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Coherent cortical and muscle discharge in cortical myoclonus

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Summary

There is increasing evidence in man that the cortical drive to motor neurons is rhythmic. This oscillatory drive may be exaggerated in patients with cortical myoclonus. Spectral analysis of surface bipolar EEG and EMG activity was performed in eight such patients. Only three cases had evidence of giant cortical evoked potentials or a cortical correlate on back-averaging at the time of study. In six subjects, significant coherence between contralateral and vertex EEG and EMG was observed in ranges similar to that previously reported for normal subjects (15–30 and 30–60 Hz). Three out of these six subjects also had significant coherence at higher frequencies (up to 175 Hz). All eight patients had a correlate in the cumulant density estimate between EEG and contralateral EMG. EMG lagged EEG by about 14, 25 and 35 ms for the muscles of the forearm, hand and foot, respectively. These delays were estimated from the slope of the phase curves and the timing of the peaks in the cumulant density estimates, and are appropriate for conduction in fast pyramidal pathways. The results provide clear evidence of a cortical drive synchronizing muscle discharge over a broad range of frequencies in patients with cortical myoclonus. Fourier analysis is a promising technique in the diagnosis and investigation of such patients.

Keywords: myoclonus; coherence; electroencephalography

Abbreviations: 1DI = first dorsal interrosseus muscles; MEG = magnetoencephalographic activity

Introduction

Single motor units may synchronize their discharges over a short time-scale during isometric contractions in man (Datta and Stephens, 1990; Farmer *et al*., 1993*a*, *b*). There is increasing evidence that short-term synchronization is associated with rhythmicities in the cortical drive to muscle (Farmer *et al*., 1993*a*; Conway *et al*., 1995; Salenius *et al*., 1997; Brown *et al*., 1998). Patients with cortical myoclonus have involuntary muscle jerks due to the synchronous discharge of many motor units. The timing relationships between motor units in cortical myoclonus may reflect abnormal high-frequency oscillations in the EEG of these subjects (Brown and Marsden, 1996). The study of patients with cortical myoclonus may therefore provide a rare insight into the rhythmic influence that the sensorimotor cortex has on human muscle discharge, particularly with regard to the range of frequencies involved and the phase relationship between cortex and muscle.

In the present study we describe for the first time the application of frequency domain analysis to the study of cortical myoclonus. We demonstrate that the cortical drive to muscle has a complex rhythmic organization over a frequency band that may extend beyond 100 Hz. At the same time, we show that this method of analysis has major advantages over the established time domain technique of back-averaging.

Patients and methods

Eight patients with suspected cortical myoclonus were studied as part of their routine clinical investigation. The clinical details and basic electrophysiological findings are summarized in Table 1. All the patients had multifocal action myoclonus most prominent in the distal limb, with a mean duration of myoclonic EMG bursts of <50 ms. Patients with clinical evidence of corticobasal degeneration, multiple system atrophy or the jerking stiff limb syndrome were excluded. Cases 2, 5, 6, 7 and 8 had the syndrome of progressive myoclonic ataxia, defined as myoclonus and progressive cerebellar ataxia, with frequent seizures and little or no cognitive dysfunction.

Surface EMG and EEG were recorded with 9-mm diameter silver–silver chloride electrodes. A bipolar montage (C3–F3,

Table 1 *Clinical and basic electrophysiological details*

Case number	Age (years)	Sex	Aetiology	Drug treatment (daily dose)	Giant SEPs (to median nerve stimulation, unless otherwise stated)	C-reflex	Time-locked EEG correlate preceding action jerks (back-averaging)
1	63	F	Coeliac disease	Clonazepam 0.5 mg Levodopa 100 mg + carbidopa 25 mg	+	–	+ (27 ms before myoclonus in ADM)
2	31	M	Progressive myoclonic ataxia*	Clonazepam 8 mg Primidone 500 mg Piracetam 19.2 g Sodium valproate 3 g	–	–	– (but a correlate was recorded 8 years earlier)
3	27	F	Postanoxic myoclonus	Clonazepam 4 mg Piracetam 2.4 g Sodium valproate 1.5 g	–	–	– (but a correlate was recorded 2 years earlier)
4†	68	F	Coeliac disease	None	+ (to tibial nerve stimulation)	+ (to tibial nerve stimulation)	+ (34 ms before myoclonus in EDB)
5	18	F	Progressive myoclonic ataxia*	Clonazepam 1 mg Sodium valproate 2 g	–	–	+ (14 ms before myoclonus in f. ext.)
6	42	F	Progressive myoclonic ataxia	Clonazepam 0.5 mg Piracetam 14.4 g Sodium valproate 2 g	–	–	– (but a correlate was recorded 8 years earlier)
7	27	F	Progressive myoclonic ataxia*	None	– (to tibial nerve stimulation)	–	–
8	46	F	Progressive myoclonic ataxia*	None	–	–	–

ADM = adductor digiti minimi; EDB = extensor digitorum brevis; f. ext = forearm extensor muscles; SEPs = cortical sensory evoked potentials. *Idiopathic progressive myoclonic ataxia despite extensive investigation. †Previously reported in detail as case 1 by Bhatia *et al.* (1995).

Cz–Fz and C4–F4) was used. EMG and EEG were bandpass-filtered at 16–300 and 5.3–300 Hz, respectively. High- and low-pass filters were first- and second-order, respectively. Signals were amplified and digitized with 12-bit resolution by a CED 1401 analogue-to-digital converter. Recordings were sampled at 625 Hz. Signals were displayed and stored on a PC microcomputer by a software package (CED Spike 2). EMG and EEG activity were also recorded with an FM tape recorder.

