

THE FREQUENCY CONTENT OF COMMON SYNAPTIC INPUTS TO MOTONEURONES STUDIED DURING VOLUNTARY ISOMETRIC CONTRACTION IN MAN

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(Received 2 September 1992)

SUMMARY

1. The discharges of pairs of individual motor units were recorded from intrinsic hand muscles in man. Single motor unit recordings were obtained either when both members of the motor unit pair were within first dorsal interosseous muscle (1DI:1DI recordings) or where one motor unit was within 1DI and the other in second dorsal interosseous muscle (1DI:2DI recordings). The pairs of motor unit spike trains were cross-correlated in the time domain and the results compared to those of coherence analysis performed on the same spike train data. Central peaks were present in the cross-intensity functions, indicating the presence of common synaptic input to the motoneurone pair. Coherence analysis of these data indicated significant association between motor unit firing in the frequency ranges 1–12 and 16–32 Hz.

2. Analysis of sequential non-overlapping segments of data recorded from individual motor unit pairs, demonstrated that both the central cross-intensity peak and coherence in the frequency bands 1–12 and 16–32 Hz were consistent features throughout a long recording. In these sequential recordings, the size of the central cross-intensity peak and the maximal value of coherence in the frequency band 16–32 Hz covaried from segment to segment. Analysis of the entire population of motor unit pairs confirmed a positive relationship between the magnitude of peak coherence and the size of the central cross-intensity peak.

3. Voluntary sinusoidal co-modulation of the firing rates of pairs of individual motor units recorded from within 1DI was found to produce significant values of coherence corresponding to the frequency of the common modulation. However, firing rate co-modulation was not found to affect either the size of the central cross-intensity peak or the maximum value of coherence in the frequency band 16–32 Hz.

4. Pairs of single motor units were recorded from within 1DI and biceps brachii muscles of healthy subjects. The number and size of the central cross-intensity peaks and coherence peaks detected were compared for the two muscles. The incidence and size of central cross-intensity peaks and the incidence and magnitude of 16–32 Hz coherence peaks were both found to be greater for 1DI recordings when compared to biceps brachii recordings.

5. Single motor unit recordings were made from the intrinsic hand muscles of a patient with severe peripheral deafferentation. Time- and frequency-domain analysis of these recordings revealed cross-intensity peaks and frequency bands of coherence similar to those seen in healthy subjects.

6. Cross-correlation and coherence analysis was performed between 1DI:1DI motor unit pairs from the affected and unaffected hands of eleven stroke patients. In comparison to recordings from sixteen healthy subjects, recordings from the affected 1DI of stroke patients showed a reduction in the incidence and size of central cross-intensity peaks. The incidence and size of significant peaks in the coherence spectra were also reduced. The difference between the healthy subjects and the stroke patients was most marked for the frequency range 16–32 Hz.

7. Results using a conductance-based model of the motoneurone suggest that common motoneurone EPSPs may exert a low-pass filtering effect on the coherence detectable between pairs of motor unit spike trains. EPSPs do not contribute discrete frequency components to motor unit coherence. Coherence spectra in the frequency ranges 1–12 and 16–32 Hz are likely, therefore, to reflect periodicities in the firing of common motoneurone inputs.

8. It is concluded that significant values of coherence may be found in the frequency ranges 1–12 and 16–32 Hz. The higher frequency range of coherence may reflect periodic activity in the presynaptic inputs responsible for the production of central peaks in the cross-intensity function. The lower frequency range may reflect periodic activity in other types of input common to pairs of motoneurons. Evidence from recordings made from healthy subjects and from subjects with central and peripheral neurological lesions suggests that the presynaptic inputs responsible for central cross-intensity peaks and 16–32 Hz coherence arise from central motor rather than peripheral afferent neural pathways.

INTRODUCTION

Motor unit spike trains may be treated as stochastic point processes and as such may be analysed in both the time and the frequency domain (Sears & Stagg, 1976; Brillinger, Bryant & Segundo, 1976; Rosenberg, Amjad, Breeze, Brillinger & Halliday, 1989). Although mathematically equivalent, it can be shown that time and frequency domain analyses emphasize different aspects of a finite amount of data (Tukey, 1978; Rosenberg *et al.* 1989).

Cross-correlation methods in the time domain can yield useful information about the presence, strength and time course of the temporal association between motor unit firing, which in turn can be used to make inferences about the presynaptic organization, strength and synaptic time course of common inputs to motoneurons (Sears & Stagg, 1976; Kirkwood & Sears, 1978; Kirkwood, Sears, Stagg & Westgaard, 1982). Cross-correlation analysis of the firing of pairs of individual motor units has also been used in order to make similar inferences about the behaviour of common inputs to motoneurons in man (Datta & Stephens, 1990; Bremner, Baker & Stephens, 1991 *a, b*).

A useful extension of cross-correlation analysis of motor unit firing in man would be to perform the frequency domain equivalent, coherence analysis. This approach detects the frequency components that are common to a pair of motor unit spike

trains. This in turn may enable a determination of the frequency content of common presynaptic inputs to human motoneurons. Until now studies using coherence analysis of human electromyographic recordings have been concerned either with the detection of high-frequency oscillations in the firing of respiratory motor units (Bruce & Goldman, 1983) or with the investigation of the output consequences of motor unit synchronization such as tremor (Elble & Randall, 1976; Clarke, Matthews & Muir, 1981).

In the present study, coherence analysis has been performed between the firing of pairs of hand muscle motor units in healthy control subjects and in patients with central and peripheral neurological lesions. The same motor unit recordings have been analysed using cross-correlation analysis. Overall the results demonstrate that significant values of coherence can be detected between the firing of pairs of single motor units in man. Coherence was found to be maximal in the frequency bands 1–12 and 16–32 Hz, suggesting that the spike trains of common inputs to human hand motoneurons contain frequency components in these ranges. Studies of patients with neurological lesions suggest that in healthy individuals a large proportion of the presynaptic inputs responsible for 16–32 Hz coherence between motor unit firing arises from central motor pathways.

A preliminary account of these results has been presented to the Physiological Society (Farmer, Bremner, Halliday, Rosenberg & Stephens, 1990*b*; Venning, Engert, Evans, Farmer & Stephens, 1990; Farmer, Bremner & Stephens, 1990*c*).

