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Time–frequency analysis of tremors

Padraig E. O'Suilleabhain and Joseph Y. Matsumoto

Department of Neurology, Mayo Clinic, Rochester, USA

Correspondence to: Dr Joseph Y. Matsumoto, Department of Neurology, Mayo Clinic, 200 1st St SW, Rochester, MN 55905, USA

Summary

Time–frequency analysis methods were applied to surface EMG records of patients with tremor. Variation in tremor frequency over time and between muscles was measured in subjects with Parkinson's disease ($n = 20$), essential tremor ($n = 8$) and psychogenic tremor ($n = 7$). The effect of externally paced voluntary contractions on tremor frequency was also characterized. Psychogenic tremor involved fewer limbs and fewer limb segments than Parkinson's disease rest tremor and essential tremor, and its frequency was less consistent. In all subject groups, muscles within a single extremity generally had identical instantaneous frequencies. Frequency dissociation, used here to describe a modal contemporaneous frequency difference of more than 0.1 Hz between two extremities, was demonstrated for symptomatic tremors in 17 subjects with Parkinson's disease, in four subjects with essential tremor and in none of the subjects with psychogenic tremor. Dissociation between tapping and tremor limbs was demonstrated in an additional two subjects with Parkinson's disease and in all four remaining essential tremor subjects but in none of the psychogenic tremor subjects. Tremor maintained a different frequency from the tapping limb in Parkinson's disease and essential tremor, and its frequency in many cases shifted by at least 0.3 Hz compared with the non-tapping condition. For example, arm and leg tremors at 5.2 and 3.8 Hz, respectively, shifted to a common frequency of 4.6 Hz in one Parkinson's disease patient while using the contralateral arm to perform a tapping movement in time with a metronome at 2 Hz. These observations suggest the existence of distinct oscillator systems projecting to each tremoring limb, which can be linked to a variable degree, and which can be modulated by voluntary activation of another limb. Psychogenic tremor was not maintained while tapping with the contralateral arm: tremor either dissipated or shifted to the metronome's frequency. The latter response was also seen in normal volunteers mimicking tremor, but not in Parkinson's disease or essential tremor. We suggest that maintenance of phasic contraction in psychogenic tremor is not due to intrinsic instability of the motor system and that muscle activation in involved limbs may instead be synchronized to a common oscillator. As in voluntary movements, only a single rhythm may be easily followed at a time. Coexistence of muscle groups phasically contracting at consistently different instantaneous frequencies is evidence against a psychogenic aetiology of tremor.

Keywords: tremor; Parkinson's disease; essential tremor; psychogenic tremor; synchrony

Abbreviation: SNR = signal-to-noise ratio

Introduction

Pathological tremor is excessive and involuntary rhythmic movement of a body part. Paired discharge (Elek *et al.*, 1991) and synchronization (Dietz *et al.*, 1974; Freund and Dietz, 1978; Young and Shahani, 1978; Dengler *et al.*, 1986) of motor units in essential tremor and in the rest tremor of Parkinson's disease implicates the nervous system in the production of these movements. The basic mechanisms have not yet been identified. As the parameters that determine a system's tendency to oscillate also influence its frequency characteristics, it is not surprising that frequency has been the focus of many attempts to elucidate the pathophysiology of tremor-generating motor systems.

A previous study showed that physiological tremors in subjects' right and left arms had similar peak frequencies, though they were not usually identical (Arblaster *et al.*, 1990). 'Remarkably uniform' tremor frequency was reported across cranial and hand muscles in three patients with Parkinson's disease using spectral analysis methods (Hunker and Abbs, 1990), though frequency dissociation between right and left sides (Schwab and Cobb, 1939) and between arm and leg (Bishop *et al.*, 1948) tremors has been demonstrated. We use the term 'frequency dissociation' to describe the simultaneous occurrence in separate muscle groups of tremors with different frequencies. This phenomenon is of interest as it may shed light on the complexity of tremor generators and the levels within the nervous system at which frequencies are determined. In this paper we report time–frequency analyses of tremors. Instantaneous frequencies of the muscle groups involved as well as relationships between extremities are characterized.