Data analysis

The EEG, denoted by *x*, and unrectified EMG, denoted by *y*, were assumed to be realizations of stationary zero-mean time series. The principal statistical tool used for data analysis in this study was the discrete Fourier transform and parameters derived from it, all of which were estimated by dividing the records into a number of disjoint sections of equal duration (1024 data points), and estimating spectra by averaging across these discrete sections (Halliday *et al.*, 1995). In the frequency domain, estimates of the autospectrum of the EEG, $f_{xx}(\lambda)$, and EMG, $f_{yy}(\lambda)$, were constructed, along with estimates of coherence, $|R_{xy}(\lambda)|^2$. Timing information between the EEG and EMG signals was calculated from the phase spectrum $f_{xy}(\lambda)$, defined as the argument of the cross-spectrum: $f_{xy}(\lambda) = \arg[f_{xy}(\lambda)]$. In the time domain, the cumulant density function, $q_{xy}(u)$, with EMG as reference, was estimated from the cross-spectrum, $f_{xy}(\lambda)$, via an inverse Fourier transform. Confidence intervals for all parameters were estimated (for further details see Halliday *et al.*, 1995). It should be noted that we used unrectified EMG in this study, although the coherence spectra and phase slopes (but not intercepts) calculated from rectified EMG were similar. The difference in the intercepts relates to the biphasic nature of the unrectified EMG.

Results

Basic electrophysiology

Figure 1A illustrates an example of the raw EEG and EMG recorded in Case 5. Brief myoclonic bursts are evident in the EMG from the extensor muscles of the left forearm. These are preceded by rather variable positive–negative wave complexes, maximal over the contralateral hemisphere. Only Cases 1 and 4 had giant cortical somatosensory evoked potentials, and only Case 4 had a C-reflex (Table 1). Cases 1, 4 and 5 had time-locked EEG correlates preceding action jerks by a short interval (Table 1). An example of the cortical correlate obtained through back (jerk-locked) averaging is shown in Fig. 1B. The remaining patients had no such correlate on the date of study, although Cases 2, 3 and 6 had had such a feature when studied 2–8 years previously. Failure

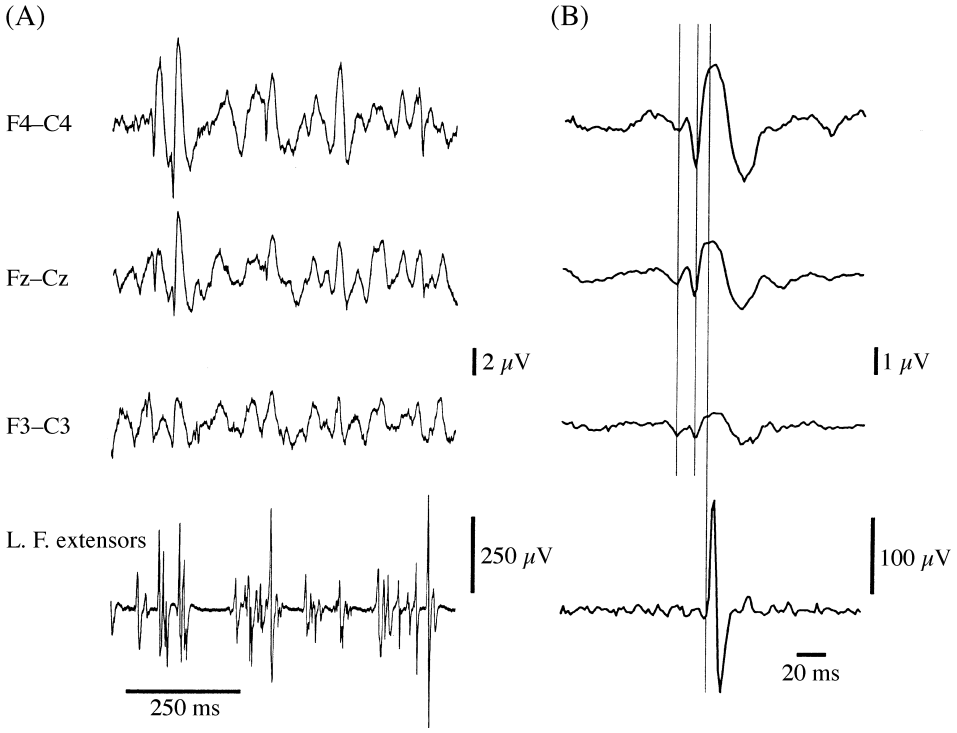


Fig. 1 (**A**) Raw record of the EEG and EMG during action myoclonus in Case 5. (**B**) Back-average of the EEG accompanying action myoclonus in Case 5. The collection of EEG was triggered by passing the unrectified surface EMG recorded from the left forearm (L.F.) extensor muscles through a level detector. The myoclonic EMG burst is preceded 11 ms earlier (middle vertical line) by a positive wave biggest over the contralateral cerebral hemisphere (C4–F4). This is in turn preceded 13 ms earlier (first vertical line) by a smaller positive wave, which is biggest in the midline channel (Cz–Fz). Average of 512 unselected trials. EMG and EEG were bandpass-filtered at 16–300 and 5.3–300 Hz in this and subsequent figures.

to record a cortical correlate was attributed partly to the high frequency and irregularity of the myoclonic jerks. Successful back-averaging requires the absence of EMG activity for a period of $\geqslant$100 ms prior to the EMG burst used to trigger the collection of EEG (to be sure that EEG correlates precede rather than follow EMG events in the time domain).

Frequency domain analysis

Four principal measures were derived through application of the Fourier methods: autospectra, coherence spectra, phase and cumulant density functions. Representative examples of these measures are shown in Fig. 2, which is derived from frequency analysis of the same signals as Fig. 1, and in Figs 3 and 4. The results in each subject are summarized in Table 2.

Cases 1, 3, 4 and 5 had regular action jerks at low frequency, apparent in raw EMG records and power spectra of EMG activity. Despite this, only Cases 3 and 4 had significant coherence between the contralateral EEG and EMG at the frequency of these jerks (Table 2). Examples of the absence and presence of significant coherence between EEG and EMG at a frequency corresponding to the repetition rate of the myoclonic jerks are shown in Figs 2 and 3, respectively.

Significant coherence between EEG and EMG was seen in all subjects at frequencies >15 Hz (Table 2). In Cases 7 and 8 the coherence was confined to the frequency range 15–30 Hz. In Cases 1, 2 and 6 coherence was seen in the ranges 15–60, 30–60 and 15–90 Hz, respectively. In Cases 4 and 5 it encompassed the range 15–150 Hz. Coherence was most extensive in Case 3, in whom there was coherence between EEG and EMG from 30 to 175 Hz.