METHODS

Subjects

Electromyographic (EMG) recordings were made with informed consent and Ethical Committee approval from all groups of subjects. Data from sixteen healthy subjects aged between 21 and 56 years were used as controls. Similar recordings were made from eleven patients aged 49–74 who had suffered a clinically unilateral stroke between 1 and 9 months previously. In the patients the presence of a cerebral lesion was confirmed using computerized tomography (CT scan) in all cases. The lesions were either in the internal capsule or in the cerebral peduncle contralateral to the affected hand. At the time of EMG recording marked spasticity of the affected limb was generally not a feature. Detailed accounts of the clinical and neurophysiological findings of these patients are included in data published previously (Datta, Farmer & Stephens, 1991; Farmer, Swash, Ingram & Stephens, 1993). In addition, EMG recordings were also obtained from a severely deafferented patient aged 32. This patient has been described in detail by Cole, Katifi & Sedgwick (1986) and Baker, Bremner, Cole & Stephens (1988).

Experimental procedure

The subjects were seated at a small table. The elbow was flexed at a right angle and the pronated arm supported on a cushioned frame, with the hand immobilized in a Plasticine mould. Two monopolar concentric needle electrodes (Medelec type E/NO1, core area 0.019 mm²) were inserted into the muscle(s) under study. The amplified EMG signal was heavily filtered (–3 dB at 2 and 16 kHz), and the needle positions adjusted so that the activity of an individual low-threshold motor unit could be recorded from each electrode. The recordings were stored on magnetic tape (Racal 4DS) for subsequent analysis.

In the healthy subjects, pairs of motor unit spike trains were recorded either from two needle electrodes inserted within the first dorsal interosseous muscle (1DI), denoted as 1DI:1DI recordings, or from a needle electrode in 1DI and a needle electrode in the second dorsal interosseous muscle (2DI), denoted as 1DI:2DI recordings. Recordings were made from the subject's dominant hand. In six healthy subjects, additional recordings were made from two needle

electrodes inserted into biceps brachii, denoted as Biceps:Biceps recordings. In the deafferented patient recordings were made from within the 1DI of his dominant (right) hand.

In the eleven stroke patients EMG recordings were made from within the 1DI of the affected hand at various times between 1 and 9 months after the stroke. In a subgroup of seven of these patients it was possible to obtain EMGs during a single recording session from both the stroke-affected and unaffected 1DI muscles when there were clear differences in the speed of performance of rapid finger movements between the two hands (i.e. the time taken to perform twenty rapid finger-thumb oppositions using the affected hand exceeded by 20% the time taken to perform the same task using the unaffected hand; see Farmer *et al.* (1993) for further details).

Subjects were instructed to maintain a weak isometric abduction of the index finger (1DI:1DI recordings) or weak isometric flexion of the elbow (Biceps:Biceps recordings) so that an individual motor unit recorded from each needle discharged at a steady rate of approximately 10 impulses/s. In the case of 1DI:2DI recordings subjects were required to co-abduct the index and middle fingers. Subjects were aided in these tasks by visual and auditory feedback of the unprocessed EMG signal. In addition, subjects were given feedback of the instantaneous firing rate of both motor units on a storage oscilloscope with a slowly 'rolling' time base. Detailed descriptions of the method of recording and experimental procedure are given in Bremner *et al.* (1991a).

In another series of experiments, performed on two subjects, the subject was required to voluntarily co-modulate the firing rates of both members of a motor unit pair recorded from within 1DI. In the 'modulated' condition, the subject was instructed to track a 0.3 Hz sinusoidal target with the instantaneous firing rate of each of the two motor units, displayed on the same storage oscilloscope as the target. In the control (steady) condition, the subject was instructed to maintain the instantaneous firing rates of both motor units as constant as possible. During this steady condition the target was adjusted so as to display the mean amplitude of the sine wave used in the modulated condition, thus ensuring that the mean firing rates of the recorded motor units remained similar under the two conditions. Successive 'steady' and 'modulated' recordings were repeated between six and fifteen times on the same pair of motor units.

Finally, sections of spike train data assumed to have come from independent samples, because they were recorded from different subjects on separate occasions, were analysed in both the time and frequency domains. In addition, data were analysed in the frequency domain in which no evidence of association could be detected in the time domain. These cases were obtained from cross-intensities constructed between motor unit spike trains in which the contributory motor units of each pair were recorded from a variety of different finger muscles, e.g. first dorsal interosseous and index finger flexor.

Data collection

The motor unit recordings were stored on magnetic tape. The preparation for statistical analysis of the spike trains involved converting the raw EMG signals into sequences of standard pulses by passing the EMG signal through a simple level-detection circuit (Neurolog NL 200). The time of occurrence of a motor unit spike was taken as the time of occurrence of the leading edge of the standardized pulse generated every time the leading edge of the waveform of the motor unit action potential crossed the threshold of the level-detection circuit. The reliability of this procedure was verified for each spike train by monitoring the waveform of the motor unit action potential using an oscilloscope triggered by the standard pulses. In addition, it was ensured that only one trigger pulse was generated per occurrence of the action potential and that no two trigger pulses were derived from a motor unit spike train with an interval of less than 10 ms. Finally, data were only selected for analysis in which the motor unit waveforms remained invariant throughout the procedure used for generating the standardized pulses.

The times of occurrence of the motor unit spikes were assumed to represent realizations of stochastic point processes (Rosenberg *et al.* 1989). Further preparation for the analysis of the discriminated spike trains consisted of creating data files containing the ordered times of occurrence of the spikes from the two trains.

Statistical procedures

The coupling between two spike trains was described by the sample cross-intensity function and the sample coherence.

An unbiased estimate of the cross-intensity function may be obtained from the cross-correlation histogram using the procedure described by Brillinger (1976). The cross-intensity function is proportional to the probability of a motor unit from one spike train occurring in a particular time interval relative to the occurrence of a reference spike from the other train at time zero. To construct the cross-correlation histogram one of the two recorded spike trains was arbitrarily taken as the reference train and the times to spikes in the other train measured up to 100 ms either side of the reference spike. The intervals between spikes from the different trains are referred to as lag times (u); these may take positive or negative values relative to the occurrence of the reference spike. The number of counts in the cross-correlation histogram at lag $u = 0$ gives the number of events in the response spike train that occur synchronously with a reference event. Approximate 95% confidence intervals for the square root of the cross-intensity and its asymptotic (mean) value are given by $\sqrt{P_1 \pm \{\beta N_2(T)\}^{-1}}$ and $\sqrt{P_1}$, respectively (Brillinger, 1976), where $N_2(T)$ is the number of spikes in the reference train, P_1 the mean rate of the response train, and β the bin width of the cross-correlograms (1 ms in the case of the present study).

