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Clinical Neurophysiology 114 (2003) 624–635

www.elsevier.com/locate/clinph

Characteristics of physiologic tremor in young and elderly adults

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Accepted 30 December 2002

Abstract

Objective: To determine the prevalence of tremor-related motor-unit entrainment in young and elderly adults.

Methods: Postural hand tremor in neurologically healthy people, age ranges 20–42 (59 women and 41 men) and 70–92 (50 women and 50 men) years, was studied with accelerometry and forearm electromyogram (EMG). Tremor was recorded with and without a 300 g load distributed over the distal half of the horizontally extended hand and was analyzed with Fourier spectral techniques.

Results: No tremor-related spectral peak was found in the EMG of 59 young and 65 elderly controls, and inconsistent EMG peaks were observed in 29 young and 21 elderly. Twelve young and 14 elderly people exhibited a well-defined tremor-coherent EMG peak with and without 300 g loading, and the frequency of the EMG peak decreased less than 1 Hz in 8 young and 7 elderly. The EMG peak frequency was 9–12 Hz during mass loading in all 8 young adults but in only two elderly adults. The other 5 elderly people had peak frequencies at 5–7 Hz. Age had no significant effect on the frequency and amplitude of the mechanical-resonant component of hand tremor.

Conclusions: Approximately 8% of young and elderly adult controls have an EMG-acceleration pattern that is indistinguishable from mild essential tremor.

Significance: These results provide a framework for the interpretation of electrophysiologic studies in patients with suspected essential tremor.

Keywords: Essential tremor; Movement disorders; Aging; Physiologic tremor

1. Introduction

Physiologic limb tremor consists of two distinct oscillations, mechanical-reflex and central-neurogenic (Elble, 1996). These two oscillations are superimposed upon a background of irregular fluctuations in muscle force and limb displacement. The mechanical-reflex component is the larger of the two oscillations and its frequency is governed by the inertial and elastic properties of the body (Elble, 1996). These mechanical attributes allow damped oscillations in response to pulsatile perturbations, such as those produced by irregularities in motor-unit firing and by the force of blood ejection during cardiac systole (Elble and Randall, 1978; Marsden et al., 1969a). The frequency ω of these passive mechanical oscillations depends upon the inertia I and stiffness K of the joint, according to the equation $\omega = (K/I)^{1/2}$ (Elble, 1996). Consequently, normal elbow tremor has a frequency of 3–5 Hz, wrist tremor 7–10 Hz, and metacarpophalangeal joint tremor 17–30 Hz (Elble and Randall, 1978; Fox and Randall, 1970; Stiles and Randall, 1967). Somatosensory receptors (e.g. muscle spindles) respond to these passive mechanical oscillations, but this response is usually too weak to entrain motoneurons at the frequency of tremor (Hagbarth and Young, 1979; Young and Hagbarth, 1980). However, the stretch reflex response to mechanical oscillation can be increased by fatigue, anxiety, and some medications, producing a modulation of motor-unit activity and so-called enhanced physiologic tremor. This involvement of the stretch reflex can increase tremor or suppress it, depending upon the dynamics of the reflex loop and limb mechanics (Elble, 1996).

In contrast to the mechanical-reflex oscillation, the central-neurogenic component of physiologic tremor is invariably associated with modulation of motor-unit activity, even when the central-neurogenic oscillation is much smaller than the mechanical-reflex oscillation. This observation suggests that the rhythmic motor-unit activity is driving the limb oscillation and is not simply a passive

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1388-2457/03/$30.00
doi:10.1016/S1388-2457(03)00006-3

response to sensory feedback. Participating motor-units are entrained at about 8–12 Hz, regardless of their mean frequency of discharge (Elble and Randall, 1976). The frequency of the central-neurogenic tremor is not governed by the equation $\omega = (K/I)^{1/2}$ or by the length of the stretch reflex arc. For these reasons, the central-neurogenic tremor is believed to originate from an oscillating neuronal network within the central nervous system (Elble, 1996). The location of this network is unknown. Thalamocortical rhythmicity contributes to this tremor but may not be its primary origin (Deuschl et al., 2000; Raethjen et al., 2000a). Olivocerebellar rhythmicity has long been a proposed site of origin, based on similarities with the tremor induced by harmaline in laboratory animals (Elble, 1998; Wilms et al., 1999), and some support for this hypothesis was recently found in a magnetoencephalogram (MEG) study by Gross et al. (2002).

In general, any of the following 4 electrophysiologic outcomes may occur when inertial (mass) loads are used to study hand tremor and forearm electromyogram (EMG, Deuschl and Elble, 2000; Elble and Deuschl, 2002):

1. There is no rhythmic entrainment of EMG despite rhythmic oscillation of the limb, measured with accelerometry. The tremor frequency decreases when an inertial load is attached to the limb, according to the equation $\omega = (K/I)^{1/2}$. This behavior is characteristic of normal tremor that emerges from the mechanical properties of the trembling hand, without a significant contribution from the stretch reflex or central oscillation.
2. Evidence of motor-unit entrainment is found in the EMG, and the frequency of the hand oscillation and EMG entrainment both decrease more than 1 Hz with inertial loading and are equal. Hence, the mechanical-resonant frequency of the wrist is imposed on the EMG pattern or, in other words, the oscillating musculoskeletal system dictates the frequency of motor-unit entrainment through somatosensory feedback. Many patients with enhanced physiologic tremor have this pattern.
3. The wrist oscillation and EMG entrainment have the same frequencies in the unloaded condition. In the loaded condition, two frequencies are seen in the accelerometry: a lower frequency oscillation corresponding to the mechanical-reflex resonance frequency and a higher frequency oscillation with associated EMG entrainment. This high-frequency oscillation is interpreted as a central-neurogenic oscillation because its frequency does not decrease with inertial loading and bears no relationship to reflex arc length (i.e. loop conduction time).
4. The wrist oscillation and EMG entrainment have the same frequency in the loaded and unloaded conditions, and the frequency decreases less than 1 Hz with inertial loading. This result is interpreted as a sign of strong central-neurogenic oscillation, with the stretch reflex and limb mechanics playing a minor or secondary role in rhythmogenesis.

Patients with advanced essential tremor have outcome 4, but outcomes 2 and 3 are common in mild essential tremor (Deuschl et al., 1996; Elble, 1986; Elble and Deuschl, 2002; Louis and Pullman, 2001). Outcome 2 may occur when a central-neurogenic oscillation is so irregular and intermittent that it produces only a series of perturbations to the mechanical-reflex system, resulting in an enhanced mechanical-reflex oscillation. Progression from outcome 2 to 4 is believed to reflect an increasing strength of central-neurogenic oscillation as essential tremor progresses or is enhanced by drugs, fatigue, or other provocative maneuvers. Outcome 4 also occurs when the central-neurogenic oscillation frequency is close to the mechanical-resonant frequency of the wrist (~6–9 Hz). Outcome 1 is unequivocally normal. This approach to tremor analysis produces an equivocal result when EMG entrainment is present only in the unloaded or loaded condition, making it impossible to determine whether the EMG entrainment is a central-neurogenic oscillation or a mechanical-reflex oscillation.

