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REVIEW

Linking Essential Tremor to the Cerebellum: Clinical Evidence

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Abstract Essential tremor (ET) might be a family of diseases unified by the presence of kinetic tremor, but also showing etiological, pathological, and clinical heterogeneity. In this review, we will describe the most significant clinical evidence, which suggests that ET is linked to the cerebellum. Data for this review were identified by searching PUBMED (January 1966 to May 2015) crossing the terms "essential tremor" (ET) and "cerebellum," which yielded 201 entries, 11 of which included the term "cerebellum" in the article title. This was supplemented by articles in the author's files that pertained to this topic. The wide spectrum of clinical features of ET that suggest that it originates as a cerebellar or cerebellar outflow problem include the presence of intentional tremor, gait and balance abnormalities, subtle features of dysarthria, and oculomotor abnormalities, as well as deficits in eye-hand coordination, motor learning deficits, incoordination during spiral drawing task, abnormalities in motor timing and visual reaction time, impairment of social abilities, improvement in tremor after cerebellar stroke, efficacy of deep brain stimulation (which blocks cerebellar outflow), and cognitive dysfunction. It is unlikely, however, that cerebellar dysfunction, per se, fully explains ET-associated dementia, because the cognitive deficits that have been described in patients with cerebellar lesions are generally mild. Overall, a variety of clinical findings suggest that in at least a sizable proportion of patients with ET, there is an underlying abnormality of the cerebellum and/or its pathways.

Keywords Essential tremor · Cerebellum · Clinical

Introduction

Essential tremor (ET) is the most common of the 20 known tremor disorders and is also one of the most common neurological disorders among adults [1–3]. ET is a widespread condition, affecting people of all races and cultures, from the remote Araihazar, Bangladesh, to the urban area of Madrid, Spain (NEDICES study) [1, 4]. Its most recognizable clinical feature is a 4–12-Hz kinetic tremor of the arms (i.e., tremor during voluntary movement), which often is later accompanied by head and voice tremors [5–8]. The traditional view of ET as a monosymptomatic condition is being replaced, as a spectrum of clinical features is increasingly being documented. These features comprise both motor and non-motor elements, including gait abnormalities [9], parkinsonism [10], cognitive impairment [11–13], dementia [14, 15], personality disturbances [16], depressive symptoms [17], sensory abnormalities (e.g., mild olfactory dysfunction and hearing impairment) [18–20], voice disturbances [21], and sleep disorders [22]. The emerging view is that ET might be a family of disease unified by the presence of kinetic tremor, but also showing etiological, pathological, and clinical heterogeneity [5–8].

The idea that ET is linked to the cerebellum is not novel. In the landmark paper by Critchley and Greenfield, published in 1949, the authors wrote: "Although anatomical proof is as yet lacking, there are at least a number of clinical points to make

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question whether 'essential tremor' may not, at times any rate, represent an incomplete or a premature variant of one of the cerebellar atrophies" [23]. Although not further elaborated on by those authors, these clinical characteristics include its insidious onset, association with advanced aging (i.e., both prevalence and incidence rates increase with age), gradually progressive nature, and the presence of "cerebellar" features (e.g., intention tremor and ataxia) on examination [23]. Indeed, these are many of the clinical features typical of neurodegenerative diseases of the cerebellum [24].

In this review, we will describe the most significant clinical evidence, which suggests that ET is linked to the cerebellum.

Methods

Data for this review were identified by searching PUBMED (January 1966 to May 2015) crossing the terms "essential tremor" (ET) and "cerebellum," which yielded 201 entries, 11 of which included the term "cerebellum" in the article title. This was supplemented by articles in the author's files that pertained to this topic. Of note is that a recent review of the 100 most cited papers on ET revealed that only one was related to the cerebellum [25, 26].

Clinical Evidence That Links Essential Tremor to the Cerebellum

Intention Tremor

Tremor is an involuntary, rhythmic, muscle movement involving oscillations of one or more parts of the body, resulting from repeated contraction and relaxation of opposing muscle groups [5–7]. Tremor can be classified according to the consensus statement of the Movement Disorder Society [27]. Tremor at rest is separated from action tremor, which is produced by voluntary muscle contraction. Action tremor includes postural, isometric, and kinetic tremors, and the latter form including intention tremor [27].