The criteria for assessing the significance of a given cross-intensity peak were set at three standard deviations of a cumulative sum constructed from the cross-correlation histogram (cf. Davey, Ellaway & Stein, 1986). The size of the peak in the cross-intensity centred about lag $u = 0$ was expressed as the number of counts in the peak exceeding the asymptotic value of the cross-intensity function, divided by the mean cross-intensity bin count, normalized to a bin width of 1 ms. This index of the strength of motor unit synchronization is denoted E/M (see Harrison, Ironton & Stephens, 1991). The duration of the peak in the cross-intensity function was defined by the time interval between inflections of the cumulative sum, constructed from the histogram.

In general, a minimum of 1000 reference spikes were used to construct the cross-intensity estimates and associated cumulative sums; however, where long sections of data were analysed, the data were broken down into segments containing 500 reference spikes.

The coherence may be defined as the correlation between the frequency components of two spike trains (Rosenberg *et al.* 1989). Calculation of the coherence provides a bounded measure of the association between the two processes. The coherence at any given frequency necessarily takes on values between zero and one, with zero occurring in the case of linear independence of the two processes. The coherence between two spike trains, N_1 and N_2 , is denoted by $|R_{12}(\lambda)|^2$ and is written as

$$|R_{12}(\lambda)|^2 = \frac{|f_{12}(\lambda)|^2}{f_{11}(\lambda)f_{22}(\lambda)}, \tag{1}$$

where λ is the frequency in Hertz, $f_{12}(\lambda)$ represents the cross-spectrum and $f_{11}(\lambda)$ and $f_{22}(\lambda)$ represent the autospectra of the two-component processes. An estimate of the coherence is obtained by inserting the estimated spectra into expression (1). The procedure used to obtain the spectral estimates involved dividing the sample record of duration R into L disjoint sections each of duration T , where $R = LT$. If the finite Fourier transform of the l^{th} section from process N_1 is denoted by $d_1^T(\lambda, l)$, with a similar expression for process N_2 , then an estimate of the cross-spectrum between these two processes is

$$f_{12}(\lambda) = \frac{1}{2\pi LT} \sum_{l=1}^L d_1^T(\lambda, l) \overline{d_2^T(\lambda, l)}, \tag{2}$$

where the overbar indicates the complex conjugate. This procedure is equivalent to applying a data window to the sample record (Bloomfield, 1976) and has the advantage that it leads to a particularly simple expression for the confidence interval for the coherence (Brillinger, 1975). In addition, the final spectral estimate was obtained by ‘Hanning’ the result of expression (2) to further suppress the rippling introduced by the sampling process, where Hanning refers to a running smoothing procedure using the weights 1/4, 1/2, 1/4.

If the above procedure is used to estimate all of the spectra using eqn (1), then an approximate confidence interval for the coherence, under the assumption that the two spike trains are independent, may be set as $Z = 1 - (1 - \alpha)^{1/(L-1)}$, where α is the desired level of confidence and L the number of disjoint sections obtained from the sample record. The hypothesis of independence at each frequency λ is rejected if the estimated coherence at that frequency (λ) exceeds the value Z . In our examples a 95% confidence limit was used (shown by a dashed line in the figures). The

frequency resolution for the coherence spectra was set at 1 Hz; at this frequency resolution the choice of a 95% confidence level means that on average 5 of the 100 data points between 1 and 100 Hz will exceed the confidence level due to chance interactions alone.

Where it was necessary to compare coherence spectra obtained from the same motor unit pair during different task conditions, the statistical test given in Rosenberg *et al.* (1989) was used to test the equivalence of the coherences at each frequency λ . Under the hypothesis that $|R_{AB}(\lambda)| = |R_{CD}(\lambda)|$, for all values of λ , $\{\tanh^{-1}|R_{CD}(\lambda)| - \tanh^{-1}|R_{AB}(\lambda)|\}$ will be, for large values of T , approximately normally distributed with a mean of zero and variance of $1/L$, where L is the number of disjoint sections of length T averaged in order to estimate the spectra of $|R_{AB}(\lambda)|$ and $|R_{CD}(\lambda)|$.

The coherence spectra were calculated from the same data files as used to calculate the cross-intensity estimates using a suite of programs on a Glasgow.vme mainframe computer written by D. M. Halliday and J. R. Rosenberg. These programs were accessed and run directly from the laboratory via the JANET network.

RESULTS

Coherence spectra in healthy subjects

Figure 1A shows the estimated cross-intensity function constructed between two motor unit spike trains recorded from within 1DI. The cross-intensity is dominated by a narrow central peak, the time course of which is consistent with that of short-term motor unit synchronization as described by Sears & Stagg (1976, see Discussion). In addition, the cross-intensity shows smaller and more dispersed secondary peaks, displaced 39 ms to the left and 43 ms to the right of time zero. Figure 1B shows the coherence computed between the same two spike trains used to construct the cross-intensity shown in Fig. 1A. It can be seen that there are two frequency bands, 1–7 and 18–29 Hz, where the coherence is significant ($\alpha = 0.95$).

The generality of this finding was investigated by performing coherence analysis on thirty-seven motor unit pairs from within 1DI (twelve subjects). In all cases, time domain analysis produced cross-intensity functions with narrow central peaks. In the frequency domain, analysis revealed a high incidence of coherence between the spike trains in the ranges 1–12 and 16–32 Hz. Significant values of coherence in the range 1–12 Hz were detected between the firing of 36/37 1DI:1DI motor pairs; in the range 16–32 Hz significant values of coherence were detected between the firing of 33/37 1DI:1DI motor unit pairs. These results are summarized in Fig. 1C, which shows the percentage of the thirty-seven motor unit pairs studied that showed significant values of coherence at each frequency between 1 and 100 Hz. It can be seen that there are two frequency ranges which show a high incidence of significant coherence (1–12 and 16–32 Hz). The most frequently occurring value of coherence in the lower frequency band was 5 Hz (77% of motor unit pairs). The most frequently occurring value of coherence in the higher frequency band was 22 Hz (66% of motor unit pairs). It can also be seen from Fig. 1C that for frequencies in excess of 60 Hz the percentage of cases showing significant values of coherence approaches the 5% level expected due to chance interactions alone.