The electrophysiologic properties of mild essential tremor in young adults are identical to those of the 8–12 Hz central-neurogenic component of physiologic tremor (Elble, 1986). Therefore, the diagnostic utility of electrophysiologic testing will depend on the prevalence of central-neurogenic tremor in normal people. Normal postural hand tremor recorded 14 cm from the wrist contains rhythmic oscillations with a mean peak-to-peak amplitude of 0.009–0.153 mm displacement and 3–33 cm/s^2 acceleration (Elble, 1986). These mean amplitudes overlap with mild essential tremor, and tremor amplitude fluctuates so much that it is not useful for distinguishing physiologic tremor from mild essential tremor (Elble, 1986). Rhythmic entrainment of motor-units is the sine qua non of essential tremor, and it has long been our impression that the electrophysiologic diagnosis of mild essential tremor should be based on the existence of rhythmic motor-unit activity at a frequency that is independent of reflex loop time and mechanical loads (Elble, 1986; Elble and Deuschl, 2002). However, the utility of this approach will depend upon the prevalence of a prominent central-neurogenic component of physiologic tremor in clinically normal people.

Most, if not all, people exhibit 8–12 Hz bursts of EMG in the wrist and finger extensor muscles during slow wrist or finger flexion, but the tendency for 8–12 Hz motor-unit entrainment is too weak in most healthy adults to contribute significantly to tremor during horizontal extension of the hand or finger (Kakuda et al., 1999; Wessberg and Vallbo, 1996). Raethjen et al. (2000b) found that about 30% of normal adults had statistically significant 8–12 Hz tremor during horizontal extension of the hand or finger. However, the magnitude of motor-unit entrainment was typically much less than in patients with essential tremor, and only 13 of their 117 controls were older than 70 years. In the present

study, we sought to determine the prevalence of motor-unit entrainment in the forearms of ostensibly normal young and elderly adults during horizontal extension of the hand. In particular, we determined the prevalence of EMG-accelerometry patterns comparable to those of mild essential tremor. This investigation is important because it provides a framework for the interpretation of electrophysiologic studies in patients with suspected essential tremor.

2. Methods

Hand tremor was studied with accelerometry and forearm EMG in 200 ostensibly normal adults, age ranges 20–42 (59 women and 41 men) and 70–92 (50 women and 50 men) years. Each volunteer gave informed consent to participate in this study, which was approved by the Springfield Committee for Research Involving Human Subjects.

Everyone in this study was white non-Hispanic except one black woman and one black man in the 70–92-year group, and one Hispanic woman and one black man in the 20–42-year group. The general population in our region of central Illinois is 97.4% white and 2.0% black (compiled by the Illinois Center for Health Statistics using the 1990 Census Modified Age–Race–Sex (MARS) tables from the US Bureau of the Census, http://www.census.gov).

The volunteers in the young and older age groups were recruited by two methods to check for the effects of potential recruitment bias. Half of the people in the 20–42-year age range were recruited through an advertisement for healthy volunteers. The advertisement asked for neurologically healthy adults to participate in a study of normal hand tremor. The advertisement was posted around our medical center and at our local senior citizens center, and was published in a newsletter for the general public. These 'biased' people were then asked to identify a genetically unrelated friend or colleague of comparable age for recruitment into an 'unbiased' group. Similarly, half of the people in the 70–92-year age range were recruited into a biased control group through advertisement. The unbiased elderly volunteers were recruited sequentially from the spouses of new patients referred to our center for dementia or Parkinson disease. Twenty people refused to participate because they were not interested ($n = 15$), were too busy ($n = 4$), or had no transportation ($n = 1$).

Nineteen biased (10 young and 9 elderly) and 8 unbiased controls (5 young and 3 elderly) had at least one parent or sibling with a history of tremor (Pearson chi square = 0.385, df = 1, $P = 0.535$ for family history vs. age group; chi square = 5.181, df = 1, $P = 0.023$ for family history vs. recruitment method). Nevertheless, for both age ranges, the EMG and accelerometry results from the biased and unbiased groups did not differ statistically, so the data from the biased and unbiased groups were pooled for much of this report.

All of the 70–92-year-old volunteers were examined by the author. A laboratory technician with 15 years of experience examined the 20–42-year-old controls during horizontal extension of the upper limbs and during writing and drawing. Young controls with visible or symptomatic tremor in the hands were examined by the author. People were excluded if they had clearly abnormal tremor (grade 2 or worse on the tremor rating scale of Fahn et al. (1993)) or if they had clinical evidence of some other neurologic condition, substance abuse, or drug-induced tremor. The Drugdex (R) computer database (Gelman et al., 1997) and the Physician's Desk Reference (1997) were used to compile a list of 214 drugs that may cause tremor or tremulousness. This list included well-known tremorogenic drugs such as lithium, neuroleptics, antidepressants, sympathomimetics and methylxanthines but also included many other drugs that cause tremor rarely (<1%). Rather than exclude people taking medications of questionable significance, we excluded only those who acknowledged shakiness with the use of any medication, and also patients taking lithium, neuroleptics, tricyclic antidepressants, sympathomimetics, or methylxanthines for major psychiatric or medical illness. Only two mildly demented patients on multiple psychotropic drugs were excluded for any of the above reasons.

None of the young controls were taking medications other than birth control pills. Eight 70–92-year-old people were taking drugs with more than a 1% incidence of tremor as a side effect (amiodarone – 1, nifedipine – 2, paroxetine – 1, quinidine – 2, sertraline – 1 and trazodone plus tocainamide – 1). Nineteen others in this age group took drugs with less than a 1% incidence of tremor (amlodipine – 7, diltiazem – 5, doxazosin – 2, fosinopril – 1, nabumetone – 2 and omeprazole – 2). None of them could recall any problem with tremor or tremulousness when these drugs were prescribed. The remaining elderly people were taking no drugs ($n = 29$) or were taking one or more drugs that were not tremorogenic ($n = 44$), but 8 of these people were taking drugs that could suppress tremor. Six were taking beta-adrenergic blockers for hypertension (atenolol-4, propranolol-1, and metoprolol-1), and two alprazolam for mild anxiety.

Postural tremor of the horizontally extended hand was recorded with the hand splinted and the forearm pronated and supported so as to restrict motion to the wrist (hand tremor). A 15 g triaxial piezoresistive accelerometer was secured to a 57 g plastic splint that was fastened to the dorsum of the hand with Velcro straps. The accelerometer was thereby located over the middle finger, 14 cm from the distal wrist fold, and the fingers were splinted in extension. The accelerometer had a sensitivity of 5.9 mV/G (G = acceleration of gravity). Hand tremor was recorded with and without a 300 g load distributed over the distal half of the horizontally extended hand. This was accomplished by fastening small lead weights on the plastic splint with Velcro adhesives.

Forearm EMG was recorded with 7 mm diameter Ag–AgCl skin electrodes that were positioned in a bipolar arrangement near the motor points of the extensor carpi radialis brevis (ECRb) and flexor carpi radialis. EMGs were full-wave rectified and low-pass filtered (−3 db at 30 Hz).