Method

Subjects

Surface EMG recordings from patients referred for electrophysiological characterization of tremor between September 1996 and August 1997 were reviewed. Data collected from all of those who had received a diagnosis of Parkinson's disease ($n = 20$), essential tremor ($n = 8$) or psychogenic tremor ($n = 7$) from a movement disorders specialist during the same period are included in this report. Median ages of the Parkinson's disease, essential tremor and psychogenic tremor groups were 69 years (range 38–80 years), 72 years (59–80 years) and 39 years (17–65 years), respectively; 14, 5 and 3 group members were male. Among the Parkinson's disease patients, medication used at the time of recording included levodopa, dopamine agonists, trihexyphenidyl or selegiline ($n = 13$), propranolol ($n = 2$) and benzodiazepines ($n = 2$). Essential tremor subjects were using propranolol ($n = 2$), primidone ($n = 3$), levodopa ($n = 1$) and benzodiazepines ($n = 1$). Among psychogenic tremor subjects, three were taking benzodiazepines and one was taking baclofen. One eligible Parkinson's disease patient was excluded having declined to give permission for the use of his medical records for research purposes. The study was approved by the review board of the Mayo Clinic.

Data acquisition

The surface EMG was recorded simultaneously from two to eight sites in two to five extremities (i.e. in some cases all limbs plus either neck or jaw muscles). One site was selected on every limb segment with clinical evidence of a tremor site, so that only one member of each agonist–antagonist pair was recorded. A typical montage was biceps, wrist flexors, thenar and anterior tibial muscles bilaterally. It should be noted that fewer sites were recorded in psychogenic tremor subjects, as these had fewer limbs and in particular fewer arms with visible tremor. Pairs of silver–silver chloride surface electrodes were applied over muscle bellies separated by ~3 cm. The preamplifier pass band was 30–500 Hz and the digitization rate was either 2000 or 2500/s over 16 bits with resolution of 0.168 μV per least significant bit (Neuroscan, Sterling, Va., USA). Periods of 1–3 min were recorded in the baseline condition: patients with Parkinson's disease were either supine or seated with arms and legs supported; patients with essential tremor were seated with their arms extended; and patients with psychogenic tremor were seated with their limbs either outstretched ($n = 6$) or supported ($n = 1$) depending on which posture produced the symptomatic tremor. Twenty-six subjects were also recorded in an externally paced condition. For this, the subject was encouraged to use the unaffected or less affected arm to perform a tapping movement in time with a metronome, while ignoring the more symptomatic arm. The metronome rate was either 2 Hz (21 subjects) or 3 Hz (five subjects with tremor frequencies around 4 Hz). Baseline and paced recordings were completed over a period of ~10 min.

Data analysis

Off-line, EMG was rectified, filtered and downsampled so that the tremor envelope was ultimately represented at 50 samples/s with a bandpass DC to 20 Hz. For each muscle group, periods recorded under baseline and paced conditions were analysed separately using three steps: first, the presence or absence of tremor was determined using classical spectral analysis methods; secondly, the instantaneous frequency over time was estimated for those muscle groups in which tremor was confirmed; finally, numerical tremor indices were calculated.

Identification of tremors

Power spectral density was estimated by the Welch method of averaging periodograms (Fast Fourier transform length 128, kaiser windowed segments overlapping 50%; DeFatta *et al.*, 1988). Spectral density was invariably high at frequencies below 1.5 Hz due to the slow fluctuations in the rectified EMG, and was low above the filter cut-off, with peaks at intermediate frequencies where rhythmic activity was concentrated. To identify spectra containing a peak which was considerably higher than the background broadband noise, the signal-to-noise ratio (SNR) was the parameter used. This was calculated by dividing the power at the peak frequency in the range of 1.5–20 Hz by the mean power at the other frequencies. Tremors were distinguished from arrhythmic EMG using a threshold SNR of 4.

Estimation of instantaneous frequency

The time–frequency distribution of each tremor was calculated as a filtered Wigner distribution. For non-stationary biomedical as well as engineering processes, frequency changes can be temporally located in the Wigner distribution and its adaptations (Akay, 1996). In the Choi–Williams adaptation, one can optimize the trade-off between the competing goals of resolution and suppression of unwanted cross-terms by adjusting the sigma coefficient (Choi and Williams, 1989). We chose a value of 0.01 for this coefficient to emphasize cross-term suppression. The DC component of the time series segments was initially removed by subtracting their linear trends, and sharp EMG impulses were smoothed with a fifth-order median filter to prevent broadband smearing. The adapted Wigner algorithm (Matlab, Nantucket, Mass., USA) was applied to sequential 128-point segments overlapping by 103 points, and energy estimates over the central 25 time indices were averaged. These parameters were chosen to allow largely independent yet stable estimates every 0.5 s with a resolution of 0.1 Hz. The peak frequency for each interval was identified, and a time series of instantaneous frequency estimates was built up in this way. For selected pairs of muscles, a time series of the frequency difference can be calculated by subtracting the instantaneous frequency of one from the other.

