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Review

EEG–EMG, MEG–EMG and EMG–EMG frequency analysis: physiological principles and clinical applications

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1. Introduction

The fact that muscle discharge tends to be rhythmic has been known for 200 years. William Wollaston, using a precursor of the stethoscope, was the first to describe this in 1810 (Wollaston, 1810). He determined the rhythm to be in the beta band by comparing the pitch of the sound picked up over his muscles with that from a horse drawn carriage driven over the cobbled streets of London at different speeds. A century later, the pioneering German neurophysiologist, Hans Piper, delineated a further modulation of motor unit discharge in the low gamma band, at around 40 Hz (Piper, 1907, 1912). However, it was not until the early 1990s that the first evidence emerged supporting a central origin for motor unit synchronisation in humans (McLachlan and Leung, 1991; Farmer et al., 1993) and other primates (Murthy and Fetz, 1992, 1996a,b; Sanes and Donoghue, 1993). The past decade has seen steadily growing interest in this field, with attention also being turned to whether specific patterns of oscillatory drives to muscle may be of pathophysiological or even diagnostic significance.

Frequency analysis is a useful way of analysing neuronal synchrony and is based on the cross-correlation between two separate signals in the time and frequency domain. Examples of some of the measures that can be derived are given in Fig. 1. The principal measure of the linear dependence or correlation between two signals in the frequency domain is coherence. It is mathematically bounded between zero and one, where one indicates a perfect linear relationship and zero indicates that the two signals are not linearly related at that frequency. Thus oscillatory coupling between motor elements of the central nervous system and electromyographic (EMG) discharge is most clearly measured as coherence between the motor cortex and muscles (Fig. 1C) while the phase difference can provide an estimate of the temporal delay between cortex and EMG (Fig. 1D) We will begin with an overview of those physiological descending drives that may modulate motor unit discharge followed by some basic methodological considerations concerning frequency analysis. However, the main thrust of this review is to critically evaluate the utility of frequency analysis techniques in the investigation of pathophysiological mechanisms in the motor system and as a diagnostic tool.

2. Physiological drives to muscle

The human central nervous system drives muscle discharges at a number of frequencies and, although the function of these oscillations is far from clear (Farmer, 1998; Brown, 2000; Brown and Marsden, 2002), one of the interests from the clinical point of view is that these different activities may be characteristic of functional activities in distinct circuits. The different physiological oscillatory drives to spinal motoneurones are summarised in Table 1.

The first is a low frequency drive at 2–3 Hz, that has been, in retrospect, rather confusingly termed ‘common drive,’ even though there are many such drives (DeLuca et al., 1982). This rhythm can be picked up during isometric contraction or slow movements, even in muscles without muscle spindles (Kamen and DeLuca, 1992; DeLuca and Erim, 1994). The site of its generation is unclear. As it is preserved in patients with cortical or capsular strokes (Farmer et al., 1993) it is not likely to have an origin within the corticospinal system.

Oscillations in the 6–12 Hz range may arise through mechanical resonance phenomena (Elble and Randall, 1978) but have also been related to the pulsatile organisation of slow movements at ~10 Hz (Vallbo and Wessberg,

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Abbreviations: EEG, electroencephalogram; EMG, electromyogram; MEG, Magnetoencephalogram; FFT, fast Fourier transform; MAR, multivariate autoregressive.