Canonically, the dominant clinical feature of ET was considered to be a "postural tremor not made strikingly worse during action" (i.e., tremor while the arms are outstretched against gravity) [28]. However, growing evidence point to a kinetic tremor (i.e., tremor during voluntary motion), affecting mainly the arms and hands, which often is later accompanied by head and voice tremors, as the primary type of tremor in ET [29–31]. Kinetic arm tremor occurs during any voluntary movement, including pouring water into a cup, drinking from a cup, eating with utensils, or drawing Archimedes' spirals [5–8]. The kinetic tremor in ET often has an intentional component; for instance, during visually guided movements, such as the finger-to-nose maneuver, the amplitude of the tremor increases as the target is approached [5–8]. This characteristic provides further support for an abnormality of cerebellar function in ET. Kinetic tremor leads to difficulties with eating, drinking, writing, dressing, and various other activities of daily living [5–8]. The intentional component of kinetic tremor in ET is usually more evident in more advanced ET cases and may occur in approximately one in three ET cases [32, 33]. In a quantitative analysis of a grasping movement, involving two subgroups of ET patients (one with predominant postural tremor and another with intention tremor), and two control groups (one with cerebellar disease and another of normal subjects), the amplitude measurements of intention tremor were clearly abnormal and of comparable magnitude for ET patients with intention tremor and those with cerebellar disease [32]. The occurrence of intention tremor therefore suggests abnormalities of cerebellar functions in ET [32].

Gait and Balance Abnormalities

Gait and balance abnormalities in ET patients have been described in a number of studies; these abnormalities include slower gait speed [34–36], impaired dynamic balance (indicated by greater number missteps) [36–39], gait asymmetry [36], and balance impairment during tandem walk [36]. Unlike controls, significant correlations between older age and quantitative gait measures have been described [36, 39, 40], suggesting that the effect of age on ET-related gait abnormalities is more obvious than in a healthy population, even in advanced ages. Moreover, ET patients report greater subjective functional gait, experiencing more fear of falls and near falls than controls [41], which indicates that gait and balance problems in ET are not merely a subclinical phenomenon. However, no increased stride-to-stride variability—considered an important hallmark of cerebellar pathology—has been found in ET patients [34, 36, 42], suggesting that the changes in ET are not as advanced as those seen in the cerebellar ataxias.

Although early studies failed to find an association between impairments of balance and gait and tremor severity in ET patients [37, 43, 44], more recent studies have consistently revealed significant correlations between tandem gait abnormalities and the severity of intention tremor of the hands [42], hands and legs [35], and cranial tremors involving the neck, jaw, and voice [9, 39, 41]. The finding that the subgroup of ET patients with head tremor is the most functionally impaired [9, 41] is consistent with a voxel-based morphometry magnetic resonance imaging (MRI) study [45], which demonstrated atrophy of the cerebellar vermis, especially in ET patients with head tremor, and one postmortem analysis that revealed more vermal Purkinje cell axonal swellings in ET patients than in controls, with the highest vermal torpedo counts in ET cases with voice, jaw, and neck tremors [46]. Taken together, these results suggest that ET-related

abnormalities of balance and gait found may correspond to lesions of the medial regions of the cerebellum that play a primary role in the control of balance and locomotion [47].

Dysarthria

Subclinical signs of dysarthria (increased syllable duration) may be seen in a subset of patients, which would suggest that ET is associated with an impairment of the cerebellum [48].

Oculomotor Abnormalities

Deficits of pursuit initiation that correlate with the intensity of intention tremor, and pathological suppression of the vestibulo-ocular reflex have been reported in ET patients [49]. These oculomotor deficits may indicate an impairment of the caudal vermis in ET. [49]

Eye–Hand Incoordination

In a study on eye–hand coordination, abnormal kinematic changes in the early phase of pointing movements have been reported in ET patients [50]. In contrast to normal subjects, ET patients' saccadic latency did not decrease during combined eye–hand movements compared with saccades performed in isolation [50]. In addition, hand movements had a longer duration in ET patients, with decreased peak acceleration, an increased latency of the peak velocity, and peak deceleration [50]. Altogether, these changes suggest an underlying abnormality of the cerebellum and/or its pathways [50].

Motor Learning Deficits

Disordered acquisition and retention of the classically conditioned eyeblink response—a well-established model to study motor learning—has been described in ET patients, providing further evidence that ET is caused by a functional disturbance of olivo-cerebellar circuits, which may cause cerebellar dysfunction [51].

