

PAPER

Abnormal vibration induced illusion of movement in essential tremor: evidence for abnormal muscle spindle afferent function

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Objectives: Vibration induced illusion of movement (VIIM) is abnormal in patients with idiopathic focal dystonia, an abnormality which corrects with fatigue of the vibrated muscle. Since dystonia and essential tremor sometimes coexist in families, we investigated the perception of VIIM and the effect of fatigue on VIIM in patients with essential tremor.

Methods: VIIM in 18 patients with essential tremor was compared with VIIM in 18 healthy control participants before and after volitional fatigue of the vibrated muscles.

Results: Vibration of the immobilised biceps produced a subnormal VIIM in patients with essential tremor (12.81° (SEM 2.15)) compared with healthy control subjects (28.55° (1.66)). The perception increased following volitional fatigue of the vibrated arm in patients with essential tremor (16.23° (2.50)) but not in healthy controls (27.55° (1.66)). No difference was observed in patients with alcohol or non-alcohol responsive tremor.

Conclusions: The VIIM decreased with increasing age in healthy control subjects. Abnormal VIIM implies abnormal sensorimotor processing in patients with essential tremor, similar to that found in idiopathic focal dystonia, and the change of the perception with age could explain the age related onset of the disorder.

Clinically heterogeneous, essential tremor is usually diagnosed after exclusion of other causes of tremor. Response to drug treatments such as alcohol, primidone, or propranolol is variable and there is no simple method of distinguishing between subtypes of tremor. The pathophysiology of essential tremor is unclear. Essential tremor and dystonia share some common pathophysiological features.^{1–3} We recently described abnormalities in perception of vibration induced illusion of movement (VIIM) in patients with idiopathic focal dystonia which corrected with volitional fatigue.⁴ In the present study we investigated the pathophysiology of essential tremor by examining the perception of VIIM in patients with essential tremor and the effect of fatigue. The study aimed to ascertain whether the abnormal muscle spindle sensorimotor afferent processing observed in patients with dystonia is a characteristic of essential tremor and whether this abnormality corrects with volitional fatigue implying a similar pathophysiology to idiopathic focal dystonia.

METHODS

Subjects

We tested 18 patients with “probable or definite” benign essential tremor⁵ recruited from the movement disorders clinic at the Royal Hallamshire Hospital, Sheffield, UK. All had a persistent postural or kinetic tremor of the hands. None had head tremor, but one subject had a tremor of the left leg. There was no evidence of any other neurological abnormality. None of the patients with tremor had clinical evidence of dystonia in the form of co-contraction of agonist and antagonist muscles, abnormal posture, or prolonged duration tremor bursts. Eighteen healthy control subjects were recruited from a healthy control database held at the department. None of the patients or healthy controls had a family history of dystonia or evidence of diabetes and psychiatric or other neurological impairment beyond the

patients' primary diagnosis. Table 1 summarises the patients' characteristics and drug treatment.

The protocol was approved by the South Sheffield Research Ethics Committee (SS94/280) and all patients and healthy control subjects gave written informed consent to the study.

Experimental design

Details of the experimental design are reported elsewhere^{6,7} and are therefore described briefly here. The subjects were seated with their elbows resting on a table and blindfolded. One arm was placed in a custom made polypropylene splint, with the elbow flexed to approximately 100° in the vertical plane (vibrated arm). The arm was secured in place with Velcro straps and volunteers were instructed to flex the “tracking arm” until they felt it was parallel with the splinted arm. The participants were asked to relax their arms whilst maintaining arm position, and relaxation of the biceps was confirmed by surface electromyography (EMG) recordings. Electrical silence of the EMG was obtained before starting the vibratory stimulus. An 80 Hz frequency, 0.5 mm amplitude vibration was applied transcutaneously to the biceps brachii tendon just above the elbow joint for 45 seconds using a battery operated vibrator (FertiCare personal, Multicept A/S, 2970 Horsholm, Denmark). The volunteers were asked to copy the sensation of movement they perceived in the vibrated arm with the tracking arm as accurately as possible.

The participants' strength was estimated using a dynamometer and dumbbell weight (1–5 kg) selected depending on their strength, to ensure gradual fatigue of their muscles. The volunteers then performed repeated biceps curls in the arm chosen to be vibrated until they felt they could no longer raise the dumbbell. Each task was performed on both arms and the side tested first was chosen randomly. As the biceps muscle recovered strength, the participants were instructed to raise the weight again in between the tasks to maintain fatigue.