Figures 2 and 3 illustrate the findings in patients with coherence at very high frequency between EEG and involuntary muscle activity in the upper (Case 5) and lower (Case 4) limbs, respectively. High-frequency coherence was best seen in Cz–Fz, although in Case 3 (not illustrated) more modest high-frequency coherence was also seen over the motor areas contralateral (but not ipsilateral) to the EMG. In contrast, Fig. 4 is taken from the results in Case 1, in whom coherence between EEG and hand was confined to the frequency ranges 15–30 and 30–60 Hz.

Figure 2 shows the EEG/EMG coherence with the corresponding cumulant density estimates in Case 5. It can be seen that the largest range of frequencies with significant coherence is present for vertex recordings (Fig. 2B). Sensorimotor cortex recordings contalateral to the active forearm show the coherence to be more restricted to the

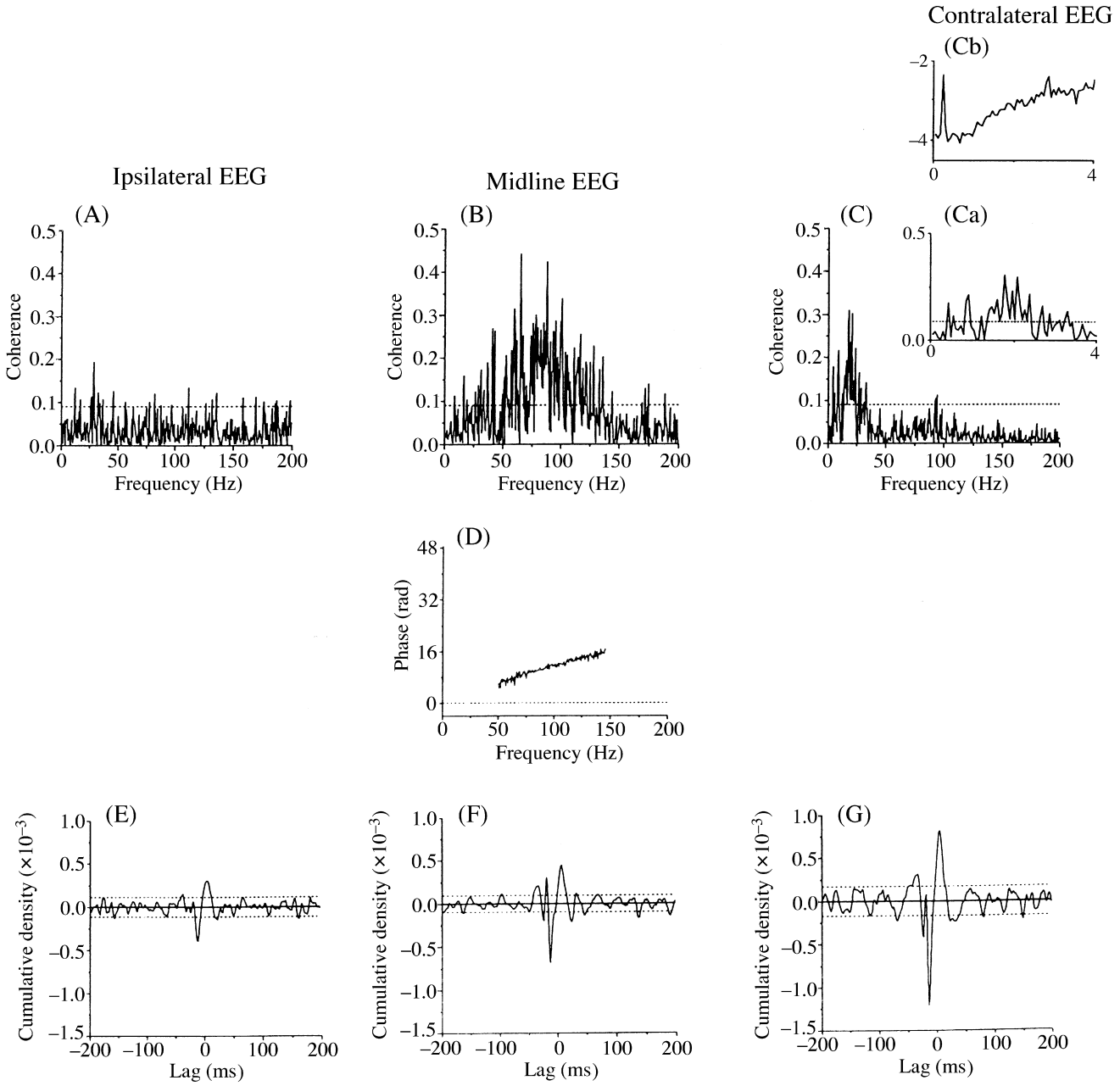


Fig. 2 Frequency analysis of the EEG and EMG recorded during action jerks of the left forearm in Case 5 (using the same data as in Fig. 1). There is barely any significant coherence (**A**) between the unrectified surface EMG from the forearm extensor muscles and the ipsilateral EEG (C3–F3). A very small feature is seen in the corresponding cumulant density (**E**). In contrast, two bands of coherence are seen between EMG and midline EEG (Cz–Fz) at around 25–40 and 50–130 Hz (**B**). Phase was more or less constant over these frequencies, EMG lagging behind EEG activity by 14 ms (**D**). A clear EEG correlate is seen in the cumulant (**F**). Note that the latter has two significant positive deflections separated by ~13 ms, both preceding the EMG. A band of significant coherence is seen between the contralateral EEG (C4–F4) and forearm EMG centred around 20 Hz (**C**). The EEG correlate in the cumulant has two significant positive deflections, both preceding the EMG (**G**). Note that although the autospectrum of the forearm EMG has a clear peak at 5 Hz (inset **Cb**) (the repetition frequency of the more regular myoclonic discharges), there is no significant coherence between any EEG channel and EMG at this frequency (**A**, **B**, **C**; see especially inset **Ca**). Analysis was of a continuous recording lasting 55 s. In this and ensuing frequency analyses, the interrupted horizontal lines in the coherence spectra and cumulant densities and the vertical bar in autospectra give the magnitude of the upper and lower 95% confidence limits, and power is in log units.

