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# Essential Tremor is not Only a Movement Disorder; Its Relationship with Sleep and Anxiety

**Bilgehan Atılgan ACAR, Türkan ACAR**

Department of Neurology, Sakarya University Faculty of Medicine, Sakarya, Turkey

## ABSTRACT

**Introduction:** Essential tremor (ET) is the most common movement disorder, and some studies suggest that there are non-motor symptoms as well as motor symptoms. This study aims to investigate the relationship between ET and anxiety and sleep disorder.

**Methods:** The study was conducted with 38 healthy individuals in the control group and 40 patients who admitted to the neurology clinic of our hospital and had definite ET according to the *Consensus statement of the Movement Disorder Society on Tremor. Pittsburgh Sleep Quality Index* (PSQI) and *Hamilton Anxiety Rating Scale* (HAM-A) were applied to both groups. Statistical analysis was carried out with SPSS 22.0 for Windows.

**Results:** The patient and control groups were similar in terms of age, gender and educational status. The PSQI and HAM-A scores in the patient group were significantly higher than the control group ($p<0.000$, $p<0.000$, respectively). Both scores were higher in female patients compared to male patients ($p<0.05$, $p<0.05$, respectively), and in married patients compared to single patients ($p<0.05$, $p<0.05$, respectively).

**Conclusion:** Sleep disorder and anxiety are more common in patients with ET than in healthy individuals. We believe that more severe sleep disorders and anxiety in female and/or married patients are indicative of the psychosocial component of the disorder, and that this condition should not be overlooked and should be studied more comprehensively in this regard.

**Keywords:** Essential tremor, sleep, anxiety

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## INTRODUCTION

Essential tremor (ET) is the most common movement disorder in adults, and is characterized by postural and/or kinetic tremor. The prevalence of ET is 0.9%, which is slightly higher in those aged 65 years and over (1). The cause of ET is not known precisely and the central nervous system region associated with its pathophysiology has not yet been identified. There is some evidence that ET may be a neurodegenerative disorder (2); however, another hypothesis that suggests ET as a functional disorder in subcortical region without neurodegeneration has also been reported (3). A common view with these pathophysiologic factors is that ET may have other symptoms in addition to motor symptoms.

## METHODS

Successive, forty adult patients (11 males and 29 females) who admitted to Sakarya University, Training and Research Hospital, Neurology Clinic between May 2016 and May 2017 and had a definite diagnosis of ET according to the *Consensus statement of the Movement Disorder Society on Tremor* (4) as well as 38 adult, healthy volunteers (12 males and 26 females) with matched age and gender were included in our study. The control group was selected from volunteers who admitted for blood donation to a blood center without any known chronic illness or psychiatric disease. Individuals who were below age 18, illiterate, have known mental disorder and/or have a "Mini-Mental State Examination" score less than 24, have any thyroid disease history, have a history of alcohol and drug abuse, have signs of lateralization except tremor in neurological examination, those who use thyroid hormones, amphetamine, beta-adrenergic agonists, theophylline, antiepileptic, antidepressant, neuroleptic medication, and in addition only patients with abnormal cranial MRI and/or patients with abnormal values in any of thyroid function tests were excluded from the study. The Sociodemographic Data Form, *Mini-Mental State Examination* (MMSE) (5,6) and *Hamilton Anxiety Rating Scale* (HAM-A) (7,8) were filled out by the clinician with face-to-face interviews with the patients, and the *Pittsburgh Sleep Quality Index* (PSQI) (9,10) was filled out by the patients themselves.

The ethical approval was obtained from the Sakarya University Faculty of Medicine Ethics Committee in order to conduct the study.

### Scales Used

- **Consensus statement of the Movement Disorder Society on Tremor for Definite Essential Tremor Diagnosis** (4)

**A. Inclusion criteria:** 1) Bilateral postural tremor with or without kinetic tremor, involving hands and forearms, that is visible and persistent. (Tremor may be in the upper extremities or additional other parts of the

**Correspondence Address:** Bilgehan Atılgan ACAR , Department of Neurology, Sakarya University Faculty of Medicine, Sakarya, Turkey • **E-mail:** bilgehanacar@hotmail.com
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body sometimes. Bilateral tremor may be asymmetric, and have variable amplitude, despite stated the patient as continuous. May or may not cause disability). 2) Duration greater than 5 years.

**B. Exclusion criteria:** 1) Other abnormal neurological signs (except Froment's sign; and neurological examination must be within normal limits of the age, except tremor). 2) Presence of known causes of increased physiological tremor. 3) Concurrent or recent exposure to tremorogenic drugs or the presence of a drug withdrawal state. 4) Direct or indirect trauma to the nervous system within 3 months before the onset of tremor. 5) Historical or clinical evidence of psychogenic origins. 6) Convincing evidence of sudden onset or evidence of stepwise deterioration (4).

