

# Absence of enhanced physiological tremor in patients without muscle or cutaneous afferents

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**SUMMARY** Patients with proprioceptive loss due to a neuropathy affecting large myelinated sensory nerve fibres were studied to determine the role of somesthetic sensory inputs in enhanced physiological tremor. Involuntary movements in patients and controls attempting to hold the outstretched arm immobile were recorded during prolonged arm extension. Fatigue led to increased movements in both controls and patients but only the controls developed a rhythmic tremor. These data indicate that enhanced physiological tremor is dependent on somesthetic afferent input.

The role of somesthetic afferent input in the generation of normal and enhanced physiological tremor is a subject of debate. It has been reported that a patient without peripheral inputs developed physiological tremor after several minutes of arm extension.<sup>1</sup> There is also abundant information from intact subjects suggesting that normal physiological tremor is mediated, at least in part, by somesthetic inputs to the central nervous system. For example, Hagbarth and Young<sup>2,3</sup> have shown that muscle spindle discharge was synchronous with the small limb oscillations of normal and enhanced physiological tremor, and that manoeuvres that altered the sensitivity of the segmental stretch reflex also modified physiological tremor. In addition, it has been shown that physiological tremor was sensitive to peripheral inputs since it was reset by mechanical perturbations that were delivered randomly with respect to the observed tremor.<sup>3,4</sup> With regard to the role of afferents in fatigue tremor, Stiles<sup>5,6</sup> has demonstrated a significant reflex contribution to the development of fatigue tremor in the hand. It should be noted though that Brown *et al*<sup>7</sup> have argued that tremor in the frequency range of normal physiological tremor (8–12 Hz) observed in the human thumb is unlikely to be caused by stretch reflex mechanisms. In particular, the timing of the reflex loop is

inappropriate to generate oscillations between frequencies of 8–12 Hz.

In an attempt to clarify the extent to which fatigue and normal and enhanced physiological tremors are dependent on peripheral inputs we examined a series of patients with large-fibre sensory neuropathy without significant pathological involvement of motor neurons, muscle or spinal cord. The role of somesthetic afferents in the development of enhanced physiological tremor was examined in these patients since their lesion was more selective than the dorsal root sectioned patient described by Marsden.<sup>1</sup> We now report that while prolonged exercise in the patients with large-fibre sensory neuropathy caused an increase in instability it did not result in development of an enhanced physiological tremor similar to that observed in controls.

## Methods

Three patients with large-fibre sensory neuropathy were evaluated. The patients have a sensory neuropathy clinically characterised by slowly progressive ataxia and an absence of position and vibration sense to the most proximal joints which was accompanied by a moderate decrease in pin prick and light touch sensation below the shoulders and hips. Deep tendon and stretch reflexes were absent but muscle strength was normal. Histochemical examination of biceps muscle either revealed no abnormalities or only occasional signs of minor degenerative processes. Motor nerve conduction velocities were normal but sensory nerve potentials were absent. Nerve obtained by biopsy was characterised by absence of the large myelinated fibres in the Ia and Ib range of diameters. The patients ages were 58, 61 and 75 years. The duration of illness ranged from

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11–25 years.

Patients and age-matched controls ( $n = 5$ ) were seated with a triaxial accelerometer (Wilcoxon Research Inc., Model 139) strapped to the dorsal surface of the right hand between the metacarpophalangeal and wrist joints. The accelerometer had three piezoelectric strips mounted orthogonally within protective shields to detect motion in the x (lateral), y (vertical) and z (sagittal) planes. The protective shield around each piezoelectric element was placed within a plastic case measuring 2.5 cm  $\times$  2.5 cm  $\times$  2.5 cm that in turn was mounted on a 3.5 cm  $\times$  3.5 cm  $\times$  1.5 mm thick plexiglass base with Velcro backing. The complete apparatus weighed 22.5 gms. The sensitivity of the piezoelectric elements was approximately 60 mV/g. The voltages proportional to displacement of the piezoelectric elements were amplified with a band pass frequency of 2–40 Hz. The amplifier roll off was 6 dB per octave below 2 Hz and 18 dB per octave above 40 Hz. After amplification and filtering, data from each axis of movement were led to separate channels of a 10 bit A/D converter of an PDP 11/03 minicomputer and sampled at 100 Hz.

