric disorders with ET may lead to difficulties in diagnosis. ET can be an important cause of disability. Initially, the frequency is fast and the amplitude is low, but over time the tremor amplitude increases and the frequency decreases. This leads to deterioration in activities of daily living. While some patients respond to medical treatment, others may need more advanced treatments such as deep brain stimulation. The need for more invasive treatments for ET makes it even more important to distinguish it from FT.

ET tremor and FT tremor are common conditions, and the intertwining of many of the findings leads to difficulties in diagnosis and treatment. How the demographic and psychometric characteristics differ between patients diagnosed with ET and FT remains elusive, as do the factors that contribute to the high misdiagnosis rate between these tremor types. Our study uniquely identified and quantified differences in the demographic and psychometric profiles between patients with ET and FT, emphasising the requirement for tailored diagnostic approaches to reduce the rate of misdiagnoses and improve treatment outcomes. ET and FT, which are often confused due to their overlapping clinical manifestations, require precise diagnostic criteria for patient care and the optimisation of treatment outcomes. Although our primary focus was not on treatment modalities, understanding the nuances of symptoms and patient-reported outcomes is critical to formulating effective therapeutic strategies.

In this study, we delineated the differences between ET and FT using comprehensive demographic and psychometric analyses, offering novel insights into the differential diagnosis and management of these conditions. FT cannot be explained by psychiatric findings alone and ET cannot be explained by organic findings alone. This situation requires a more comprehensive assessment and a multidisciplinary approach to these patients. In addition, the inclusion of other causes of tremor in the differential diagnosis may lead to confusion, unnecessary investigations and inappropriate treatment. Collaboration and jointly designed studies will increase awareness.

#### **Materials and Methods**

## Study Design

This study included 104 patients diagnosed with ET and FT who visited the movement disorder unit at our neurology outpatient clinic between 2020 and 2024. Each patient underwent a double-blind examination by two doctors specialising in movement disorders. Of the patients diagnosed with FT, only patients with tremor complaints were included in the study. In the case of a difficult diagnosis, the patient underwent electrophysiological tests. We excluded eight patients as

their diagnoses could not be confirmed. This study was approved by the local ethics committee (04/05/2020-039). The International Parkinson and Movement Disorder Society diagnostic criteria were used for the diagnosis of essential tremor in this study. These criteria consist of four parts: Presence of isolated action (kinetic and postural) tremor in bilateral upper extremities without other motor abnormalities. Duration of at least three years. With or without tremor in other locations (eg head, voice or lower extremities). Absence of other neurological signs such as dystonia, ataxia or parkinsonism. For the diagnosis of FT, axis 1 criteria such as sudden onset of symptoms, inconsistency and variable features in terms of topographic distribution, frequency and activation were used in our study.<sup>3,6–8</sup>

## **Participants**

The exclusion criteria were as follows: patients with cognitive disorders, additional neurological diseases, potential tremor-inducing drug use (B-adrenergic and antipsychotic drugs), potential tremor-inducing accompanying diseases, and those diagnosed with FT and accompanying movement disorders other than tremors (eg, myoclonus, dystonia, or chorea). Finally, we included patients diagnosed with FT or ET who provided informed consent. Our study comprised a cohort of 96 patients, and detailed clinical assessments and psychometric testing were performed to identify unique patterns and associations within each tremor type. We meticulously analysed variables including age, sex, body mass index (BMI), tremor symptom onset, and disease duration. Beyond the distribution of tremors and misdiagnoses, we performed electrophysiological tests and other imaging methods on the relevant patients. Additional psychometric assessments included the Mini-Mental Status Examination (MMSE), Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), Barratt Impulsivity Scale-Short Form (BIS-SF), Buss-Perry Aggression Questionnaire (BPAQ), and Body Image Scale (BIS). The patients' psychometric test results were evaluated by a psychiatrist.