range 15–30 Hz (Fig. 2C). Despite the presence of a small time domain component (Fig. 2E), no clear EEG/EMG coherence is present for ipsilateral sensorimotor cortex recordings (Fig. 2A). It is of interest that this subject also demonstrated a double-peaked correlate in the back-averaged EEG (Fig. 1B). These peaks were separated by ~9 ms

(equivalent to a frequency of ~110 Hz) and were larger over the vertex than laterally. It should be noted that the coherence is a normalized measure of the linear association between two signals at a given frequency. It is derived from the cross-spectrum through division by the product of the autospectra of the two signals. Thus, the coherence spectrum is not directly comparable with either the back-average or cumulant density, which are directly related to the absolute amplitude of the signal. This distinction is highlighted in Fig. 2, where coherence is greatest between the midline EEG and EMG (Fig. 2B), although the cortical correlate is biggest over the EEG channel contralateral to the active limb (Figs 2G and 1B). Conversely, the high-frequency activity evident in coherence spectra may be of very small amplitude relative to activities of lower frequency, and therefore may not be evident in cumulant density estimates or back-averages (compare, for example, the coherence spectrum and cumulant density in Fig. 3D and H).

It seems unlikely that the shape information contained in the EEG correlate (as opposed to periodicities in the timing of correlates) contributed much to the pattern of EEG/EMG coherence. Thus, there was little difference in the shape of the EEG correlate in Figs 3H and 4H, and yet the corresponding coherence spectra in Figs 3D and 4E were quite different, particularly with respect to the degree of coherence at high frequency. The same is true of the cumulant density estimates and coherence over the midline and contralateral cerebral hemisphere in Fig. 3. Conversely, the principal features evident in the different coherence spectra were not due to variations in the shape the EMG potentials, as shown on the right-hand side of Fig. 3. Here, the EMG signal used to the left of Fig. 3 was reanalysed by passing the analogue EMG signal through a level detector. In this analysis only information pertaining to the timing of EMG events was preserved. The resulting coherence (Fig. 3E) was very similar to that in Fig. 3D. The range of frequencies represented remained between 15 and 150 Hz. Thus coherence spectra such as that in Fig. 3D provide strong evidence that high frequencies in the EEG may affect the timing of myoclonic muscle discharges (see also Brown and Marsden, 1996).

Time domain representations (cumulant density function) were derived from the frequency domain measures through application of the inverse Fourier transform. All eight Cases were found to have a time-locked EEG correlate over the contralateral motor cortex or vertex preceding muscle activity in the cumulant. In contrast, back-averaging techniques using the same signals revealed such a feature in only three patients (Table 1).

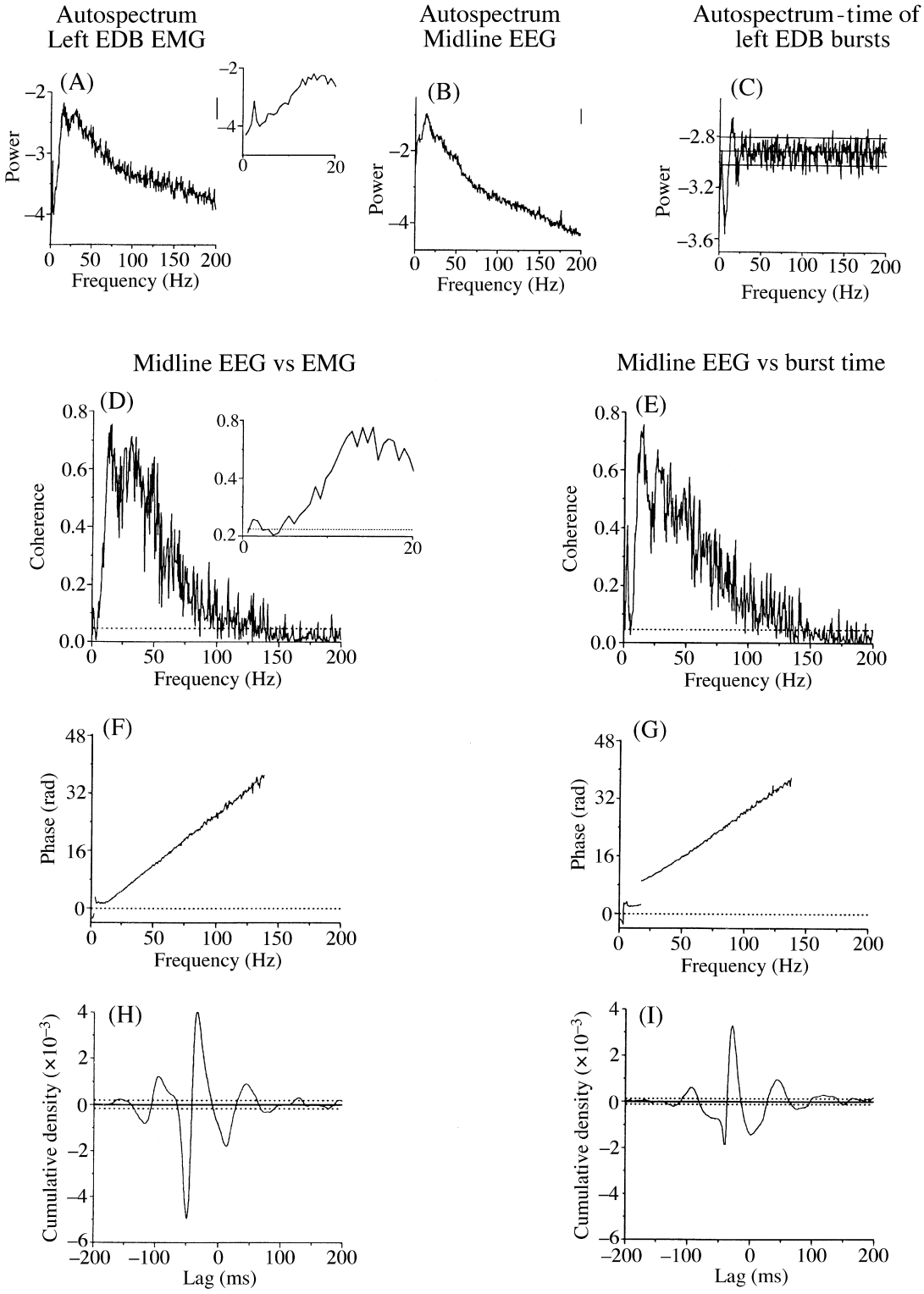
The principal feature in the EEG/EMG cumulants was a sharp downward deflection followed by an upward deflection. The downward defection occurred at negative lag when the EMG was used as the reference, indicating that there was a time-locked component in the EEG that preceded the EMG burst. The timing of this component was appropriate for conduction in fast pyramidal pathways (Rothwell *et al.*, 1991). Thus it was around 14, 20–26 and 35 ms for muscles of the forearm, hand and foot, respectively (Table 2). It is of interest that the phase delays for any given subject were similar at all frequencies at which coherence was present. For example in subject 4 (Fig. 3F), in whom a broad spread of frequencies were coherent, the phase delay was constant from 15 to 150 Hz, corresponding to a lag of ~35 ms. This suggests that the pyramidal tract and spinal motor neurons transmit information faithfully at a variety of frequencies.

