Evidence for a non-orthostatic origin of orthostatic tremor

B Boroojerdi, A Ferbert, H Foltys, C M Kosinski, J Noth, M Schwarz

Abstract

***Objectives*—Orthostatic tremor was first described by Heilman in 1984. It usually occurs in the legs during stance and decreases markedly during sitting or walking. The aim of this study was to determine if orthostatic tremor is invariably associated with the orthostatic and weight bearing conditions in the arms and legs, and to investigate the features of orthostatic tremor under different levels of peripheral loading.**

***Methods*—Multichannel surface EMG recordings were obtained under different conditions (body posture and peripheral loading) from the proximal arm and leg muscles of seven patients fulfilling the clinical and electrophysiological criteria of orthostatic tremor.**

***Results*—In weight bearing positions (stance; weight bearing on the hands on all fours), all patients showed 13 Hz-16 Hz tremor activity, predominantly in the active limb. No tremor activity could be found in a supine position with muscles at rest. Isometric contraction of the limbs in the supine position led to synchronous 13 Hz-16 Hz rhythmic activity in five patients. No tremor was seen when the subjects were suspended in a harness with relaxed legs. Isometric contraction of the legs in this position produced tremor in two patients. A stepwise reduction of the body weight by a harness reduced the tremor activity. Additional loading (10 kg-20 kg) during stance led to an increase in tremor amplitude, but tremor frequency remained unchanged.**

***Conclusions*—Orthostatic tremor is invariably present during stance or other weight bearing positions. It is not, however, always associated with orthostasis. In at least some patients it can be classified as an orthostasis independent action tremor. The failure of peripheral loading to modify tremor frequency indicates that orthostatic tremor may have a central, rather than a peripheral, origin.**

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Keywords: orthostatic tremor; essential tremor; central oscillator; action tremor

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List of the investigated patients: clinical and treatment data

Patient No	*Age*	*Sex*	*Duration of disease (y)*	*Leg tremor frequency in stance (Hz)*	*Treatment and daily dose*
1	66	F	6	13	3 mg clonazepam 625 mg primidone
2	71	F	7	15	3 mg clonazepam
3	62	F	17	15	1.5 mg clonazepam 125 mg primidone
4	71	F	5	14	3 mg clonazepam
5	64	M	18	15	0.5 mg clonazepam
6	62	F	8	16	2 mg clonazepam
7	67	M	7	14	3 mg clonazepam

Primary orthostatic tremor is a rapid (14 Hz-16 Hz) tremor, which usually affects the lower limbs during stance. It is much less apparent when leaning against an object or during walking. This disorder was first described in 1984 by Heilman.[1] It has originally been classified by some authors as a variant of essential tremor,[2–4] but several features such as a high degree of synchrony between different muscles in orthostatic tremor,[5 6] its lack of response to β blocking agents such as propranolol and to alcohol,[1] a usually negative family history,[6] and its higher frequency, suggest that orthostatic tremor and essential tremor are different disease entities.[7] Unlike essential tremor, orthostatic tremor cannot be reset by a peripheral nerve stimulus.[6 8] It has been shown in PET studies that the tremor of the upper limbs in patients with orthostatic tremor is associated with abnormal bilateral cerebellar activity.[9] A similar overactivity has been seen in other tremulous disorders such as essential tremor or writing tremor.[7 10–11] The clinical response of orthostatic tremor to therapeutical interventions with clonazepam, primidone, and phenobarbitone has been reported to be good.[6] Most authors have suggested that orthostatic tremor has a central oscillator.[5 12–14] An unresolved question is the relation of orthostatic tremor to orthostatic and weight bearing body postures. An invariable connection to such positions would suggest the involvement of vestibular pathways in this disorder. In this case it would be difficult to explain the decrease in orthostatic tremor during leaning or walking. Several case reports have suggested a possible involvement of the arm muscles at rest or in weight bearing positions and a gradual decrease in the tremor by reduction of the active body weight.[6 7 14 15] However, a systematic analysis of these phenomena has yet to be performed.

A change in peripheral loading in peripherally generated tremor disorders leads to a modification of the resonance and the tremor frequency of the limb, whereas in central tremors the EMG tremor frequency has a constant peak, irrespective of peripheral loading.[16–20] This feature may help to distinguish between central and peripheral tremor entities. There are no reports concerning analysis of the tremor frequency of the legs in

orthostatic tremor with different peripheral loadings.