## Statistical Analysis

The data were summarised using descriptive statistics. Continuous variables, depending on their distribution, were presented as the mean ± standard deviation or median and minimum and maximum values. Categorical variables were presented as counts and percentages. To assess the normality of the numerical variables, we applied the Shapiro–Wilk and Kolmogorov–Smirnov tests. These tests are crucial for determining the appropriate statistical methods for data analysis, as they help verify whether the data distribution conforms to the assumption of normality, which influences the choice of parametric versus non-parametric tests. The Pearson chi-square, Fisher's exact, Mann–Whitney U, and Anderson–Darling tests were used in subsequent analyses, as appropriate. In addition, we applied a classification and regression tree (CART) analysis for the model that could separate ET and FT patients. We used age at illness onset and the BDI, BAI, BMI, BPAQ, BIS-SF, and BIS scores as independent variables in the analysis. Furthermore, we considered the prior probabilities for each class to be equal and used the Gini criterion for node division. We determined the model to be the optimal tree within one standard error of the minimum misclassification cost and validated the model using a 10-fold cross-validation.

#### **Results**

The median age of the participants was 33.0 years; 41.7% (n = 40) were male and 58.3% (n = 56) were female. The total misdiagnosis rate for men and women is 14.5%. Findings showed that the higher prevalence of ET in males (p= 0.015). On examination, patients with ET displayed a significantly lower body mass index and a lower age of onset compared to those with FT (p = 0.050 and p = 0.023, respectively) which means statistically FT diagnosis are significant compared to ET. The disease duration was significantly longer in the ET group than in the FT group (p < 0.001). Table 1 summarises the demographic and clinical results.

Pairwise comparisons revealed that the MMSE and BIS scores were higher in ET patients than in FT patients, whereas the BDI, BAI, BPAQ, and BIS-SF scores were significantly lower in ET patients than in FT patients (p < 0.05). Table 2 summarises the psychometric data.

Univariate analyses of the demographic and clinical variables indicated that the female gender increased the risk of FT by 3.11-fold (95% confidence interval (CI): 1.32-7.34, p = 0.010), and each 1-year increase in the age of onset raised the risk of FT by 5% (95% CI: 1.01-1.09, p = 0.020). An analysis of psychometric variables indicated that each one-unit increase in the BDI,

**Table I** Demographic and Clinical Characteristics and Pairwise Comparisons Between the ET and FT Groups of Tremor Patients

	Overall (n = 96)	Groups	p-values	
		Essential Tremor (n = 52)	Functional Tremor (n = 44)	
Age (years)§	33.0 [18.0–55.0]	34.0 [18.0–55.0]	28.5 [18.0–54.0]	0.265**
Gender <sup>‡</sup>				
Male	40 (41.7)	28 (53.8)	12 (27.3)	0.015*
Female	56 (58.3)	24 (46.2)	32 (72.7)	
Body Mass Index (BMI)§	24.6 [17.8–34.8]	23.9 [17.9–34.8]	26.8 [17.8–33.5]	0.050**
Body Mass Index (BMI) Groups <sup>‡</sup>				
Underweight	6 (6.2)	2 (3.8)	4 (9.1)	0.148*
Normal	49 (51.0)	32 (61.5)	17 (38.6)	
Overweight	29 (30.2)	13 (25.0)	16 (36.4)	
Obesity Class I	12 (12.5)	5 (9.6)	7 (15.9)	
Age of Onset (years)§	25.0 [3.0–54.0]	24.0 [3.0–45.0]	27.5 [17.0–54.0]	0.023**
Duration of Disease (years)§	2.0 [0.0–31.0]	5.5 [1.0–31.0]	1.0 [0.0–7.0]	<0.001**
Misdiagnosis, present ‡	14 (14.5)	7 (13.4)	7 (15.9)	0.927*
Correct Diagnosis <sup>‡</sup>				
Essential Tremor (ET)	6 (42.8)	0 (0.0) <sup>a</sup>	6 (85.7) <sup>b</sup>	0.004*
Functional Tremor (FT)	4 (28.5)	4 (57.2) <sup>a</sup>	0 (0.0) <sup>b</sup>	
Wilsons Disease	2 (14.2)	2 (28.5) <sup>a</sup>	0 (0.0) <sup>a</sup>	
Dystonia	1 (7.1)	I (14.3) <sup>a</sup>	$(0.0)^a$	
Neurodegenerative Disease	1 (7.1)	0 (0.0) <sup>a</sup>	I (14.3) <sup>a</sup>	
Hand Tremor <sup>‡</sup>	81 (84.4)	46 (88.5)	35 (79.5)	0.359*
Hand Tremor Symmetry/Asymmetry <sup>‡</sup>				
Symmetry	50 (61.7)	40 (87.0)	10 (28.6)	<0.001*
Asymmetry	31 (38.3)	6 (13.0)	25 (71.4)	
Head Tremor, present <sup>‡</sup>	20 (20.8)	14 (26.9)	6 (13.6)	0.179*
Jaw Tremor, present <sup>‡</sup>	3 (3.1)	I (I.9)	2 (4.5)	0.592*
Leg Tremor, present <sup>‡</sup>	13 (13.5)	6 (11.5)	7 (15.9)	0.746*
Leg Symmetry/Asymmetry <sup>‡</sup>				
Symmetry	11 (84.6)	6 (100.0)	5 (71.4)	0.462*
Asymmetry	2 (15.4)	0 (0.0)	2 (28.6)	
Trunk Tremor, present <sup>‡</sup>	10 (10.4)	4 (7.7)	6 (13.6)	0.505*

