

# Prevalence of mood and/or anxiety disorders in patients with essential tremor: an integrative review

Ayssa Carneiro Castor de Vasconcelos<sup>1\*</sup>, Calil Darzé Neto<sup>2</sup>

<sup>1</sup>Escola Bahiana de Medicina e Saúde Pública. Discente no Departamento de Medicina, Salvador, BA, Brazil.

<sup>2</sup>Escola Bahiana de Medicina e Saúde Pública. Mestre, Professor Assistente de Neurologia, Salvador, BA, Brazil.

**\*Corresponding Author:** Ayssa Carneiro Castor de Vasconcelos, 1Escola Bahiana de Medicina e Saúde Pública. Discente no Departamento de Medicina, Salvador, BA, Brazil.

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## Abstract

**Introduction:** Essential tremor is a highly prevalent movement disorder worldwide. Characterized by tremors in the upper limbs, it can also affect other regions of the body and often compromises patients' ability to perform daily activities. The disease has a strong relationship with family history, commonly appearing between the second and sixth decades of life, and its prevalence is proportional to the population's age. While its pathophysiology is not entirely understood, several hypotheses exist, such as the neurodegenerative, GABAergic, and central oscillatory network hypotheses. Treatment options for this condition include pharmacological or surgical approaches. Although it was long considered a monosymptomatic disease, it is now known that essential tremor is correlated with psychiatric symptoms. These symptoms may arise from the condition's underlying pathophysiology or from the social stigma experienced by individuals due to the tremor, leading to anxiety and depression. Thus, studying the prevalence of these symptoms in this population is essential. **Objectives:** To describe the prevalence of mood and anxiety disorders in patients with essential tremor. **Methods:** A literature review was conducted using the databases PubMed, EMBASE, LILACS, Scielo and Pepsic. Cross-sectional studies, cohort studies, and clinical trials were included. Studies were excluded if the patients were not diagnosed with essential tremor according to the Movement Disorder Society criteria or if mood and anxiety disorders were not diagnosed according to the DSM-IV criteria. **Results:** Initially, 1,288 articles were identified, of which 4 met the eligibility criteria for this review. A significant association was found between the studied variables, with the prevalence of depression ranging from 15% to 27% and anxiety ranging from 16% to 42% in patients. **Conclusion:** The prevalence of mood and/or anxiety disorders in patients with essential tremor is higher than in healthy individuals.

**Keywords:** essential tremor; mood disorders; anxiety; prevalence

## Introduction

Essential Tremor is one of the most common movement disorders, with an estimated prevalence of about 1% in the general population [1]. It has a clinical diagnosis, defined as bilateral tremor of the upper limbs lasting at least three years, which may or may not involve other parts of the body, such as the head, vocal cords, and, less frequently, the lower limbs [2]. This condition can develop at any stage of an individual's life; however, it has peaks of onset around the ages of 20 and 60 years old. It often occurs in individuals with a family history of the disorder [1].

Studies on the pathophysiology of Essential Tremor consistently show a relationship between this condition and alterations in the cerebellar-thalamic-cortical circuit of affected individuals, and Purkinje cells are significant components in this dynamic, as they are involved in degenerative processes associated with the disease's development [1,3].

Essential Tremor typically has an insidious onset, worsening progressively over the years and its intensity may increase with stress and decrease with the use of small amounts of alcohol [1,2]. Treatment for this condition can be pharmacological or surgical. Propranolol and primidone are the first-line medications aiming to reduce tremor severity. Surgical treatment involves deep brain stimulation or thalamotomy [4].

On the other hand, Essential Tremor, which for a long time was considered to be a purely motor disease, has shown, through studies, a pattern with a varied spectrum of non-motor symptoms such as depression and anxiety [3,5,6], which may be due primarily to the neurodegenerative nature of the disease [7], and/or due to situations secondary to the embarrassment and shame experienced by patients as a result of tremor on occasions of social contact [8].

Thus, given the evidence in the literature demonstrating the presence of neuropsychiatric symptoms in patients with Essential Tremor, along with the lack of integrative reviews on this topic, this study aims to analyze the prevalence of mood and anxiety disorders in the described population.

## Materials And Methods

### Study design

The present paper is an Integrative Review of the literature on scientific bases, in which the prevalence of mood and anxiety disorders in people with essential tremor will be described.