Incoordination During Spiral Drawing Task

The Spiral Width Variability Index (SWVI) is a graphonomic measure of the variability around an ideal trajectory, which may be increased in patients with cerebellar pathology [52, 53]. The finding that ET cases exhibit higher SWVI than controls and that higher SWVI scores correlated not only with more severe kinetic tremor but also with the presence and severity of other cerebellar signs in ET (e.g., intention tremor and tandem gait mis-steps) provides additional support for the notion that the underlying pathology in ET is at least in part cerebellar [54].

Motor Timing and Visual Reaction Time

ET patients present significantly impaired motor performance, at least in some tasks, such as rapid repetitive finger movements (finger tapping and frequency) and visual reaction time than normal controls, suggesting a severe deficit of event-based rhythm generation on both sides in ET [55, 56]. The finding that both spinocerebellar ataxia and ET patients are significantly worse at intercepting moving target than are patients with early Parkinson's disease and normal controls suggests that the cerebellum may play an essential role in integrating incoming visual information with motor output in a timely manner [57].

Impairment of Social Abilities

Cognitive aspects of the theory of mind have been reported to be selectively impaired in ET patients [58]. Theory of mind is the ability to attribute mental states (beliefs, intents, desires, pretending, and knowledge) to oneself and others, and to understand that others have beliefs, desires, and intentions different from one's own, and thus, it may be regarded as an essential prerequisite for successful human social interaction [59]. The dorsolateral prefrontal cortex is anatomically and functionally connected with the posterior lobule of neocerebellum [60], and this neural circuit is thought to be involved in several cognitive functions [61, 62], including social cognition [63]. Based on these facts, the selective impairment of cognitive theory of mind found in ET patients might be conceived of as a further consequence of dysfunctional dorsolateral prefrontal cortex–cerebellum circuit [58].

Improvement in Tremor After Cerebellar Stroke

Vascular lesions of cerebellar–thalamic–cortical pathway have been reported to improve the tremor of ET patients [64–66]. There are anectodical cases of ET patients in whom tremor improved or disappeared after stroke. There are several described cases in the literature. For example, an ET patient in whom tremor disappeared on the right side after a homolateral cerebellar infarct has been reported [64]. In another case, an ET patient improved after a sensorimotor stroke related to a small cortical infarct near by the left precentral region of the brain [66]. Finally, the unilateral tremor of an ET patient with a large area of damage in the right hemisphere, as a result from two strokes, disappeared in the left arm after the second stroke [65]. Contrary to the previous observations, lesions of the cerebellum may also trigger ET. For example, a patient who developed ET ipsilateral to cerebellar hemispherectomy has been described [67].