Coherence between co-activated muscles

In three subjects simultaneous EMG recordings were obtained from upper limb muscles co-activated by the myoclonic jerks. Coherence between motor units recorded from different muscles is an expression of the frequency content of the common presynaptic input to the two sets of motor neurons (Farmer *et al.*, 1993*b*). Coherence analysis of EMGs co-activated by the myoclonus revealed correlation between a wide range of frequencies. In particular, the coherence between different muscles revealed the frequency of repetition of the myoclonic jerks and expressed the range of frequencies detected between the EEG and EMG. Figure 5 shows an example of coherence between forearm extensor muscles and first dorsal interrosseus (1DI) muscles in Case 5. Significant coherence is present at the frequency of the jerks (~5 Hz) and in the frequency range 20–180 Hz. The corresponding coherence between the EEG and left forearm extensor muscles is shown in Fig. 2. Although not identical, the EEG–muscle coherence encompasses the same range of frequencies expressed between the two EMGs. Thus coherence between the EMGs of muscles co-activated by the myoclonic volley reveals the frequency content of the descending common input. Time-domain analysis of the data revealed the expected highly synchronous EMG bursts. The peak in Fig. 5E is offset from time zero by ~6 ms, indicating that the more proximal forearm extensor muscle discharges slightly earlier than 1DI. This lag corresponds to the approximate difference in motoneuron–muscle conduction time between the two muscles. Thus, it may be inferred that, at the level of the spinal cord, the presynaptic drive to the forearm extensor muscles and 1DI motor neurons resulting from the myoclonic discharge is synchronous.

Discussion

We have shown that the cortical drive to muscle has a complex rhythmic organization extending over several frequency bands in patients with cortical myoclonus. This cortical drive is reflected in both the EEG–EMG coherence and, importantly, in the coherence between the EMGs of different muscles, further validating the latter as a measure of the common presynaptic drive to motor neurons. In addition, our results demonstrate that frequency domain analysis has significant advantages over the established time domain technique of back-averaging, and may therefore have diagnostic potential in myoclonic disorders.



Coherence between EEG and EMG at frequencies in excess of 60 Hz

Perhaps the most remarkable finding was the presence of coherence between EEG and EMG at frequencies of >60 Hz in four subjects. A previous study of cortical myoclonus demonstrated periodicities of comparable frequency in the precise timing of EMG discharges (Brown and Marsden, 1996), and here it is shown that these periodicities are driven by the motor cortex. Thus, with jerks in the hand, coherence between EEG and muscle is greatest over the vertex and contralateral hemisphere, and the phase lag between EEG and EMG is appropriate for conduction in fast pyramidal pathways. Cumulant density functions confirmed the presence of positive EEG waves of high frequency preceding EMG discharges in some patients. Although there are no reports of coherence between scalp-recorded EEG and EMG at such high frequencies in healthy subjects, activity of comparable frequency has been recorded in pyramidal tract fibres in the lightly anaesthetized cat (Adrian and Morruzzi, 1939) and the unanaesthetized cat (Calma and Arduini, 1954) in response to peripheral stimulation, and is a consistent feature of activity in cortical neurons projecting to the pyramidal tract during voluntary movement in subhuman primates (Evarts, 1965; Porter, 1985). The present results are important in showing that this high-frequency efferent activity may be found in man and is synchronized across many neurons. This must be the case as large populations of cortical neurons must be synchronized to give a surface-recorded EEG wave. Similarly, many motor units must be synchronously activated to give the myoclonic jerks, which are often large (Brown and Marsden, 1996). How this comes about may be best understood by drawing an analogy with the CA1 region of the rat hippocampus (Buzsaki *et al*., 1992). Inputs to this region set off fast (200 Hz) oscillations in field potentials, with the discharge of pyramidal cells time-locked to the negative peaks of these oscillations.

It is important to note that volume conduction of EEG discharges from the ipsilateral hemisphere could contribute to high-frequency coherence. Such ipsilateral discharges might arise from transcallosal spread, which takes ~10 ms between cortical representations of the distal upper limb (Brown *et al*., 1991). However, this does not seem to account for the coherences in the present cases, as any volume conduction would be expected to be two-way, and yet there was no high-frequency coherence over the ipsilateral motor areas in Cases 3 and 5. Moreover, transcallosal spread would be expected to be more rapid between the cortical representations of the lower limb, leading to coherence at even higher frequencies. However, the upper limit of the high-frequency coherence seen in leg jerks in Case 4 was no higher than that picked up in the upper limb jerks of Cases 3 and 5.