Cross-correlated activity may also be detected between the firing of pairs of motor units recorded from different muscles (Bremner *et al.* 1991a; Datta *et al.* 1991). Cross-intensity and coherence analyses were performed between the firing of pairs of motor units where one member of the motor unit pair was in the first dorsal interosseous muscle (1DI) and the other in the second dorsal interosseous muscle (2DI). Figure 2A shows, for the same subject as in Fig. 1A, a cross-intensity function constructed

between the spike train of a motor unit in 1DI and that of a motor unit in 2DI. The cross-intensity contains a narrow central peak. Figure 2*B* shows the coherence estimated from the data used to construct the cross-intensity in Fig. 2*A*. Significant coherence can be observed principally in the frequency bands 1–7 and 18–29 Hz. In

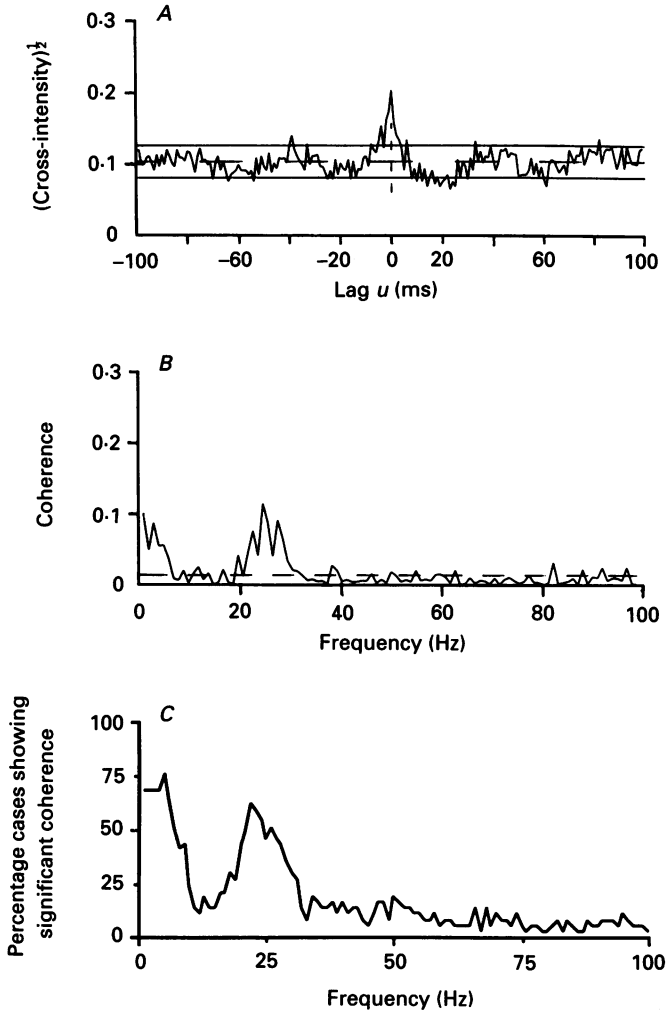


Fig. 1. *A*, cross-intensity (1945 reference spikes, bin width 1 ms) constructed between the firing of two motor units recorded from within 1DI during a steady isometric contraction. The peak, centred around $u = 0$, indicates short-term synchronization between the firing of the motor unit pair. The dashed horizontal and continuous lines in this and other figures denote the mean level of the cross-intensity and an approximate 95% confidence interval, respectively, under the assumption that the two processes are independent. *B*, coherence analysis (frequency resolution 1 Hz) performed on the data used in *A*. Significant coherence peaks are present in the frequency bands 1–7 and 18–29 Hz. The dashed horizontal line in this and other figures denotes the upper level of an approximate 95% confidence level for the coherence under the assumption that the two processes are independent (see Methods). *C*, histogram of the percentage of the thirty-seven 1DI:1DI motor unit pairs that exhibited significant coherence peaks at each frequency in the range 1–100 Hz.

this example, coherence is detectable in similar ranges to those observed between the firing of two motor units recorded from within 1DI (compare to Fig. 1*B* and *C*). In Fig. 2*C* the incidence of significant values of coherence detected between twenty-six 1DI:2DI motor unit pairs (eight subjects) is shown. Again there is a high incidence

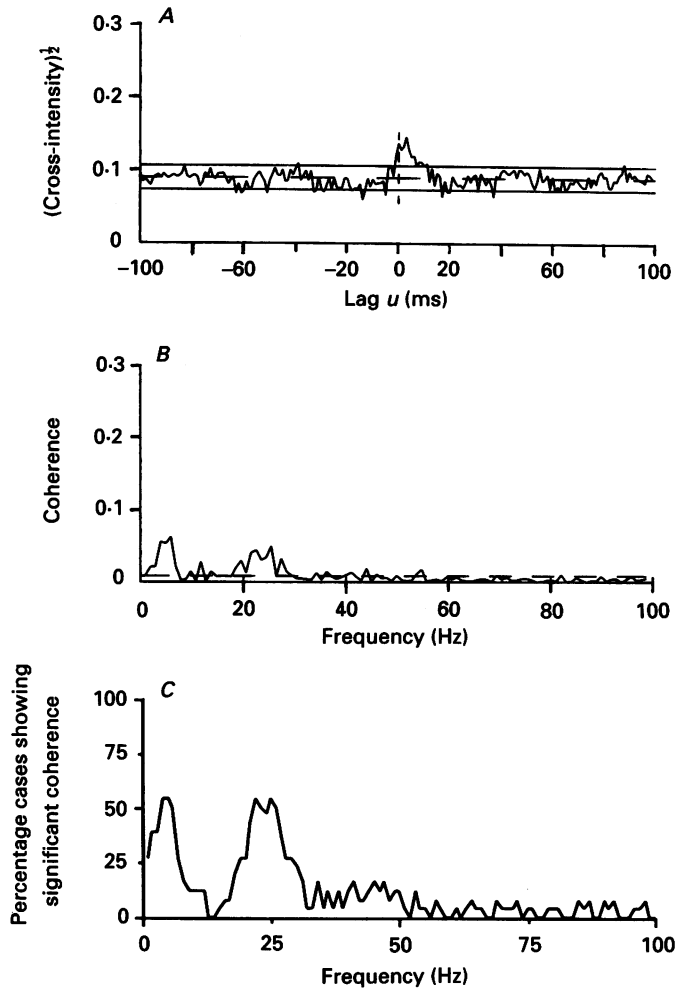


Fig. 2. *A*, cross-intensity (3903 reference spikes, bin width 1 ms) constructed between the firing of a motor unit in 1DI (reference) and a motor unit in 2DI (response). Motor units recruited during steady isometric co-contraction of 1DI and 2DI (same subject as in Fig. 1). The cross-intensity contains a narrow central peak. *B*, coherence analysis (frequency resolution 1 Hz) performed on the data used in *A*. Significant coherence peaks are present in the frequency bands 1–7 and 18–29 Hz. *C*, histogram of the percentage of the twenty-six 1DI:2DI motor unit pairs that exhibited significant coherence peaks at each frequency in the range 1–100 Hz.