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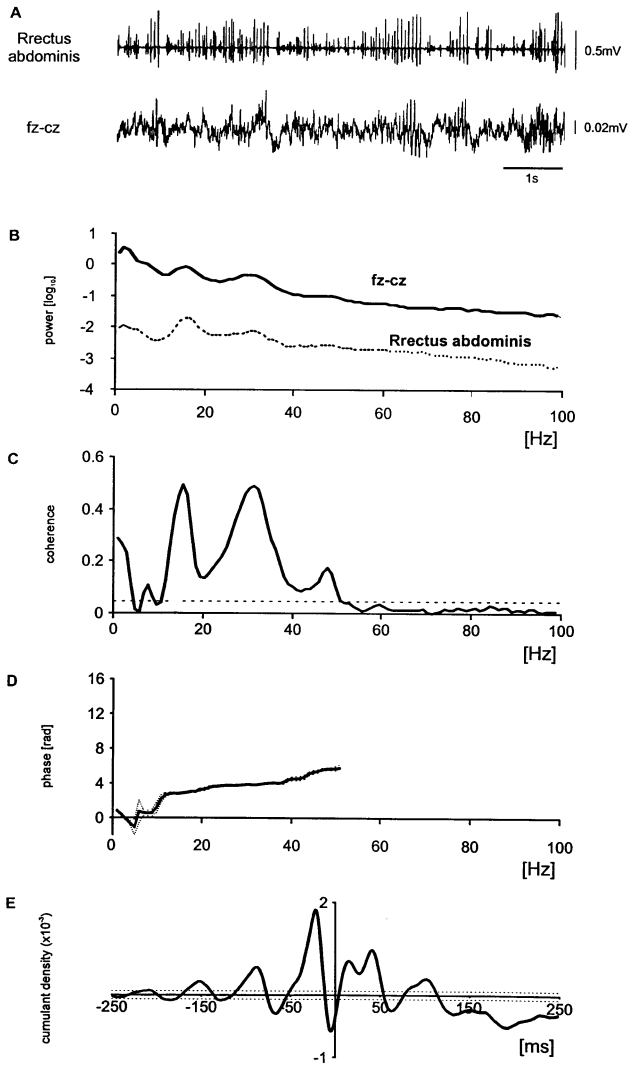

Fig. 1. Frequency analysis in a patient with spontaneous and action-induced irregular, multi-focal myoclonus of the abdominal wall and proximal parts of the lower extremities. (A) EMG from right-sided rectus abdominal muscle and midline EEG. EMG shows myoclonic bursts at variable frequencies with premyoclonic spikes in the EEG. (B) Autospectra of Fz–Cz and right-sided rectus abdominal muscle. (C) Coherence between Fz–Cz and right-sided rectus abdominal muscle. EEG–EMG coherence is exaggerated with peaks at 16 and 32 Hz; (D) Phase between Fz–Cz and right-sided rectus abdominal muscle. EEG precedes EMG. Regression analysis gives a time difference between the two signals of 14.9 ms (±1.2 ms, 95% confidence limits). (E) Cumulant density estimate showing a positive–negative deflection with peaks at about 21 and 2 ms before the onset of EMG. Interrupted thin lines in C–E are 95% confidence levels.

1993) – identical to physiological action tremor and to the central component of physiological postural tremor (force tremor) (Conway et al., 1995a). In these instances, 6–12 Hz oscillations prove to be unaffected by alterations of the limb mechanics (Halliday et al., 1999; Vallbo and Wessberg, 1996). The olivary–cerebellar system has been suggested as a possible generator for the 6–12 Hz oscillations (Llinàs and Pare, 1995) based on findings in the animal harmaline-tremor model (Llinàs and Volkind, 1973). Consistent with this, some studies have failed to show a cortical correlate at ~10 Hz (Kilner et al., 1999; Mima et al., 2000). Nevertheless the exclusivity of the subcortical generation of this drive has been challenged as other studies have detected significant cortico-muscular coherence at this frequency (Mima and Hallett, 1999; Raethjen et al., 2000; Salenius et al., 1997a) indicative of sensorimotor cortex involvement. In part, this variability in findings may be accounted for by task dependency. Thus a recent magnetoencephalographic–electromyographic (MEG–EMG) study found coherence at 6–12 Hz in force tremor with a source unequivocally originating in the primary motor cortex but no such coherence in action tremor (Marsden et al., 2001a).

In contrast, there is general agreement that motor unit synchronisation in the beta (15–30 Hz) and low gamma (30–60 Hz) bands is predominantly driven from the primary motor cortex, with less influential contributions possibly from supplementary motor and premotor cortices (Feige et al., 2000; Marsden et al., 2000a). Coupling between primary motor cortex and muscle has been demonstrated by both MEG (Conway et al., 1995b; Salenius et al., 1997a; Salenius et al., 1997b; Brown et al., 1998b; Gross et al., 2000) and surface EEG (Halliday et al., 1998; Mima et al., 1998), although coherence in the gamma band is best seen with the former technique due to the low pass filtering charactaristics of the skull and scalp (Fig. 2). Cortico-muscular coherence seems ubiquitous and is even demonstrated by those muscles with small representation in the motor cortex such as the paraspinal and abdominal wall muscles (Murayama et al., 2001). The coherence in the beta band appears during weak tonic contraction, particularly when attention is directed towards the motor task (Kristeva-Feige et al., 2002) and is abolished by movement, whereas that in the gamma band is more obvious in strong contractions and may persist during slow movements (Baker et al., 1997; Brown et al., 1998b; Kilner et al., 1999).