Tremor and rectified–filtered EMG (hereafter EMG) were recorded simultaneously for 62 s, with and without a 300 g load attached to the hand. Each measurement was performed twice. Tremor and EMG were digitized at 200 samples per second using a personal computer and a 16 bit analog-to-digital converter. Spectral and coherence analyses of the tremor and EMG were computed using a fast Fourier transform, as previously described (Elble, 2000). Autospectra of 6 sequential 10.24 s data epochs tremor and EMG were averaged to produce smoothed autospectra with a frequency resolution of 0.098 Hz. We computed one-half peak-to-peak tremor amplitude (i.e. baseline to peak amplitude) in the vertical direction by taking the square root of the total power within the acceleration (cm/s^2) spectral peak of wrist tremor. The displacement amplitude (cm) was estimated by dividing the acceleration amplitude by the squared tremor frequency in radians per second.

Tremor frequency was computed from the EMG and acceleration autospectra. A weighted average measure of tremor frequency was computed by summing the product of spectral amplitude and frequency for each spectral band within a tremor spectral peak and dividing this sum by the sum of the spectral amplitudes. This measure of tremor frequency, rather than peak frequency, is less dependent on trial-to-trial variations in the shape of the spectral peak and produces the measure of tremor frequency with the least trial-to-trial variability (Elble et al., 1994).

The principal aim of this study was to determine the prevalence of prominent motor-unit entrainment in postural wrist tremor of ostensibly normal people. Motor-unit entrainment was considered significant when the EMG spectral peak was significantly greater than the background activity ($P < 0.01$) and had a bandwidth less than 3 Hz at half-peak power. The coherence (squared linear correlation) between EMG and acceleration is typically more than 0.5 when these criteria are met, and these characteristics are typical of the EMG spectral peaks in patients with essential tremor (Elble, 1986).

All statistical analyses were performed using SYSTAT software (http://www.systat.com). Repeated-measures analysis of variance (ANOVA) was used to examine the effects of age (elderly vs. young), recruitment bias, gender (male vs. female), mass loading (0 vs. 300 g) and trials (1 and 2) on tremor frequency and amplitude. Post hoc comparisons were performed with Bonferroni-corrected t tests. In no instance did we find any trials effect ($P > 0.2$ for all variables studied), so the groups mean ± SD were computed using the average of two trials. All means are expressed ± SD. The boxes of the box-and-whisker plots in this paper represent the range between the 25th and 75th percentiles, and the whiskers are the 95th percentiles. The line within each box is the median.

3. Results

The young and elderly controls produced 4 EMG–acceleration patterns (Table 1): (a) no tremor spectral peak in the ECRb EMG with and without mass loading; (b) a tremor spectral peak in the EMG only in the condition of no mass loading; (c) a tremor spectral peak in the EMG only in the condition of 300 g loading and (d) a tremor spectral peak in the EMG with and without 300 g loading. The proportions of people with these patterns did not differ statistically between the young and elderly people (Pearson chi square = 7.344, df = 3, $P = 0.062$).

3.1. Tremor with no spectral peak in the EMG

Fifty-nine young and 65 elderly controls had a statistically flat rectified–filtered ECRb EMG spectrum in the frequency range of tremor (0–15 Hz), and the frequency of the tremor (vertical acceleration spectrum) decreased with mass loading (Fig. 1). This ultra-normal accelerometry–EMG pattern corresponds to outcome 1 given in Section 1. Twenty-seven of the 59 young controls and 29 of 65 elderly controls were biased (Pearson chi square = 0.016, df = 1, $P = 0.898$), indicating no effect of recruitment bias.

Repeated-measures ANOVA revealed no effect of age on tremor frequency with and without mass loading ($F = 2.742$, df = 1,119, $P = 0.100$). The distributions of tremor frequencies were nearly identical for the two age groups (Fig. 2). However, there was a statistically significant gender effect on tremor frequency ($F = 20.865$, df = 1,119, $P < 0.001$), due to the greater effect of mass loading on the women's tremor frequency. With no mass loading, the elderly women tended to have slightly lower tremor frequencies (average of two trials: 7.480 ± 0.652 Hz) than the young women (8.015 ± 0.852 Hz), young men (8.047 ± 0.469 Hz) and elderly men (7.949 ± 0.885 Hz, $F = 3.229$, df = 1,120, $P = 0.075$). With mass loading, the young (5.182 ± 0.507 Hz) and elderly women (5.096 ± 0.510 Hz) had significantly lower frequencies than did the young (5.763 ± 0.501 Hz) and elderly men (5.741 ± 0.456 Hz, $F = 45.239$, df = 1,120, $P < 0.001$).

Tremor frequency decreased significantly with mass loading ($F = 1691.186$, df = 1,119, $P < 0.0001$). The frequency of tremor decreased by an average of 2.64 ± 0.694 Hz in the young controls and by 2.30 ± 0.633 Hz in the elderly ($F = 4.972$, df = 1,120, $P = 0.028$, Fig. 3). This small difference between groups was due to a slightly greater frequency change (average of two trials) in the 38 young women (2.833 ± 0.712 Hz) than the 21 young men (2.284 ± 0.505 Hz), 34 elderly women

Table 1
Occurrence of tremor-coherent EMG spectral peaks in controls

	Young controls (age 20–42 years, $N = 100$ people)	Elderly controls (age 70–92 years, $N = 100$ people)
No tremor spectral peak in ECRb	59	65
Tremor spectral peak in the ECRb only without mass loading	27	14
Tremor spectral peak in the ECRb only with mass loading	2	7
Tremor spectral peak in the ECRb with and without mass loading	12	14
Total	100	100

(2.384 ± 0.665 Hz), and 31 elderly men (2.208 ± 0.594 Hz, $F = 9.463$, df = 1,120, $P = 0.003$).

The acceleration amplitude of tremor did not change significantly with inertial loading ($F = 0.176$, df = 1,118, $P = 0.676$), and there was no effect of age ($F = 0.685$, df = 1,118, $P = 0.410$). The mean acceleration amplitudes of the young (without loading: 14.087 ± 7.993 cm/s^2; with loading: 13.292 ± 4.829 cm/s^2) did not differ significantly from those of the elderly (without loading: 14.468 ± 7.088 cm/s^2; with loading: 15.021 ± 5.886 cm/s^2). There was a small gender effect of marginal statistical significance ($F = 0.036$, df = 1,118, $P = 0.036$) because the young (without loading: 13.201 ± 8.930 cm/s^2; with loading: 12.803 ± 4.655 cm/s^2) and elderly women (without loading: 12.786 ± 6.469 cm/s^2; with loading: 14.277 ± 5.658 cm/s^2) had slightly lower tremor amplitudes than the young (without loading: 15.690 ± 5.793 cm/s^2; with loading: 14.176 ± 5.125 cm/s^2) and elderly men (without loading: 16.313 ± 7.376 cm/s^2; with loading: 15.837 ± 6.114 cm/s^2).