of coherence between the two spike trains in the ranges 1–12 and 16–32 Hz. In total, 20/26 motor unit pairs showed significant coherence in the range 1–12 Hz; 22/26 motor unit pairs showed significant coherence in the range 16–32 Hz. The most

frequently occurring values of coherence in the lower frequency band were 4 and 5 Hz (54% of motor unit pairs). In the higher frequency band the most frequently occurring values of coherence were 22 and 25 Hz (54% of motor unit pairs). The percentage of 1DI:2DI motor unit pairs showing significant values of coherence in

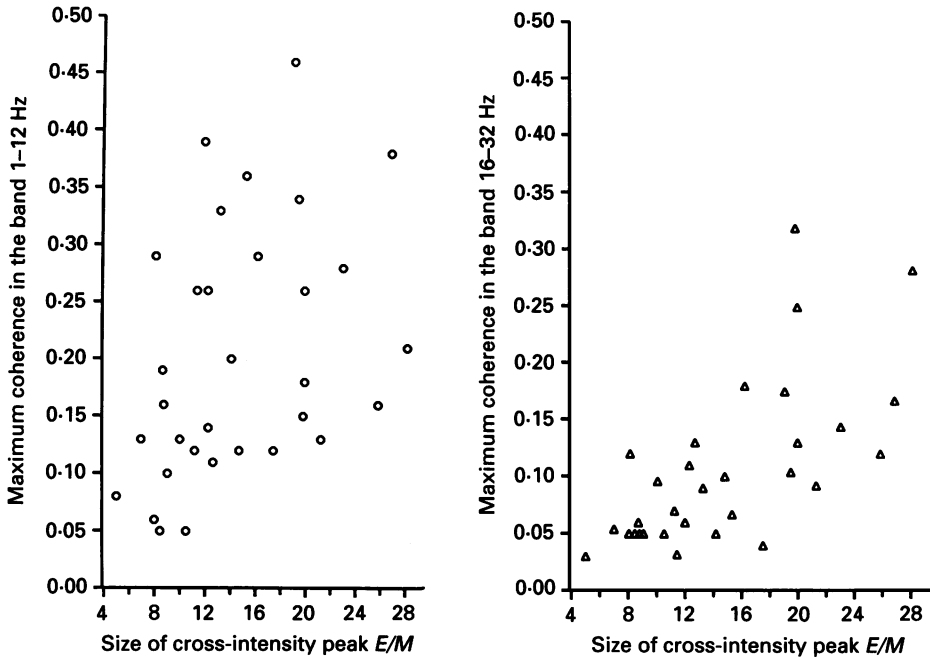


Fig. 3. Scatter diagrams illustrating the relationship between the maximum value of coherence and the size (E/M) of the central cross-intensity peak detected for the same 1DI:1DI motor unit pair. Each point represents data from a single motor unit pair. The relationship is shown for coherence in the two frequency bands, 1-12 Hz (A) and 16-32 Hz (B).

excess of 50 Hz approaches the 5% level expected due to chance interactions alone. In all cases time domain analysis revealed a central peak in the cross-intensity function.

Time and frequency domain analyses were performed on sections of independent spike train data. Both the cross-intensity function and the coherence spectra corresponded to those expected for two independent processes in that they showed only occasional crossings of the 95% confidence limits. In addition, frequency domain analysis was performed on data in which no evidence of significant association could be found in the time domain: for example, between a motor unit recorded from 1DI and one recorded from the index finger portion of flexor digitorum superficialis in the same subject. In 25% of these cases ($n = 28$ motor unit pairs), the coherence spectra showed a weak association between the spike trains at frequencies of 3 Hz and below. However, for values of coherence in excess of 3 Hz no more than chance levels of coherence were detected (i.e. approximately 5% of motor unit pairs showing coherence at any particular frequency).

We further investigated the relationship between the time domain measure of association and the coherence present in the two frequency bands by constructing scatter diagrams relating the maximal coherence in the frequency ranges 1–12 Hz (Fig. 3A) and 16–32 Hz (Fig. 3B) to the size of the central cross-intensity peak (E/M) detected when the same data were analysed in the time domain. Both the 1–12 and 16–32 Hz frequency ranges show a positive relationship with the time domain index; the relationship was closer for the higher 16–32 Hz frequency band ($r = 0.41$, $P < 0.02$, $n = 36$ and $r = 0.67$, $P < 0.001$, $n = 33$; for the 1–12 and 16–32 Hz bands of coherence, respectively). A similar relationship between the size of the central cross-intensity peak and the magnitude of maximum coherence was found for data from the 1DI:2DI motor unit pairs.

Cross-correlation analysis has shown that the mean size of the central cross-correlogram peak detected between the firing of motor unit pairs within 1DI (1DI:1DI) is approximately twice as great as that found between 1DI:2DI motor unit pairs (Bremner *et al.* 1991*b*). A similar result has been obtained in the present study. The mean size (E/M) of the central cross-intensity peak was 13.7 ± 6.4 (mean \pm s.d.) for the thirty-seven 1DI:1DI motor unit pairs and 8.6 ± 2.6 for the twenty-six 1DI:2DI motor unit pairs. This difference was significant (unpaired t test, $P < 0.01$). In the frequency domain, the mean magnitude of the maximum coherence in the range 16–32 Hz detected between 1DI:1DI motor unit pairs was approximately twice that observed between 1DI:2DI motor unit pairs (0.11 ± 0.07 , $n = 33$ and 0.06 ± 0.02 , $n = 22$, respectively). This difference was also significant (unpaired t test, $P < 0.01$). The mean magnitude of maximal coherence in the frequency range 1–12 Hz detected between 1DI:1DI motor unit pairs was three times that observed between 1DI:2DI motor unit pairs (0.21 ± 0.11 , $n = 36$ and 0.07 ± 0.03 , $n = 20$, respectively). Again this difference was significant (unpaired t test, $P < 0.01$).