Cortical oscillations coupled to motor unit discharge may arise intrinsically within the cortex or may be under extrinsic, subcortical influence. The intrinsic generation of cortical oscillations may involve pacemaker cells, such as the 'chattering cells' (Jefferys et al., 1996; Steriade et al., 1993), which fire rhythmically and may drive neuronal networks (Conners and Amitai, 2001) or result from network properties. The latter include recurrent circuits between excitatory and inhibitory cells and circuits involving the mutual inhibition of inhibitory neurons (Wilson and Bower, 1992; Jefferys et al., 1996).

Striking evidence in favour of a subcortical influence on cortical rhythmicity was initially found non-invasively in patients with Parkinson's disease through muscle sound recordings using a stethoscope. In untreated patients, the normal sound due to the Piper (around 40 Hz) rhythm of muscle was replaced by a 10 Hz rhythm, although the Piper drive could be restored by treatment with levodopa (Brown, 1997). The implication was that the pattern of cortical drive to muscle was critically dependent on the effects of the basal

Table 1
Physiological oscillatory drives synchronising motor units in humans

Frequency range (Hz)	Origin	Task in which manifest	Detection	References
~ 2 ('common drive')	Unknown	Sometric contraction, slow movements	EMG–EMG	DeLuca and Erim, 1994; Kakuda et al., 1999
6–12	Unknown	Isometric contraction, slow movements	MEG–EMG, EMG–EMG	Vallbo and Wessberg , 1993; Conway et al., 1995b; Marsden et al., 2001a
15–30	Motor cortex	Submaximal voluntary contraction	MEG–EMG EEG–EMG	Conway et al., 1995b; Halliday et al., 1998
30–60 ('piper rhythm')	Motor cortex	Strong voluntary contraction, slow movements	MEG–EMG	Brown et al., 1998
60–90	Brainstem	Eye movements	EMG–EMG	Brown and Day, 1997; Spauschus et al., 1999
60–100	Brainstem	Respiration	EMG–EMG	Carr et al., 1994

ganglia on the motor areas of the cerebral cortex. This hypothesis has recently been confirmed by MEG–EMG studies (Salenius et al., 2002).

Oscillatory drives above 60 Hz have also been described, both in electrocorticographic recordings from the motor cortex (Marsden et al., 2000a), and through EMG–EMG frequency analysis in the striated ocular muscles (Brown and Day, 1997; Spauschus et al., 1999) and respiratory muscles (Carr et al., 1994). These drives will not be considered further here.

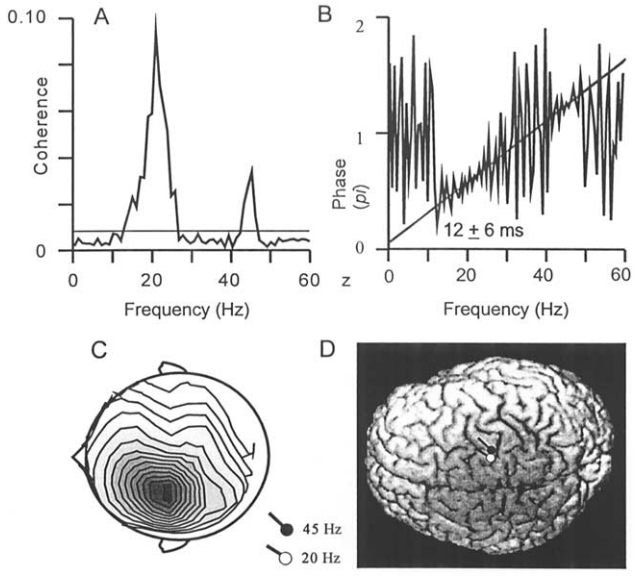

Fig. 2. (A) Coherence spectrum between EMG of right forearm extensors and MEG over the contralateral Rolandic area in a healthy subject. The horizontal line indicates the 1% confidence level. (B) Phase spectrum in the same subject. The correlation coefficient was >0.90 ($P < 0.01$), and the MEG–EMG time difference (±99% confidence limit) calculated from the regression coefficients is shown. The positive phase slope and MEG–EMG time difference means that MEG leads EMG. EMG was the input. (C) Spatial distribution of the strongest peak (20 Hz) of the coherence spectrum in (A). The head is viewed from above, nose points leftward. (D) Sources of cortical oscillatory signals associated with contraction in same subject, superimposed on the surface rendering of their brain. The black lines indicate the current directions. Filled circles represent the sources for the beta and gamma activities. Both overlie the hand area of the motor cortex.