Calculation of tremor indices

The following were chosen to summarize numerically tremor behaviour in the baseline condition: (i) a tremor's modal frequency is the instantaneous frequency occurring most often; (ii) tremor consistency is the proportion of time spent at modal frequency; (iii) bandwidth, a related measure, is the range of contiguous non-empty bins around the mode in a histogram of instantaneous frequency estimates calculated for the first 60 s recorded; (iv) a tremor pair's modal frequency difference is the difference in instantaneous frequencies occurring most commonly, and a modal frequency difference of >0.1 was taken to indicate frequency dissociation; and (v) a tremor pair's similarity index is the Pearson correlation coefficient for instantaneous frequency estimates of each member, excluding as invalid those estimates $\geqslant 0.5$ Hz above or below the immediately preceding estimates, and estimates $\geqslant 1.5$ Hz above or below the modal frequency. The majority of the invalid estimates, as determined by these empirically derived criteria, were due to noise, such as a sporadic muscle contraction, temporary absence of tremor, or the presence of harmonics briefly at higher power than the tremor fundamental.

Statistics

For all comparisons between groups, Kruskal–Wallis tests were used, followed by the Wilcoxon test for comparison of the essential tremor with the Parkinson's disease group, and the psychogenic tremor with the combined essential tremor–Parkinson's disease group if the former difference was not significant. Measures compared among the groups were: number of tremoring limbs and limb segments identified per subject; modal tremor frequency; tremor consistency; and bandwidth. For each patient, the single tremor with the highest consistency score was selected for the last three of these comparisons. Modal frequency differences of tremor pairs were compared within each diagnostic group. The four pairs of interest were: (i) proximal and distal levels of an individual arm, (ii) right and left arms, (iii) ipsilateral arm and leg and (iv) cranial and limb tremors. A pair from each of these categories was selected from as many patients as possible. For subjects with multiple pairs within a category, the pair for which both members had valid estimates for the greatest proportion of time windows was chosen.

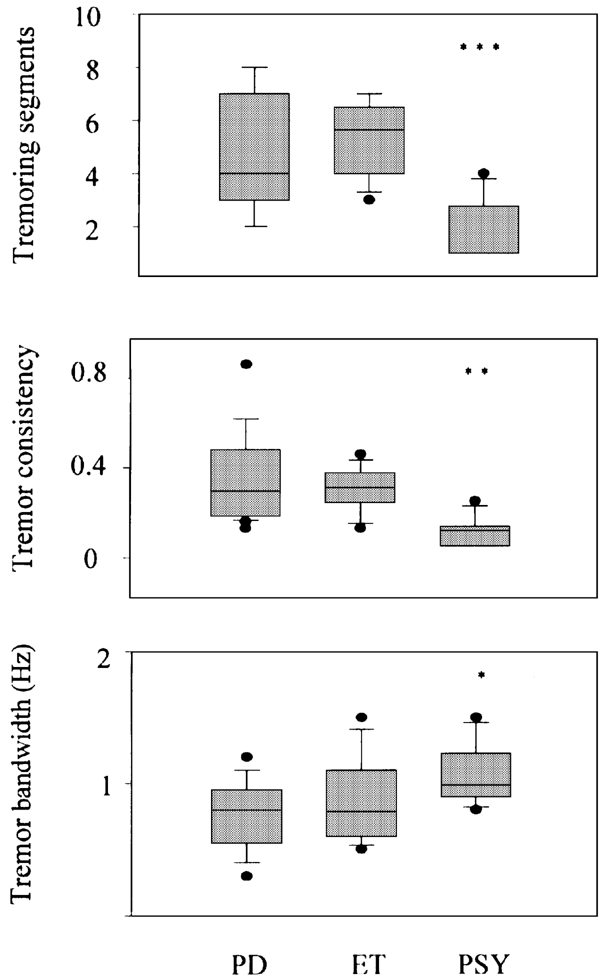

Fig. 1 Box plots showing that psychogenic tremor involves fewer limb segments, is less consistent and has wider bandwidth than were found in the combined Parkinson's disease + essential tremor group. The boxes extend from the 25th to the 75th centile with a line marking the median, whiskers extend to the 10th and 90th centile, and each outlier is identified with a disc. PD = Parkinson's disease; ET = essential tremor; PSY = psychogenic tremor. *$P \leqslant 0.05$; **$P \leqslant 0.005$; ***$P \leqslant 0.0005$.