Time and frequency domain analysis of non-overlapping segments of data recorded from the same motor unit pair were compared. Figure 4 shows the results of cross-intensity and coherence analysis performed on non-overlapping 57 s segments of spike train data recorded from a single 1DI:1DI motor unit pair. Figure 4A and B shows the results of cross-intensity and coherence analysis performed on a segment of data in a time window 116–173 s from the start of the recording. The cross-intensity function of this data segment contains a central peak ($E/M = 20.0$); in the frequency domain, significant coherence is observed in the ranges 1–13 and 20–32 Hz (peak magnitudes: 0.27 and 0.26, respectively). Figure 4C and D shows the results of time and frequency domain analysis for a segment of data in a time window 290–347 s from the start of the recording. In this segment, the central cross-intensity peak (Fig. 4C) is smaller than that of Fig. 4A ($E/M = 12.2$); in the frequency domain, significant coherence is observed in the ranges 1–3 and 20–29 Hz (Fig. 4D). The maximum value of coherence in the lower range is similar to that of Fig. 4B (peak magnitude: 0.25); however, the magnitude of coherence in the range 20–29 Hz is considerably smaller (peak magnitude: 0.11).

Similar results were obtained for segmented data obtained from a further two 1DI:1DI motor unit pairs and three 1DI:2DI motor unit pairs, indicating that significant coherence remains constrained to the frequency ranges 1–12 and 16–32 Hz

during successive recording epochs from any given motor unit pair. It has been demonstrated previously that the strength of cross-correlated activity between the motor unit discharges shows variability with time (Bremner *et al.* 1991*b*). The results of the present study suggest that the variability in size of the central cross-intensity

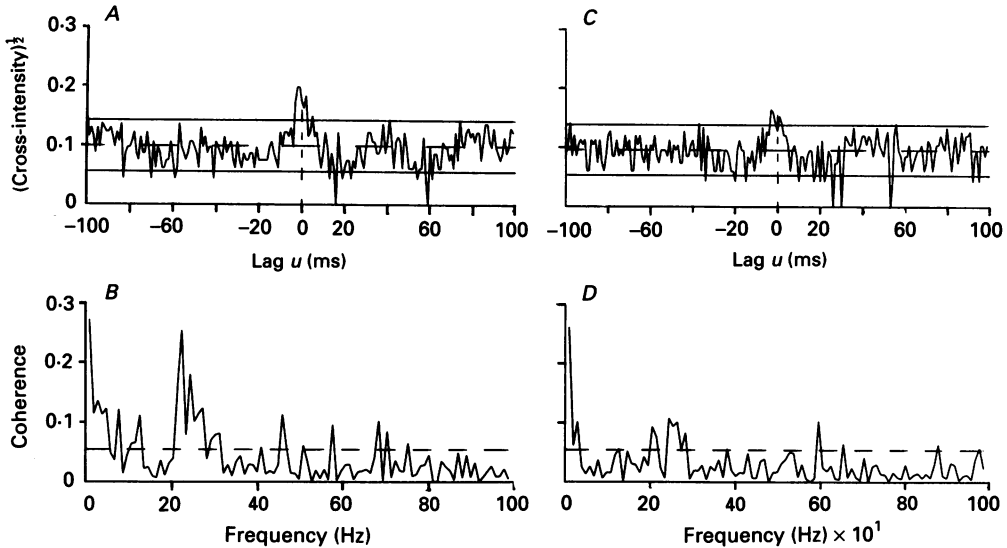


Fig. 4. Comparison of the cross-intensity and coherence estimated from two different 57 s segments of a continuous recording from a pair of 1DI motor units. Cross-intensity (*A*) and coherence (*B*) between motor unit discharges in a time window 116–173 s from the start of the recording, containing 549 reference spikes. Cross-intensity (*C*) and coherence (*D*) between the discharges of the same pair of motor units in a time window 290–347 s from the start of the recording, containing 572 reference spikes. The size of the central cross-intensity and the magnitude of maximal coherence in the range 16–32 Hz were both smaller for the 290–347 s time window when compared to the 116–173 s time window. Bin width *A* and *C*: 1 ms; frequency resolution *B* and *D*: 1 Hz.

peak is reflected in a similar variability in the magnitude of coherence detected in the frequency range 16–32 Hz. There was no relationship between the size of the central cross-correlogram peak and the magnitude of coherence in the 1–12 Hz range.

The cross-intensity function reflects the auto-intensity functions of common inputs as well as the auto-intensity functions of the output spike trains (Moore, Segundo, Perkel & Levitan, 1970). Cross-intensity peaks displaced to either side of the central peak, with a lag shorter than the mean interspike interval of either the reference or response motor unit spike train, have been observed in both this (see Fig. 1*A*) and a previous study (Bremner *et al.* 1991*a*). In the present study secondary peaks were present in approximately 50% of cases. In the study of Bremner *et al.* (1991*a*) secondary peaks were present in only 7% of the cross-intensities. It should be noted that in the study of Bremner *et al.* (1991*a*), the majority of cross-correlations were between motor units recorded from different muscles. In such recordings the size of central cross-intensity peaks is much smaller than for within-1DI recordings;