3. Methodological considerations

The coherence between signals a and b at frequency λ is an extension of Pearson's correlation coefficient and is defined as the absolute square of the cross-spectrum normalised by the autospectra:

$$|R_{ab}(\lambda)|^2 = \frac{|f_{ab}(\lambda)|^2}{f_{aa}(\lambda) f_{bb}(\lambda)}$$

In this equation, f_{aa}, f_{bb} and f_{ab} give the values of the auto and cross-spectra as a function of frequency λ.

Spectra are usually determined using the fast Fourier transform (FFT). Data are divided into serial, usually non-overlapping windows, transformed and then averaged. The basic trade-off that one has to consider in the FFT approach is between frequency resolution and spectral variance. As the size of the windows decreases, the variance goes down, but the spectral resolution becomes poorer. Spectra derived from a FFT approach are defined pointwise, and the frequency difference between two adjacent points is given by the sampling rate divided by the FFT window size (in samples).

Alternatively, spectra can be determined using multivariate autoregressive (MAR) models. The latter have the desirable property of representing the characteristics of a signal with just a few coefficients, which can then be used to calculate the relevant spectra. Because of this property, MAR models are often useful for modelling short data sets. In addition, MAR spectra are continuous functions of frequency, and thus avoid the spectral resolution problems encountered with the FFT approach. In practice, however, the calculation of true confidence limits is problematic and the approximate limits that can be calculated are generally wider than their FFT counterparts. (Cassidy and Brown, 2002). A detailed comparison between FFT and MAR approaches to spectral estimation can be found in Cassidy

and Brown (2002), which shows that MAR and FFT derived spectra are in good agreement if a large amount of data are available for analysis.

It is worth noting that the computation time for FFT methods is much faster than for MAR modelling. However, if one wants to model more than two signals at a time, the MAR model provides a superior representation by modelling all channels simultaneously without having to look at individual pairs, as with the FFT approach. The MAR representation can also be embedded into more complex non-stationary models, which are often necessary in the analysis of biomedical signals whose statistical properties change substantially over time. However, as the number of channels to be modelled increases, the calculating time scales as the number of channels squared, so one can see that a full MAR model for 64 or 128 channels is unfeasible.

The biggest problem that anyone working with static MAR models faces is the choice of model order to be used. If one thinks in terms of a univariate model, the model order can be interpreted as twice the number of peaks that one wants in the power spectrum. This is tantamount to assuming a specific model for the data. The question is therefore, how does one know how many peaks to include? One may have some prior reason to expect that there will be peaks in particular frequency bands but really one would like to have some objective measure of what to choose for the model order. Potential MAR modellers have a number of model order selection criteria at their disposal, which can be derived from reasonable statistical assumptions. We have used Bayesian methodology to derive a unifying approach to both MAR parameter estimation and model order selection, so that these can be handled in a rigorous, objective manner (Cassidy and Brown, 2002). This effectively removes the only remaining free parameter of the MAR model (i.e. the model order), which is now completely determined by the data.

Whichever technique is used, whether FFT or MAR, autospectra and cross-spectra may be derived, and from these coherence, phase and cumulant density function determined. Phase, $\phi_{ab}(\lambda)$, is expressed mathematically as the argument of the cross-spectra:

$$\phi_{ab}(\lambda) = \arg\{f_{ab}(\lambda)\}$$

It comprises two factors, the constant time lag given by the slope of the phase spectrum, when linear, and a constant phase shift, which is reflected in the intercept and is due to differences in the shapes of the signals (Mima and Hallett, 1999).

The cumulant density, which is in many ways similar to the cross-correlation between signals, is calculated from the inverse Fourier transform of the cross-spectrum. When the input/reference signal is EMG, this cumulant density estimate resembles a back-averaged electroencephalographic (EEG) record.

For a general introduction to coherence, readers are referred to Challis and Kitney (1991), and for a more detailed discussion of the measures derived from frequency analysis to Rosenberg et al. (1989) and Halliday et al. (1995) for FFT approaches and Cassidy and Brown (2002) for MAR approaches.

3.1. Problems of recording and interpretation

In this section, we will consider some specific problems of recording and interpretation relevant to the investigation of corticomuscular coupling.