Patients and controls were required to position the right arm at 90° of horizontal flexion, with the elbow fully extended and with the forearm in a pronated position for 10 min while either grasping a 1 kg weight or having a 1 kg weight attached to the wrist. Samples of movement were taken for 20 s at intervals of one min from the onset or arm extension until the 10 min test expired.

Data were analysed offline with PDP-11 computers. Acceleration data from each of the x, y and z axes were first analysed independently and then combined (after digital filtering and integration) to derive a statistic of total distance travelled. Spectral analysis was done with standard fast-Fourier analysis procedures and the proportion and absolute values of power in 0.5 Hz band widths between 1.5–25 Hz were derived. For each individual patient and control subject, the frequency band with the peak proportion of activity at minute 10 of extension was chosen as a reference point (as noted in *Results* this varied from 5.0 to 9.0 Hz). The percentage of power in a 1.5 Hz band about this peak frequency was calculated for each axis for minute 0 to 10. These data and the total distance travelled were analysed with a repeated measures analysis of variance.

## Results

The primary finding was that while muscle fatigue in the patients with large-fibre sensory neuropathy caused an increase in postural instability it did not cause an enhanced physiological tremor similar to that observed in intact subjects. This lack of enhanced physiological tremor was evident despite the observations that patients as a group showed greater arm instability than controls if involuntary movements were summed over the 10 min test ( $p < 0.05$ ) and that patients showed a greater increase in movement from the beginning to the end of the 10 min test ( $p < 0.01$ ). Figure 1 illustrates the typical results for one control subject (left) and one patient

with the sensory neuropathy (right). In the upper panels, the raw acceleration record, and frequency spectrum for the complete 20 s test in the y-axis (vertical dimension) are shown when the horizontal arm flexion was begun. Although most activity was observed in the y axis, acceleration in the x and z axes paralleled that seen in the y axis. In the section marked acceleration, the absence of any fluctuations in arm posture for the control and some minimal acceleration of the arm for the patient with sensory loss should be noted. All patients with sensory loss described in the study had these minor fluctuations at the beginning of horizontal arm flexion. This observation could have been a result of the pseudo-athetoid movements that were often seen in these patients or the impaired ability of patients to maintain constant postures.<sup>8,9</sup> The spectral analyses of the movements in the y-axis are displayed on the right half of each of the upper diagrams. Each bar represents the percentage of power contributed by a one-half Hz band width around the frequencies 1.5–25.0 Hz. Note the absence of a peak in power at a specific frequency in both the patient and control at the beginning of arm extension.

The middle panels of fig 1 show the acceleration and spectrum of the same control and patient evaluated after 10 min of horizontal arm flexion. For these subjects, and for all others, the arm moved more after being held in horizontal flexion for 10 min. This control subject developed rhythmic movements with maximal power at about 8.0 Hz evident in both the spectral analysis and raw acceleration record. The remaining control subjects developed rhythmic movements with maximal power at 5.0 Hz, 7.5 Hz, 8.0 Hz or 9.0 Hz. In contrast to the distinct rhythmic involuntary movements that developed in a restricted frequency band in the arm of the control subjects, the patients with sensory loss still showed movements that were almost equally distributed across 1.5–7.0 Hz and diminished power in higher frequencies. The patients with large-fibre sensory neuropathy showed somewhat greater relative power in the frequency spectrum at 5.0 Hz, 5.5 Hz or 6.0 Hz. The lower sections of fig 1 show the total movement in the 20 s test. The movements of the control and patient increased from the beginning to the end of the test.