Results

Distributions, modal frequency and consistency and bandwidth of tremors

The numbers of limbs and of limb segments recorded were 1–5 and 2–8 (median, 4 and 7.5, respectively) in Parkinson's disease subjects, 2–5 and 4–8 (median, 3 and 7) in essential tremor and 1–4 and 2–6 (median, 2 and 4) in psychogenic tremor. Phasic activity meeting the criterion for tremor was found in 2–8 (4.5), 3–7 (5.5) and 1–3 (1) segments per subject. Fewer limb segments were recorded in psychogenic tremor ($P = 0.03$), reflecting less widespread clinically suspected tremor. The number of limbs and limb segments in which tremor was confirmed was similar in the Parkinson's disease and essential tremor groups and less in the psychogenic tremor group ($P = 0.0005$) (Fig. 1). Even when expressed as a proportion of sites recorded, tremor was

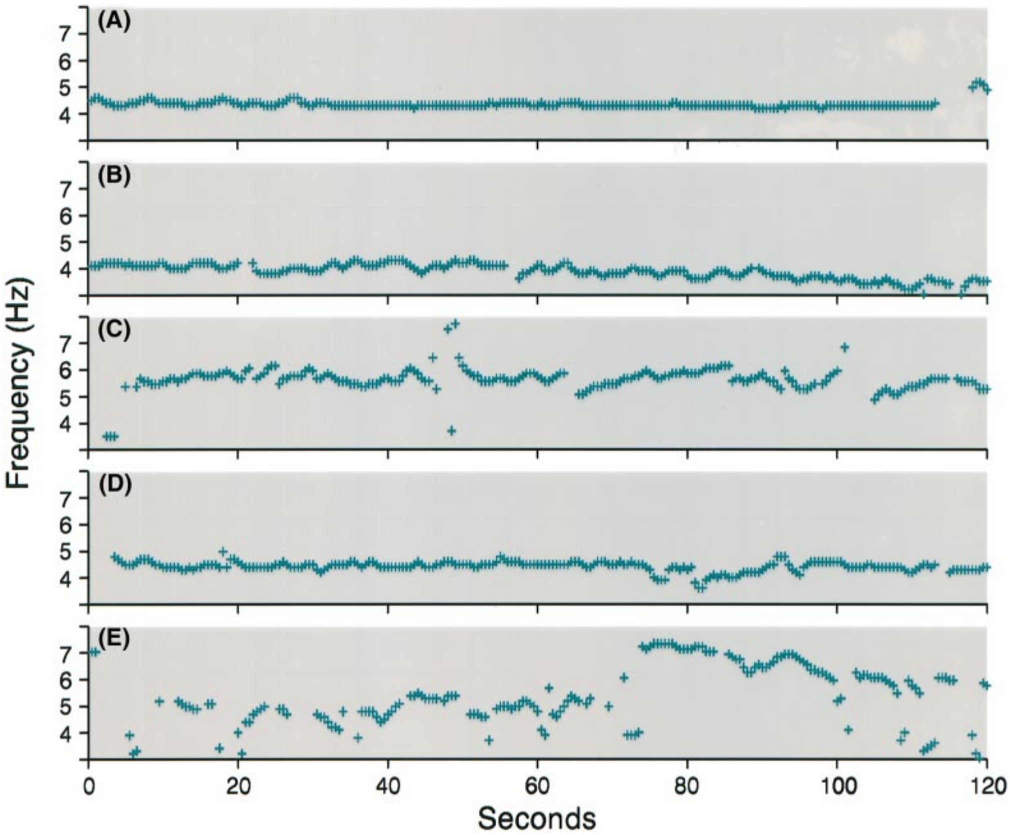

Fig. 2 Variation over time of tremor frequency. (**A**) Relatively stationary Parkinson's disease rest tremor. (**B**) Gradual slowing of Parkinson's disease rest tremor. (**C**) Small fluctuations of rest tremor in Parkinson's disease. (**D**) Small fluctuations of postural tremor in essential tremor subjects. (**E**) Large fluctuations in psychogenic tremor.