The signal and its collection: The first problem is the signal itself and the question of how closely it matches the activity to be modelled. For example, the skull and scalp act as a low pass filter so that scalp EEG may not reflect cortical activities at higher frequencies, which are otherwise evident in electrocorticographic or MEG recordings. Another factor is the focality of the cortical area sampled by scalp EEG. This can be increased by Laplacian derivations such as the current source density and Hjorth transformation. The latter also tend to give higher EEG–EMG coherence estimates, whereas common average references and balanced non-cephalic references may give misleading results because of possible EMG contamination (Mima and Hallett, 1999). In addition, it is necessary to sample the signal at a rate that is greater than twice the low-pass filter setting so as to avoid aliasing and the identification of spurious spectral elements.

Coherence: Another important point is that as coherence is a measure of linear dependence between two signals in the frequency domain, any artefact common between channels leads to high coherence values over the relevant frequency band. This is most commonly evident in the case of mains artefact, but any volume conduction of signals between electrodes or cross-talk within leads or amplifiers will also lead to inflated coherences. Such artefacts occur with zero phase delay, and are reasonably obvious in paradigms in which biologically related signals would be expected to demonstrate phase differences, such as when investigating the coupling between EEG and EMG or EMG and tremor. In addition, because coherence ranges between 0 and 1, its variance should be stabilised by transformation before statistical comparison. In practice, this makes relatively little difference to small coherences, but is important with coherences of more than 0.6. The usual transform used is the arc hyperbolic tangent transformation (Rosenberg et al., 1989).

Phase: The other major information provided by frequency analysis is the phase spectrum. The phase estimate from a single point is ambiguous (Gotman, 1983). Measuring phase relationships that are linear over a band of frequencies reduces this ambiguity. Under these circumstances, the temporal delay between the signals can be calculated from the gradient of the line. A negative gradient indicates that the input/reference signal leads. The temporal delay between the two signals is equal to the gradient (in radians/ms) multiplied by $1/2\pi$. Two confounding factors must be remembered when the temporal delay between two

signals is calculated from the phase. First, low pass filters, such as the skull and scalp, may introduce phase shifts that may underestimate real conduction delays (Lopez da Silva et al., 1989). Second, it is possible that more than one coherent activity may overlap in the same frequency band, in which case the phase estimate will be a mixture of the different phases. This may help explain why the temporal differences calculated between EEG or MEG and EMG are often shorter than those predicted from transcranial stimulation of the motor cortex (Brown et al., 1998b; Mima et al., 1998; Salenius et al., 1997a), as both efferent and afferent cortico-muscular coupling may occur in overlapping frequency bands (Mima et al., 2001a). Co-existing bi-directional oscillatory flows between neural networks can be separated through application of the directed transfer function (Kaminski and Blinowska, 1991), although so far there has been only one report of the use of this in the motor sphere (Mima et al., 2001a).

Cumulant density estimate: This measure is equivalent to the cross-correlogram, with the advantage that the 95% confidence limits are easier to derive. Like the cross-correlogram, it is difficult to resolve common activities of more than one frequency (Challis and Kitney, 1990).

3.2. EMG–EMG frequency analysis

The recording of scalp EEG is not always easy, for example in children, and in movement disorders, in particular, the signal can be marred by muscle artefact. Thus it is fortunate that the same drive that leads to coherence between cortex and muscle also leads to coherence between the EMG signals of agonist muscles coactivated in the same task (Kilner et al., 1999). EMG–EMG coherence analysis can be performed using single or multi-motor unit intramuscular needle recordings or surface EMG. Studies of single units tend to be less informative (smaller signal to noise ratio in coherence spectra) than multi-unit needle or surface recordings (Christakos, 1997). Surface EMG is more practical but may be limited by volume conduction between muscles. The latter can be ruled out if there is a constant phase lag between the two EMG signals in the range of significant coherence. Thus it is generally best to choose muscle pairs that are separated (such as forearm extensors and intrinsic hand muscles), where one would expect physiological coupling to involve a phase difference. Alternatively, volume conduction can be limited by appropriate levelling of both signals and analysing the coherence between the resulting point processes. The principle that intermuscular coherence may give comparable information about descending cortical drives as cortico-muscular coupling has been validated in cortical myoclonus (Brown et al., 1999). Examples of EMG–EMG coherence are illustrated in Fig. 3. These are taken from the data of the same myoclonic patient as in Fig. 1 and show that the pattern of EMG–EMG coherence is qualitatively similar to that of the EEG–EMG coherence in the same subject.