Table 1 Summary of main studies that link essential tremor to cerebellum

	Authors	Number of patients	Main results	Links to cerebellar-like disorder
Gait and balance abnormalities	Louis et al. [9]	122 ET patients	Number of tandem mis-steps increased markedly with cranial tremor score	Tandem gait difficulty and cranial tremors may be both symptomatic of a disturbance of cerebellar regulation of the midline
	Earhart et al. [34]	13 ET patients with bilateral DBS versus 13 controls	ET walked more slowly and had lower cadence and lower tandem relative to control	ET patients present cerebellar-like gait difficulties
	Fasano et al. [35]	11 ET patients treated with DBS versus10 controls.	(1) ET had more mis-steps and slower gait velocities during stimulation off and supra-therapeutic stimulation than during stimulation on; (2) improvements in ataxia were not a function of reduced tremor in the lower limbs or torso	The cerebellar movement disorder of ET is due to a typical cerebellar deficit, not to t rembling extremities
	Rao et al. [36]	104 ET subjects versus 40 controls	ET showed deficits related to gait speed, dynamic imbalance, and gait asymmetry under both standard and tandem walk on level ground	ET patients present cerebellar-like gait abnormalities
	Singer et al. [37]	36 ET patients versus 40 controls	ET patients exhibited tandem gait abnormalities compared to controls.	
	Hubble et al. [38]	40 ET patients versus 40 controls	ET patients showed significantly more mis-steps when tandem walking in comparison to controls	
	Hoskovcova et al. [39]	30 ET patients versus 25 controls	(1) ET patients showed lower tandem gait velocity, more mis-steps, and increased postural sway in tandem stance; (2) the step width of normal gait correlated with midline tremor subscore	Abnormalities of balance and gait may correspond to lesions of the medial regions of the cerebellum
	Stolze et al. [42]	25 ET patients (10 PT, 15 IT) versus 8 patients with cerebellar diseases versus 21 controls	1) ET patients showed abnormalities in tandem gait with an increased number of mis-steps and an ataxic and dysmetric gait; (2) the gait disorder was much more pronounced in the IT group	ET-related gait difficulties were indistinguishable from those of the cerebellar diseases group
	Kronenbuerger et al. [48]	25 ET patients (8 ETpt; and 7 ETc) versus 25 controls	(1) ET patients exhibited an increased number of mis-steps and shortened stride length with tandem gait; (2) ETc patients had increased postural instability in dynamic posturography conditions	ETc, but not ETpt patients exhibited significantly increased syllable durations
Eye movements abnormalities	Helmchen et al. [49]	14 ET patients (6PT , 8 IT) versus11 controls	ET patients showed an impaired smooth pursuit initiation as well as pathological suppression of the VOR time constant by head tilts (pathological VOR dumping)	(1) IT patients were significantly more affected than PT patients; (2) the oculomotor deficits may indicate an impairment of the caudal vermis in ET
Eye-hand coordination	Trillenberg et al. [50]	12 ET patients versus 14 controls	(1) ET patients revealed abnormal kinematic changes in the early phase of pointing movements; (2) ET patients did not have saccadic dysmetria	Pathological kinematic hand parameters would indicate a cerebellar disorder that is probably independent of saccadic behavior and spares the oculomotor posterior vermis
Motor learning deficits	Kronenbuerger et al. [51]	23 ET patients versus 23 controls	The ability to acquire conditioned eyeblink responses was significantly reduced in ET patients	Evidence of motor learning deficits strengthens the hypothesis of olivo-cerebellar

Table 1 (continued)

	Authors	Number of patients	Main results	Links to cerebellar-like disorder
				involvement in ET
Motor incoordination	Louis et al. [54]	145 ET patients versus 34 controls	Compared to controls, ET patients showed higher SWVI scores during drawing Archimedean spirals	Higher SWVI scores correlated markedly with the presence and severity of other cerebellar signs in ET (e.g., intention tremor, tandem gait mis-steps)
Regularity of rhythmic movements	Farkas et al. [55]	34 ET patients versus 41 controls	Variability of rhythmic finger tapping and alternating hand movements was significantly higher compared to controls	Timekeeping operations deficits, which are regulated by cerebellar structures, are affected in ET patients
Impairment of social abilities	Santangelo et al. [58]	30 ET patients versus 30 controls	ET patients achieved significantly lower scores than controls on task assessing cognitive ToM	Cognitive ToM scores correlated with frontal tasks among ET patients, suggesting dysfunctional dorsolateral prefrontal cortex–cerebellum circuit
Cognitive deficits	Gasparini et al. [78]	27 ET patients (15 EFT; 12 EPT), versus 15 PD patients, versus 15 controls	ET patients showed significant impairments both in attentional and conceptual thinking tasks, similar to PD	The observed cognitive deficits among ET patients suggest involvement of frontocerebellar circuits
	Lombardi et al. [79]	18 ET patients versus18 PD patients	(1) ET patients had deficits on verbal fluency, naming, mental set-shifting, verbal memory, and working memory; (2) compared to PD group, ET group had greater impairment in verbal fluency, and working memory	
	Lacritz et al. [80]	13 patients with severe ET	12/13 subjects demonstrated impairment on one or more cognitive measures	
	Sahin et al. [81]	16 ET patients versus 16 controls	ET patients had deficits on visuospatial functions, verbal memory, and executive functions.	
	Higginson et al. [82]	33 ET patients versus 33 PD patients versus 21 controls	ET group performed significantly worse across multiple cognitive domains, but performed remarkably similar to PD patients	
	Ki et al. [83]	34 ET patients versus 33 controls	ET patients showed severe impairments in most domains, including attention, language function, verbal memory, and frontal executive functions.	
	Benito-León et al. [11]	232 ET patients versus 696 controls	ET performed worse on tests of frontal executive function	