- **Mini Mental State Examination (MMSE)**

The maximum score of this scale, used in the short-term evaluation of the cognitive status, is 30, and a score between 24 and 30 is considered normal (5,6).

- **Hamilton Anxiety Rating Scale (HAM-A)**

It is a 14-item scale applied by the clinical observer to measure the level of anxiety, the distribution of symptoms and the change in its intensity. A HAM-A global score in the range of 0-5 was considered as no anxiety, 6-14 as mild anxiety, 15-24 as moderate anxiety, and a score ≥24 was classified as intense anxiety (7,8).

- **Pittsburgh Sleep Quality Index (PSQI)**

It's a 19-item scale to evaluate sleep quality and sleep disorder over the past month. The total score ranges between 0 and 21. In PSQI, global score <5 indicates a good sleep quality, and a score ≥5 considered poor sleep quality (9,10).

### Statistical Analysis

Mean, standard deviation, median, minimum, maximum, frequency and ratio values were used in the descriptive statistics of the data. The distribution of the variables was measured by the Kolmogorov-Simirnov test. Mann-Whitney u test was used in the analysis of quantitative independent data. Chi-square test was used to analyze qualitative independent data, and Fischer test was used when chi-square test conditions were not met. Spearman's correlation analysis was used for correlation analysis. The effect level and cut-off value were investigated by ROC curve. SPSS 22.0 program was used in the analysis.

## RESULTS

The mean age of 40 patients (29 females, 11 males) with essential tremor was 33.6±12.2, and the mean age of the healthy volunteers (26 females, 12 males) of the control group was 33.2±10.1. There were no significant differences between the two groups in terms of age, gender distribution, education level and marital status. In the patient group, Pittsburg sleep score and the rate of patients with poor sleep quality were significantly higher than the control group ($p<0.05$). According to the Hamilton anxiety scale, anxiety levels were not severe in both groups; however, the Hamilton anxiety score and the rate of patients with moderate anxiety in the patient group were significantly higher than the control group ($p<0.05$). Demographic data of patients and control group and statistical comparison of PSQI and HAM-A scores are shown in Table 1. The PSQI is shown in Fig. 1A and its comparison with HAM-A is shown in Fig. 1B.

In the patient group, Pittsburg sleep score and the rate of patients with poor sleep quality were significantly higher in the female patients than in male patients ($p<0.05$). Again in the patient group, the Hamilton anxiety score and the rate of patients with moderate anxiety were also significantly higher in females than males ($p<0.05$) (Table 2).

In the patient group, Pittsburg sleep score and the rate of patients with poor sleep quality were significantly higher in the married patients than the single patients ($p<0.05$). Again in the patient group, the Hamilton anxiety score and the rate of patients with moderate anxiety were significantly higher in married patients than in male patients ($p<0.05$) (Table 3).

There was no significant correlation between age and Pittsburg sleep score ($r=0.399$ / $p=0.051$) in the patient group. There was no significant correlation between age and Hamilton anxiety score ($r=0.144$ / $p=0.377$) in the patient group.

## DISCUSSION

ET, which has been characterized by postural tremor previously, has been traditionally thought to be monosymptomatic. However, ET is the most common movement disorder in adults, and non-motor features of this disorder have also been started to be defined in recent years (11-14). These non-motor features include psychiatric symptoms and sleep disorders, which together with ET restrict activities of daily living (15,16). In the first studies on this subject, it was determined that anxiety symptoms were common in patients with ET and it was stated that this effect social communication negatively. A presumed mechanism for this is the social withdrawal due to patient's physical complaint (17,18). Especially depression and anxiety may increase due to the effect and severity of tremor. Anxiety and depression are the most common psychiatric disorders and clear results have been obtained regarding the underlying neural mechanisms in current human and animal studies (19). Therefore, another possible mechanism has been reported that ET may be a neurodegenerative disorder similar to Parkinson's disease,