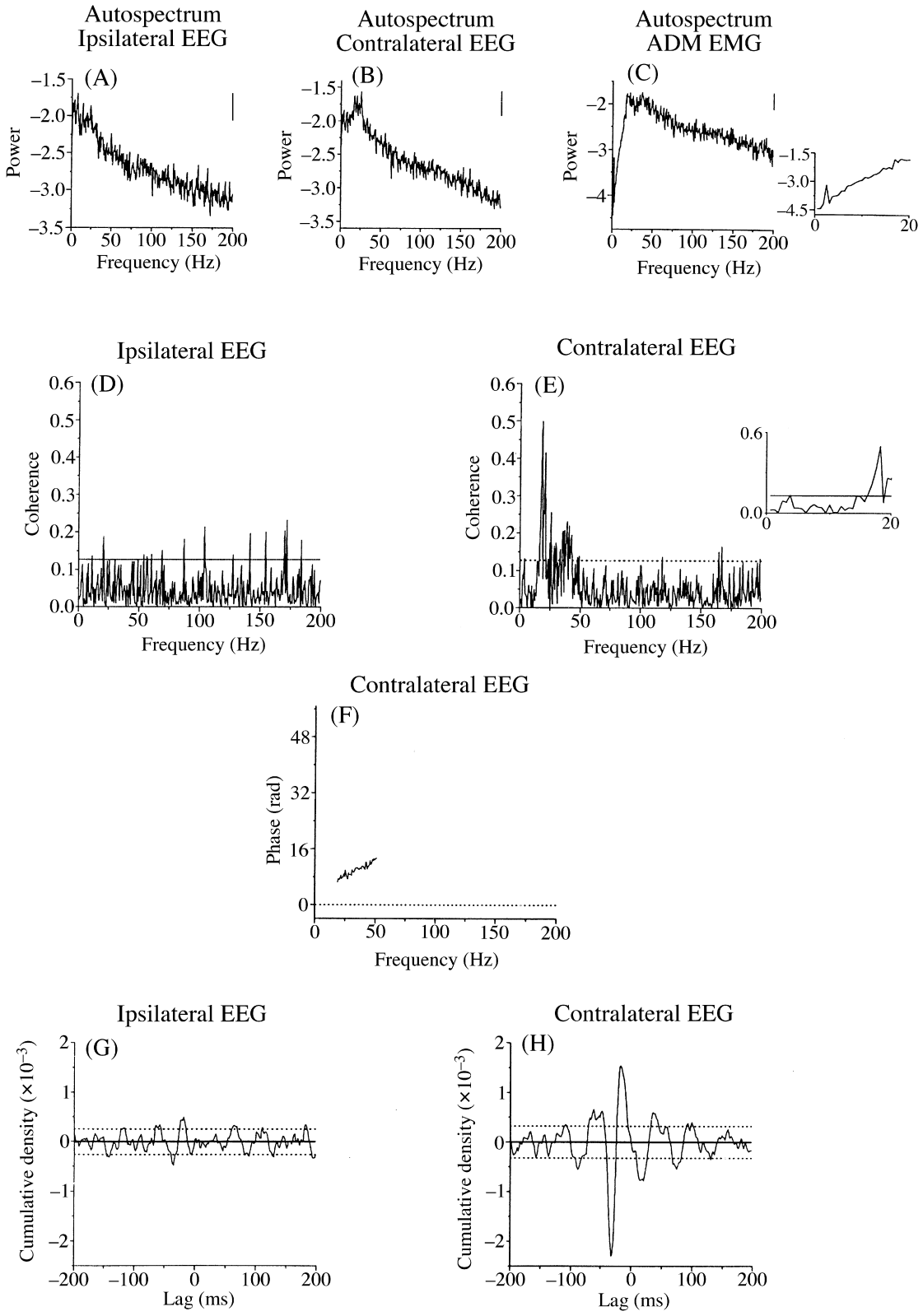
Finally, the period (<16 ms for frequencies of >60 Hz) of these high-frequency rhythmicities in brain and muscle and the similarity of the frequencies seen in the hand and foot argue against a simple re-afferance mechanism. Combined afferent and efferent loop times from the hand and foot would be ~45 and 90 ms, respectively.

Coherence between EEG and EMG in the 30–60 Hz band

Six out of eight of the cases demonstrated coherence between EEG and EMG in this band, with a phase lag between EEG and muscle appropriate for conduction in fast pyramidal pathways (Rothwell *et al*., 1991). There has been increasing interest in this frequency of oscillatory activity at both the cortical (Singer, 1993) and the motoneuron (Brown, 1997) level. In particular, this is the frequency range of the Piper rhythm of muscle, which is now recognized as a feature of both movement and tonic, particularly strong, contractions (Piper, 1912; Hill, 1921; Hagbarth *et al*., 1983; Brown, 1997; McAuley *et al*., 1997). Although coherence between scalp-recorded EEG and EMG has been reported only exceptionally in this band (Halliday *et al.*, 1998), recent magneto-encephalographic (MEG) recordings have demonstrated consistent coherence between the cortical signal from the motor cortex and EMG activity in the Piper band during strong contractions and movement in healthy subjects (Brown *et al*., 1998). It is likely that an exaggeration of this normal rhythmic drive plays an important role in the involuntary muscle activity seen in patients with cortical myoclonus. As such, one might predict that coherence between cortex and muscle in the 30–60 Hz band would be particularly prominent in those myoclonic jerks occurring during movement or strong tonic contractions.

It remains unclear whether the Piper rhythm and oscillations of even higher frequency, which are manifest in muscle and paralleled in the motor cortex, are intrinsic to the latter or imposed from elsewhere, possibly the basal

Fig. 3 Frequency analysis of the EEG and EMG recorded during action jerks of the left foot in Case 4. To the left of the figure (**A**, **D**, **F** and **H**), EMG is unrectified surface activity from extensor digitorum brevis. The autospectrum of the latter has a clear peak at 4 Hz, the repetition frequency of the more regular myoclonic discharges (inset in **A**). The coherence spectrum between the EEG recorded over the midline (Cz–Fz) and EMG also demonstrates a small but significant peak at 4 Hz (inset in **D**). This is followed by a broad band of coherence extending from ~10 to ~140 Hz (**D**). The phase slope was more or less constant over this band, EMG lagging behind EEG by 35 ms (**F**). A clear EEG correlate is seen in the cumulant, the major positive wave preceding the EMG discharge by ~50 ms (**H**). This is one in a series of significant positive deflections, repeating with a frequency of ~18 Hz. To the right of the figure (**C**, **E**, **G** and **I**) EMG is represented by a digital signal triggered from a level detector. The range of coherence (**E**) and phase estimate (**G**) were similar to those seen in **D** and **F**. All graphs are derived from the same continuous recording lasting 104 s.



ganglia and/or the cerebellum. It is therefore of interest that pathological changes in patients with cortical myoclonus occur in the cerebellum rather than the cerebral cortex (Hauw *et al*., 1986), and that cerebellothalamocortical projections are characterized by activity at 40 Hz (Steriade, 1995) or even higher frequencies (Timofeev and Steriade, 1997).