Abbreviations: VIIM, vibration induced illusion of movement

Table 1 Characteristics of the patients with essential tremor and healthy controls

	Essential tremor (n = 18)	Controls (n = 18)
Sex (M/F)	10/8	9/9
Age in years (SEM)	62.2 (2.5)	58.9 (3.0)
Alcohol response		
Yes	12	
No	4	
Teetotal	2	
Average duration of disease in years (SEM)	9 (2.87)	
Right/left handed	17/1	16/2
Medication* (yes/no)	11/7	

*Medication included one or more of the following drugs: propranolol, topiramate, primidone.

The perception of arm movement as a result of the vibration induced illusion of movement in the vibrated arm was measured as angular displacement of the tracking arm from the initial to the final position using a digital camera (Olympus Camedia) and measured on the digital images using Adobe PhotoShop software.

Statistical analysis

Paired and unpaired *t* tests, repeated measures ANOVA, and Pearson’s correlation test were used where appropriate. Statistical significance was determined as $p < 0.05$. Results are presented as mean (standard error of the mean (SEM)).

RESULTS

Tremor was generally less conspicuous in the relaxed, immobilised arm during the experiment and was more prominent when a posture was maintained. Vibration of the restrained arm’s biceps brachii tendon elicited the sensation of arm extension in all healthy control subjects, but had no measurable effect on the amplitude or frequency of the observed tremor. There was no dystonic posturing induced by the stimulus in any patient. After 45 seconds, the extension of the tracking arm was significantly less ($p < 0.001$, independent samples *t* test) in patients with essential tremor (12.81° (SEM 2.15)) compared with healthy controls (28.55° (1.66)) (fig 1). No difference was observed between the dominant and non-dominant arms, and so the results from both arms were averaged for each subject. After fatigue, the perception of movement of the vibrated arm increased significantly in patients with essential tremor (16.23° (2.50)) compared with the perception prior to fatigue ($F_{1,34} = 21.55$; $p < 0.01$, repeated measures ANOVA). This was not observed in the healthy controls who showed no significant effect of fatigue on the perception of illusory arm movement (mean post-fatigue value 27.55° (1.66)) (fig 1).

There was no significant difference (independent samples *t* test) in the perception of movement between patients with alcohol responsive and non-alcohol responsive essential tremor (alcohol responsive 13.83° (2.60), non-alcohol responsive 9.23° (2.95)) before or after volitional fatigue (alcohol responsive 17.80° (2.87), non-alcohol responsive 10.73° (4.6)).

The perception of VIIM decreased with age in healthy controls ($r^2 = -0.295$, $n = 32$; $p < 0.05$, Pearson correlation) but this trend did not reach significance in patients with essential tremor. Figure 2 shows the relation between age and perception of VIIM in healthy controls and patients with essential tremor.

There was no significant difference between the perception of VIIM in patients on medications ($n = 11$) and those not on

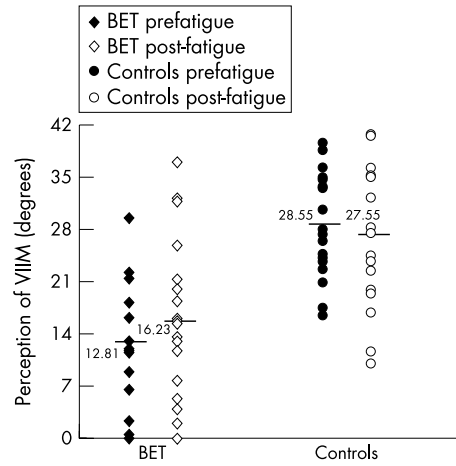


Figure 1 The perception of vibration induced illusion of movement (VIIM) in patients with benign essential tremor (BET) and healthy control subjects, before and after fatigue of the vibrated arm. Perception of VIIM is measured as movement of the tracking arm over 45 seconds.

medications ($n = 7$) (see table 1) before ($p = 0.250$, independent samples *t* test) or after fatigue of the vibrated arm. ($p = 0.814$, independent samples *t* test).