**Notes**: This table illustrates demographic and clinical characteristics along with pairwise comparisons between essential tremor (ET) and functional tremor (FT) groups among patients with tremor using various statistical methods and data representations. The  $^{\ddagger}$ symbol indicates that data are displayed in number and percentage format (n (%)). The  $^{\$}$ symbol denotes that values are presented as median and range [minimum–maximum]. The symbols used for statistical tests are as follows: \*signifies the use of Pearson Chi-Square, Fisher's exact, or Fisher–Freeman–Halton test, which were employed to determine the significance of differences in categorical data across groups. \*\*represents the Mann–Whitney *U*-test, used for comparing median values between two independent samples. Different superscripts  $^{a,b}$ within the table indicate statistical differences between groups in each row, with no statistical difference being marked where superscripts are the same.

BAI, BPAQ, and BIS-SF scores increased the risk of FT by 13% (95% CI: 1.05-1.21, p < 0.001), 11% (95% CI: 1.06-1.15, p < 0.001), and 6% (95% CI: 1.03-1.09, p < 0.001), respectively. Conversely, each one-unit increase in the BIS score decreased the risk of FT by 3% (95% CI: 0.95-0.98, p < 0.001). In the multivariate analyses, each one-unit increase in BPAQ and BIS-SF scores was associated with an 8% (95% CI: 1.03-1.12, p < 0.001) and 4% (95% CI: 1.01-1.07, p = 0.009) increase in the risk of FT, respectively. Table 3 summarises the clinical and psychometric variables.

Table 2 Comparison of Psychometric Parameters in Patients with ET and FT

	Groups	p-values	
	Essential Tremor (n = 52)	Functional Tremor (n = 44)	
Mini-Mental State Examination (MMSE)§	29.0 [26.0–30.0]	28.0 [25.0–30.0]	0.007**
Beck Depression Inventory (BDI) <sup>§</sup> Beck Depression Inventory (BDI) Groups <sup>‡</sup>	7.0 [0.0–26.0]	14.0 [3.0–26.0]	<0.001**
Normal Mild Depression Moderate Depression	32 (61.5) <sup>a</sup> 12 (23.1) <sup>a</sup> 8 (15.4) <sup>a</sup>	14 (31.8) <sup>b</sup> 16 (36.4) <sup>a</sup> 14 (31.8) <sup>a</sup>	0.013*
Beck Anxiety Inventory (BAI) <sup>§</sup> Beck Anxiety Inventory (BAI) Groups <sup>‡</sup> Normal Anxiety	9.0 [3.0–34.0] 43 (82.7) 9 (17.3)	15.0 [5.0–56.0] 24 (54.5) 20 (45.5)	<0.001** 0.006*
Buss-Perry Aggression Questionnaire (BPAQ)§	28.0 [11.0–68.0]	63.5 [23.0–94.0]	<0.001**
Barratt Impulsiveness Scale–Short Form (BIS-SF)§	31.5 [12.0–78.0]	67.0 [15.0–113.0]	<0.001**
Body Image Scale (BIS) <sup>†</sup> Body Image Scale (BIS) Groups <sup>‡</sup> Poor Low Perception	140.2 ± 24.8 18 (34.6) 34 (65.4)	114.9 ± 28.8 30 (68.2) 14 (31.8)	<0.001*** 0.002*

