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Short communication

Action tremor of the legs in essential tremor: Prevalence, clinical correlates, and comparison with age-matched controls

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ABSTRACT

The hallmark feature of essential tremor (ET) is action tremor of the arms. Leg tremor may also occur yet it has not been the central focus of previous studies. Its prevalence has only rarely been reported, its clinical correlates have yet to be explored. Our aims were to report the prevalence and analyze the clinical correlates of leg action tremor in patients with ET and, given the propensity for normal elderly individuals to manifest mild limb tremors, compare the prevalence with that in age-matched controls. Kinetic leg tremor rated ≥ 1 occurred in 28/63 (44.4%) ET cases and in only 9/63 (14.3%) controls ($p < 0.001$); moderate leg tremor occurred in 14.3% of cases. Leg tremor severity modestly correlated with disease duration ($r = 0.31$, $p = 0.02$). However, the severity and laterality of leg tremor did not correlate with those of arm tremor. The pathophysiological implications of this finding deserve further exploration.

1. Introduction

The most characteristic feature of essential tremor (ET) is arm tremor [1,2]. This tremor is predominately kinetic, but it may also be postural. ET typically begins in the hands and several years after symptom onset may begin to involve other body regions (e.g., head, voice) [3].

Although leg tremor is known to occur in ET, considerably more attention is focused on arm tremor [4]. Postural and kinetic leg tremors are not regularly tested on routine neurological examinations, although they may be tested by specialists with an interest in tremor. While the Fahn–Tolosa–Marin Tremor Rating Scale (TRS), one common rating scale used in clinical trials, includes an assessment of leg tremor [5], this assessment is brief in comparison to the more lengthy assessment of arm tremor. Aside from occasional published observations [2,6], the literature is silent regarding the prevalence of leg tremor in ET. Larsson and Sjögren reported leg tremor in 13.8% of ET cases in rural Sweden [2], and Lou and Jankovic, in 13.7% attending a specialty clinic in the USA [6]. Moreover, it is not clear how much mild leg tremor is merely due to aging as there have been no prior comparisons with age-matched controls. Finally, the clinical correlates of leg tremor in ET have not been explored. For example, is leg tremor correlated with disease duration? Our aims were to: (1) estimate the prevalence of leg action tremor in ET, (2) compare this with age-matched controls, and (3) examine the clinical correlates of this tremor in cases.

2. Methods

Sixty-three ET cases and 63 controls were enrolled in an epidemiological study at the Neurological Institute at Columbia University. Each participant signed an informed consent approved by our Human Ethics Committee. As documented previously, ET cases were patients at the Institute [7] and patients with a diagnosis of other movement disorders (e.g., Parkinson's disease, dystonia) were excluded. Controls, ascertained from the same set of zip codes in New York, New Jersey and Connecticut as cases, were recruited using random-digit telephone dialing and were frequency-matched on age (5-year strata), gender, and race categories [7]; each was initially screened for tremor using a questionnaire and later underwent the same detailed neurological examination and tremor examination as the cases to ensure that they did not have ET. All participants underwent a demographic and medical history questionnaire and a videotaped routine neurological examination (including an assessment of limb strength) and tremor examination [7]. Assessment of leg tremor began in August 2007.

During the videotaped tremor examination, postural leg tremor was assessed separately in each limb with subjects seated in a chair with footwear off during sustained (10 s) leg extension (hip flexed, knee extended and leg held at level of hip parallel to the ground). Kinetic tremor was also assessed with subjects seated in a chair with footwear off during the big toe-to-examiner's finger maneuver (10 repetitions with each leg). During this standardized maneuver, subjects fully