established in fewer extremities ($P = 0.02$) and in fewer segments ($P = 0.04$) in psychogenic tremor. Comparing the single most consistent tremor per subject, modal frequencies were higher in psychogenic tremor (4.5–7.1; median, 6.2) than Parkinson's disease (2.5–6.8; median, 4.9) or essential tremor (4.3–6.1; median, 5.1; Parkinson's disease + essential tremor versus psychogenic tremor, $P = 0.01$). In Parkinson's disease, the most consistent tremors were recorded most often at wrist flexors. Masseters, biceps, thenar and tibial muscles were more consistent in a few patients. Qualitative assessment of time–frequency distributions demonstrated a fluctuating frequency for most tremors, though most fluctuations were brief in duration and small in degree: fluctuations of 0.2 Hz lasting 5 s or so were typical (Figs 2C and D, 3 and 4). A gradual progressive frequency change of 0.5 or so over a period of tens of seconds was apparent in four Parkinson's disease subjects (Figs 2B, 3A and 4A). In three of the psychogenic tremor subjects fluctuations appeared to be 1.5–2.5 Hz (Figs 2E and 4C); such large fluctuations were not detected in Parkinson's disease/essential tremor. Consistency scores are an attempt to quantify frequency invariability over time. Scores differed between the groups ($P = 0.002$): consistency was similarly high in Parkinson's disease (0.13–0.86; median, 0.3) and essential tremor (0.13–0.46; median, 0.32), and was significantly lower in psychogenic tremor (0.05–0.25; median, 0.13; $P = 0.004$). The tremor with highest consistency overall involved wrist flexors in Parkinson's disease; instantaneous frequency was 4.3 ± 0.05 Hz for 102 of 120 time windows of 0.5 s (Fig. 2A). Bandwidth of instantaneous frequency was also broader in psychogenic tremor than in the combined Parkinson's disease + essential tremor group ($P = 0.034$) (Fig. 1).

Relatedness of tremors in different muscles

For contralateral tremors, dissociation characterized nine of 12 Parkinson's disease resting tremors and four of seven essential tremors but neither of the two psychogenic tremor subjects with eligible tremor pairs. As noted in the previous section psychogenic tremor affected fewer limbs, and these were the only two of the seven psychogenic tremor subjects with spontaneous tremors of adequate quality simultaneously present in separate limbs; four others had involuntary phasic movements affecting different limbs but movements were not adequately rhythmic simultaneously, while the last had symptoms confined to one limb. The modal difference between dissociated right- and left-side essential tremor and Parkinson's disease tremors ranged from 0.2 to 1.6 Hz (Fig. 3C and D). In a few cases, a common frequency was sustained briefly for tremors with different modal frequencies