Coherence between EEG and EMG in the 15–30 Hz band

Six out of the eight cases demonstrated coherence between EEG and EMG in this band, with an appropriate phase lag between EEG and muscle, although these were not necessarily the same cases as those that showed coherence in the Piper band. The coherence evident during involuntary action myoclonus between 15 and 30 Hz is likely to be an exaggeration of a parallel drive to muscle in healthy voluntary contraction (Farmer *et al*., 1993*b*). Recent MEG and EEG recordings have demonstrated coherence between the cortical signal from the motor cortex and EMG activity in this frequency band during sustained contraction in healthy subjects (Conway *et al*., 1995; Salenius *et al*., 1997; Halliday *et al*., 1998). Similar results have been obtained in monkeys (Murphy and Fetz, 1992; Sanes and Donoghue, 1993; Baker *et al*., 1997). The MEG and EEG results in man have proved difficult to interpret as cortical and muscle activity may appear to be synchronized with zero delay (Conway *et al*., 1995; Halliday *et al*., 1998). In these experiments the subjects

Table 2 *Results of frequency-domain analyses*

Case no.	Regular low-frequency action jerks (<10 Hz)	EEG–EMG coherence* (NB: often merged between bands, without clear peaks)					Phase lag (contralateral EEG to hand, or vertex EEG to leg)	Time-locked EEG correlate preceding muscle activity in cumulant
		<10 Hz	15–30 Hz	30–60 Hz	60–90 Hz	>90 Hz		
1	+	–	+	+	–	–	25 ms to ADM from both phase and cumulant plots	+
2	–	–	–	+ (only seen over vertex for ADM)	–	–	25 ms to ADM from cumulant plot only	+
3	+	+	–	+	+	+ (up to 175 Hz)	26 ms to 1DI from both phase and cumulant plots	+
4	+	+	+	+	+	+ (up to 150 Hz)	35 ms to EDB from both phase and cumulant plots	+
5	+	–	+	+	+ (best seen over vertex	+ (up to 150 Hz and best seen over vertex)	14 ms to f. ext from both phase and cumulant plots	+
6	–	–	+	+ (only vertex for biceps)	+ (only seen for forearm extensors)		–13 ms to biceps from both phase and cumulant plots	
7	–	–	+	–	–	–	44 ms to tib. ant. from both phase and cumulant plots	+
8	–	–	+	–	–	–	20 ms to 1DI from cumulant plot only	+

1DI = first dorsal interosseus; biceps = biceps brachii; tib. ant. = tibialis anterior; remaining abbreviations as for Table 1.
*Coherence greater than 95% confidence level in ⩾2 contiguous bins for activities at frequencies <Hz, and ⩾4 contiguous bins for rest.

Fig. 4 Frequency analysis of the EEG and EMG recorded during action jerks of the right hand in Case 1. There is barely any significant coherence (**D**) between the unrectified surface EMG from the adductor digiti minimi and the ipsilateral EEG (C4–F4). A very small feature is seen in the corresponding cumulant density (**G**). In contrast, the contralateral EEG (C3–F3) shows a large peak of coherence centred on 20 Hz, with a broader band of lesser coherence from ~25–45 Hz (**F**). Phase slope was more or less constant over these frequencies, EMG lagging behind EEG activity by 25 ms (**E**). A clear EEG correlate is seen in the cumulant, the major positive wave preceding the EMG discharge by a similar amount (**H**). This is one in a series of significant positive deflections, repeating with a frequency of ~20 Hz. Note that although the autospectrum of the hand EMG has a clear peak at 5 Hz (inset in **C**) (the repetition frequency of the more regular myoclonic discharges), there is only a small peak in coherence between EEG and EMG at this frequency (inset in **F**). Analysis was of a continuous recording lasting 37 s.