**Notes**: This table details the comparison of psychometric parameters between patients with essential tremor (ET) and functional tremor (FT), employing various statistical techniques and data presentation methods. The <sup>‡</sup>symbol indicates that data are displayed in number and percentage format (n (%)). The <sup>§</sup>symbol denotes that values are presented as median and range [minimum-maximum]. The <sup>†</sup>symbol represents values given as mean ± standard deviation. The symbols used for statistical tests include \*for Pearson Chi-Square, Fisher's exact, or Fisher-Freeman-Halton tests, which assess the significance of differences in categorical data across groups; \*\*for the Mann-Whitney *U*-test, used to compare median values between two independent samples; and \*\*\*for the independent samples t-test, which compares mean differences between two independent groups. Different superscripts <sup>a,b</sup> within the table denote statistical differences between groups in each row, with no statistical difference indicated where superscripts are the same.

**Table 3** Results of Logistic Regression Analyses for the Predictive Effect of Clinical and Psychometric Variables on Tremor Type

Dependent: Groups (Essential Tremor vs Functional Tremor)	Univariable OR (95% CI), p-values	Multivariable OR (95% CI), p-values
Gender: Female vs Male	3.11 (1.32–7.34), p = 0.010	2.26 (0.54–9.46), p = 0.265
Body Mass Index (BMI)	1.09 (0.98–1.22), p = 0.098	-
Age of Onset (years)	1.05 (1.01–1.09), $p = 0.020$	1.06 (0.99–1.15), p = 0.111
Hand Tremor: Present vs Absent	0.51 (0.17–1.56), p = 0.236	-
Head Tremor: Present vs Absent	0.43 (0.15–1.23), p = 0.116	-
Beck Depression Inventory (BDI)	1.13 (1.05–1.21), p < 0.001	1.02 (0.89–1.15), p = 0.744
Beck Anxiety Inventory (BAI)	1.11 (1.05–1.18), p < 0.001	1.03 (0.96–1.11), p = 0.393
Buss-Perry Aggression Questionnaire (BPAQ)	1.11 (1.06–1.15), p < 0.001	1.08 (1.03–1.12), p < 0.001
Barratt Impulsiveness Scale—Short Form (BIS-SF)	1.06 (1.03–1.09), p < 0.001	1.04 (1.01–1.07), p = 0.009
Body Image Scale (BIS)	0.97 (0.95–0.98), p < 0.001	0.98 (0.96–1.01), p = 0.199

**Notes**: This table presents the results of logistic regression analysis for predicting tremor type (essential tremor vs functional tremor) based on clinical and psychometric variables. The table displays odds ratios (ORs) with corresponding 95% confidence intervals (Cls) and *p*-values for both the univariable and multivariable models. The analysis examines variables such as gender, body mass index (BMI), age of onset, presence or absence of hand and head tremors, and scores from the Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), Buss-Perry Aggression Questionnaire (BPAQ), Barratt Impulsiveness Scale-Short Form (BIS-SF), and Body Image Scale (BIS). The *p*-value indicates the statistical significance of each variable's predictive power on tremor classification, guiding insights into factors that may differentially influence the development of these tremor types.

The confusion matrix used to evaluate the performance of the model revealed that in the training data, 45 of the 52 ET cases were predicted correctly, resulting in an accuracy of 86.5%. Similarly, 34 of the 44 FT cases were predicted correctly with an accuracy of 77.3%, leading to an overall accuracy of 82.3%. In the test data, 44 and 32 of the 52 and 44 ET and FT cases were correctly predicted (accuracies of 84.6% and 72.7%), respectively, with an overall accuracy of 79.2%. The sensitivities of the model were 86.5% and 84.6% for training and test data, respectively. The false positive rate was 22.7% and 27.3% in the training and test data, respectively. The false negative rate was 13.5% and 15.4% in the training and test data, respectively. These findings are summarised in Table 4. Additionally, data for ET and FT patients are summarized in Table 5.