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extended the leg as the big toe approached and touched a fixed target 1.5 feet from the floor then returned the foot to the floor. During these maneuvers, the arms were resting in the lap so as to avoid transmission of postural or kinetic arm tremors to the legs. As documented previously, the videotaped examination also included detailed assessment of arm tremor during six tasks (five kinetic, one postural), head, voice, and jaw tremor and an assessment of parkinsonian features [7]. Each videotaped examination was reviewed by a senior neurologist (E.D.L.) who did not receive information regarding intake status (i.e., enrollment as a case or as a control). Leg postural and kinetic tremors were rated separately in each leg using a 0–3 scale: 0, no visible tremor; 0.5, questionably present; 1, low amplitude tremor; 1.5, intermittently moderate amplitude tremor (e.g., during <50% of repetitions); 2, consistently moderate amplitude tremor; and 3, large amplitude tremor. This resulted in a total kinetic leg tremor score (range = 0–6), a total postural leg tremor score (range = 0–6), and a total leg tremor score (range = 0–12). A unilateral leg tremor score for each leg was the sum of kinetic and postural tremor scores in that leg (range = 0–6). This leg tremor rating scale was not validated against previously published scales; however, a second diagnostically blinded neurologist (K.L.P.) independently rated 20% of videotaped examinations and the inter-rater agreement was high (intraclass correlation coefficient = 0.90).

Postural and kinetic tremor in each arm was rated during each of six tests using a 0–3 scale, resulting in a total arm tremor score (range = 0–36) [7]. A unilateral arm tremor score was the sum of six test scores in each arm (range = 0–18). Rest, voice, head, and jaw tremor were coded as present if visualized during the videotaped examination.

After review of the history and videotaped examination, the diagnosis of ET was then reassessed (E.D.L.). The cases included in these analyses met published criteria for ET (moderate or greater amplitude kinetic tremor of the arms during at least three tasks or head tremor, in the absence of Parkinson's disease, dystonia, or another neurological disorder) [7]. The presence of bradykinesia or any other sign of parkinsonism (except isolated rest tremor) was an exclusionary criterion for ET.

3. Results

Cases and controls were similar in terms of demographic characteristics (Table 1). In ET cases, the mean age of onset was 46.0 ± 22.3 years and mean disease duration was 22.1 ± 18.1 years (Table 1); 27/63 (42.9%) cases were taking medication for ET.

Nearly one-half of the cases (28/63, 44.4%) had mild or greater kinetic tremor in either leg (rated ≥1) vs. only one in seven (9/63, 14.3%) controls ($p < 0.001$, Table 1). One in seven cases (9/63, 14.3%) had moderate or greater amplitude kinetic tremor in either leg (rated ≥1.5) vs. only one (1.6%) control ($p = 0.008$, Table 1); none of these had reported leg tremor when asked during the medical history questionnaire. No cases or controls had leg tremor scores = 3. Few cases or controls had postural leg tremor (Table 1). When leg tremor was treated as a continuous variable, both the total kinetic leg tremor score and the total leg tremor score were higher in cases than controls (both p-values < 0.001), whereas the total postural leg tremor score was marginally different (Table 1). The use of ET medication did not affect the results: mild or greater kinetic tremor in either leg occurred in 11/27 (40.7%) ET cases who were taking ET medication vs. 17/36 (47.2%) who were not (chi-square = 0.26, $p = 0.61$).

We examined the clinical correlates of leg tremor, comparing the 28 ET cases with mild or greater kinetic leg tremor to the remaining 35 ET cases (Table 2). The two groups did not differ by age, sex, or a number of other factors. In the 28 ET cases with mild or greater kinetic leg tremor, severity of leg tremor was modestly associated with age of disease onset (Spearman's $r = -0.27$, $p = 0.03$), disease duration (Spearman's $r = 0.31$, $p = 0.02$), and presence vs. absence of voice tremor on examination (median total leg tremor score = 1.5 vs. 1.0, Mann–Whitney $z = 2.67$, $p = 0.008$). In ET patients with leg tremor, 17/28 (60.7%) had asymmetric tremor severity in either the arms or the legs. Arm and leg tremor were concordant for side of worse severity in 8/28 (28.6%) cases, discordant in 9/28 (32.1%) cases, and with equal bilateral tremor in either the arms or the legs in 11/28 (39.3%) cases. The unilateral leg tremor score did not correlate with the ipsilateral unilateral arm tremor score (Spearman's $r = 0.10$, $p = 0.45$ for right arm and leg, Spearman's $r = 0.16$, $p = 0.23$ for left arm and leg) in these 28 cases.