Nevertheless, it should be remembered that oscillatory presynaptic drives to spinal motoneurons other than those of cortical origin will also be reflected in the synchronisation of motor unit discharge, where these contribute to muscle activity. Thus EMG–EMG coherence may afford an additional insight into subcortical motor drives.

4. Frequency analysis in pathological conditions

Frequency analysis is being increasingly applied in the investigation of movement disorders. So far, studies have usually involved relatively small numbers of patients, so that the degree to which findings may be true across large populations (and consequently the clinical utility of these techniques) remains largely unclear.

4.1. Cortical myoclonus

Frequency analysis shows the most diagnostic potential in cortical myoclonus. To date, the diagnosis of cortical myoclonus has relied on the detection of giant cortical sensory evoked potentials, which are not always present, and of a cortical correlate upon back-averaging (Shibasaki and Kuroiwa, 1975). Frequency analysis may, however, have several advantages over the time domain technique of back-averaging. High-frequency myoclonic discharges with low amplitudes, such as in minipolymyoclonus (Wilk-

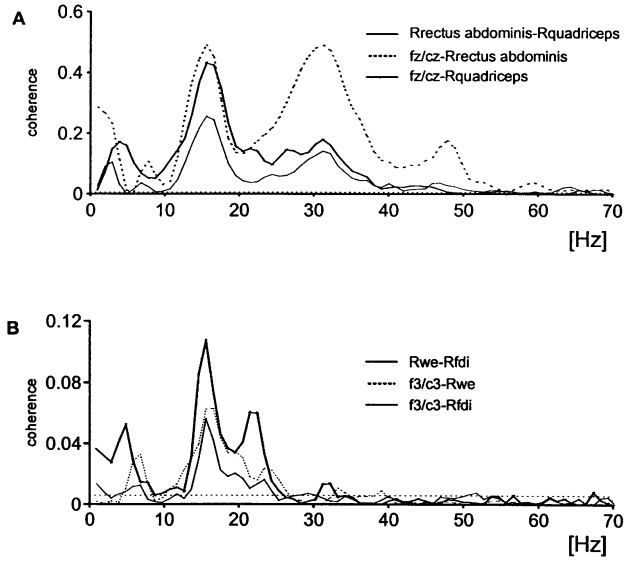

Fig. 3. EMG–EMG and EEG–EMG coherence in the same patient as in Fig. 1. (A) Coherence between the right rectus abdominal muscle compared to the right quadriceps muscle (thick line). In this case, rectus abdominal muscle leads the right quadriceps muscle by 3.5 ms (±0.7 ms, 95% confidence limits). (B) EMG–EMG coherence in an ispilateral muscle pair in the upper extremity (right wrist extensor and first dorsal interosseus muscle). Although no myoclonus was clinically evident in this limb, coherence was nevertheless exaggerated. In this case the wrist extensor leads the first dorsal interosseus by 11 ms (±3.5 ms, 95% confidence limits). Note that in both A and B, the overall pattern of EMG–EMG coherence is similar to that of the EEG–EMG coherence. Interrupted horizontal lines are 95% confidence levels.

ens et al., 1985), do not preclude analysis, no arbitrary trigger level has to be chosen so that jitter is less, statistical evaluation of the results is possible and the technique is quick and automated, so that long sections of data may be analysed. Thus in a recent study, it was possible to demonstrate cortical activity related to myoclonic jerking through frequency analysis in 8 patients in whom classical back-averaging failed to show a cortical correlate in 5 (Brown et al., 1999). Three of the patients in this study also showed exaggerated coherence that encompassed not only the physiological frequency range between 15 and 60 Hz, but also much higher frequencies. This report described patients with large amplitude jerks of low frequency typical of post-anoxic myoclonus and progressive myoclonic epilepsy and ataxia. Recently significant coherence between EEG and EMG has also been reported in genetically determined mini-polymyoclonus (Guerrini et al., 2001) and Fig. 1 illustrates the findings in one such patient. Similarly, the tremor of hepatic encephalopathy, which shares many featuresof minipolymyoclonus, has also been found to involve exaggerated cortico-muscular coupling (Timmermann et al., 2002). Regardless of aetiology, phase spectra confirm that cortical activity precedes EMG by a delay appropriate for conduction in the fast conduction pyramidal pathway (see Fig. 1D). However, it should be noted that occasional exceptions to this rule are met at low frequencies, where the cortical activity lags (Marsden et al., 2000b).