We evaluated the performance of the CART model using several statistical methods. The mean log-likelihood values were 0.4668 and 0.5287 for the training and test data, respectively. The area under the receiver operating characteristic curve (AUC) values were 0.8191 for training and 0.7340 for testing, with 95% CIs of 0.06453–1 and 0.6257–0.8423, respectively. We calculated the lift values to be 1.5105 and 1.2088 for training and testing, respectively. In addition, the misclassification costs were 0.3619 and 0.4266 for training and testing, respectively. These measurements indicate that the model performed better on the training than on the test data. Although the decrease in performance indicators on the test data suggests certain limitations in the model's generalisability, the obtained values were still within acceptable limits.

Table 4 Confusion Matrix and Statistics for Training and Test Data

	Predicted Class (Training)		Predicted Class (Test)	
Actual Class	ET	FT	ET	FT
ET FT All	45 (86.5% accuracy) 10 55 (82.3% accuracy)	7 34 (77.3% accuracy) 41	44 (84.6% accuracy) 12 56 (79.2% accuracy)	8 32 (72.7% accuracy) 40
Statistics			Training (%)	Test (%)
False Positive False Negative	Rate (Sensitivity) Rate (Type I Error) e Rate (Type II Error) e Rate (Specificity)		86.5 22.7 13.5 77.3	84.6 27.3 15.4 72.7

**Notes**: This table presents the confusion matrix and associated statistics for both the training and test datasets. It illustrates the accuracy of the model in classifying patients into essential tremor (ET) and functional tremor (FT) groups during the training and testing phases. The sensitivity (true positive rate) and specificity (true negative rate) are highlighted along with the rates of type I and type II errors, providing a comprehensive view of the model's performance in differentiating between ET and FT.

Table 5 Summary of Positive Findings Between Both Groups

	Overall (n = 96)	Groups		p-values
		Essential Tremor (n = 52)	Functional Tremor (n = 44)	
Gender				
Male	40 (41.7)	28 (53.8)	12 (27.3)	0.015*
Female	56 (58.3)	24 (46.2)	32 (72.7)	
Body Mass Index (BMI)	24.6 [17.8–34.8]	23.9 [17.9–34.8]	26.8 [17.8–33.5]	0.050**
Age of Onset (years)	25.0 [3.0–54.0]	24.0 [3.0-45.0]	27.5 [17.0–54.0]	0.023**
Duration of Disease (years)	2.0 [0.0–31.0]	5.5 [1.0–31.0]	1.0 [0.0–7.0]	<0.001**
Misdiagnosis, present	14 (14.5)	7 (13.4)	7 (15.9)	0.927*

(Continued)

Table 5 (Continued).

	Overall (n = 96)	Groups		p-values
		Essential Tremor (n = 52)	Functional Tremor (n = 44)	
Correct Diagnosis				
Essential Tremor (ET)	6 (42.8)	0 (0.0) <sup>a</sup>	6 (85.7) <sup>b</sup>	0.004*
Functional Tremor (FT)	4 (28.5)	4 (57.2) <sup>a</sup>	0 (0.0) <sup>b</sup>	
Wilsons Disease	2 (14.2)	2 (28.5) <sup>a</sup>	0 (0.0) <sup>a</sup>	
Dystonia	1 (7.1)	I (14.3) <sup>a</sup>	0 (0.0) <sup>a</sup>	
Neurodegenerative Disease	1 (7.1)	0 (0.0) <sup>a</sup>	I (14.3) <sup>a</sup>	
Hand Tremor	81 (84.4)	46 (88.5)	35 (79.5)	0.359*
Hand Tremor Symmetry/Asymmetry				
Symmetry	50 (61.7)	40 (87.0)	10 (28.6)	<0.001*
Asymmetry	31 (38.3)	6 (13.0)	25 (71.4)	
Beck Depression Inventory (BDI)		7.0 [0.0–26.0]	14.0 [3.0–26.0]	<0.001**
Beck Anxiety Inventory (BAI)		9.0 [3.0–34.0]	15.0 [5.0–56.0]	<0.001**
Buss-Perry Aggression Questionnaire (BPAQ)		28.0 [11.0–68.0]	63.5 [23.0–94.0]	<0.001**
Barratt Impulsiveness Scale–Short Form (BIS-SF)		31.5 [12.0–78.0]	67.0 [15.0–113.0]	<0.001**
Body Image Scale (BIS)		140.2 ± 24.8	114.9 ± 28.8	<0.001***