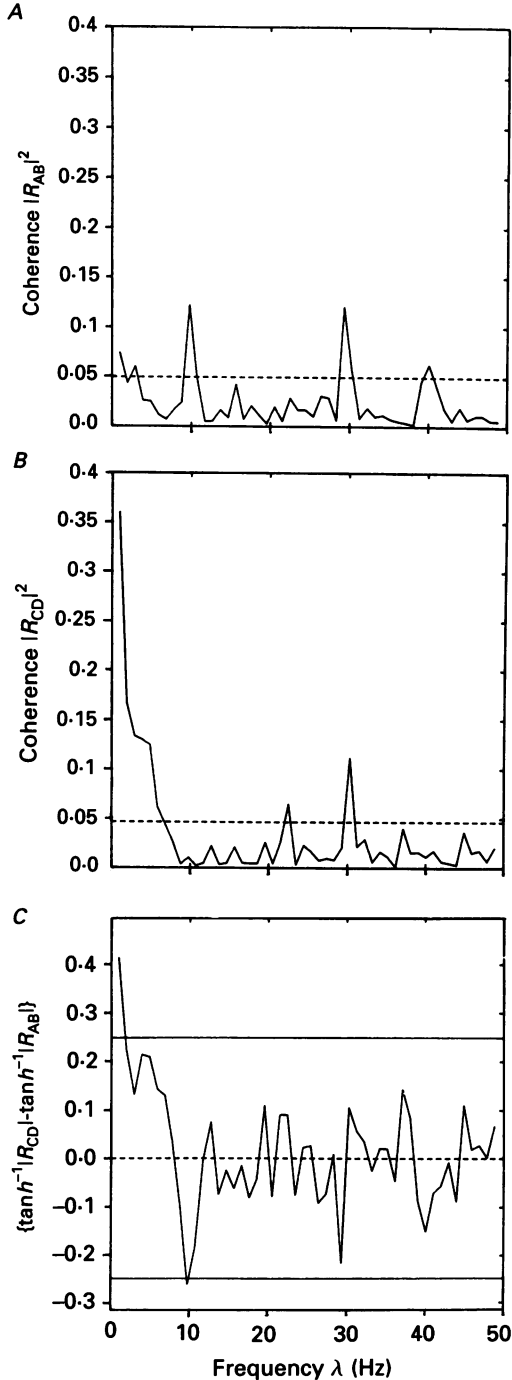


Fig. 5. *A*, coherence between two motor unit spike trains recorded from within 1DI during voluntary abduction of the index finger (490 reference spikes). The subject was instructed to maintain the motor unit firing rates as steady as possible. *B*, coherence between the same pair of motor unit spike trains when the subject was instructed to voluntarily co-modulate the discharge rates of both motor units by matching their instantaneous firing frequencies to a 0.3 Hz target sinusoid (471 reference spikes). *C*, graph of the difference of the $\tan h^{-1}$ of the moduli of the coherences of *A* and *B*. The continuous lines define the 95 %

the size and incidence of secondary cross-intensity peaks is also much less. Secondary peaks are likely to result from a mapping of the auto-intensity function of the common inputs onto the cross-intensity functions. It would be expected that cross-intensities showing prominent secondary peaks should also display prominent coherence at a frequency corresponding to the reciprocal of the secondary peak displacement from the central peak. This was confirmed by plotting the reciprocal of the temporal displacement of the secondary cross-intensity peaks from the central peak against the frequency at which maximal coherence was detected in the higher frequency range. A strong linear relationship was found between the frequency of maximal coherence and the reciprocal of the temporal displacement of the secondary peaks both for positive and negative lags ($r = 0.80$, $P < 0.05$, $n = 35$ and $r = 0.72$, $P < 0.05$, $n = 34$, respectively). This relationship suggests that these secondary features in the cross-intensity may reflect periodic frequency components common to the motoneurone pair.

Significant values of coherence in the lower frequency range (1–12 Hz) may either reflect low-frequency modulation of the 16–32 Hz 'carrier frequency' of branched presynaptic inputs or the frequency content of other common branched or non-branched presynaptic inputs. In an attempt to distinguish the synaptic mechanisms involved in generating coherence in the low- and high-frequency bands, common modulation of the firing rates of five 1DI:1DI motor unit pairs (two subjects) was performed.

Figure 5A shows coherence spectra constructed between the firing of a pair of 1DI:1DI motor units during voluntary abduction of the index finger. In this recording, the subject was instructed to maintain the motor unit firing rates as steady as possible. Figure 5B shows coherence spectra for the same motor units as used in Fig. 5A; however, in this case, the subject was instructed to co-modulate the firing of the two motor units by using displays of their instantaneous firing rates to track a target 0.3 Hz sinusoid. The coherence peak present at 29 Hz in the steady condition (Fig. 5A) is also present in the modulated condition (Fig. 5B). However, in the lower frequency range of 1–6 Hz, the two conditions show a marked change in the magnitude of the coherence. It can be seen from Fig. 5A that there are no significant values of coherence below 8 Hz. In contrast, Fig. 5B shows a marked increase in coherence in the range 1–6 Hz. When the data in Fig. 5B were analysed at a frequency resolution of 1/4 Hz it was apparent that the majority of the increase in coherence in the low-frequency range occurred at 1/4–1/2 Hz, the frequency of voluntary common firing rate modulation. Figure 5C shows a coherence difference plot in which the two coherence spectra shown in Fig. 5A and B have been compared by plotting the difference between the moduli of the \tanh^{-1} of the coherencies (see Methods and Rosenberg *et al.* 1989). At low frequencies (≈ 1 Hz) the coherence difference between the steady and the modulated conditions is significant (i.e. the 95% confidence limits shown by the continuous line have been exceeded). In this figure there is a significant difference between the two conditions at 10 Hz. However,

confidence interval for the hypothesis that the two moduli are equal at any given frequency. Common modulation induces a low-frequency component (≈ 1 Hz), which differs significantly between the two conditions. The higher frequencies of coherence are not affected by voluntary common firing rate modulation.

repeated analysis of different segments of 'modulated' and 'steady' data from this motor unit pair and studies of different motor unit pairs indicated that the only consistent differences between the two conditions were at the frequency of modulation. Time domain analysis of these data confirmed the previous finding that common rate modulation of the firing of pairs of motor units does not alter the size or duration of the cross-intensity peak detected between their discharges (Bremner *et al.* 1991*a*). Similar results to those illustrated were found when a further ten recordings were made for this pair of motor units (five steady, five modulated). Moreover, the same findings were obtained from all five motor unit pairs studied in the two subjects.

In six of the healthy subjects, motor unit recordings were also obtained from within biceps (twenty motor unit pairs). In the recordings from biceps, there were five instances (25%) in which cross-correlation analysis failed to reveal a central peak. All recordings from within 1DI in these subjects contained central peaks in the cross-intensity ($n = 19$ motor unit pairs). The mean size (E/M) of the nineteen cross-intensity peaks detected for within-1DI motor unit pairs was considerably greater than that of the fifteen significant peaks detected for within-biceps motor unit pairs (mean \pm s.d.: 14.6 ± 8.9 and 4.9 ± 2.5 , respectively), recorded from the same six subjects. The difference between these means was significant (unpaired t test, $P < 0.001$).