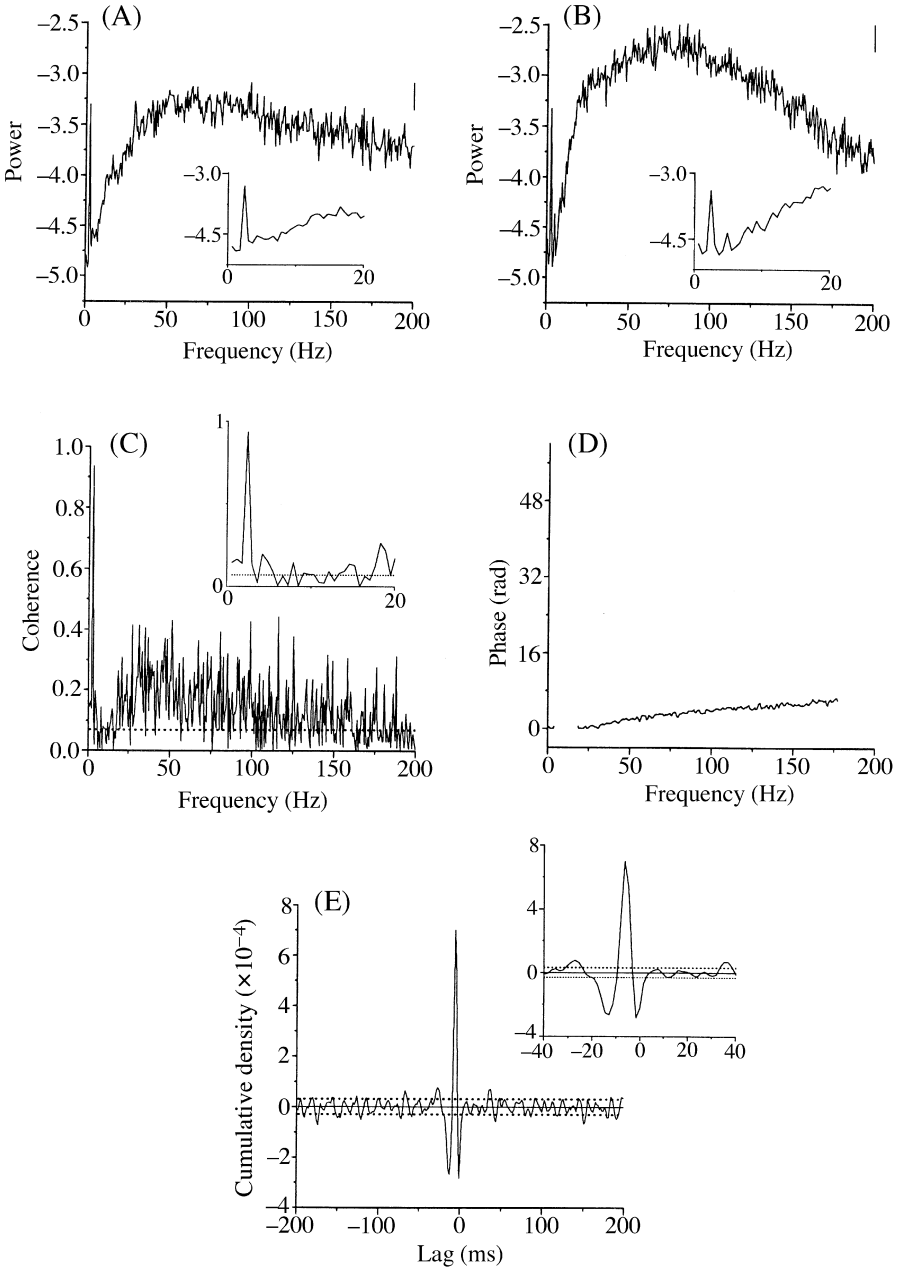


Fig. 5 Frequency analysis of the EMG recorded during action jerks of the left forearm extensor muscles and left 1DI in Case 5. (**A**) Power spectrum of the EMG in 1DI. (**B**) Power spectrum of the EMG in the forearm extensor muscles. (**C**) Coherence between the two muscles. (**D**) Phase. (**E**) Cumulant density. Significant coherence is present at the frequency of the jerks (~5 Hz) and in the frequency range 20–180 Hz. The phase and cumulant indicate that EMG bursts lead in the forearm extensor muscle by ~6 ms. Analysis was of a record lasting 55 s.

maintained a steady, gentle isometric or postural contraction. In this situation much of the input to motor neurons depends on afferent feedback, which maintains corticomotoneuronal drive through transcortical reflex pathways (Matthews and Miles, 1988; Matthews *et al.*, 1990). The presence of strong closed-loop feedback may lead to the synchronization (without delays in phase) of rhythmically firing neurons despite significant interneuronal conduction delays (Engel *et al.*, 1991; Singer, 1993).

The recordings of myoclonic activity afford an opportunity to study phase relationships outside this steady state. Under such open-loop conditions, the 15–30 Hz cortical drive to muscle is associated with a phase lag appropriate for conduction in fast pyramidal pathways. The function of this descending drive is unclear. Baker *et al*. (1997) and Halliday *et al.* (1998) considered it a function of the motor cortex acting in a 'holding' postural mode, and it remains to be seen if the coherence between cortex and muscle in the 15–

30 Hz band is particularly represented in those myoclonic jerks occurring during sustained posture as opposed to action.

It is important to note that although, under some circumstances, the EEG activity recorded over the motor cortex may be coherent with muscle activity in healthy subjects in the 15–30 Hz band, the strength of this coherence is considerably less than that seen in our patients with cortical myoclonus (Halliday *et al.*, 1998).

Low-frequency coherence between EEG and muscle

Four of the patients had regular series of EMG bursts with a frequency of <10 Hz during action myoclonus. However, only two of these subjects had significant coherence between EEG and EMG at the frequency of rhythmic jerks. This variability of the cortical and muscle locking is also seen in the pathological tremors. Patients with parkinsonian tremor demonstrate coherence between MEG and EMG at frequencies corresponding to that of the tremor (Volkmann *et al.*, 1996), although MEG–EMG coherence has not been demonstrated at higher frequencies. Patients with essential tremor demonstrate the reverse picture, with coherence between MEG and EMG at 15–30 Hz, the same frequency range as is associated with steady muscle contraction in healthy subjects. However, in essential tremor the tremor frequency does not seem to be expressed in the MEG–EMG correlation (Halliday *et al*., 1997). Thus different movement disorders show differing frequencies of cortical–EMG coupling and may differ in the extent to which the pathological frequency of the tremor, be it essential, Parkinsonian or myoclonic, involves the motor cortical neurons.

Diagnostic use of frequency domain analysis techniques

Hitherto, the time domain analysis technique of back-averaging has, together with the presence of giant cortical sensory evoked potentials, formed the principle method for diagnosing myoclonus of cortical origin. Such physiological characterization may have implications for aetiology and treatment (Brown, 1995). In the present study only three of the eight patients had evidence of a time-locked EEG correlate preceding action jerks, as determined by back-averaging. A further three subjects had no EEG correlate at the time of study, but had been shown to have such a correlate during earlier studies. In contrast, a time-locked EEG correlate preceding muscle activity was evident in the cumulant in all eight cases. Fourier analysis may have several advantages over traditional diagnostic techniques. High-frequency myoclonic discharges do not preclude analysis, no arbitrary trigger level has to be chosen so that jitter is less, statistical evaluation of results is possible and the technique is quick and automated, so that long sections of data may be analysed. The result is that a cortical correlate may be demonstrated using coherence analysis in patients in whom classical back-averaging has failed to demonstrate such a feature.

Conclusion

The present study has identified several frequency bands in which there may be coherence between EEG and EMG in cortical myoclonus. The importance of this is threefold. First, these activities are likely to represent pathological exaggerations of physiological central rhythmicities relating to movement. Two such activities have recently been found in the human motor cortex, in the frequency bands 15–30 and 30–60 Hz, and the present results suggest that more remain to be identified. Secondly, the precise pattern of coherence in myoclonic patients may have potential diagnostic value in distinguishing between different pathological processes. Finally, it remains to be seen whether frequency-domain analysis is able to demonstrate a cortical correlate to the myoclonic activity in conditions such as corticobasal degeneration, where existing techniques have failed to show such a feature.

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