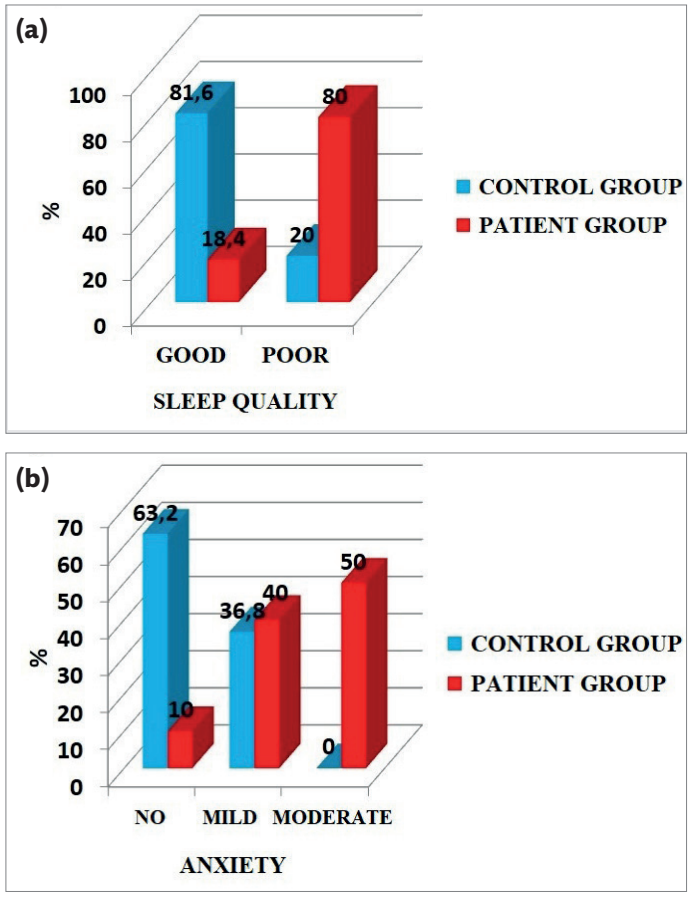


**Figure 1.** Pittsburg sleep quality index of patients with essential tremor and volunteer control group (A) Hamilton Anxiety Scale (B) comparison of results.

**Table 1.** Demographic data of the patient and control groups and Pittsburg Sleep Quality Index and Hamilton Anxiety Rating Scale scores

| | | Control Group | | | | | Patient Group | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Avg. ± S.D. / n-% | | | Median | | Avg. ± S.D. / n-% | | | Median | p | |
| Age | | 33.2 | ± | 10.1 | 32.0 | | 33.6 | ± | 12.2 | 33.0 | 0.944 | m |
| Gender | Female | 26 | | 68.4% | | | 29 | | 72.5% | | 0.693 | $X^2$ |
| | Male | 12 | | 31.6% | | | 11 | | 27.5% | | | |
| Education status | Literate | 2 | | 5.3% | | | 3 | | 7.5% | | 0.186 | $X^2$ |
| | Primary school | 6 | | 15.8% | | | 10 | | 25.0% | | | |
| | Secondary school | 1 | | 2.6% | | | 2 | | 5.0% | | | |
| | High School | 21 | | 55.3% | | | 12 | | 30.0% | | | |
| | University | 8 | | 21.1% | | | 13 | | 32.5% | | | |
| Marital Status | Single | 14 | | 36.8% | | | 18 | | 45.0% | | 0.464 | $X^2$ |
| | Married | 24 | | 63.2% | | | 22 | | 55.0% | | | |
| Pittsburg Sleep Scale | | 2.7 | ± | 1.7 | 2.0 | | 6.2 | ± | 1.9 | 6.0 | 0.000 | m |
| Sleep Quality | Good | 31 | | 81.6% | | | 8 | | 20.0% | | 0.000 | $X^2$ |
| | Poor | 7 | | 18.4% | | | 32 | | 80.0% | | | |
| Hamilton Anxiety Scale | | 4.4 | ± | 4.0 | 3.0 | | 13.8 | ± | 5.6 | 14.5 | 0.000 | m |
| Anxiety | No | 24 | | 63.2% | | | 4 | | 10.0% | | 0.000 | $X^2$ |
| | Mild | 14 | | 36.8% | | | 16 | | 40.0% | | | |
| | Moderate | 0 | | 0.0% | | | 20 | | 50.0% | | | |

[m] Mann-Whitney u test / [X²] Chi-square test

**Table 2.** Distribution of Pittsburg Sleep Quality Index and Hamilton Anxiety Rating Scale scores by gender in the patient group.

| | | Female | | | | | Male | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Avg. ± S.D. / n-% | | | Median | | Avg. ± S.D. / n-% | | | Median | p | |
| Pittsburg Sleep Scale | | 6.7 | ± | 1.9 | 7.0 | | 4.6 | ± | 1.0 | 5.0 | 0.001 | m |
| Sleep Quality | Good | 3 | | 10.3% | | | 5 | | 45.5% | | 0.041 | $X^2$ |
| | Poor | 26 | | 89.7% | | | 6 | | 54.5% | | | |
| Hamilton Anxiety Scale | | 15.3 | ± | 5.0 | 16.0 | | 9.6 | ± | 5.1 | 12.0 | 0.005 | m |
| Anxiety | No | 1 | | 3.4% | | | 3 | | 27.3% | | 0.015 | $X^2$ |
| | Mild | 10 | | 34.5% | | | 6 | | 54.5% | | | |
| | Moderate | 18 | | 62.1% | | | 2 | | 18.2% | | | |

[m] Mann-Whitney u test / [X²] Chi-square test

and therefore cognitive changes and psychiatric symptoms may be seen in addition to tremor (17,18,20-22). In our study, the anxiety score in patients with ET was significantly higher than the control group.