There was no effect of age ($F = 1.999$, df = 1,118, $P = 0.160$) or gender ($F = 0.360$, df = 1,118, $P = 0.550$) on the displacement amplitude of tremor. However, mass loading increased the amplitude of tremor in the young (without loading: 0.006 ± 0.003 cm; with loading: 0.012 ± 0.006 cm) and elderly (without loading: 0.006 ± 0.003 cm; with loading: 0.014 ± 0.006 cm, $F = 192.831$, df = 1,118, $P < 0.0001$) due to the reduction in tremor frequency with mass loading (displacement amplitude = acceleration amplitude/tremor frequency squared, where tremor frequency is expressed in radians/s).

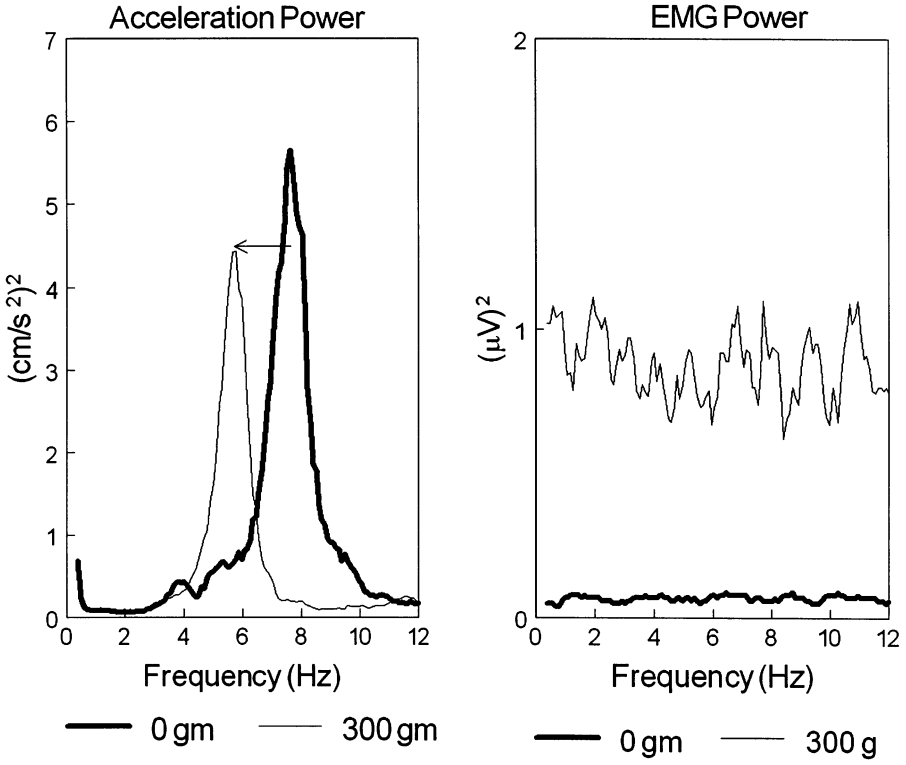

Fig. 1. Wrist tremor and rectified–filtered EMG (ECRb) from a 27 year old woman with no evidence of motor-unit entrainment with and without 300 g loading. Note the 2 Hz reduction in the acceleration spectral peak with 300 g loading (arrow).

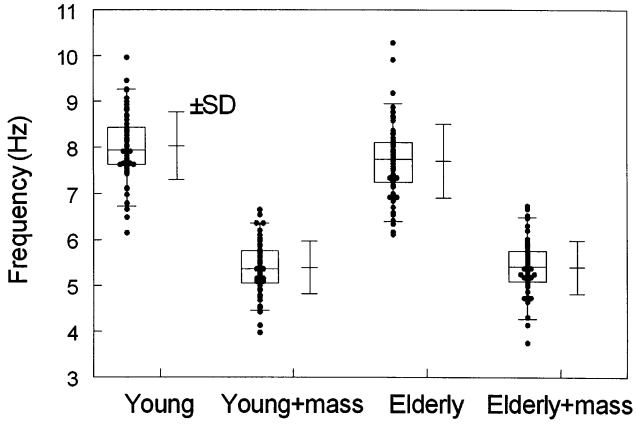

Fig. 2. Box-and-whisker plots of tremor frequency (average of trials 1 and 2) with and without mass loading for the young and elderly controls with statistically flat EMG spectra. The mean ± SD is also shown for each distribution.

3.2. Inconsistent EMG spectral peaks

Twenty-seven young and 14 elderly controls exhibited ECRb motor-unit entrainment at the frequency of tremor without mass loading, but the EMG spectral peak disappeared during mass loading (Fig. 4). The EMG spectral peak occurred at the frequency of the mechanical-resonant tremor peak, and the EMG and acceleration spectra were highly coherent (>0.5) at this frequency. Thirteen of the people with this EMG-acceleration pattern (4 young and 9 elderly controls) also had poorly formed EMG spectral peaks at 9–14 Hz, but there was no corresponding spectral activity in the acceleration spectra (Fig. 4).

Two young and 7 older adults produced an ECRb EMG spectral peak only during mass loading. This EMG peak occurred at the mechanical-resonant tremor frequency in all but one person, who exhibited an EMG spectral peak at 9–10 Hz without appreciable corresponding activity in the acceleration spectrum. Regardless, the EMG peaks were highly coherent (>0.5) with the acceleration spectra.

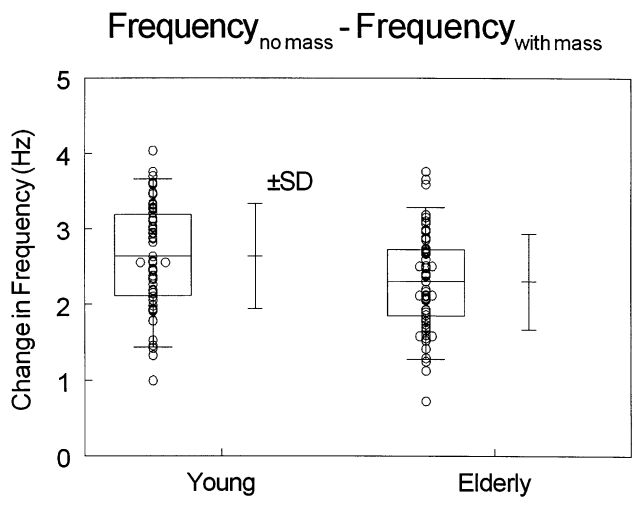

Fig. 3. Box-and-whisker plots of the change in acceleration peak frequency (average of trials 1 and 2) with and without mass loading for the young and elderly controls with no EMG spectral peaks with and without mass loading. The mean ± SD is also shown for each distribution.

3.3. EMG spectral peak with and without mass loading

Twelve young and 14 elderly controls produced an ECRb EMG spectral peak with and without mass loading. Five of the 12 young and 9 of the 14 older controls were biased (Pearson chi square = 1.330, df = 1, $P = 0.249$). Eight of the 12 young and 4 of the 14 elderly controls were women (Pearson chi square = 3.773, df = 1, $P = 0.052$). Thus, there was no significant effect of age, gender or recruitment bias.