DISCUSSION

The VIIM of patients with essential tremor and its change with fatigue is variable, underlining the heterogeneity of the disease, as shown in fig 1. We have recently reported abnormal perception of VIIM in patients with idiopathic focal dystonia.^{4,7} In this study we have demonstrated that perception of VIIM was also impaired in patients with essential tremor compared with healthy control subjects. The vibration induced illusion of arm extension elicited in the relaxed, immobilised arm probably occurs as a result of the interpretation by the brain of the Ia afferent volley of activity without equivalent increase in fusimotor activity.^{8,9}

To exclude a contribution to the abnormality in patients with essential tremor from their medication we compared the 11 patients with essential tremor on medications (taking a number of different drugs, see table 1), with the seven patients who were not taking any medication for their essential tremor. Since both, the patients taking medications and those not taking medications, had the same response to VIIM and fatigue the results cannot be attributed to medication effects.

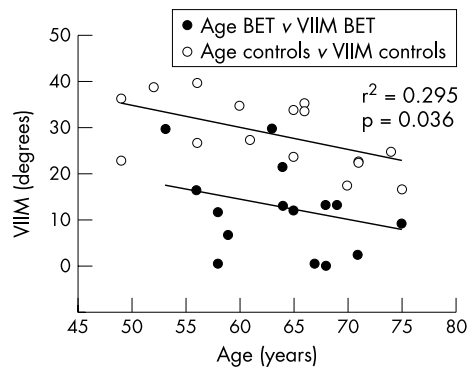


Figure 2 Correlation of perception of vibration induced illusion of movement (VIIM) in patients with essential tremor and healthy control subjects with age. Perception fell significantly with age in the control subjects, but the fall was not statistically significant in patients with benign essential tremor (BET).

Although some patients may have had “dystonic tremor” mimicking essential tremor, we excluded patients with any clinical signs or symptoms suggestive of a dystonic phenotype. Subjects with abnormal H reflexes, which are found in dystonic subjects, were not specifically excluded, but an abnormal H reflex has not been demonstrated to be sensitive or specific enough to exclude a dystonic predisposition in this context.¹⁰ The tremor itself had minimal impact on the experimental measurements, but may have increased the variability of the measurements slightly.

This impaired perception of VIIM in essential tremor may have several possible explanations. One involves the physical properties of the muscle spindles themselves. The findings of this experiment are consistent with excessive stiffness of muscle spindle dynamic nuclear bag 1 fibres which improves with volitional fatigue. A sluggish response of the relatively inelastic muscle spindle to dynamic stimuli may result in a slightly delayed and inappropriately prolonged activation of Ia afferent fibres during muscle stretch. As the muscle fatigues during repeated muscle stretches, the stretching of nuclear bag fibres may change their elasticity increasing their sensitivity to vibration. The cerebellum may normally function to compensate by adjusting timing of the feedback loop to minimise tremor. Essential tremor may become apparent only if such compensatory mechanisms are inadequate.

Another explanation relies on abnormal central processing of the afferent information from muscle spindles. It is possible that subnormal responsiveness of the central nervous system to normal Ia afferent input improves when the muscle is fatigued, although a physical basis of this explanation is less straightforward to propose.

Essential tremor and dystonia have some common pathophysiological features. Both disorders involve reduced spinal presynaptic inhibition and abnormal stretch reflexes.¹ Tremor is frequently observed in dystonic patients, and essential tremor has been observed in relatives of dystonic patients.² Patients with essential tremor may be predisposed towards developing dystonia in response to trauma.¹¹ Recently, we described an abnormal response in the perception of VIIM in patients with idiopathic focal dystonia that corrects with volitional fatigue.⁴ This implies that both disorders share some similar pathophysiological features, perhaps based on abnormal elasticity of muscle spindles.

Subgroup analysis of the results showed that there was no difference in the response of patients with alcohol responsive versus non-alcohol responsive tremor to vibration. However, this analysis should be treated with caution as the study was

not powered sufficiently to undertake a full analysis of the clinical correlates of abnormal VIIM. The perception of VIIM decreased with age in healthy controls, and this could explain the age related onset of benign essential tremor. The explanation of this phenomenon we favour involves decrease in the elasticity of muscle spindles with age, tremor becoming apparent only when the response lag of muscle spindles to limb displacement exceeds the capacity of the central nervous system to compensate. There may be other explanations based on age related changes in the central nervous system. That we could not demonstrate a significant correlation between age and VIIM in patients with essential tremor may be explained by abnormally low values of VIIM, such that reduction in the VIIM with age is less easily measurable, but a trend similar to that found in the healthy control subjects was apparent.

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