**Notes**: This table summarizes the data in patients with essential tremor and functional tremor. The symbols used for statistical tests include \*for Pearson Chi-Square, Fisher's exact, or Fisher–Freeman–Halton tests, which assess the significance of differences in categorical data across groups; \*\*for the Mann–Whitney *U*-test, used to compare median values between two independent samples; and \*\*\*for the independent samples *t*-test, which compares mean differences between two independent groups.

We expressed the relative importance of the predictors as a percentage, with the most effective predictor rated at 100%. According to our analysis, the BPAQ scores displayed the highest level of importance at 100%, followed by BIS, BDI, BIS, BMI, sex, BDI, and age at illness onset at 60.3%, 45.6%, 36.6%, 19.0%, 17.8%, 9.1%, and 3.9%, respectively (Figure 1). In our analysis, we used the CART methodology to divide patients into two main groups based on various clinical and demographic parameters: ET and FT. We identified key features (such as age at onset of illness, BDI, BAI, BMI, BPAQ, BIS-SF, and BIS) as the primary predictors for classifying the patients. The results showed that the patients in the dataset were grouped according to their risk profiles, initially based on BIS-SF values. The first division was made at BIS-SF ≤ 43.5 and BIS-SF, followed by further subdivisions into more detailed subgroups based on BDI, BAI, and BIS-SF values.

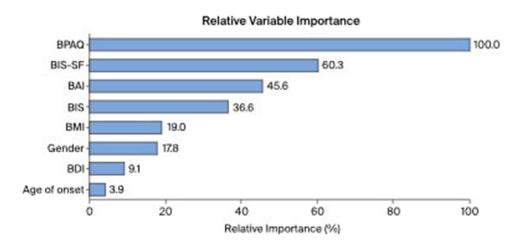


Figure 1 The relative importance of the predictors as a percentage.

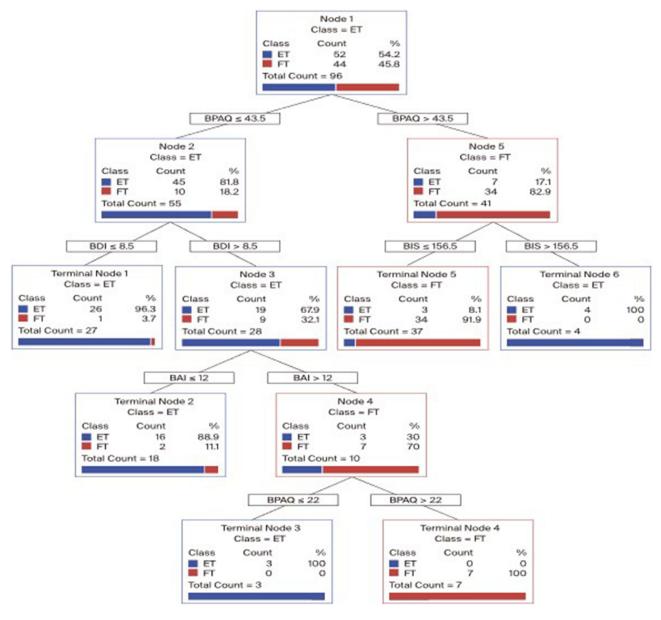


Figure 2 Classification and regression tree (CART) methodology to divide patients into two main groups.

Each terminal node contains the final classification of the model, which includes the number of patients and the percentage distribution within these groups. The high accuracy rates observed at these terminal nodes demonstrated the efficacy of the model in predicting the disease states. Notably, one terminal node, which included 26 patients in the ET group, correctly classified 96% of patients (Figure 2).

