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FAMILIAL ORTHOSTATIC TREMOR: AN ADDITIONAL REPORT IN SIBLINGS

Orthostatic tremor (OT) was a term first used to describe tremor that occurred in the legs while patients were standing, and which was relieved while patients were walking, seated, or supine.¹ The disorder can be very disabling, and the treatment, which is largely unsuccessful, remains empiric.^{2,3} Although there is some evidence of a dopaminergic deficit,⁴ the exact circuit responsible for the high frequency, 13–18 Hz tremor that is pathognomonic for this disorder remains unclear. OT is thought to be sporadic rather than familial, which makes the search for a pathophysiologic mechanism particularly challenging. There are only 2 prior case reports of OT in siblings.^{5,6} Here we report a third sibling pair, each of whom had clinical and electrophysiologic evidence of OT.

Case reports. The patients were brother (B) and sister (S), aged 79 and 75 years, respectively. Both also shared a history of coronary artery disease and hypothyroidism. Symptoms started at age 73 in both and were described as tremulousness in the legs after 10–30 seconds of standing, which improved when walking or leaning to the side. To aid with stability, S had used a walker for the past year. Both had mild action tremor but no rest tremor in the arms. B reported heavy ethanol use in the past, while S reported only social ethanol consumption.

By report, their mother, now deceased, had been witnessed on at least one occasion to have been similarly tremulous while standing. They had 3 other siblings, including a deceased sister with alcoholism and tremor (unspecified location). One of B's daughters also possibly had tremor on standing; however, permission could not be obtained to contact her for verification.

S was evaluated by a movement disorders specialist (E.D.L.), who learned that B had also been evaluated several years earlier by another movement disorders specialist (C.W.) at the same center. On examination, both had normal extraocular movements without square wave jerks or nystagmus and cranial nerve examination was normal. Neither had rest tremor, but both had mild kinetic tremor of the arms with an intentional component, although too mild to qualify for a diagnosis of essential tremor.⁷ There was no bradykinesia or rigidity. Neither had postural instability on the pull test. Within 30 seconds of standing, both had high-frequency tremor of their legs, which resolved with walking (videos 1 and 2 on the *Neurology*[®] Web site at www.neurology.org).

S had a peripheral neuropathy with absent deep tendon reflexes in the legs, and felt more comfortable using a walker. Neurologic examinations were otherwise normal.

Both underwent clinical motor physiologic testing (S.L.P.). During finger-nose-finger maneuver, there was a mild kinetic tremor (4.3–5.4 Hz on right in B, and 5.9–8.5 Hz bilaterally in S). Upon standing, B had tremor in the tibialis anterior (TA) and gastrocnemius (GM) muscles, with alternate bursts in this agonist-antagonist muscle pair on surface EMG recordings (figure), while S showed similar alternating synchronized bursts between the TA and vastus lateralis (VL) muscles (figure). Power spectra showed a sharp peak frequency at 13.5 Hz in all muscles tested in B, and 13.3 Hz in S, with a high coherence between frequencies observed in the left and right TA muscles in each patient (figure). When standing on alternate feet, tremor was demonstrated on EMG only in the weight-bearing limb, and while walking in place, alternate activation of agonist-antagonist pairs was observed in the limb that was on the ground (data not shown).

Both patients were treated with clonazepam, with mild subjective improvement in tremor reported at subsequent visits. The dose was limited by the development of imbalance and falls in B (2 mg/day); somnolence limited the total dose in S (1 mg/day).

Discussion. We describe a family in which 2 siblings have clinically and physiologically documented OT. Other family members also possibly had leg tremor, including the patients' mother and B's daughter. Interestingly, both patients reported onset of tremor at age 73, had similar symptomatic improvement with clonazepam, and although the electrophysiologic studies were performed 3 years apart without the knowledge of the other's results, both had a remarkable similarity in tremor frequency (13.5 and 13.3 Hz). While the vast majority of cases of OT appear to be sporadic, this family, taken together with prior reports of familial OT,^{5,6} suggests there may be a heritable component as well. Further analysis into such kindreds could lead to the identification of putative genes, a greater understanding of disease pathogenesis, and eventually more targeted therapies for both the symptomatic treatment of the disorder and potentially the underlying abnormalities.

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Supplemental Data

(A, C, E) Patient B; (B, D, F) patient S. (A, B) Sample rectified surface EMG recordings of tremor from the tibialis anterior (TA) and gastrocnemius (GM) muscles (A, patient B), and TA and vastus lateralis (VL) muscles (B, patient S), with both patients standing. (C, D) Power spectra analyses of traces above showing a peak in frequency of discharges at 13.5 Hz (C, patient B) and 13.3 Hz (D, patient S). (E, F) Coherence analysis between limbs showing good correlation in frequency of tremor on standing between the right and left TA in patient B (E) and S (F).

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