The 26 controls with EMG peaks had a tremor frequency without mass (8.002 ± 1.387 Hz) that did not differ significantly from the mean tremor frequency of controls with no EMG spectral peaks (7.857 ± 0.784 Hz, $t = -0.516$, df = 28.4, $P = 0.610$). Mass loading produced one of 4 different EMG–acceleration patterns:

1. The EMG and acceleration spectral peaks had the same frequency, but their frequency decreased more than 1 Hz (outcome 2 in Section 1).
2. The frequency of the EMG spectral peak increased to 9–12 Hz with mass loading. The acceleration spectrum contained spectral peaks at 9–12 Hz and at the lower mechanical-resonant frequency (Fig. 5), but there was no EMG spectral peak at the mechanical-resonant frequency (outcome 3 in the Section 1).
3. Same as #2, except that the EMG spectrum contained peaks at 9–12 Hz and at the lower mechanical-resonant frequency (Fig. 6, outcome 3 in Section 1).
4. The frequency of the EMG and acceleration spectral peaks changed less than 1 Hz with mass loading, and the acceleration spectrum contained a single spectral peak with and without mass loading (Fig. 7, outcome 4 in Section 1).

Only one person (21 year old male unbiased control) exhibited two peaks in the acceleration and EMG spectra with mass loading (Fig. 6). The remaining 25 controls exhibited a single EMG spectral peak with and without mass loading.

The distributions of the EMG frequency change are shown in Fig. 8 for the 11 young and 14 elderly controls with a single EMG spectral peak with and without mass loading. Four of the 11 young controls exhibited a reduction in EMG peak frequency comparable to the change in mechanical-resonant frequency exhibited by the controls with no EMG spectral peaks. Seven of the 11 young controls exhibited an increase in the EMG peak frequency to 9–12 Hz with mass loading, as illustrated in Fig. 5. By contrast, only two of the 14 elderly controls exhibited an increase in frequency to 9–12 Hz. The remaining 12 elderly controls exhibited acceleration and EMG peaks that

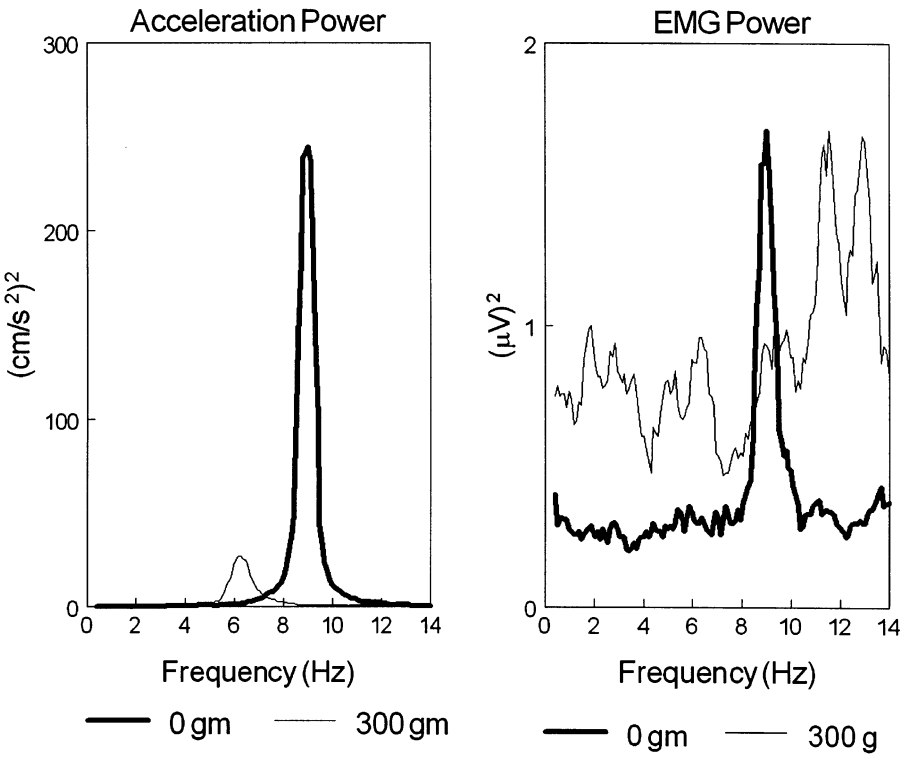

Fig. 4. Wrist tremor and rectified–filtered EMG from a 31-year-old man with prominent motor-unit entrainment only in the absence of mass loading. Mass loading produced a 3 Hz reduction in the acceleration spectral peak and a reduction in amplitude, but there was no corresponding peak in the EMG (ECRb).

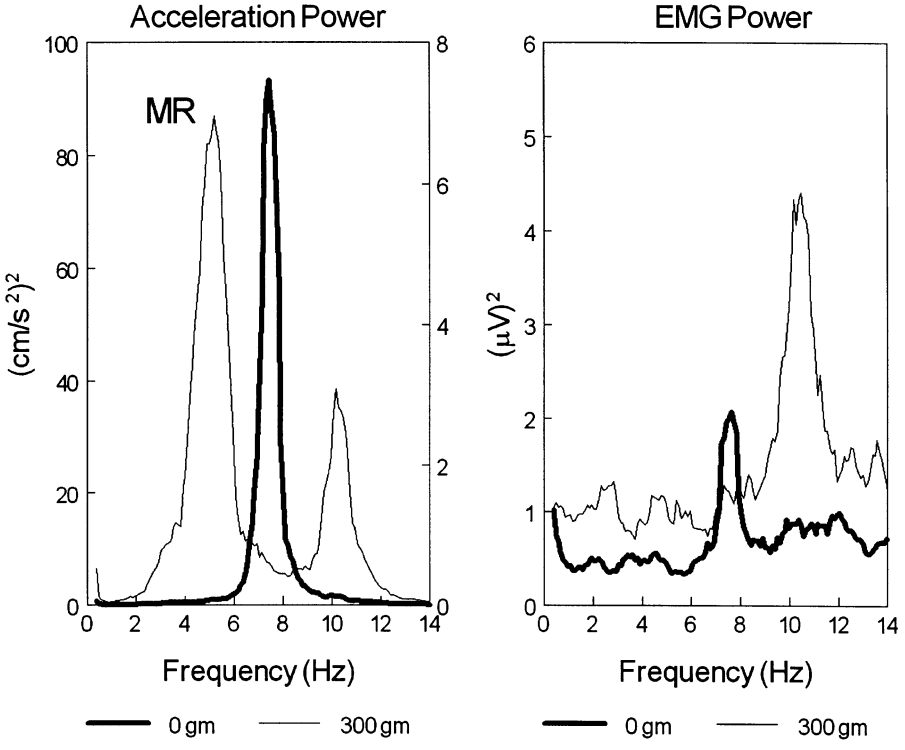

Fig. 5. Wrist tremor and rectified–filtered EMG (ECRb) from a 76-year-old woman with prominent motor-unit entrainment with and without mass loading. With no mass loading, the acceleration and EMG spectra contained a single coherent peak at 7.8 Hz. Mass loading produced peaks in the acceleration spectra at 5 and 10.5 Hz. Left vertical axis of the acceleration spectrum: 0 g load and right vertical axis: 300 g load.