Figure 2 illustrates the development of tremor about the peak frequency (left panel) and total distance travelled in the 20 s test (right panel) for the group of patients and control subjects. Note that for control subjects and patients with sensory loss, the distance travelled increased nearly linearly from the beginning to the end of the 10 min test ( $p < 0.0001$ ). In control subjects, the increased movement was accompanied by an increased tendency for

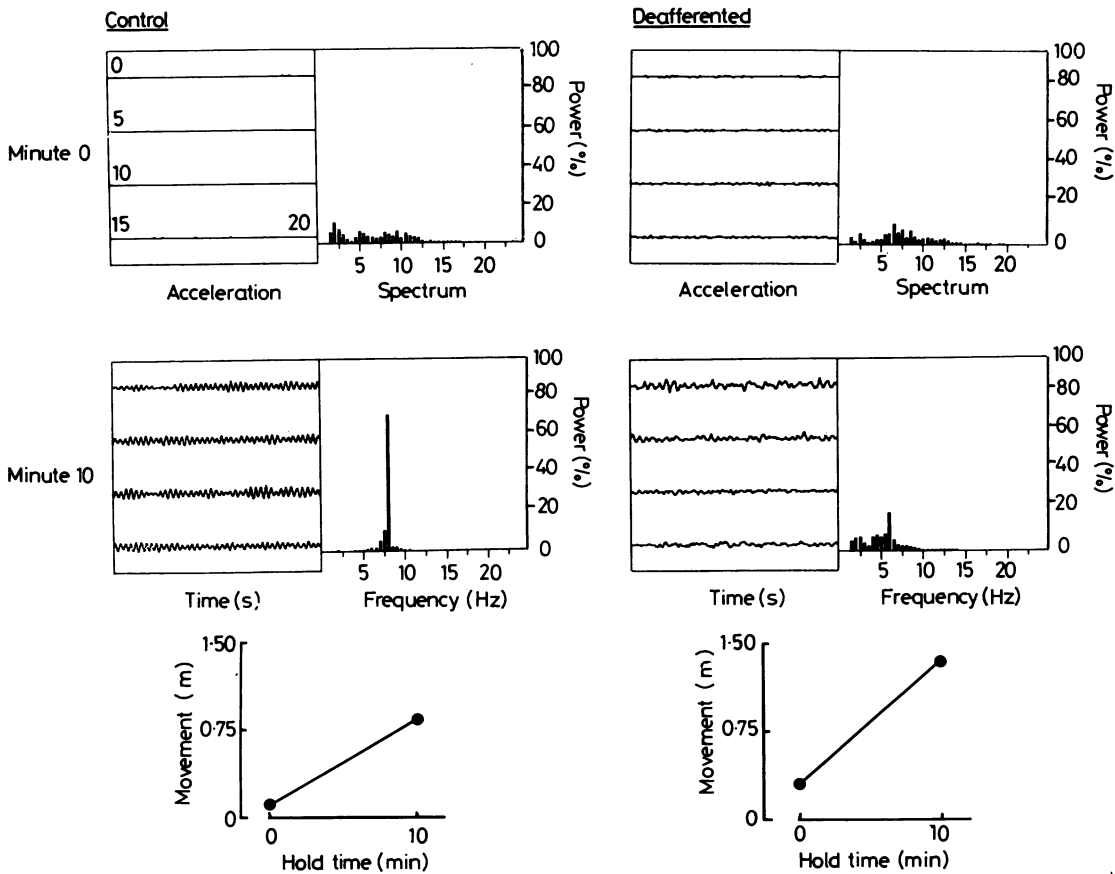


Fig 1 Movement during horizontal arm flexion. Normal control in left panels, patient with sensory loss in right panels. Labelling for all panels with acceleration data as in upper left panel. Each of the four upper panels represents the 20 s digitised acceleration records (left portions) and spectral analysis of the acceleration data (right portions) for movement in the y-axis. The four lines in the acceleration records show motion for successive 5 s intervals constituting the 20 s test. Each bar in the frequency spectrum represents the percentage power contained with a 0.5 Hz band width. The two upper panels illustrate motion when subjects first positioned the arm in horizontal flexion, while the two middle panels show motion after 10 min of continuous horizontal arm flexion. The two lower panels illustrate total movement only for minute 0 and 10.

movement to be predominantly restricted to a particular frequency between 5.0 and 9.0 Hz whereas for patients the spectral analysis did not show any dramatic increase in any particular frequency band. Statistical analysis revealed that patients differed from control subjects in the development of rhythmic movement over the course of the 10 min test ( $p < 0.05$ ).