### Search strategies

This review was conducted on November 9, 2023. Data collection was carried out in the electronic databases PubMed, Embase, LILACS, Scielo and PsychInfo by searching the combination of health descriptors and synonyms, evidenced by the Descriptors in Health Sciences (DeCS), Medical Subject Headings (MeSH) and Emtree, with the inclusion of works in English, Portuguese, Spanish and French. The terms to be searched, following a POT strategy as a guide for the integrative review, will be related to the population of interest (Essential Tremor) and related to the outcome (Mood Disorders OR Anxiety).

The search strategies and selection of studies followed the PRISMA protocol (Preferred Reporting Items for Systematic Reviews and Meta-Analyses).

### Inclusion and exclusion criteria

We included Articles published from 1998 onwards that fit the design of cross-sectional studies, cohort studies, or clinical trials, considering only the

baseline data in the latter two. Male and female patients aged 16 years or older diagnosed with essential tremor by medical evaluation according to the 1998 Movement Disorder Society criteria were included. These patients may come from the community or specialized centers. The endpoints, mood and anxiety disorders, should be diagnosed according to DSM-IV criteria onwards. Were excluded articles containing patients who, upon further analysis, were not diagnosed with essential tremor based on medical evaluation using the Movement Disorder Society (MDS) criteria, or whose prevalence data were not clearly defined or extractable.

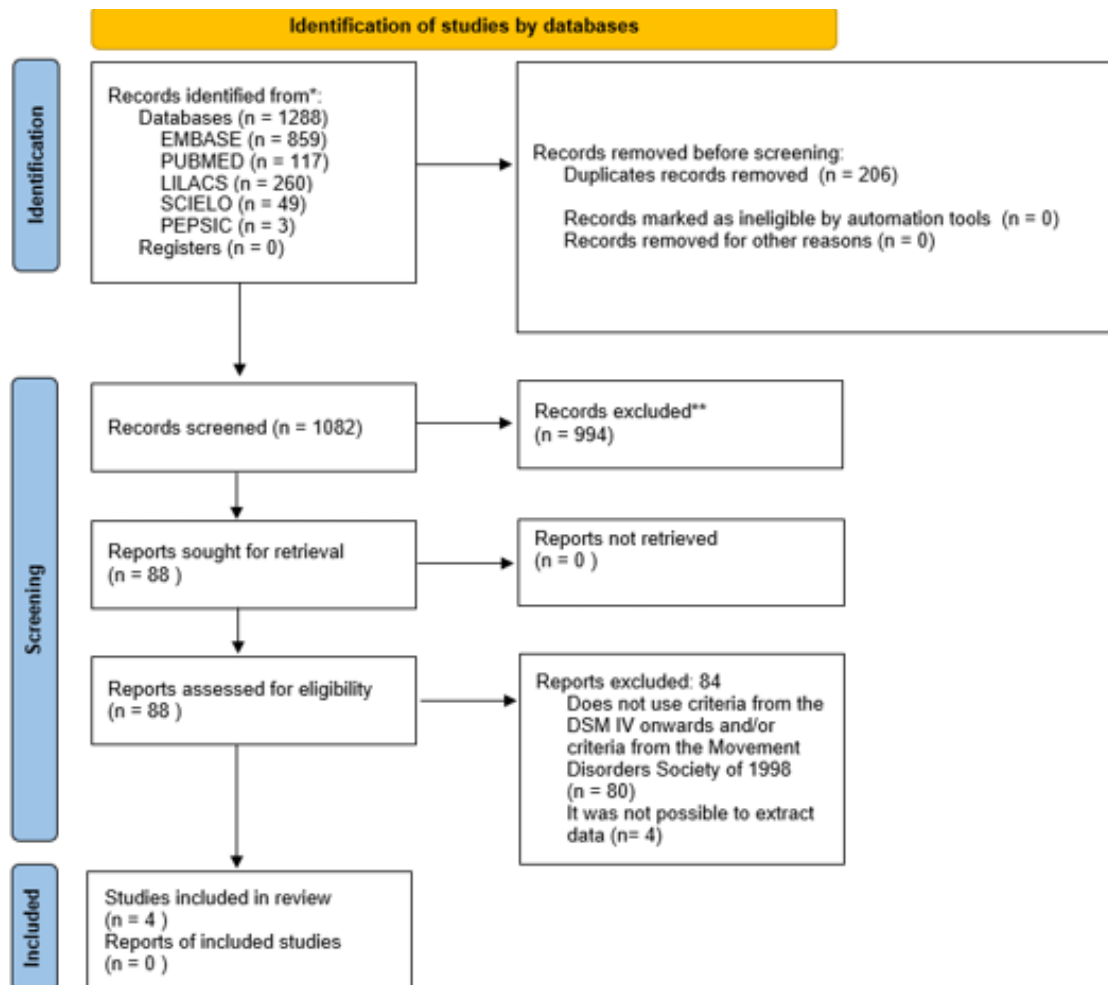
### Evaluation of the methodological quality of the selected articles