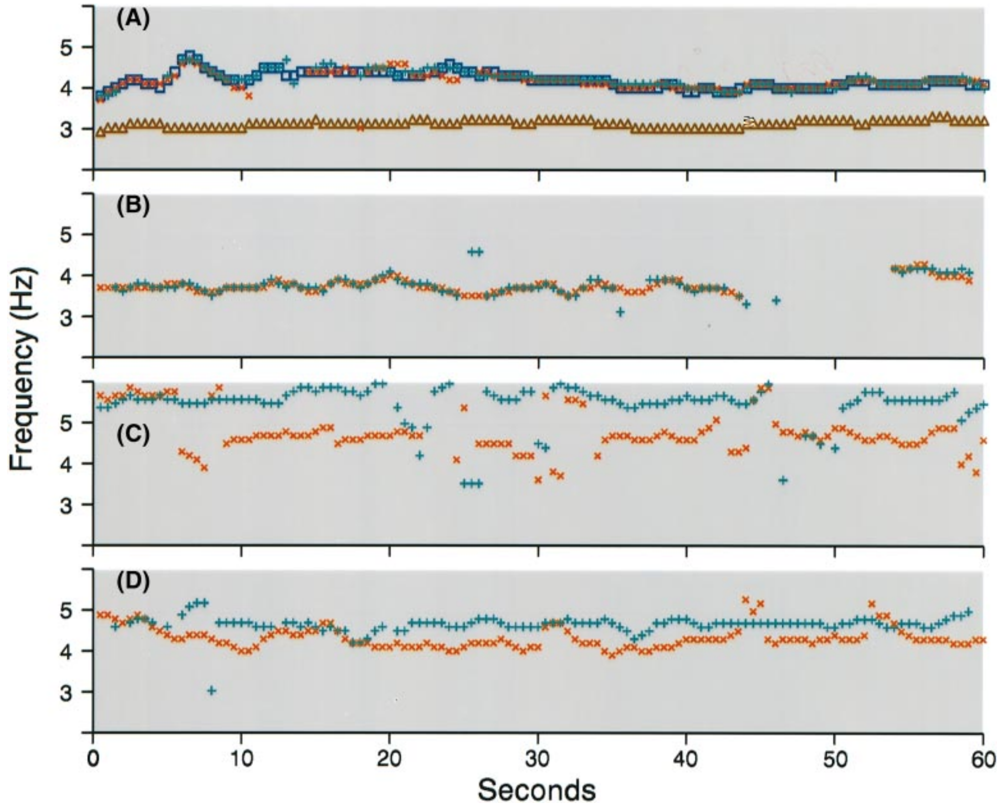

Fig. 3 Instantaneous frequencies of simultaneous tremor in separate limb segments. (**A**) Parkinson's disease rest tremor involving biceps (green +), wrist flexors (orange ×), thenar (blue open square) and anterior tibial (brown open triangles) muscles. (**B**) The single Parkinson's disease patient out of 12 with essentially identical tremors in arm (green +) and leg (orange ×). (**C**) Parkinson's disease rest tremors in left (green +) and right (orange ×) arms; note period of similarity at beginning. (**D**) Frequency dissociation between left (green +) and right (orange ×) arms in essential tremor.

(Fig. 3C). Frequency dissociation between arm and leg tremors was also prevalent, occurring in 12 of 14 Parkinson's disease subjects (Figs 3A and 4) and in two of three essential tremor subjects. Leg tremors were in some cases faster and in some cases slower than ipsilateral arm tremors, with modal differences of up to 1.5 Hz. Cranial–limb tremor pairs were dissociated in five of six Parkinson's disease and one of two essential tremor subjects; modal differences ranged from 0.3 to 1.2 Hz. In some subjects, the cranial tremor was faster than the limb tremor with the highest consistency score; in others it was slower. Similarity indices were uniformly low (<0.1). Multiple tremors within an individual limb were recorded in most but not all subjects. Proximal and distal tremors were dissociated in only two, one and none of the 18 Parkinson's disease subjects, eight essential tremor subjects and two psychogenic tremor subjects with simultaneous tremors at multiple levels of a limb (Fig. 3A). The dissociated tremors affected biceps and wrist flexors in each case, with modal differences of 0.2 and 0.3 Hz in the two Parkinson's disease patients and 1.3 Hz in the essential tremor patient.

The psychogenic tremor group was excluded from statistical tests of tremor pairs as numbers were insufficient. The Kruskal–Wallis statistic demonstrated significantly different absolute modal frequency differences among tremor pair categories in both Parkinson's disease ($P = 0.0001$) and essential tremor ($P = 0.02$) groups. *Post hoc* tests confirmed that the absolute modal difference was smaller for the within-limb pair than for all other tremor pairs. The magnitudes of the arm–leg and arm–contralateral arm discrepancies were not statistically different.

Effect of voluntary rhythmic action

Tremor was recorded in both baseline and paced conditions in 14, 7 and 5 subjects in the Parkinson's disease, essential tremor and psychogenic tremor groups, respectively. The voluntary tapping was confirmed to be at the metronome frequency in 9, 7 and 1 of these subjects, as the EMG of the designated muscle had a SNR of >4 at the prescribed frequency. The EMG spectra in another 3, 0 and 2 subjects did not have a definite peak at the paced frequency, while the voluntary EMG was not recorded in the rest. Some, though not necessarily all, of a subjects' tremors continued to beat steadily in the Parkinson's disease and essential tremor subjects in whom voluntary pacing was confirmed.