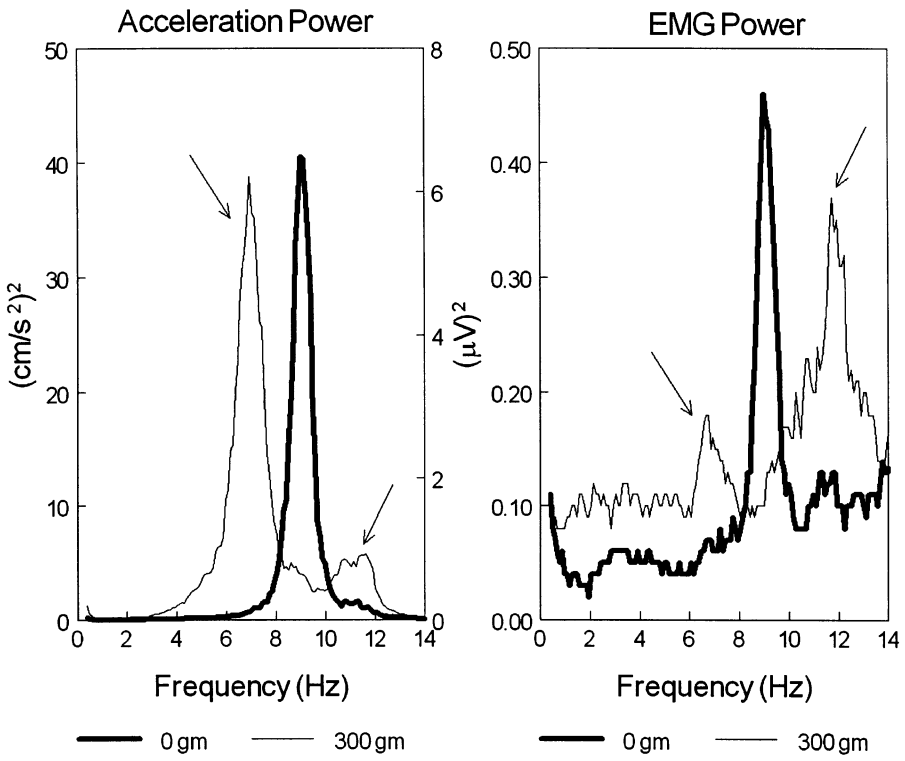

Fig. 6. Wrist tremor and rectified–filtered EMG (ECRb) from a 21-year-old man with prominent motor-unit entrainment with and without mass loading. With no mass loading, the acceleration and EMG spectra contained a single coherent peak at 9.4 Hz. Mass loading produced coherent peaks in the EMG and acceleration spectra at 6–7 and 11–12 Hz (arrows). Left vertical axis of the acceleration spectrum: 0 g load and the right vertical axis: 300 g load.

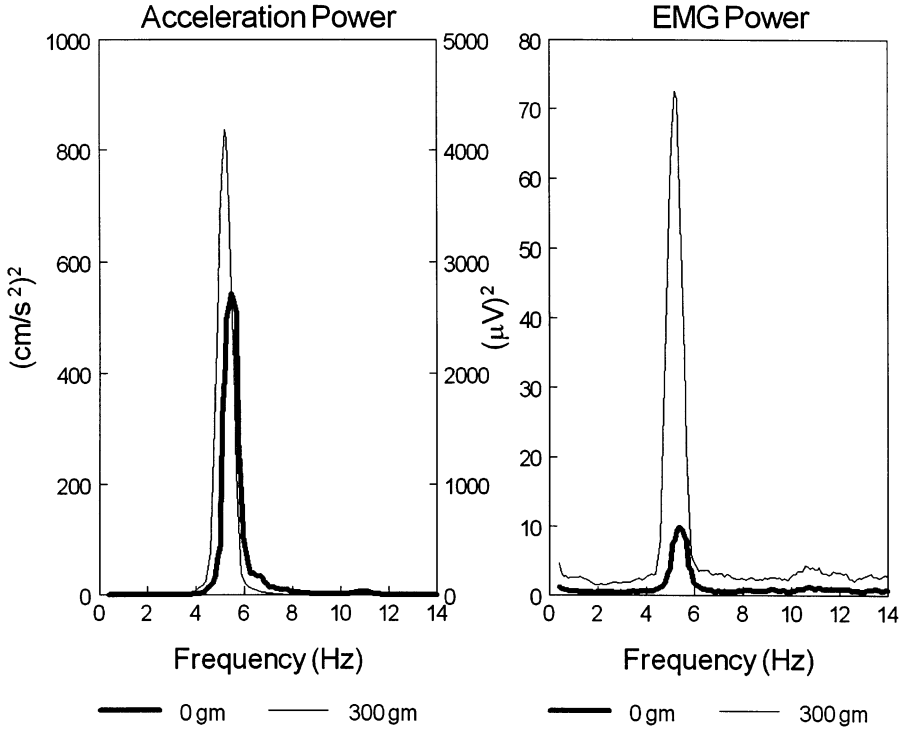

Fig. 7. Wrist tremor and rectified–filtered EMG (ECRb) from an 80-year-old man with prominent motor-unit entrainment that changed less than 1 Hz with mass loading. Left vertical axis of the acceleration spectrum: 0 g load, and right vertical axis: 300 g load.

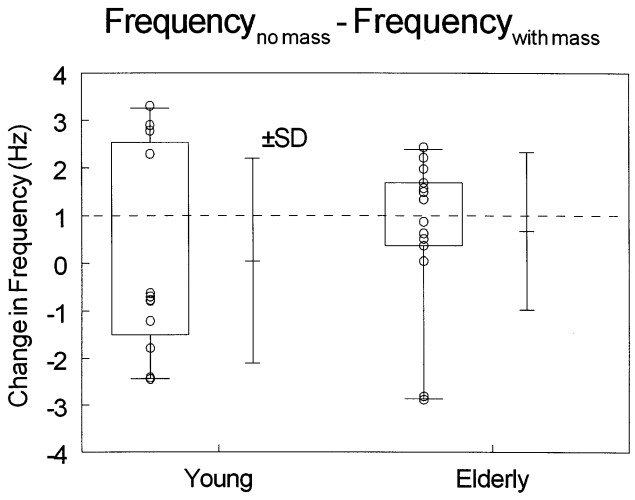

Fig. 8. Box-and-whisker plots of the change in EMG (ECRb) peak frequency (average of trials 1 and 2) with and without mass loading for the young and elderly controls with EMG spectral peaks with and without mass loading. The mean ± SD is also shown for each distribution. A horizontal broken line is drawn at 1 Hz change in frequency.

decreased by 0.04–2.43 Hz to a frequency of 5–7 Hz (Fig. 8).