To assess the risk of bias, the critical tool for use in systematic reviews, JBI (Joanna Briggs Institute), was used for cross-sectional studies, in addition to cohort studies and randomized clinical trials, since only the baseline (cross-sectional) of the latter two will be used. Assessment of the risk of bias was not included as an exclusion criterion for the articles, but was useful for analyzing heterogeneity and studying subgroups.

## Results

### Identification and selection of studies

After an initial search of the PubMed, EMBASE, Scielo, LILACS and PsycINFO databases, 1288 articles were found, of which 1200 were excluded. Of these, 206 were duplicates, and 994 articles were excluded because they did not fit the study design or did not address the studied topic. A total of 88 articles remained for full-text reading, of which 84 were excluded for not meeting the eligibility criteria or for impossibility to extract the necessary data for the study.



**Figure 1:** Flowchart of article selection (according to PRISMA)

## Characteristics of the included studies

The general characteristics, including study designs and the diagnostic criteria for essential tremor, mood disorders, and anxiety disorders present in the selected journals, are listed in alphabetical order of author, year and country in Table 1.

All four included articles were published in English and the studies were conducted in Turkey [17], Latvia [19], Serbia [18] and Italy [20]. The studied populations consisted entirely of adults and elderly individuals, with sample sizes ranging from 37 to 63 patients. Three of the articles included patients followed up or investigated in Neurology departments and/or specialized centers for movement disorders as the authors described [17,19,20], while one article did not describe the study location [18].

The data was extracted from one clinical trial and three cross-sectional studies, totaling a sample of 190 patients. Major Depressive Disorder and Anxiety disorder were the main psychiatric conditions observed in the articles, being the topics studied in the review. Additionally, two of the articles also highlighted the presence of other psychiatric comorbidities. (17, 19) All the studies used the 1998 Movement Disorders Society criteria for

diagnosing essential tremor, and one of them described the additional use of the Fahn, Tolosa, Marin Tremor Rating Scale [19].

Regarding mood and anxiety disorders, all authors used DSM-IV criteria onwards, with the aid of scales to screen for psychiatric symptoms, such as the Symptom Check List (SCL-90R), General Symptom Index (GSI), Structural Clinical Interview-Nonpatient (SCID-NP), Depression Anxiety Stress Scale (DASS), Beck Depression Inventory – 2nd Edition (BDI II), Social Interaction Anxiety Scale (SIAS), Social Phobia Scale (SPS), State-Trait Anxiety Inventory form Y (STAI test), Structured Clinical Interview (SCID-I and SCID-II), Hamilton Depression Rating Scale (HDRS), Hamilton Anxiety Rating Scale (HARS), Mini Mental State Examination (MMSE), and Millon Clinical Multiaxial Inventory III (MCMI III).

As far as the quality of the studies is concerned, none of them completed the items proposed by the checklist of the JBI (Joanna Briggs Institute) critical tool for use in systematic reviews. The articles with the lowest risk of bias were those by Fabbrini et al. (2021) [20], followed by Smeltere et al. (2017), conducted in Latvia [19].