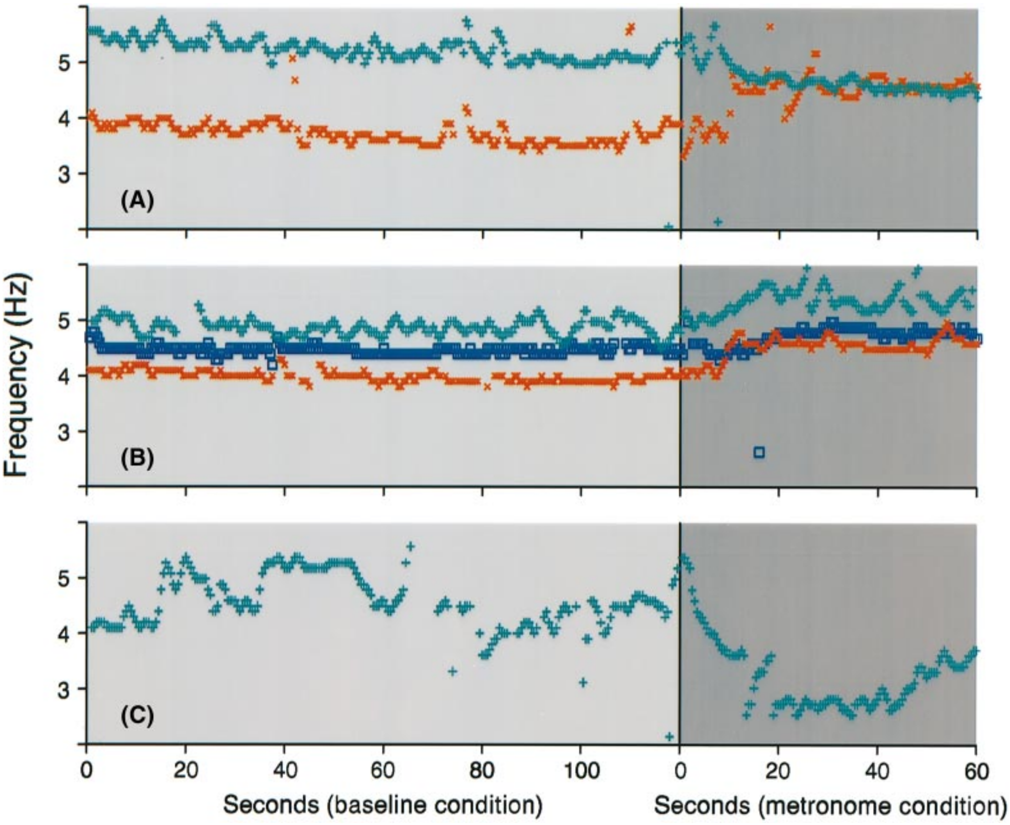

Fig. 4 Change from baseline frequency (0–120 s) when another limb taps in time with a metronome. (**A**) Parkinson's disease: left biceps (green +) and left anterior tibial (orange ×) tremors both shift to 4.6 Hz from baseline modal frequencies of 5.2 and 3.8 Hz, respectively, when the right hand taps at 2 Hz; note that frequency ramps down slowly and tends to fluctuate simultaneously in both extremities. (**B**) Parkinson's disease: shift of modal frequency of masseter (green +) from 4.8 to 5.5, of right wrist flexors (blue open square) from 4.5 to 4.8, and of left anterior tibial muscles (orange ×) from 4.2 to 4.6 when left hand taps at 2 Hz. (**C**) Psychogenic tremor: wide fluctuation of right thenar tremor, which shifts when left hand taps at 2.8 Hz.

In each case, the frequencies of involuntary tremor and of voluntary tapping and its harmonics were different. A distinct shift in frequency of the subject's most consistent tremor (by 0.2–1.1 Hz) was produced by tapping of the contralateral arm in seven of the nine Parkinson's disease subjects and in four of the seven essential tremor subjects (Fig. 4). This resulted in faster tremor in some and slower tremor in others. In one subject, left arm and leg rest tremors at different frequencies jumped to a common intermediate frequency when the right arm tapped voluntarily (Fig. 4A).

Among the five psychogenic tremor subjects attempting contralateral paced contractions, the effects on tremor were quite unlike those seen in Parkinson's disease and essential tremor subjects attempting the task. In two subjects the most symptomatic tremor adopted the metronome frequency (Fig. 4C), an effect not seen in any Parkinson's disease or essential tremor cases. In the other three subjects the involuntary tremor essentially discontinued during the manoeuvre. Brief periods of tapping were observed to alternate with shuddering displacements of the symptomatic limb.

Discussion

In this study of tremor, we compared time–frequency distributions rather than purely frequency domain measures such as coherence and autospectral density. While coherence quantifies the extent to which activity within a particular frequency band is common to two processes, neither low nor high coherence values can reveal whether their peak frequencies are the same or different. Autospectra, typically estimated by averaging Fourier transformations of a segmented time series, allow frequency comparisons between processes which are stationary and have sharp isolated spectral peaks. We have demonstrated that tremor frequency may vary over time. Time–frequency distributions register slow frequency modulations and small fluctuations around the tremor modal frequency. Not only are these undetectable using ensemble-averaged time segments, but resulting broad spectral peaks blur comparisons between tremors. Using time–frequency distributions, we observed frequency dissociation between contralateral tremors of fractions of 1 Hz in most subjects with essential tremor and Parkinson's disease. Leg and cranial tremors were also most often dissociated from arm tremors in these subjects.