The aim of this study was to examine the relation between orthostatic tremor and orthostatic (weight bearing) conditions and a possible relation of the different features of this tremor (frequency and severity) to a stepwise reduction in body weight.

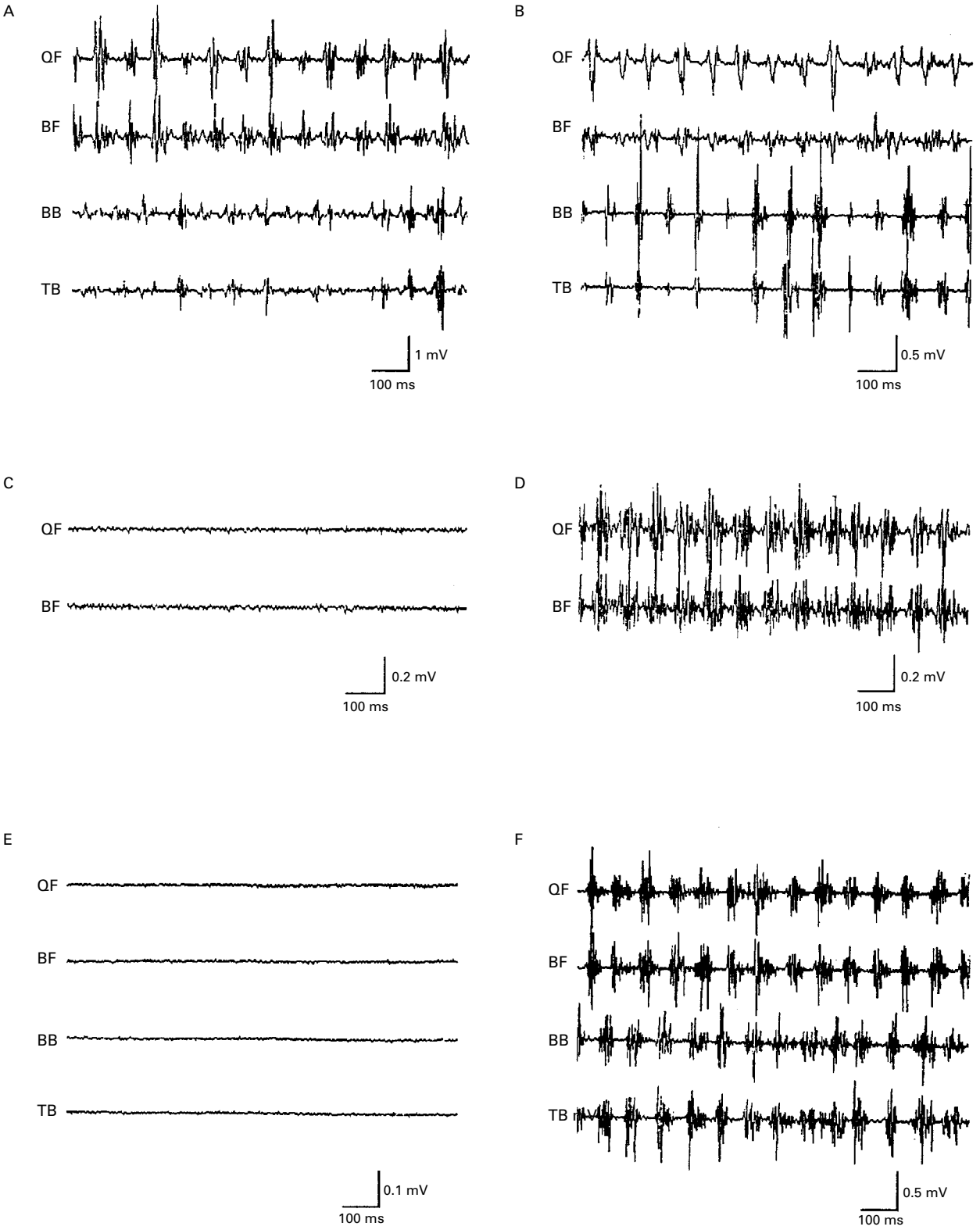

Figure 1 Surface EMG recordings from leg and arm muscles (QF=M quadriceps femoris; BF=M biceps femoris; BB= M biceps brachii; TB=M triceps brachii) in different positions in patient 4. (A) Stance with full weight bearing; (B) weight bearing on all fours in crouching position; (C) suspended upright in a harness with relaxed legs; (D) suspended upright with isometric contraction of the legs; (E) supine position with relaxed legs and arms; and (F) supine position with isometric contraction of arms and legs.