4. Discussion

Anecdotally, patients with ET may exhibit tremor in a variety of anatomic regions, yet there were few published data on the prevalence of leg tremor in ET and no data on the clinical severity of that tremor, its clinical correlates or its occurrence in a normal elderly comparison population [8]. The focus of this study was leg tremor in ET. Nearly one-half (44.4%) of ET cases had leg action tremor, and this tremor was of moderate amplitude in 14.3%. This value of 44.4% compared to a prevalence of only 14.3% in age-matched controls, indicating that 30% of cases have leg tremor that is in excess of that seen in controls. Epidemiological studies have not reported the prevalence of leg tremor in ET [1,2,9]. One exception was a report in Sweden where 29/210 (13.8%) familial ET cases had leg tremor, although the method of assessing that tremor was not specified nor was the severity [2]. There is one clinic-based series of the clinical features of 350 ET cases, which briefly noted that 13.7% had leg tremor [6]; however, tremor severity, description of leg tremor and the clinical correlates of the tremor were not reported in that broad clinical study.

Compared to the two prior observational reports of patients with ET, we found a higher prevalence of leg tremor. This is most likely explained by our inclusion of low amplitude, mild tremor in our prevalence estimate. If we had used a less sensitive measure (i.e., limiting our prevalence estimate to moderate or greater amplitude tremor) the prevalence would have dropped from 44.4% to 14.3%. Similarly, in our study, mild leg tremor was detected in 14.3% of normal subjects, but if we had used a less sensitive measure, this would have been only 1.6%. Our control subjects did not meet the criteria for ET nor did they exhibit other features of ET, such as head or voice tremor. A general neurological examination performed on all cases and controls ruled out other causes of tremor, such as weakness. Therefore enhanced physiologic tremor is the most likely explanation for mild leg tremor in most controls.

As in the upper extremities, tremor in the legs was predominantly kinetic. A clinical and electrophysiological study of arm tremor similarly showed kinetic tremor to be more severe than postural tremor in most ET cases [10].

The clinical correlates of leg tremor have not been studied previously. In this study, severity of leg tremor was modestly associated with younger age of onset and longer disease duration. Most likely, as the disease progresses, tremor spreads, suggesting ongoing neurodegeneration. Prior studies have similarly demonstrated that arm tremor severity in ET is associated with disease duration [7].

Although generally bilateral, ET is usually mildly asymmetric, with arm tremor more severe in one arm than the other [11]. Interestingly, although 60.7% of patients with leg tremor had asymmetric tremor severity, there was no correlation between the side of greater leg tremor severity and the side of greater arm tremor severity nor between unilateral leg tremor score and ipsilateral unilateral arm tremor score. This is unlike Parkinson's disease, in which the side of greater upper limb and lower limb involvement is usually the same. In Parkinson's disease, the laterality of symptoms is due to pathology in the contralateral substantia nigra. The full spectrum of pathology for ET is unclear; however, involvement of structures with bilateral projections, such as the cerebellum, rather than mostly contralateral projections, could explain our findings [12].

The significance of leg tremor in patients with ET is not entirely clear. Unlike orthostatic tremor, which is accompanied by feelings of unsteadiness, ET patients do not typically complain of symptoms related to leg tremor. When compared with the upper limbs, the lower limbs are less frequently used in precise movements. However, balance difficulty while walking and loss of postural control occur in some patients with ET. It is conceivable that leg