The 124 controls (59 young and 65 elderly) with no EMG tremor spectral peak had lower amplitude tremor (acceleration: 14.287 ± 7.503 cm/s^2; displacement: 0.006 ± 0.003 cm) than the 26 controls (12 young and 14 elderly) with EMG spectral peaks with and without loading (acceleration: 38.463 ± 25.569 cm/s^2; displacement: 0.018 ± 0.019 cm, $P < 0.001$ for acceleration and displacement). The exclusion of two outliers from the group with EMG spectral peaks did not eliminate the statistical difference between this group (acceleration: 32.081 ± 13.352 cm/s^2; displacement: 0.013 ± 0.006 cm) and the group with no EMG spectral peaks (acceleration: 14.287 ± 7.503 cm/s^2; displacement: 0.006 ± 0.003 cm, acceleration: $t = -6.212$, df = 24.6, $P < 0.001$; displacement: $t = -4.827$, df = 24.3, $P < 0.001$).

Repeated-measures ANOVA revealed no significant effect of age, gender, or trials on the coherence between the extensor EMG and acceleration tremor peaks ($P > 0.5$). The coherence without (mean 0.760 ± 0.101; range 0.585–0.943) and with 300 g loading (mean 0.722 ± 0.107; range 0.497–0.932) did not differ significantly ($t = 1.699$, df = 24, $P = 0.102$), and all but one coherence value was greater than 0.5.

3.4. Flexor EMG

Spectral peaks occurred in the flexor carpi radialis at the frequency of tremor in 17 people (9 young and 8 elderly): 12 of 26 with tremor-coherent extensor EMG peaks with and without mass loading, two of 41 with tremor-coherent extensor EMG peaks without mass loading, and 3 of 9 with tremor-coherent extensor EMG peaks with mass loading. The 124 people with no extensor EMG peaks also had no peaks in the flexor EMG. In all instances, the flexor EMG activity was at least an order of magnitude smaller than the extensor activity, and the coherence between the flexor EMG peak and acceleration was statistically insignificant ($P > 0.05$) in 5 of the 17 people with flexor peaks (two young and 3 elderly). These 5 had extensor EMG peaks with and without loading. The phase between coherent extensor and flexor EMG peaks varied greatly but had a bimodal distribution centered around 0 and 180°, with and without 300 g loading. Thus, flexor EMG was variable and made little or no contribution to hand tremor under the conditions of this study. Similar results and conclusions were reported by Raethjen et al. (2000b).

3.5. Clinical data

Three elderly people with no EMG peaks and 3 elderly with EMG peaks with and without loading had mild intermittent wrist tremor that was questionably abnormal (grade 1 by the Fahn–Tolosa–Marin tremor rating scale (Fahn et al., 1993)) during horizontal extension of the hands and during finger–nose–finger testing. All 6 drew slightly tremulous Archimedes spirals and, therefore, may have had mild essential tremor.

4. Discussion

The people in this study were not a random sample of the general population, so we cannot exclude an effect of recruitment bias. We recruited controls by two methods to check for effects of bias and found only a more frequent family history of tremor in the biased controls (19 biased and 8 unbiased people with a tremulous parent or sibling). We found no effect of recruitment bias on the electrophysiologic data. Therefore, we believe our results are representative of the general population.

This is the largest published study of physiologic tremor in young and elderly adults. The results of this study are very similar to those of Raethjen et al. (2000b). Both studies found that the mechanical-resonant oscillation is the main source of physiologic tremor, and there is no significant effect of aging on the frequency of this oscillation. The mechanical-resonant tremor frequencies in our controls were nearly identical to those published by Raethjen et al. (2000b). They used larger mass loads (500 and 1000 g) than us (300 mg), but we distributed the mass over the distal half of the hand so as to maximize the change in moment of inertia about the wrist.

Raethjen et al. (2000b) found that men had a slightly lower mechanical-resonant tremor frequencies than women, and this gender effect correlated with the smaller hand mass in women. This gender effect disappeared when large mass loads were applied to the hand. By contrast, we found a significant gender effect on mechanical-resonant tremor frequency only when 300 g loads were applied to the hand;

the tremor frequencies in women were slightly lower than in the men. It is unclear why the gender differences in our study differed from those reported by Raethjen et al. (2000b). Minor differences in recording methods and an inability to measure and control joint stiffness could be responsible. Regardless, the gender effects observed in both studies were small and of questionable clinical significance.

We found no effect of age on the mechanical-resonant tremor frequency, even though we carefully examined the extremes of the adult age range. Other studies have produced conflicting results, as reviewed by Raethjen et al. (2000b). These studies failed to restrict motion to a single joint or did not use EMG and mass loading to separate the mechanical-resonant and central-neurogenic components of physiologic tremor (Marsden et al., 1969b). Proximal joints with greater inertia (shoulder, elbow) influence greatly the Fourier spectra of tremor recorded from the carpus or finger (Elble and Randall, 1978; Raethjen et al., 2000b). Only Raethjen and coworkers controlled for these factors, and they too found no effect of age on the mechanical-resonant tremor frequency. Similarly, age had no effect on tremor amplitude.

Raethjen et al. (2000b) found that only two of 117 people had an EMG peak that was coherent with the mechanical-resonant oscillation. By contrast, we found that 27 young and 14 elderly controls exhibited motor-unit entrainment at the frequency of mechanical-resonant tremor without mass loading, but the EMG spectral peak disappeared during mass loading. We also found two young and 7 elderly people with motor-unit entrainment at the frequency of mechanical-resonant tremor with mass loading but not without. This difference in our results suggests that more of our controls exhibited enhanced mechanical-reflex physiologic tremor or possibly a central-neurogenic component that was too weak to persist in both loading conditions. We recorded tremor for 62 s while Raethjen recorded for 30 s. Therefore, fatigue may have enhanced tremor in our study. Longer recording periods permit greater frequency resolution and spectral smoothing (Elble and Deuschl, 2002), but fatigue will eventually occur, particularly with mass loading. The optimum recording duration needs to be determined with additional study. One minute is perhaps too long.

Raethjen et al. (2000b) found tremor-correlated EMG peaks with and without mass loading in the hand tremor of 15% of their controls and finger tremor of approximately 25%. We found that 12% of the young and 14% of the elderly controls exhibited tremor-coherent motor-unit entrainment with and without mass loading. The percentages of young and elderly controls with persistent tremor-coherent EMG peaks were 15 and 16%, respectively, if all statistically significant EMG peaks were considered. However, we did not count 3 young and two elderly controls because their EMG and acceleration peaks had wide half-amplitude bandwidths, greater than 4 Hz (e.g. the 10–14 Hz EMG activity with mass loading in Fig. 4). Nevertheless, our results are comparable to those of Raethjen and coworkers.