Author, Year, Country	Study design	Study location	Diagnostic Criteria for Essential Tremor	Diagnostic Criteria for Mood Disorders and Anxiety Disorders	Relationship between essential tremor and mood and/or anxiety disorders
Fabbrini et al. (2021). Itália.	Cross-sectional study	Outpatient clinic at the Department of Neurology and Psychiatry, “Sapienza” University of Rome	1998 Movement Disorders Society diagnostic criteria	DSM IV/ Structured Clinical Interview (SCID-I e SCID-II)	The prevalence of mood and anxiety disorders secondary to essential tremor was analyzed
Günel et al. (2001). Turquia	Clinical trial	Movement disorder outpatient clinic of a University Hospital	1998 Movement Disorders Society diagnostic criteria	DSM IV/ Symptom Check List (SCL-90R), General Symptom Index (GSI) e Structural clinical interview-nonpatient (SCID-NP)	The psychiatric evaluation of the patients was frequently pathological; however, there was not enough data to estimate whether the pathologies were secondary to essential tremor
Smeltere et al. (2017). Letônia	Cross-sectional study	Neurology Outpatient Center at Pauls Stradiņš Clinical University Hospital and the Consulting Room for Parkinson’s Disease and Other Movement Disorders at Health Center 4	1998 Movement Disorders Society diagnostic criteria	DSM V/ Depression Anxiety Stress Scale (DASS), Beck Depression Inventory – 2ª edição (BDI II), Social Interaction Anxiety Scale (SIAS), Social Phobia Scale (SPS), State-Trait Anxiety Inventory form Y (STAI test)	Mood and anxiety disorders were analyzed as personality traits and secondary to essential tremor
Tomic et al. (2012). Sérvia.	Cross-sectional study	Not described	1998 Movement Disorders Society diagnostic criteria	DSM IV/ Hamilton Depression Rating Scale (HDRS), Hamilton Anxiety Rating Scale (HARS), Mini Mental State Examination (MMSE), Millon Clinical Multiaxial Inventory III (MCMI III)	The prevalence of mood and anxiety disorders secondary to essential tremor and as pre-motor symptoms was analyzed

**Table 1:** Characteristics of studies included in this review

Prevalence of Mood Disorders, Anxiety Disorders and characteristics of the study population

The most commonly described psychiatric disorders in the articles were mood and anxiety disorders, with the former varying between 15% and 27%

of patients, and the latter between 16% and 42%. Günel et al. also identified conditions such as dysthymia and social phobia in a percentage of the studied population. Additionally, Smeltere et al. also reported the presence of social phobia in a considerable percentage of their population sample. Furthermore, their study compared anxiety symptoms as a personality trait or secondary to

essential tremor, with the anxiety state secondary to the disease prevailing over anxiety as a personality trait in 37.5% of patients (19, 20).

Regarding the demographic characteristics of the participants in the selected studies, Günel et al. [17] conducted the study with patients of both sexes, including 32 men and 18 women, with a mean age of 52.2 years (range: 18–75 years). In this study, the average disease duration was 6.2 years (range: 3–25 years) [17].

Smeltere et al. [19] recruited 40 patients, 26 of whom were female. The mean age of the participants was 52.05 years with a standard deviation of  $\pm 20.18$ . The author did not describe the duration of essential tremor or the age of onset [19].

Fabbrini et al. [20] conducted the study with 37 patients, 21 of whom were male, with a mean age of 66.5 years and a standard deviation of  $\pm 9.9$ . The author also reported the age of onset of the tremor, which was 48.9 years

with a standard deviation of  $\pm 16$ , and the mean disease duration, which was 17.7 years with a standard deviation of  $\pm 15.3$  [20].

Tomic et al. [18] selected 63 patients, but it was not possible to extract sex-specific data. The mean age of the participants was 66.5 years with a standard deviation of  $\pm 14.9$ , and the mean disease duration was 16.3 years, with a standard deviation of  $\pm 13.8$  [18].

None of the studies described the race/color of the participants, and only Fabbrini et al. [20] reported the educational level of the patients, which averaged 13.8 years of schooling with a standard deviation of  $\pm 4.2$  [20]. Regarding the tremor location in patients, only Günel et al. [17] reported these data in the study, noting that all 50 patients exhibited hand tremors, with 5 patients also presenting head tremors and 3 with voice tremors [17].

Table 2 describes the psychiatric disorders reported in the studies reviewed and the characteristics of the population sample.

Author, Year, Country	Sex (male/female)	Age (years) summarized	Educational level of the population	Race/ethnicity	Age of essential tremor onset (years)	Location of essential tremor	Frequency of mood disorder	Frequency of anxiety disorders
Fabbrini et al. (2021). Itália.	37 patients: 21 men and 16 women	Mean age 66.5 $\pm$ 9.9	Years of education 13.8 $\pm$ 4.2	Not reported	Age of tremor onset: 48.9 $\pm$ 16 Mean disease duration: 17.7 $\pm$ 15.3	Not reported	10 patients (27%)	6 patients (16%)
Günel et al. (2001). Turquia	50 patients: 32 men, 18 women	Mean age 52.2 (18-75)	Not reported	Not reported	Mean disease duration of 6.2 years (3-25)	Tremor nas mãos – 50 pacientes  Tremor adicional na cabeça – 5  Tremor adicional na voz – 3 pacientes	Episodes of Major Depressive Disorder in the past – 19 patients (38%) Dysthymia – 6 patients (16%) Social Phobia – 9 patients (18%)	Anxiety disorder – 21 patients (42%)
Smeltere et al. (2017). Letônia.	40 patients - 26 women (65%), 14 men (35%)	Mean age 52.05 (standard deviation $\pm$ 20.18)	Not reported	Not reported	Not reported	Not reported	Major Depressive Disorder - 15%	Disease-related anxiety prevailed in 37.5% of the patients
Tomic et al. (2012). Sérvia.	63 patients – sex distinction not described	Mean age 66.5 $\pm$ 14.9	Not reported	Not reported	Mean disease duration 16.3 $\pm$ 13.8	Not reported	23,3%	33,3%