DBS deep brain stimulation, *EFT* ET patients with family history of ET, *EPT* ET patients with family history of Parkinson's disease, *ET* essential tremor, *ETc* ET patients with additional clinical signs of cerebellar dysfunction, *ETpt* ET patients with predominantly postural tremor without intention tremor, *IT* ET patients with clinical evidence of intention tremor, *PD* Parkinson disease, *PT* ET patients with postural and/or simple kinetic tremor, *SWVI* spiral width variability index, *ToM* theory of mind, *VOR* vestibulo-ocular reflex

Efficacy of Stereotactic Thalamotomy and Thalamic Ventralis Intermedius Nucleus Deep Brain Stimulation

Surgery has been a treatment for ET since the early 1950s [8]. Initially, a number of different brain regions were targeted for tremor control. However, the optimal target was eventually determined to be the ventralis intermedius (VIM) nucleus of the thalamus, since tremor is thought to be mediated by a neuronal loop involving cerebello-thalamo-cortical pathways [5–8]. Stereotactic thalamotomy and thalamic VIM nucleus deep brain stimulation (DBS) offer high rates of tremor reduction in the contralateral arm [5–8]. The effects of thalamic DBS on the cerebellothalamocortical pathway have been studied [68]. With DBS turned off, excitability of the cerebello-thalamo-cortical pathways was reduced [68]. Turning DBS on resulted in facilitation of the cerebello-thalamo-cortical pathways, which suggests that thalamic DBS appears to activate rather than inhibit [68].

In a recent study, using diffusion tensor imaging, a group of ET patients that had undergone unilateral, left, thalamotomy, and ET patients that did not undergo thalamotomy (control group) were compared [69]. Fractional anisotropy and increased mean diffusivity values in the right superior cerebellar peduncle leading to the left, lesioned thalamus, only in the thalamotomy group, were observed, which suggests that long-term structural changes in the cerebellorubrothalamic tract after thalamotomy may occur [69].

Neuropsychological Deficits

Although the cerebellum has been linked historically to the control of posture, gait, and skilled voluntary movement, converging clinical and neuroimaging evidence has implicated the cerebellum in many different neuropsychological non-motor functions, thereby defining a novel vision of the cerebellar contribution to cognitive processes and emotional behavior [70]. This view gives rise to the dysmetria of thought theory, which holds that cerebellar modulation of movement, cognition, and emotion is a manifestation of the same neurological process [71, 72]. Schmahmann and Sherman [73] provided clinical evidence for this theory based on a constellation of cognitive, affective, and behavioral manifestations in patients whose lesions were confined to the cerebellum. The authors argued that those non-motor dysfunctions were related to the cerebellar disorder itself, particularly when the posterior lobe was involved, which led them to propose the cerebellar cognitive affective syndrome, characterized by the following features: (1) disturbances of executive function (this includes deficient planning, set-shifting, abstract reasoning, working memory, and decreased verbal fluency), (2) impaired spatial cognition, (3) personality changes, and (4) linguistic difficulties [73]. All these deficits have been attributed to the disruption of the neural circuits linking prefrontal, temporal, posterior parietal, and limbic cortices with the cerebellum [73]. The subsequent description that patients with cerebellar stroke in the posterior lobe had no or minimal cerebellar motor signs provides further indirect support to the notion that the "motor cerebellum" is situated in the anterior lobe (lobules I–V), and the "cognitive cerebellum" within the posterior lobe (predominantly lobule VII) [74].

As in other neurodegenerative cerebellar diseases [75, 76], mild cognitive deficits, mainly in attention and frontal executive functions, verbal memory, and visuospatial processes, have been reported to occur in ET patients in a series of independent studies [11, 13, 77–86]. Taken together, these studies indicate that a disorder of the frontal cortical or frontal cortical–cerebellar pathways might occur in some patients with ET [11, 13, 77–86]. Overall, the degree of cognitive impairment in ET is mild and is thought to be due to a dysfunction in the dorsolateral prefrontal cortex and in the inferior parietal cortex, including the cerebral–cerebellar loop [87].