Multiple oscillator systems in essential tremor and Parkinson's disease, not in psychogenic tremor

The relative roles of autonomous pacemakers and enhanced reflex loops in the generation of tremor have been debated but not resolved. We simply use the term 'oscillator system' to refer to the ensemble of elements which combine to cause an excessive tremor. Synchronized activation of separate muscle groups would best be explained by a single system. Distinct arm and leg tremors imply more than one oscillator system, though neural elements common to both are not excluded by this formulation. Our data indicate that separate rhythms maintained simultaneously in separate limbs are the rule in patients with essential tremor and Parkinson's disease. This suggests that tremor production in these patients is not due to a single oscillator system. Similar logic has been applied to physiological tremor, in which tremor bursts are not co-ordinated bilaterally (Morrison and Newell, 1996). By contrast, it has been suggested that synchronized cranial and forearm discharges in patients with symptomatic palatal tremor could be explained by a common oscillator (Tahmoush *et al.*, 1972; Deuschl *et al.*, 1994).

Tremor involved fewer limbs and limb segments in psychogenic tremor. This suggests either fewer oscillator systems than in Parkinson's disease and essential tremor, or less widespread recruitment per oscillator system. The absence of frequency dissociation in psychogenic tremor is evidence for the former explanation. Even under instruction to maintain a paced second rhythm, frequency dissociation between limbs did not occur. This is reminiscent of voluntary bimanual rhythmic activity, in which a common bilateral frequency is the rule (Peters, 1977). It is presumed that such movements involve attention to a central timing or oscillator system (Lang *et al.*, 1990), and most people seem incapable of attending to more than one frequency. While trained musicians may maintain bimanual polyrhythms (Ullen *et al.*, 1997), it has been suggested that this involves a common timebase—for example two-time and three-time, both paced by a timebase of six beats (Klapp, 1979). To confirm that voluntary bimanual rhythms tend to be identical, we asked four normal volunteers to mimic bilateral postural tremor, then to keep time with a metronome at 2 Hz on one side while maintaining the contralateral arm at the unpaced frequency. In no case was frequency dissociation seen. While attempting to produce two rhythms, either the externally paced or the self-generated rhythm was poorly maintained. To the extent that bilateral rhythmic activity was sustained, both arms had the same frequency.

It thus appears that frequency dissociation segregates quite well with non-psychogenic tremors. Assuming that certain motor system elements are disrupted in Parkinson's disease and essential tremor, we speculate that the observed frequency dissociation could be explained by non-uniform pathological involvement of parallel neural pathways. In psychogenic tremor, on the other hand, we propose that the motor system *per se* is intact, and that rhythmic contractions are mediated by top-down synchronization involving a common oscillator system, perhaps at a higher cerebral level. The tendency for psychogenic tremor to attenuate when patients are distracted could be explained by a requirement for such higher level involvement, and the variability of phasic contractions in most of the psychogenic tremor cases also argues against an autonomous hard-wired motor system oscillator.

Alteration of tremor frequency in Parkinson's disease and essential tremor by externally paced motion

Frequency dissociation as seen in essential tremor and Parkinson's disease implies a degree of independence for each tremoring limb's oscillator system. Simulating tremor with one arm could induce a contralateral involuntary tremor to change its frequency, however, so the oscillator systems are not entirely autonomous. The observed frequency shift, between 0.2 and 1.1 Hz in magnitude, does not reflect tremor entrainment to the voluntary rhythm or its harmonics. Rather, assuming the paced rhythm does in fact project to the tremor oscillator, the frequency shift observed here represents a non-linear interaction of the two. Such modulation of tremor by an adjustable imposed rhythm may have potential as a model for examining the dynamics of coupled neural networks.

Conclusion

We summarize our interpretations of EMG recordings made simultaneously at multiple muscle groups as follows. Distinct oscillator systems underlying tremors in different limbs can be found in most people with Parkinson's disease and essential tremor, though a common oscillator involving arm–leg or arm–arm limb pairs is present or can be induced in a number of subjects. In Parkinson's disease and essential tremor, instantaneous tremor frequency can change by fractions of 1 Hz over a period of seconds, either spontaneously or during voluntary paced contraction of another limb. The involuntary tremors are not entrained to the frequency of the paced rhythm. In psychogenic tremor, tremors in all involved limbs appear to have a common oscillator, as do psychogenic tremors and coincident voluntary rhythmic contractions. By revealing frequency dissociation among phasically contracting muscle groups, a feature difficult to detect on clinical examination, multi-limb recording in both spontaneous and paced conditions helps in distinguishing psychogenic tremor from non-psychogenic tremors.

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