**Table 2:** Characteristics of the studies regarding the patient sample

## Discussion

In this integrative review, the prevalence of depression, the main mood disorder assessed, ranged from 15% to 27% of patients. Regarding anxiety disorders, the range was 16% to 42%. All studies included in this work used the 1998 Movement Disorders Society criteria for the diagnosis of essential tremor, although the scales used to measure tremor severity varied among authors. Similarly, all studies used DSM-IV or (DSM-)V criteria to diagnose mood and anxiety disorders, despite differences in the scales used to screen psychiatric symptoms and assess their severity. Anxiety and depression rates were higher in the essential tremor population compared to control groups, raising some hypotheses for this finding, such as the involvement of brain regions responsible for emotional control due to the disease [3,8], tremor in social situations causing discomfort and embarrassment in the individual, and the psychological burden of living with a chronic condition.

Fabbrini et al. identified a significant number of psychiatric disorders in patients with essential tremor especially depression [20]. In this study, it was

reported that anxiety and/or depression started after the onset of the motor symptom in 65% of the cases, a finding that converges with another study which points to the presence of greater psychological stress in patients with chronic diseases, showing that these individuals are 1.5 and 1.8 times more likely to report depression and anxiety, respectively, when compared to a healthy population. This may be because patients have to deal with the challenges and particularities that their illness imposes on them [21]. Drawing a parallel with the present study, essential tremor, as a chronic disease, has manifestations that patients have to live with and deal with, directly impacting on their routine and may predispose them to the development of psychiatric symptoms [22].

The authors also showed a relationship between an increased frequency of mood disorders and the presence of a family history of essential tremor in the patients in the study, suggesting that depression may be part of the clinical spectrum of essential tremor, at least in cases of a positive family history. However, this higher prevalence may occur because these patients, due to their family history, have a greater knowledge of the disease and,



consequently, a greater inclination to develop psychiatric disorders in the face of the situation experienced [20].

Smeltere et al. also found non-motor symptoms in their study population. The Beck Depression Inventory revealed that 79.49% of essential tremor patients presented depressive symptoms at varying levels of severity, with 15% meeting criteria for major depressive disorder [19]. Similarly, Günel et al. identified psychopathology in 76% of essential tremor patients, with 38% reporting past major depressive episodes. However, after psychiatric evaluation, the author concluded that these individuals did not meet the criteria for the reported pathology and were diagnosed with dysthymia per DSM-IV criteria [17], characterized by chronically depressed mood lasting most of the day for at least two years, with symptom-free intervals not exceeding two months [23]. Tomic et al. found a prevalence of 47.8% for psychiatric manifestations in essential tremor patients, with 23.3% corresponding to depression [18].

Regarding anxiety disorders, these were measured using different instruments, which may explain the variation in the percentages found, which ranged from 16 to 42%, or even more than double depending on the study evaluated. Although there are no studies comparing all the scales used in the studies included in this review, it is possible to infer that this difference is due to the variation in sensitivity between them to identify anxiety, as well as the experience of the evaluator and the way the questions were applied. With the Social Interaction Anxiety Scale and Social Phobia Scale, used in the study conducted by Smeltere et al., the authors pointed out that patients with essential tremor tend to exhibit anxious symptoms, since they have shown to be more concerned about tremor when they are being seen by other people and nervous when they have to speak in front of them or in a position of authority, as well as distress in social interactions [19].

Additionally, these authors correlated the severity of tremor with the manifestation of social phobia, supporting the hypothesis that the emotional state can imply changes in the intensity of tremor and vice-versa. Consequently, Smeltere et al. put forward the hypothesis that social phobia plays a role in influencing tremor in patients as a factor that can increase its amplitude [19]. This hypothesis is corroborated by another study, in which treatment for anxiety combined with anti-tremor medication showed the best results, with a 29.2% reduction in the intensity of the motor symptom [17].