Nearly all patients with clinically definite essential tremor have EMG spectral peaks with and without mass loading, and the change in tremor frequency is less than 1 Hz (Deuschl et al., 1996; Elble, 1986; Elble and Deuschl, 2002; Louis and Pullman, 2001). Seven of the young controls with EMG spectral peaks with and without loading exhibited a 0.5–2.5 Hz increase in EMG peak frequency with mass loading, making this central-neurogenic oscillation easily discernible from the mechanical-resonant oscillation, which decreased in frequency by 2.64 ± 0.694 Hz. The frequency of this central-neurogenic oscillation was 9–12 Hz. This type of oscillation is also seen in young adults with mild essential tremor (Elble, 1986). Four young controls had a tremor-coherent EMG spectral peak that decreased in frequency by 2.5–3.5 Hz with mass loading, which is typical of enhanced physiologic mechanical-resonant tremor (Elble and Deuschl, 2002). One young control exhibited both patterns simultaneously.

By contrast, only two of the 14 elderly controls with EMG spectral peaks with and without mass loading exhibited a 9–12 Hz peak with mass loading. The tremor-coherent EMG spectral peaks of 12 elderly controls decreased 0.04–2.43 Hz with mass loading. Five of these 12 controls exhibited a reduction in frequency of less than 1 Hz, and 7 had a reduction in frequency greater than 1 Hz. While the distribution of frequency changes had some separation at about 1 Hz (Fig. 8), too few elderly controls with this pattern of tremor were studied to comment definitively. One may simply conclude that some elderly controls exhibit an EMG spectral peak at 7.704 ± 0.801 Hz that increases to 9–12 Hz with mass loading, similar to young controls, but most elderly controls have an EMG spectral peak that decreases in frequency by 0–2.5 Hz. Thus, the tremor-related EMG activity tends to occur at frequencies below 8 Hz in the elderly. This effect of aging on physiologic wrist tremor has not been reported previously, possibly because previous studies included few people in the 70–90 year age range. This tendency for lower tremor frequencies in the elderly also occurs in essential tremor (Elble et al., 1994).

A reduction in EMG peak frequency with mass loading is consistent with a mechanical-reflex origin for the oscillation but is also consistent with a central-neurogenic oscillation that is entrained by the mechanical-reflex system. Any centrally generated oscillation must be expressed through the segmental stretch reflex and limb mechanics (Elble, 1996). A relatively weak central-neurogenic oscillation at a frequency near the mechanical-reflex resonant frequency can be influenced by mechanical-reflex dynamics in such a way as to produce a reduction in tremor frequency with inertial loading (Wenderoth and Bock, 1999). Thus, in elderly patients, it may be difficult to distinguish a weak central-neurogenic oscillation from an enhanced mechan-

ical-reflex oscillation using a 1 Hz limit for the permissible reduction in frequency.

In a previous study of 59 essential tremor patients, we found no significant difference in tremor frequency with and without 300 g loading (Elble et al., 1994). However, we failed to report the mean and range of changes in tremor frequency. These results are now displayed in Fig. 9 with the exclusion of one 15 year old patient who had 9–12 Hz tremor. The change in frequency was always less than 1 Hz. In the present study, 8 young and 7 elderly controls had tremors with these frequency characteristics, consistent with a central-neurogenic source of oscillation. These prevalence estimates in ostensibly normal people must be considered when interpreting the electrophysiologic studies of people with mild or questionable essential tremor.

In summary, 12% of our young and 14% of our elderly adults had a well-defined tremor-coherent EMG peak with and without mass loading, similar to outcomes 2, 3 or 4 in patients with clinically definite essential tremor (see Section 1). Inconsistent EMG peaks with mass loading occurred in 29% of young and 21% of elderly adults. The extent to which this occurs in very mild essential tremor is unknown because there is no definitive diagnostic test for essential tremor. Excluding the elderly adults with possible mild essential tremor, 11% of our elderly controls had tremor-coherent EMG peaks with and without loading (outcomes 2, 3 or 4 in Section 1). Assuming these people were truly normal, the false positive rate for tremor-coherent EMG peaks with and without loading when used as an indication for pathologic action tremor, is about 12%. Excluding those people with a 1 Hz or greater reduction in frequency with

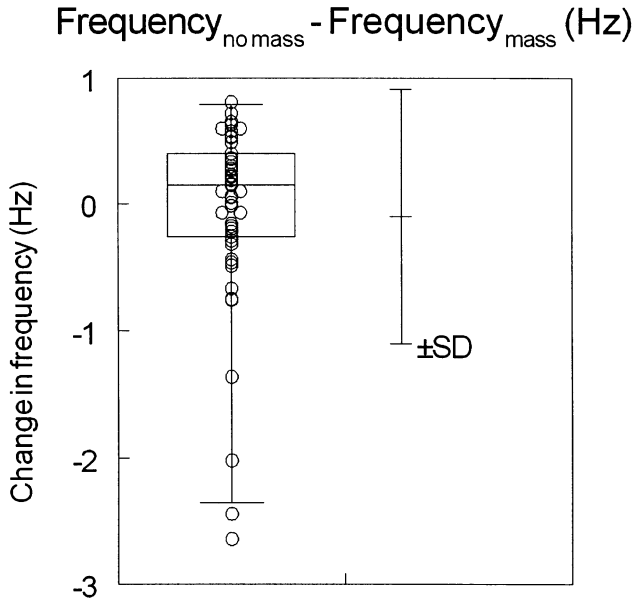

Fig. 9. Box-and-whisker plots of the change in EMG (ECRb) peak frequency (average of trials 1 and 2) with and without mass loading for 58 people, age range 20–84 (mean ± SD = 64.3 ± 14.8), with definite essential tremor, reported previously (Elble et al., 1994). The mean ± SD is also shown.

300 g loading (outcome 2 in the Section 1), the false positive rate for outcomes 3 or 4 is 7% in the elderly and 8% in the young. The clinical significance of outcomes 3 and 4 is suggested by the higher associated tremor amplitude, which falls within the range of mild essential tremor (Elble, 1986). The extent to which outcomes 3 and 4 can be considered normal is unknown because essential tremor probably occurs in at least 5% of the elderly and a reliable test for detecting mild or subclinical essential tremor in the young does not exist, making prevalence estimates uncertain (Louis et al., 1996; Louis and Ottman, 1996). Existing clinical criteria for the diagnosis of essential tremor are admittedly conservative and probably exclude people with mild disease (Deuschl et al., 1996; Elble, 1986; Elble and Deuschl, 2002; Louis and Pullman, 2001). Given the infrequent occurrence of outcomes 3 and 4 in normal volunteers and the virtual universal occurrence in clinically definite essential tremor (Deuschl et al., 1996; Elble, 1986; Elble and Deuschl, 2002; Louis and Pullman, 2001), it would appear that the electrophysiologic methods of this study are useful in confirming the diagnosis of clinically definite essential tremor and in raising the level of suspicion in people with possible essential tremor. Our methods, like all electrophysiologic studies, must be interpreted in the context of the patient's history and neurologic exam.

Acknowledgements

This study was supported by NS20973 from the National Institute of Neurological Disorders and Stroke and by the Spastic Research Foundation of Kiwanis International, Illinois-Eastern Iowa District. The author is grateful to Connie Higgins and Suzanne Elble for their help in collecting and analyzing the data in this report.

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