Patients and methods

PATIENTS

The study involved seven patients (two men and five women, age range 62–71 years, mean age 66.1 (SD 3.8) years, duration of disease 5–18 years) who fulfilled the clinical and electrophysiological criteria for orthostatic tremor. All procedures were explained fully to the patients, who then gave their informed consent. Four patients were investigated in Aachen and three in Kassel. All patients had a 13 Hz-16 Hz tremor activity in the leg muscles during stance, which caused them difficulties while standing. The patients described this as weakness, trembling, or a feeling of unsteadiness. In all cases the tremor began a few seconds to a minute after standing up and progressively worsened to a point that the patient was compelled to move or to sit down for fear of falling. All patients commented that their symptoms were abolished by sitting or lying and were improved by shifting the weight, leaning against an object, or by walking. All patients were on medical treatment with oral clonazepam or primidone,or both (table).

EMG RECORDINGS

Multichannel surface EMG recordings using Ag/AgCl electrodes were made with a VIKING I device (Nicolet Biomedical Inc) with a bandpass of 100 Hz-10 kHz. Recordings were made from the right M biceps brachii, M triceps brachii, M quadriceps femoris, and M biceps femoris. Tremor activity (frequency and maximum amplitude of EMG activity) was measured by visual inspection under several conditions: (1) during stance with full body weight and outstretched arms; (2) during weight bearing on the hands and legs on all fours; (3) in an upright position while suspended in a harness and with a stepwise reduction of body weight (2/3 body weight,1/2 body weight, 1/3 body weight) in five patients (patients 3–7) and complete suspension with relaxed legs in all patients; (4) as condition 3, but with isometric contraction of the legs; (5) with additional loading (10 kg-20 kg) in a standing position in four patients (patients 3, 4, 5, and 7) achieved by carrying a loaded rucksack. In each case a maximum additional loading of 20 kg was tried. As this load was poorly tolerated by some patients the weight of the rucksack was reduced down to a tolerable value (minimum 10 kg). The electrophysiological measurements were done using only one load in each individual subject; (6) in a supine position with relaxed muscles; (7) in a supine position with isometric contraction of the arm and leg muscles. The patients were first asked to maintain a maximum isometric contraction of their arm and leg extensors and flexors separately against resistance. A simultaneous contraction of the arm flexors and leg extensors were then performed in the second step of the experiment. In each condition the tremor frequency and the ratio of the peak tremulous EMG activity of the M quadriceps femoris to the peak EMG activity during stance was calculated.

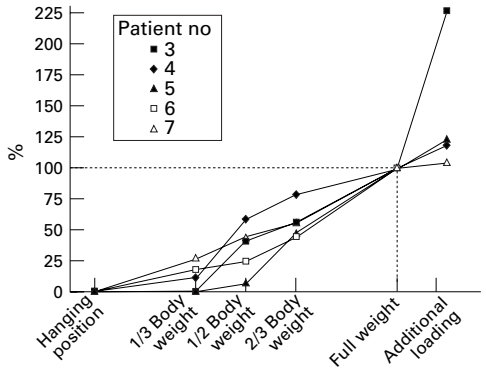

Figure 2 Peak EMG amplitude of the tremor activity in M quadriceps femoris after stepwise reduction of the body weight and after additional loading in stance in relation to peak amplitude during stance with full weight. An increase in loading weight leads to an increase in tremor amplitude in the legs.

Results

MEDICAL TREATMENT DATA

All patients were on appropriate medication with clonazepam or primidone, or both and had a moderate to good response to this treatment. The daily dose of clonazepam ranged between 0.5 mg and 3 mg, and that for primidone between 125 mg and 625 mg (table).

TREMOR ACTIVITY UNDER DIFFERENT CONDITIONS

Stance—In this position all patients had a 13 Hz-16 Hz synchronous tremor activity in the leg muscles (fig 1A). Three patients showed tremor in their outstretched arms at the same frequency, but with a lower amplitude.

Weight bearing on all fours—In this position all patients had a 13 Hz-16 Hz tremor activity in the active arms. Three patients showed a similar tremor in the leg muscles. By contrast with the findings during stance, the tremor amplitude was larger in the arm muscles than in the legs under this condition (fig 1B), although no change of the tremor frequency could be detected.

Upright, suspended position with stepwise reduction of the body weight—This procedure could be performed in five patients (patients 3–7). A decrease in the tremor amplitude accompanied the reduction in body weight (fig 2), but no change of the tremor frequency was apparent. Tremor was abolished during complete unloading with relaxed legs (Fig 1C).