More than a third of studies on ET have reported that the prevalence varies by gender and have been reported as more common in male in most studies (23). In our study, the high proportion of male/female gender in the patient group (29/11) could be methodological due to the low number of patients and due to the selection of group from the patients successively admitting to the polyclinic. However, this does not explain the high rate of sleep disorders and anxiety in female patients with ET than in male patients with ET. Demographic analysis of affective disorders shows that the prevalence is high in female gender (19). It is unclear whether these non-motor symptoms are more common in patients with ET, or whether they are a result of a disease or have a common pathophysiological background. It is also known that non-motor symptoms, particularly cognitive impairment, are not associated with ET duration or severity, which is a primary characteristic of ET (15). In the structure and functions of the brain, the effect of gender difference is evident and age-dependent fluctuations are seen (24). In anxiety and depression, many studies have reported that neuroactive steroids and steroidal hormones such as testosterone and estrogen in brain structures such as hippocampus and amygdala affect neural excitability and are associated with mood disorders (19,25-27).

One cause of general fatigue complaints in patients with ET may be the more common sleep disorder or poor sleep quality in these patients. Sleep disorder may also occur due to the disorder itself or side-effects of

**Table 3.** Distribution of Pittsburg Sleep Quality Index and Hamilton Anxiety Rating Scale scores by the marital status in the patient group.

| | | Single | | | | | Married | | | | p | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Avg. ± S.D. / n-% | | | Median | | Avg. ± S.D. / n-% | | | Median | | |
| Pittsburg Sleep Scale | | 5.3 | ± | 1.7 | 5.5 | | 6.8 | ± | 1.9 | 7.0 | 0.009 | m |
| Sleep Quality | Good | 7 | | 38.9% | | | 1 | | 4.5% | | 0.021 | $X^2$ |
| | Poor | 11 | | 61.1% | | | 21 | | 95.5% | | | |
| Hamilton Anxiety Scale | | 12.9 | ± | 4.4 | 13.0 | | 14.4 | ± | 6.4 | 16.0 | 0.046 | m |
| Anxiety | No | 1 | | 5.6% | | | 3 | | 13.6% | | 0.047 | $X^2$ |
| | Mild | 11 | | 61.1% | | | 5 | | 22.7% | | | |
| | Moderate | 6 | | 33.3% | | | 14 | | 63.6% | | | |

[m] Mann-Whitney u test / [X²] Chi-square test

medications used (20). None of the patients with ET in our study group received treatment for sleep disorder and our patients had significant sleep disorder compared to the control group. In addition, another cause of sleep disturbance may be the presence of anxiety in these patients.

An interesting finding in our study was that ET was more frequent in married patients compared to that of single patients. In a recent study investigating the relationship between marriage and quality of life, single men have been found to have a poorer quality of life compared to the married men, whereas single women have been found to have a better quality of life than the married, separate or divorced women (28). Our findings indicate that not only psychological but also environmental, social, cultural and sociological backgrounds of the disorder.

## CONCLUSION

All these findings suggest that ET, which is the most common movement disorder in adults, should not only be evaluated within the context of physical limitations but also within the psychosocial aspects as well. Further studies supporting this multidimensional evaluation will both shed a light on the etiopathology of the disorder as well as facilitating the treatment success.

### Limitations

The major limitation in our study was the limited number of subjects in patient and control groups. Apart from this, the strict inclusion criteria may be the cause of lack of intense anxiety, according to HAM-A, detected in any of our participants. The requirement in the Consensus statement of the Movement Disorder Society on Tremor for Definite Essential Tremor Diagnosis we used that necessitates the exclusion of psychogenic origin tremor may lead to evaluate all patients with intense anxiety and tremor as psychogenic, which in turn may cause exclusion of all patients with intense anxiety and ET. This may also be explained by the exclusion of antidepressant and neuroleptic users both in the patient and voluntary control groups in the study. In the study protocol, another limitation may be the fact that history and normal physical examination considered sufficient in the control group without any routine TFT tests and cranial MRI, different from the patient group.

**Ethics Committee Approval:** Ethics committee approval was received for this study from Sakarya University Faculty of Medicine Ethics Committee.

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept –BA, TA; Design – TA; Supervision –BA; Source- BA; Materials – TA; Data Collection and/or Processing – TA; Analysis and/or Interpretation – BA; Literature Search – BA; Writing Manuscript – BA, TA; Critical Review – BA, TA.

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