In addition to this hypothesis, the study carried out by Tomic et al. found that 25% of patients with essential tremor and psychiatric symptoms had psychiatric manifestations before their motor symptoms, most of which were depression and anxiety [18]. Based on this, the authors suggested that these psychiatric symptoms may be part of the clinical spectrum of essential tremor as premotor manifestations, suggesting that this disease is not monosymptomatic [18].

These findings are not unanimous. Fabbrini et al. noted that anxiety frequency was similar between essential tremor patients and controls without tremor. However, they emphasized that these results are inconclusive due to the limited statistical power of the sample [20]. Furthermore, these authors found no relationship between essential tremor duration or severity and the development of psychiatric disorders. While highlighting that 65% of patients developed these disorders after the onset of tremor, the age of onset for depressive and anxious symptoms was similar between essential tremor patients and controls. This led the authors to conclude that these disorders might not be part of the clinical spectrum of essential tremor but rather a non-specific consequence of the chronic neurological condition [20]. Günel et al. also underscored this ambiguity, stating that while psychiatric evaluations often reveal abnormalities in these patients, it remains unclear whether these are secondary to the tremor [17].

Given this ambiguous context and the lack of an assertive body of evidence to indicate whether psychiatric alterations are part of the clinical picture of essential tremor, or are associated with it, or occur independently, being related to sociodemographic, geographical and/or genetic factors, other studies not selected in this systematic review sought to answer this question.

One of these studies, carried out on Egyptian patients with essential tremor, analyzed the presence of non-motor symptoms in two groups: one group aged over 45 and the other under 45. As a result, it was found that, when compared to their respective comparison groups (without essential tremor), the younger patients had a significant tendency to develop depression, while those in the older group had higher rates of already diagnosed depression [22]. This finding seems to indicate that depression has a higher incidence in patients with essential tremor and may also be directly proportional to advancing age, since there is a tendency for motor symptoms to worsen as the disease progresses.

The study by Huang et al. found that anxiety is present more frequently in female patients with essential tremor. This condition is known to be a risk factor for the development of anxiety symptoms [5]. This is due to genetic differences between the genders, psychosocial and cultural factors. Similarly, a Chinese study also pointed out that women are more likely to develop social anxiety and added that this may be due to hormonal effects and the habit of caring more about their personal image in public, leading to greater embarrassment in the face of tremor [24]. Therefore, these studies seem to indicate that the phenomenon of anxiety disorders follows, in patients with tremors, what is observed in the general population.

Additional factors, such as geographic location, may also influence mood and anxiety disorder prevalence. Dingwei et al. highlighted that depression rates in the United States were significantly lower compared to studies in China and Spain, potentially due to cultural, socioeconomic, and environmental differences [25]. Similarly, Smeltere et al. noted higher depression prevalence in Latvia compared to Spain, likely influenced by historical, sociopolitical, economic, and comorbid factors [19].

Finally, Smeltere et al. pointed out that psychiatric conditions such as depression and anxiety are poorly recognized in routine consultations with patients with movement disorders, since no tests are carried out to look for them. They therefore suggested adapting the clinical interview to a neuropsychiatric approach in order to better track these symptoms associated with tremor [19]. This research should be carried out given that the association between essential tremor and higher rates of depression and anxiety is notorious, since both the impairment of the cerebello-thalamo-cortical circuit in the pathophysiology of the disease and the neurodegenerative theory can also lead to an impairment of regions of the brain corresponding to emotional regulation and, consequently, the emergence of psychiatric symptoms [3,8]. In addition, the social component involving the embarrassment and discomfort caused by tremor in front of other people and the impact on patients' quality of life can contribute to the development of depression and anxiety.

## Conclusion

It is concluded that the prevalence of mood disorders and/or anxiety in patients with essential tremor is high and statistically significant, exceeding that observed in healthy populations. This finding underscores a meaningful relationship between these conditions, highlighting the need to systematically evaluate psychiatric symptoms during consultations with patients experiencing movement disorders. Such an approach can ensure more comprehensive and effective treatment, addressing both motor and non-motor aspects of the disease.

However, further studies are needed to clarify the nature of this relationship. It is essential to determine whether mood and anxiety disorders are secondary to essential tremor, part of its clinical spectrum, or associated with independent factors. New research with larger samples and standardized methods could help answer these questions and improve the clinical management of these patients.

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