Upright suspended position with isometric leg contraction—In this position the isometric cocontraction of the leg muscles led to tremor activity in two patients (fig 1D).

Additional loading—An additional loading of 10 kg-20 kg during stance was performed in four patients (patients 3, 4, 5, and 7). It led to an increase of the tremor amplitude in all patients without any shift in frequency (fig 2).

Supine position with relaxed muscles—No tremor activity was seen under this condition (fig 1E).

With isometric contraction of the upper or lower limb tremor activity could be seen mainly in the contracted muscles. Isometric cocontraction of the arms and legs in a supine

position led to tremor in all four limbs in five patients (fig 1F).

Discussion

Orthostatic tremor is a unique tremor syndrome, characterised by a subjective feeling of imbalance in stance and a substantial relief when sitting or lying. When in the last condition only sparse clinical findings, in the form of a barely visible or palpable fine amplitude tremor of the leg muscles, are found. The diagnosis can be easily confirmed by EMG recordings from these muscles, which show a characteristic 13 Hz-18 Hz tremor. In severe cases this activity is apparent in all leg, trunk, and arm muscles. Involuntary shaking, jerking, or tremor of the legs may be a prominent symptom of several conditions such as myoclonus, cerebellar ataxia, or clonus due to spasticity. In all these conditions the shaking of the legs may also produce a severe unsteadiness in stance, with considerable relief after sitting or lying. The characteristic tremor frequency in orthostatic tremor can help to achieve a correct diagnosis.

Orthostatic tremor was always present in weight bearing conditions such as stance and crouching on all fours, predominantly in the more activated limbs. The tremor amplitude was larger in the leg muscles than in the arms during stance, whereas in a crouching position a larger amplitude could be seen in the arm muscles. This tremor activity did not depend on orthostatic conditions. No tremor could be seen when the patients were suspended upright with relaxed legs whereas there was a clear tremor activity in a considerable proportion of the patients in the non-orthostatic supine position, as well as while suspended with isometric contraction of the leg muscles. Thus the "orthostatic" tremor could be seen in many patients during muscle contraction in any position (lying, hanging, standing). This suggests that afferents signalling the body position may not play a crucial part in the generation of orthostatic tremor.

There are three principal mechanisms for the generation of tremor. Firstly, tremor generation caused by firing of motor neurons at their proper frequency. Higher order structures, such as spinal interneurons, may in this case maintain the synchronisation of motor neurons. A rhythmic firing of motor neurons with the characteristic frequency of 13 Hz-16 Hz could, theoretically, be the origin of orthostatic tremor. But needle EMG recordings in patients with orthostatic tremor have disclosed a firing frequency of only about 8 Hz.[5] A second tremor mechanism is an oscillatory system composed of central and peripheral mechanisms. An oscillating system with a central part and peripheral receptors and pathways could also be postulated in orthostatic tremor. The 13–18 Hz tremor frequency of orthostatic tremor is, however, far too high to originate in a lower limb reflex loop. Clonus, which is produced by such a mechanism, has a frequency of 6 Hz-8 Hz in the legs. By contrast with the peripherally generated tremors, the tremor in orthostatic tremor cannot be reset by peripheral nerve stimuli.[6 8] A third mechanism is a central oscillator acting alone. The high degree of regularity and synchrony between muscles in the different parts of the body in orthostatic tremor,[6 13] and the fact that the phase of orthostatic tremor can be reset by transcranial magnetic stimuli,[21] suggest that this third principal mechanism of tremor generation is the most probable in the case of orthostatic tremor.

It is known that the frequency of peripherally mediated tremors, such as normal physiological tremor, depends on the resonance frequency of the limb rather than on the frequency of any central oscillator.[17–20] This resonance frequency can be modified by external loading of the limb. Therefore changes in loading can be a useful way to distinguish between peripherally and centrally generated tremor variants. In subjects with an enhanced physiological tremor the reduction of the mechanical resonance frequency by loading can reduce the EMG frequency.[18 20] By contrast, this effect of mass loading is not seen in parkinsonian tremor or essential tremor.[20] In our study the reduction of body weight by suspension in a harness or increases in body weight by additional loading (changes in peripheral loading) did not lead to any significant changes in the EMG tremor frequency, although a marked modification of the peak EMG amplitude could be found. This would suggest a central oscillator for the tremor activity in orthostatic tremor, in agreement with the findings of many other authors.[5 12–14] In studies of hand tremor additional loads of up to twice the mass of the hand (500 g-1000 g) are often used. Compared with this loading the ratio of the additional weight in our study (10 kg-20 kg) to the total body mass (70 kg) is very modest. Thus it is conceivable that larger mass loads would have possibly changed the tremor frequency. Due to the poor toleration of the additional loading by the elderly population of patients with orthostatic tremor, loadings comparable with the body mass could not be used in our study.