#### **Discussion**

The present study, which focused on differentiating the clinical and psychometric characteristics of ET and FT, significantly contributes to our understanding of these conditions in the clinical setting. By assessing variables such as sex, BMI, age of onset, misdiagnosis rates, and various psychometric assessments, we performed a comprehensive analysis that aligns with and extends the current research on tremor pathology and diagnosis.

Our study identified a notably higher proportion of males in the ET than in the FT group. This sex disparity is not only significant in understanding the demographic distribution of tremor types but also suggests that inherent differences could exist in how these conditions manifest across sexes. This finding is consistent with the results of Govorova and Pan et al,

who explored how the clinical features of ET vary among different ethnic groups, suggesting that genetic or environmental factors might influence the disease phenotype. <sup>11,12</sup> The variation in the clinical ET features, as noted by Govorova, Pan, and Sun et al, underscores the complexity of ET as a neurodegenerative condition influenced by various factors, including sex. <sup>11–13</sup> In summary, our findings on the sex-related ET distribution not only corroborate the observations made by Govorova et al concerning ET variability across different groups but also emphasise the need for further studies focusing on the biological underpinnings that contribute to these differences. <sup>11,13</sup> Such studies could ultimately lead to more effective and personalised therapeutic interventions, enhancing the outcomes of patients with tremor-related disorders. <sup>14</sup>

In our study, the misdiagnosis rate of 14.5% emphasises that accurately distinguishing between ET and FT is a complex challenge. This high misdiagnosis rate reflects subtleties in the clinical presentations of tremor syndromes, which can often overlap, leading to diagnostic errors. Misdiagnosis delays appropriate treatment, potentially leading to ineffective therapy, underscoring the need for enhanced diagnostic criteria and methods.<sup>3,4</sup> Our findings resonate with those of Peng et al (2022), who highlighted the critical need for the reassessment and reclassification of patients with tremor syndromes to enhance diagnostic precision and treatment outcomes.<sup>10</sup> Peng et al argued that the current classification systems might not suffice, suggesting that a more nuanced approach, possibly integrating more sophisticated diagnostic tools, such as advanced imaging techniques, enhanced neurophysiological assessments, or new criteria, would be required. This recommendation aligns with our observed misdiagnosis rates, suggesting that both studies recognised the significant limitations in the current clinical framework for tremor diagnosis.<sup>10</sup> Such advancements could reduce the misdiagnosis rates by providing clearer distinctions between ET and FT at earlier stages of patient evaluation.<sup>15–18</sup>

In our study, we observed notable differences in the psychometric profiles between patients with ET and those with FT, providing crucial insights into the distinct nature of these conditions. These differences were particularly evident in the assessment scores of the psychological scales, such as depression and anxiety, which were significantly higher in patients with FT than in patients with ET. In addition, body image scales were distorted, and the rate of impulsivity and aggression was high in patients with FT. Such findings are crucial, as they not only help in differentiating between these tremor types but also in understanding the broader psychosocial impacts of these conditions on patients. 19-22 This aspect of our study aligns with the observations of S. Lidstone and A. Lang (2020), who explored the diagnostic criteria for functional tremors, emphasising the role of clinical and examination features, including psychometric evaluations, in their diagnosis.<sup>3</sup> This is particularly relevant, as psychometric evaluations could reveal underlying psychological factors that may not be immediately apparent through physical examinations alone. 19-22 The significant psychometric differences identified underline the necessity of incorporating comprehensive psychological assessments into the diagnostic process for tremors, potentially enhancing the accuracy of distinguishing between ET and FT. 23-25 By integrating detailed psychometric evaluations into the routine assessment of patients with tremors, clinicians could have a better understanding of the patient's condition, which is crucial for effective treatment planning. In addition, although the psychometric data scores of patients with ET were lower than those of patients with FT, there was also a disorder in the psychometric profiles of patients with ET. This may be related to the neurodegenerative and cognitive disorders accompanying ET.<sup>26-28</sup>