Absolute acceleration in the selected frequency band increased over the course of the 10 min test ( $p < 0.05$ ). However, there was no difference in the response of the control subjects and patients when absolute acceleration in the selected band width about the maximum frequency was evaluated statis-

tically. This result is not necessarily surprising because there was a ubiquitous increase in absolute acceleration at all frequencies below 7.0 Hz for patients that was not different than the selective increase in absolute acceleration in a restricted frequency band observed in control subjects.

### Discussion

The major result of this investigation was that patients without large fibre somesthetic sensory inputs did not seem to develop enhanced physiological tremor when muscle fatigue was induced by horizontal arm flexion for 10 min. This contrasts with

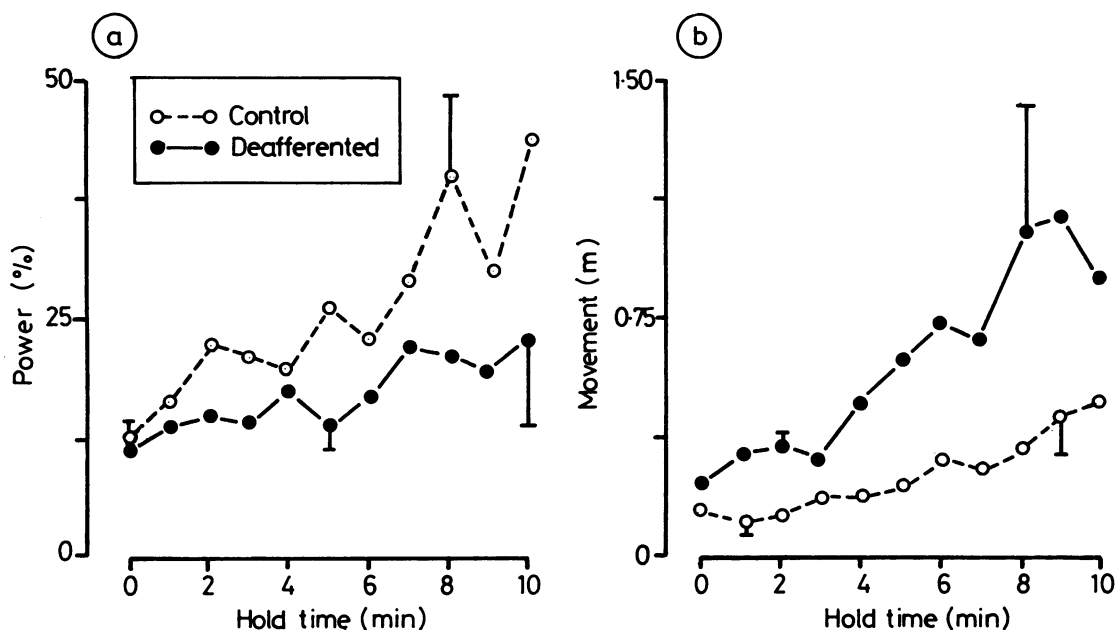


Fig 2 Development of movement during 10 min of horizontal arm flexion. (a) Percentage of power in dominant frequency band for the 20 s test taken at intervals of one min. Note the greater proportionate increase in power in a specific bandwidth (7–11 Hz) for controls than for patients with sensory loss. (b) Total distance travelled measured at successive one min intervals in the 10 min test. Note that patients showed greater instability than controls. The error bars represent the largest and smallest SEM of all the observations.