In conclusion, although orthostatic tremor can always be seen in weight bearing positions, it diminishes in pure orthostatic (vertical) positions without isometric muscle contraction. In at least some patients muscle activation while supine also leads to characteristic tremor activity. In these patients orthostatic tremor may be redefined as an orthostasis independent action tremor. The lack of EMG frequency shift with different peripheral loadings suggests a central oscillator for this disorder.

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1 Heilman KM. Orthostatic tremor. *Arch Neurol* 1984;**4**:880–1.
2 Wee AS, Subramony SH, Currier RD. Orthostatic tremor in familial essential tremor. *Neurology* 1986;**36**:1241–5.
3 Papa SM, Gershanik OS. Orthostatic tremor: an essential tremor variant? *Mov Disord* 1988;**3**:97–108.
4 Fitzgerald PM, Jancovic J. Orthostatic tremor: an association with essential tremor. *Mov Disord* 1991;**6**:60–4.
5 Deuschl G, Lücking CH, Quintern J. Orthostatischer Tremor: Klinik, Pathophysiologie und Therapie. *Z EEG EMG* 1987;**18**:13–19.

6 Britton TC, Thompson PD, van der Kamp W, *et al*. Primary orthostatic tremor: further observations in six cases. *J Neurol* 1992;**239**:209–17.
7 McManis PG, Shabrough FW. Orthostatic tremor: clinical and electrophysiologic characteristics. *Muscle Nerve* 1993; **16**:1254–60.
8 Bathien N, Rondot P, Toma S. Inhibition and synchronisation of tremor induced by muscle twitch. *J Neurol Neurosurg Psychiatry* 1980;**43**:713–18.
9 Wills AJ, Thompson PD, Findley LJ, *et al*. A positron emission tomography study of primary orthostatic tremor. *Neurology* 1996;**46**:747–52.
10 Jenkins IH, Bain PG, Colebatch JG, *et al*. A positron emission tomography study of essential tremor. Evidence for overactivity of cerebellar connections. *Ann Neurol* 1993;**34**: 82–90.
11 Wills AJ, Jenkins IH, Thompson PD, *et al*. A positron emission tomography study of cerebral activation associated with essential and writing tremor. *Arch Neurol* 1995;**52**: 299–305.
12 Elble RJ. Central mechanisms of tremor. *J Clin Neurophysiol* 1996;**13**:133–44.
13 Thompson PD, Rothwell JC, Day BL, *et al*. The physiology of orthostatic tremor. *Arch Neurol* 1986;**43**:584–7.
14 Uncini A, Onofrj M, Basciani R, *et al*. Orthostatic tremor: report of two cases and an electrophysiological study. *Acta Neurol Scand* 1989;**79**:119–22.
15 Walker FO, McCormick GM, Hunt VP. Isometric features of orthostatic tremor: an electromyographic analysis. *Muscle Nerve* 1990;**13**:918–22.
16 Joyce GC, Rack PMH. The effects of load and force at the normal human elbow joint. *J Physiol* 1974;**240**:375–96.
17 Elble RJ, Randall JE. Mechanistic components of normal hand tremor. *Electroencephal Clin Neurophysiol* 1978;**44**:72–82.
18 Hömberg V, Hefter H, Reiners K, *et al*. Differential effects of changes in mechanical limb properties on physiological and pathological tremor. *J Neurol Neurosurg Psychiatry* 1987;**50**:568–79.
19 Gantert C, Honerkamp J, Timmer J. Analyzing the dynamics of hand tremor time series. *Biol Cybernet* 1992;**66**:479–84.
20 Deuschl G, Krack P, Lauk M, *et al*. Clinical neurophysiology of tremor. *J Clin Neurophysiol* 1996;**13**:110–21.
21 Tsai CH, Semmler JG, Kimber TE, *et al*. Modulation of primary orthostatic tremor by magnetic stimulation over the motor cortex. *J Neurol Neurosurg Psychiatry* 1998;**64**:33–6.