This aspect of our study correlates with the findings reported by Hopfner and Deuschl (2016), who explored the implications of symptomatic management outcomes in patients with ET. They highlighted the variability in patient responses to treatment, and the importance of tailoring management strategies based on individual symptoms and disease characteristics.<sup>29</sup> This is particularly relevant to our findings, suggesting that the underlying psychometric differences between ET and FT could influence how patients respond to standard treatment protocols. The increased BMI in patients with FT indicates that not only psychiatry and neurology should be involved in the treatment method, but also dietitians. Furthermore, the detailed demographic analysis in our study revealed that certain therapies might be more effective in one group than in another, which are also influenced by factors such as age and sex.

Our contribution emphasises the need for further research to explore how demographic and psychometric distinctions between tremor types can be effectively translated into personalised treatment plans. Future studies should consider these factors when assessing the efficacy of different therapeutic interventions to enhance the overall management of tremor disorders and improve patient outcomes in clinical practice.

Our study raises important questions concerning the biological underpinnings that could be used to differentiate ET from FT, particularly in the progression and response to therapy. The distinct psychometric and demographic profile identification suggests that personalised treatment strategies could be more efficient than the current one-size-fits-all approaches. Furthermore, the significant rate of misdiagnosis indicates the need for improved diagnostic protocols, possibly by incorporating advanced imaging techniques or revised clinical guidelines that consider our findings.

Future studies should focus on longitudinal patient tracking to observe the progression of ET and FT under various treatment modalities. Additionally, exploring the genetic markers or environmental factors that could contribute to the phenotypic expression of these tremors would be invaluable. These efforts would not only refine the diagnostic accuracy but also enhance the therapeutic outcomes by tailoring interventions to specific tremor types and individual patient characteristics.

Despite the wide range of data obtained in our study, some limitations remain. First, the sample size, although adequate for detecting significant differences, might not have captured the full spectrum of variability within the tremor population. Second, the cross-sectional nature of our study design limited our ability to infer causality or track tremor progression over time. Additionally, while we used a robust statistical framework to analyse our data, reliance on self-reported measures for some psychometric evaluations might have introduced bias or variability in the accuracy of the data. Furthermore, incorporating objective biomarkers or neuroimaging data could enhance the reliability of distinguishing between ET and FT.

Addressing these limitations in future studies would refine our understanding and contribute to more definitive conclusions, thereby not only solidifying the foundations laid by our current study but also expanding the scope of tremor disorder management methods.

#### Conclusion

Our discoveries related to the clinical and psychometric distinctions between ET and FT underscore significant differences that are not only statistically relevant but also clinically actionable. Our analysis highlighted a higher prevalence of ET in males and an association of FT with more pronounced psychometric impairments, including higher anxiety and depression scores. These observations align with our initial hypothesis that the two tremor types would manifest distinct clinical profiles that could inform diagnostic and therapeutic strategies.

Furthermore, the substantial misdiagnosis rates in our study highlight the need for increased clinical awareness and diagnostic precision. Our study suggests that integrating more rigorous psychometric assessments into routine clinical evaluations could reduce these rates and ultimately enhance patient care.

By demonstrating clear distinctions in the clinical presentation and psychometric parameters, we pave the way for future research exploring tailored therapeutic interventions that address the specific needs of each tremor type, potentially improving outcomes and patient satisfaction.

## **Abbreviations**

BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; BIS, Barratt Impulsivity Scale-Short; BMI, Body mass index; CART, Classification and regression tree; CI, Confidence interval; ET, Essential tremor; EVA, Ethylene vinyl acetate; FMD, Functional movement disorders; FT, Functional tremor; MMSE, Mini-Mental Status Examination; OR, Odds ratios.

# **Data Sharing Statement**

The data presented in this study are available on request from the corresponding author due to ethical reasons.

# Ethics Approval and Informed Consent

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of Cukurova University School of Medicine (04/05/2020-039). Consent for publication Informed consent was obtained from all subjects involved in the study.

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Permission has been obtained from PARinc for the use of MMSE.

## **Author Contributions**

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## **Disclosure**

The authors declare that they have no competing interests.

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