Patients with cortical myoclonus also have exaggerated coherence between ipsilateral muscles co-activated by myoclonic jerks (Brown et al., 1999). Thus, EMG–EMG coherence analysis can be used to infer the pattern of coherence between motor cortex and EMG, as illustrated in Fig. 3.

4.2. Tremor

Cortico-muscular coherence in tremor with maximal coherence at the frequency of the tremor was first demonstrated in parkinsonian rest tremor using MEG (Volkmann et al., 1996). This finding has since been confirmed in studies of MEG/EEG–EMG coherence (Hellwig et al., 2000; Salenius et al., 2002), but the time delays between cortex and muscle are variable, suggestive of efferent and afferent cortico-muscular drives in different patients (Hellwig et al., 2000). Some of this variability may be explained by the presence of two types of parkinsonian tremor with differing pathophysiological mechanisms (Lance et al., 1963). In higher frequency (7–10 Hz) parkinsonian action tremors cortical signals tend to lead EMG, whereas during low frequency (3–6 Hz) parkinsonian rest tremor EMG activity in the forearm precedes cortical activity, consistent with peripheral re-afference (Volkmann et al., 1996; Salenius et al., 2002). Coherence has also been reported between the activity of units in the Globus Pallidus interna and rest tremor (Hurtado et al., 1996).

Findings in essential and exaggerated physiological tremor have been more contradictory. A single channel MEG–EMG study failed to demonstrate cortico-muscular coherence at tremor frequency in essential tremor (Halliday et al., 2000). In contrast, a recent EEG–EMG study with extensive head coverage showed coherence between the contralateral sensorimotor cortex and the tremulous arm (Hellwig et al., 2001). The same authors could not, however, demonstrate EEG–EMG coherence at tremor frequency in enhanced physiological postural tremor although this is at odds with studies on physiological tremor using EMG–EMG coherence analysis in patients with mirror movement (Köster et al., 1998; Mayston et al., 2001) and with MEG–EMG coherence studies in physiological postural (force) tremor (Marsden et al., 2001a).

In summary, there have been conflicting reports of coherence between cortex and tremor and at present EEG/MEG–EMG coherence studies do not help differentiate different tremor types.

4.3. Parkinson's disease

Parkinson's disease is characterised by a reduction in the normal cortical oscillatory drive to muscles in the beta and gamma band. Instead, in untreated Parkinson's disease MEG–EMG coherence tends to be at $\leq$10 Hz. Such synchronisation of muscle discharge at rest and action tremor frequencies leads to a sub-optimal unfused pattern of muscle activation, thereby slowing the onset of voluntary actions and decreasing contraction strengths (Brown et al., 1998a). Treatment with L-Dopa or therapeutic stimulation of the subthalamic nucleus restores the normal cortical drive and enables cortical motor elements to oscillate at higher frequencies as illustrated in Fig. 4 (Salenius et al., 2002; Marsden et al., 2001b). Muscles can then be activated at high frequencies, improving bradykinesia and weakness. Motor cortical elements are also freer to form dynamic patterns of synchronised activity at frequencies above 20 Hz that might be important in higher-order aspects of motor control (Brown and Marsden, 1998).

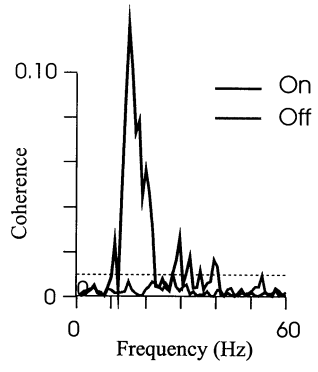

Fig. 4. Coherence spectra between EMG of forearm extensors and MEG over the contralateral Rolandic area for a patient with Parkinson's disease after withdrawal and reinstitution of levodopa treatment. Note that MEG–EMG coherence in the beta and gamma bands is restored by levodopa. The thin horizontal line indicates the 1% confidence level.

4.4. Dystonia

Patients with upper limb dystonia show abnormal coherence between extensor carpi radialis and flexor carpi radialis over 1–12 and 14–32 Hz leading to the suggestion that cortical drives may be responsible for the co-contraction of antagonistic muscles in this condition (Farmer et al., 1998). In contrast, in writer's cramp the only abnormality was a discrete peak in EMG–EMG coherence at 11–12 Hz when tremor was present.