the gradual development of an enhanced physiological tremor in controls who also maintained horizontal arm flexion for 10 min. These results are consistent with earlier reports on the abolition of finger tremor following inactivation of somesthetic afferents by ischaemia<sup>10</sup> and the absence of tremor in the 6–12 Hz range in tabetic patients.<sup>11</sup> It appears that peripheral muscle or cutaneous receptors are necessary for the development of rhythmic movements during fatigue.<sup>5,6</sup> The basis for enhanced physiological tremor could be the interaction between muscle spindle discharge<sup>2,12</sup> and increased instability because of weakness that occur when a limb is fatigued. In this regard, Hagbarth and Young<sup>2</sup> demonstrated that following fatigue muscle spindle activity is synchronous with motor unit discharge, thereby suggesting that muscle spindle discharge contributes significantly to the rhythmic limb movements seen during fatigue. The increase in movements by patients in the 10 min test, that incidentally exceeded that of controls, indicated that patients also were becoming fatigued but this did not result in rhythmic arm movements. An unsynchronised wide band movement pattern was observed in patients instead of the rhythmic movements seen in controls.

In apparent contradiction to the present results, Marsden *et al*<sup>1</sup> reported development of fatigue tremor in a surgically deafferented patient. However, although the involuntary movements observed by Marsden *et al*<sup>1</sup> were tremulous, those movements were considerably different from movements of fatigued normal subjects. First, the percentage of energy contained in the peak frequency was reduced in the patient. Secondly, the spectral analysis of movements in the deafferented patient's fatigued limb showed a much broader distribution of energy in the frequencies adjacent to the peak frequency than controls. Thus, the deafferented patient showed a less well developed fatigue tremor than controls. In some sense, this is similar to the present results, since two of the three patients developed a small spike in the spectrum at about 5–6 Hz when fatigued. It is possible that continued maintenance of the extended limb position by the patients with sensory loss would have resulted in a more classical enhanced physiological tremor. Similar results to the present observation have been recently reported in abstract form by Shahani from one patient with pansensory neuropathy.<sup>13</sup> In those studies, the normal (that is at rest) physiological tremor was evident in surface electromyograms (EMG). Slow oscillations,

at 1–3 Hz, but not enhanced physiological tremor, at higher frequencies, appeared when the patient extended the arms for up to four minutes. Shahani<sup>13</sup> concluded that stretch reflexes were not important for enhanced physiological tremor and that the observations of an 8–12 Hz tremor at rest and the slow oscillation with muscle activation were generated, at least in part, by central neural mechanisms. The present results differ from Shahani's in that there was little evidence in our patients of significant oscillatory movements at any point in the test period. It is possible that our recording methods were less sensitive than recordings of the EMG.

After 10 minutes of horizontal arm flexion the distribution of energy in the frequency spectrums for the patients with the large-fibre sensory neuropathy remained diffuse, but there was some evidence of a peak in energy in a restricted frequency band. As noted above, this contrasted with the development of peak (and nearly all of the) power in a restricted frequency band for fatigued normal controls. Thus, normal controls showed increased movement for restricted frequencies whereas the patients exhibited increased movements in a relatively broad range of frequencies. It was of some interest that the absolute energy in the peak frequency band was not different between the normal controls and patients. This result could indicate that patients also showed an enhanced physiological tremor that was superimposed upon (and obscured by) a general and non-specific (in the frequency domain) increase in abnormal movements. Alternatively, the increased movements exhibited by the patients reflected non-specific abnormalities (for example broad-band athetoid movements). Unfortunately, this issue cannot be resolved unequivocally since techniques that would decompose the acceleration records and attribute various frequency components to either tremulous activity or band-limited white noise were unavailable. It should be noted, however, that in an experiment similar to the present one, Shahani<sup>13</sup> found no increase in power for frequencies classically thought to represent enhanced physiological tremor (6–12 Hz) while observing a simultaneous increase in low frequency components (1–3 Hz). Thus, it may be that the increase in absolute energy for patients with a large-fibre, peripheral neuropathy induced by prolonged muscle activity is related to a non-specific, but band-limited, increase in movement.

These results bear on the physiological mechanisms of tremor. That is, although some tremors have central generators,<sup>5</sup> the results support the view-

point that physiological tremor, and especially enhanced physiological tremor, depends on afferent inputs.

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