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Non-motor features of essential tremor, Updated review of evolving aspects

Gharib Fawi, Hazem K Elhewag, Mohamed Nasreldin Thabit, Ahmed Ezzat Amin

Department of Neurology and Psychological medicine, Faculty of Medicine, Sohag University

Abstract

Essential tremor (ET) is defined as an action tremor syndrome with a duration of more than three years in both upper limbs with or without tremor in other areas and with no other neurological signs. ET's non-motor characteristics add to the evidence of clinical variability in ET, a disease with a wide range of pathological and etiological characteristics. Problems in frontal–executive function, comparable to Parkinson's disease (PD), were one of the most common patterns of cognitive affection in ET. ET individuals who started tremor after the age of 65 were 64 to 70% more likely than control subjects to develop dementia, but ET cases who started tremor before the age of 65 have an equal chance to develop dementia as controls. Depression rates were considerably higher in ET than controls and more severe depression is found. A strong evidence linking anxiety and ET. Many studies have documented sleep disturbances in ET.

Keywords: essential tremor, non-motor features, cognition, depression, anxiety, sleep disturbances.

Introduction:

Essential tremor (ET) is defined as an action tremor syndrome with a duration of more than three years in both upper limbs with or without tremor in other areas like head, voice, lower limbs, and/or trunk and with no other neurological signs like dystonia, ataxia, and/or parkinsonism) [1].

Rest tremors may develop in advanced E T, but they do not subside following pur poseful movements which differentiates ET from parkinsonian tremor [2]. The non-motor features of ET contribute to the evidence of clinical heterogeneity in ET, an illness with heterogeneity in pathological and etiological features [3].

Cognition:

ET has been linked to a wide range of levels of cognitive functions, from normal cognition to dementia, according to numerous research [4-6].There is growing evidence that ET patients progress to mild cognitive impairment (MCI) and dementia at a faster rate than age-matched controls despite that the majority of ET patients perform within the normal cognitive spectrum [5, 7].

Gasparini et al. were among the first to discover that ET patients had severe frontal function impairments when compared to healthy controls [8]. In a recent case-control observational study on ET

cases and matched healthy controls from Egypt were examined, and it was shown that patients with ET have significant cognitive dysfunction [9]. One of the most prominent patterns of cognitive affection in ET was problems with frontal–executive function, which are similar to Parkinson's disease (PD) [8] as well as those involving visual attention [10], verbal fluency, naming, mental set shifting, verbal memory, working memory [11], complex auditory attention, visual attention and response inhibition, recall of a word list, verbal fluency, visual confrontation naming, verbal fluency, immediate word list recall, semantic encoding, and facial matching [12].

ET individuals who started tremor after the age of 65 were 64 to 70% more likely than control subjects to develop dementia, but ET cases who started tremor before the age of 65 have an equal chance to develop dementia as controls [5]. In the same context, an older-onset ET also was connected to a slight but statistically significant increase in the risk of MCI in a recent study, whereas younger-onset ET was not [4].

The basis for cognitive dysfunction in ET is unclear. The role of the cerebellum in cognition is more and more becoming well established [13, 14]. According to (the dysmetria of mind) idea, the cerebellum regulates the pace, consistency, capacity, and appropriateness of mental or cognitive processes, much as it regulates the rate, rhythm, force, and precision of motions[14], this could give an explanation for the cerebellum's role in cognitive processes. In a study by Stoodley et al., the hypothesis was tested by the fact that lesions in the posterolateral cerebellum cause the Cerebellar cognitive affective syndrome (CCAS; Schmahmann's syndrome) using voxel-based lesion-symptom mapping [15]. They found that patients with CCAS had damage to posterior lobe regions, with lesions resulting in affected scores on tests for language, spatial, and executive function even if they did not have cerebellar motor syndrome [15]. All of the above-mentioned data suggest the role of cerebellum which is the main site of pathological changes in ET in producing cognitive dysfunction [16-18].

Another explanation for ET's MCI and dementia came from postmortem examinations, which revealed that ET's brains had more Alzheimer's type alterations than age-matched control brains [19]. Alzheimer's disease affects the majority of ET patients who develop dementia, and the risk of Alzheimer's disease is substantially higher in ET patients, according to epidemiological studies [5, 20].

Depression*:*

Lombardi et al. were among the first to study depression in ET using the Geriatric Depression Scale to assess depression in 18 individuals with ET. They discovered that individuals had severe depression that did not correlate to the degree of their tremors [11]. Depression scores were considerably higher in ET than controls in an Indian research of 50 ET cases and 50 controls [21]. A study employing Beck Depression Inventory scores yielded the same outcome [6]. A significant prevalence of depression (more than half of cases) was discovered in a recent study in China, in particular women, cases with head or voice tremors, and those having significant functional impairment [22].

Higher depression levels were linked to more severe tremors [23, 21]. Some studies have discovered a link between depression and the total Fahn-Tolosa-Marn Tremor Rating Scale, which includes overall tremor as well as a self-reported functional impairment score, implying

that depressive symptoms could be a secondary response to tremor not a primary feature of the disease [24, 25]. A point of much debate about this is that others found no relation between depression and tremor severity [26].

Anxiety:

A strong evidence linking anxiety and ET. In an Egyptian community research involving 30 ET patients, who were shown to be more anxious than controls using Hamilton anxiety rating scale [9]. In a research involving 40 ET patients, using unilateral thalamic DBS for ET treatment, patients showed lower anxiety levels (measured by mood state) 3 and 12 months following surgery [27]. The relation between anxiety and ET severity is a matter of debate. Some studies found a correlation [28, 29], and others showed no correlation [30].

Sleep disturbances:

Many investigations have established the presence of sleep problems in ET patients in the last few years [6, 24, 31-35]. Because of the probable importance of the locus calculus in sleep regulation, Lewy body depositions in this area are higher in ET patients' postmortem brains than in control brains, which could be linked to the development of sleep problems in this disease [36].

This includes excessive daytime sleepiness [37, 38-40], rapid eye movements behavior disorder [41,42], restless leg syndrome [43, 44].

Conclusion

Non-motor features of ET have underestimated aspects of the disease which adds a significant burden on the patient besides the motor features. The cognitive issues in ET involve rapid progression f rom MCI to dementia and frontal lobe dysfunction. More prevalent depression and anxiety in ET cases is a well-established finding in many studies. Sleep disturbances in ET may be explained by the pathological changes in found the brain stem of ET cases. We recommend further studies on these and other non-motor features in ET.

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