EMG–EMG frequency analysis has been used to distinguish idiopathic dystonic torticollis from voluntary torticollis in agonistic muscles. Patients with dystonic torticollis exhibit an abnormal synchronised drive in agonistic sternocleidomastoid and splenius capitis muscles between 4 and 7 Hz (Tijssen et al., 2000). The same common 4–7 Hz drive can also be found in complex cervical dystonia (Tijssen, 2002).

4.5. Stroke

Transcranial magnetic stimulation and imaging studies have suggested that the ipsilateral motor cortex may show compensatory activity in stroke patients after recovery. Mima et al. explicitly tested this hypothesis in 6 patients with longstanding subcortical lacunar, pure motor strokes, but failed to find coherence between muscle and ipsilateral motor cortex (Mima et al., 2001b). Coherence between EMG and contralateral EEG was smaller for distal but not proximal muscles on the affected side, in line with the view that pyramidal pathways are differently organised to proximal and distal muscles (Turton and Lemon, 1999; Marsden et al., 1999).

4.6. Functional neurosurgery

In the future, a specific clinical application of frequency analysis in patients with movement disorders treated with deep brain stimulation might be to identify the optimal electrode contact for stimulation. It has recently been shown that the degree of coherence between the local potential picked up by contacts on subthalamic nucleus macroelectrodes and EEG recorded over the midline scalp is correlated with the degree of clinical improvement derived from stimulation at that contact (Marsden et al., 2001b). A comparable finding for coherence between GPi and EEG in dystonia would be particularly useful as stimulation effects may be delayed for many months in this condition.

5. Perspectives

So far, many studies of the coherence between cortical activity and EMG or between EMG signals have focussed on long records of essentially stationary physiological activity, such as voluntary tonic contraction or records of persistent tremor. However, these paradigms are relatively limited. Many pathological conditions, such as hyperekplexia and paroxysmal dystonia, lead to involuntary muscle contractions that are brief. In other pathological conditions such as chorea, involuntary movement may be persistent, but vary in an unpredictable fashion. In these more complex cases, it is not appropriate to apply the standard stationary FFT based spectral estimation techniques. For these types of signal, non-stationary models can capture much more of the true structure of the data. Non-stationary signals are those whose statistical moments, such as the mean and variance (or higher order moments such as skewness and kurtosis) change in time through the signal. One way of approaching non-stationary signals is to consider them as being composed of a number of smaller stationary states in which the statistical properties stay fairly constant. The short time Fourier transform relies on this assumption and has been used successfully in a number of studies (Baker et. al., 1997; Kilner et al., 2000). In this type of model, the window length and amount of overlap is generally determined 'by hand', so free parameters still remain in the analysis.

If one desires a model with no free parameters, there are a number of standard statistical models that can be employed to probabilistically determine these smaller stationary regimes (or states) and their respective spectral properties. This approach may prove useful in the determination of the pattern of descending drive in conditions such as chorea. For example, a hidden Markov model can be used to objectively segment signals into regimes corresponding to different states of muscle activation, with a MAR model embedded to determine the spectral properties of each regime (Cassidy and Brown, 2002). In this type of model, the periods of stationary activity detected on probabilistic grounds can then be averaged for better spectral estimates. Alternatively, one can embed a MAR model into a Kalman filter, which describes a system whose properties change continuously though the data record (Shumway and Stoffer, 1982, Cassidy and Penny, 2002). Such an approach would be more suitable where signals change gradually so that discrete state change times are hard to discern, as in event-related (de) synchronisation paradigms. This model has recently been applied to short-time coherence changes in movement related local field potentials recorded from the basal ganglia in Parkinsonian patients (Cassidy et al., 2002).

Another approach to non-stationary analysis is the wavelet approach. This approach has been widely applied in studies of oscillatory activity in the sensory system. Wavelets have the advantage that they automatically take account of the natural time–frequency resolution tradeoff that exists in spectral estimation. However, at present their use is mainly limited to one-dimensional signals, and fully two or higher dimensional wavelets are tricky to construct rigorously, a fact which currently restricts their value for coherence studies.

Advances need not be solely analytical. More work is necessary on the pharmacological underpinning of corticomuscular coherence through the systematic investigation of

drug effects and ligand-gated channelopathies, and normal ranges for EEG–EMG and EMG–EMG coherences at different frequencies clearly need to be established. At present, there is a considerable way to go before frequency analysis can provide an accessible and useful tool in the assessment of movement disorders in a routine clinical practice.

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