It is worth noting how the observed ET-related neuropsychological deficits resemble those reported in the literature to occur after isolated cerebellar lesions:

1. ET patients experience cognitive difficulties impacting executive functions and frontal lobe tasks [11, 13, 77–86], and similarly, several reports of cerebellar patients have also noted impaired executive function [88–90]. For example, working memory, a cognitive process, which can be considered an example of a test of executive function, has been consistently shown to strongly engage cerebellar circuits [91, 92], suggesting that the role of the cerebellum in working memory includes aspects of encoding, maintenance, and retrieval [93]. Overactivation (abnormally enhanced cerebellar response) of posterior lobules of the cerebellum (crus I/lobule VI) during verbal working memory represents increased effort to subvocally refresh stimuli during attention-demanding conditions, such as high-load working memory trials and, hence, it may represent a brain compensatory mechanism that maintains the behavioral performances within a normal range [94]. Noteworthy, this abnormally enhanced cerebellar response has been reported in both individuals suffering from chronic alcoholism, a toxic condition associated with neurodegeneration of the cerebellum [94], and patients with ET during a verbal working memory task [95], providing evidence that disrupted functional interactions within distinct cortical–cerebellar circuits responsible for verbal working memory are an important mechanism underlying cognitive dysfunction in ET.
2. The observed fluency deficits among ET patients (more impaired on lexical than semantic verbal fluency) [77, 96] also parallel those reported after cerebellar lesions [73, 97].

3. Given that the posterior parietal cortex receives afferent connections from cerebellum via the pons and thalamus, the poor performance in visuospatial functions among ET patients may reflect the involvement of the cerebello-ponto-thalamo-parietal pathways [81].

There are also observations which suggest alternative explanations for the ET-related cognitive deficits. First, cognitive deficits in motor and premotor ET (that is, ET cases who underwent neuropsychological evaluations at a baseline visit prior to the onset of their tremor) are not static, and they appear to be progressing at a faster rate than in elders who do not develop this disease [13, 86]. In addition, an association between elderly-onset ET and prevalent mild cognitive impairment was demonstrated in the NEDICES study [12]. In line with this, in the same population, an association between elderly-onset ET and prevalent dementia was also evident; ET cases with tremor onset after 65 years of age were 70 % more likely to have dementia than were similarly aged controls [14]. Further, in an incidence cohort from the same population, ET cases with tremor onset after 65 years of age were 89 % more likely to develop incident dementia than were controls [15]. It is unlikely, however, that cerebellar dysfunctions per se fully explain dementia in ET, because the cognitive deficits that have been described in patients with cerebellar lesions are generally mild [74, 98]. Second, there is preliminary evidence to suggest that there are gray matter changes in ET patients with ET [99], the significance of which in relation to cognitive deficits requires further study. Moreover, the link between elderly patients with ET and dementia would suggest that this subgroup of patients with ET had involvement of the cerebral cortex during the course of their illness [14, 15], which raise the question whether elderly patients with ET are suffering from the same illness as younger patients with ET or whether there is a difference in pathophysiology based on age of onset. However, a recent neuroimaging study has reported that ET patients display, relative to controls, disrupted functional coupling between lobule VI and the executive control circuit (dorsolateral prefrontal cortex; parietal lobules) as well as the default mode network (precuneus cortex, ventromedial prefrontal cortex, and hippocampus) [95]. This functional imbalance can be viewed as a dysfunction of switching from default mode network to executive control circuit [95]. This "switcher role" of the cerebellum would be essential to guarantee a correct optimization of cognitive resources in accordance to ongoing needs [95]. Thus, given that diffuse abnormalities within the executive control circuit and the default mode network are the hallmarks of Alzheimer's disease [100], it could be that the fundamental brain mechanisms underlying cognitive deficits in ET resemble those implicated in Alzheimer's disease.

Table 1 summarizes the main studies that link ET to cerebellum.

Conclusion

ET may be a family of disease unified by the presence of kinetic tremor, but also showing etiological, pathological, and clinical heterogeneity. The wide spectrum of clinical features of ET that suggest that it originates as a cerebellar or cerebellar outflow problem include the presence of intentional tremor, gait and balance abnormalities, dysarthria, and oculomotor abnormalities, as well as deficits in eye-hand coordination, motor learning deficits, incoordination during spiral drawing task, motor timing and visual reaction time, impairment of social abilities, improvement in tremor after cerebellar stroke, efficacy of deep brain stimulation (which blocks cerebellar outflow), and cognitive dysfunction. It is unlikely, however, that cerebellar dysfunctions per se fully explain ET-associated dementia, because the cognitive deficits that have been described in patients with cerebellar lesions are generally mild. Overall, a variety of clinical findings suggest that in at least a sizable proportion of patients with ET, there is an underlying abnormality of the cerebellum and/or its pathways.

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Compliance with ethical standards

Conflict of interest The authors report no conflicts of interest.

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