Figure 6*A* and *D* shows cross-intensities from 1DI and biceps in the same subject. Figure 6*B* and *E* shows the results of coherence analysis performed on same spike train data used to construct the cross-intensities. This figure illustrates the previous assertion that, when present, the central cross-intensity peaks detected in biceps recordings were invariably smaller than those found in recordings from 1DI. The corresponding coherence spectra for both sets of data showed significant peaks in essentially two frequency ranges: 1–8 and 16–32 Hz. However, the number and magnitude of the significant coherence peaks detected for the 1DI:1DI motor unit pair were greater than those observed for the Biceps:Biceps motor unit pair. The difference between these two recordings was most apparent for the higher frequency band (16–32 Hz).

The incidence of significant coherence peaks detected at each frequency between 1 and 100 Hz is summarized in Fig. 6*C* and *F* for nineteen 1DI:1DI motor unit pairs and twenty Biceps:Biceps motor unit pairs, respectively. In comparison to recordings from 1DI, there was a lower incidence of significant coherence peaks between biceps motor unit discharges at all frequencies between 1 and 60 Hz. The most striking difference between the two sets of data was the reduction in the number of motor unit pairs displaying significant coherence peaks in the higher frequency band (16–32 Hz) in the biceps recordings.

The size of coherence was quantified by recording the magnitude of the peak coherence in each of the two major frequency ranges of interest i.e. 1–12 and 16–32 Hz. In the case of the 1DI:1DI recordings, the mean \pm s.d. peak coherence in the frequency range 1–12 Hz was 0.24 ± 0.11 ; that for the frequency range 16–32 Hz was 0.06 ± 0.04 ($n = 19$). The corresponding values for biceps recordings were 0.22 ± 0.11 and 0.03 ± 0.03 , for the lower and higher frequency ranges respectively ($n = 20$). In the lower frequency range (1–12 Hz), the mean magnitude of peak

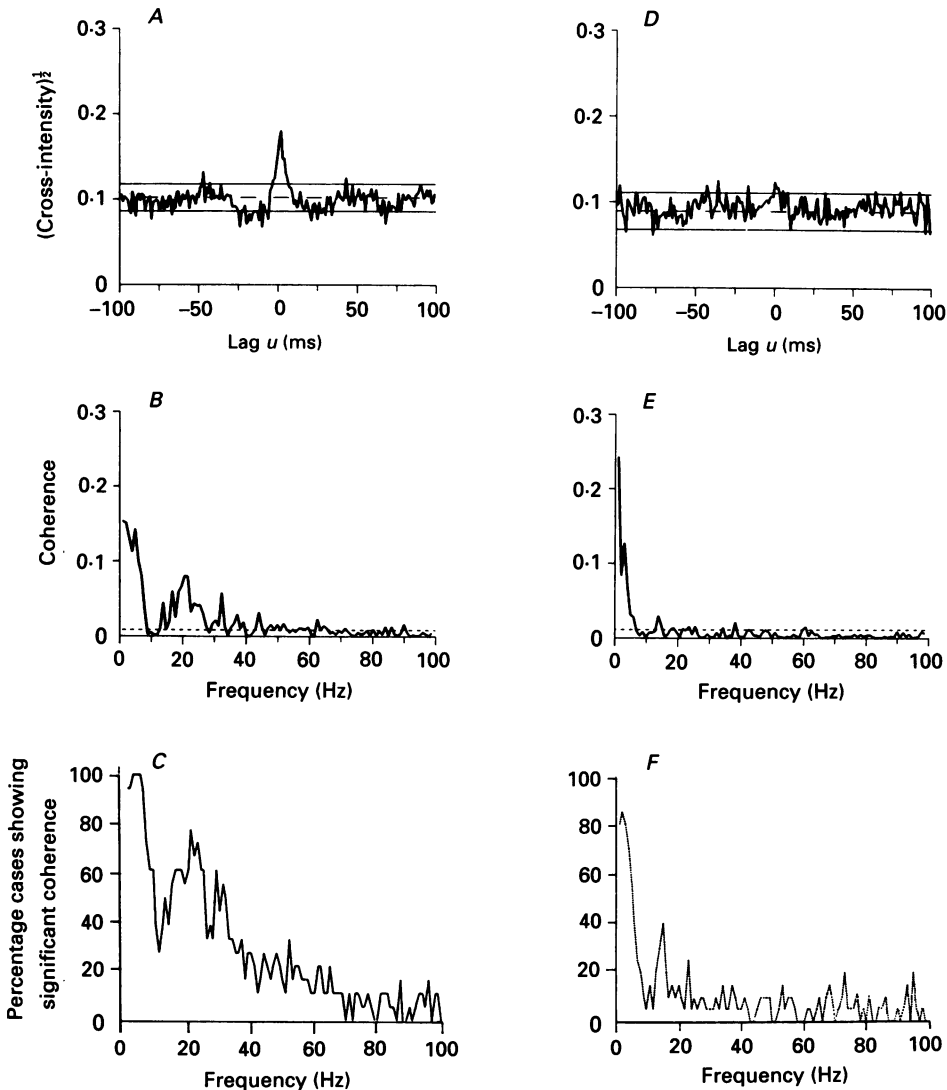


Fig. 6. *A*, cross-intensity constructed between the discharges of two motor units recorded from within 1DI (4000 reference spikes). *B*, coherence spectra for the data used to construct the cross-intensity in *A*. *D*, cross-intensity constructed between the discharges of two motor units recorded from within biceps for the same subject as in *A* (2170 reference spikes). *E*, coherence spectra for the data used to construct the cross-intensity in *D*. When compared to the biceps motor unit pair, the size of the central cross-intensity peak and the number and magnitude of significant peaks in the coherence spectra detected for the 1DI motor unit are both greater. Bin width *A* and *D*: 1 ms; frequency resolution *B* and *E*: 1 Hz. The percentages of 1DI:1DI ($n = 19$) and Biceps:Biceps ($n = 20$) motor unit pairs that demonstrated significant coherence at each frequency between 1 and 100 Hz are shown in *C* and *F*, respectively.

coherence did not differ significantly between biceps and 1DI recordings (unpaired t test, $P > 0.1$). However, the mean magnitude of peak coherence in the higher frequency band (16–32 Hz) was found to be larger in 1DI compared to biceps recordings (unpaired t test, $P < 0.01$).

In all cases, the motor unit firing rates were well controlled by the subjects. The mean \pm s.d. firing rates of the reference and response motor units were 9.4 ± 1.3 and 9.6 ± 1.2 Hz for 1DI ($n = 19$); those of the reference and response motor units recorded from biceps were 9.6 ± 1.2 and 10.2 ± 1.3 Hz ($n = 20$). These values did not differ significantly between the two sets of recordings (unpaired t test, $P > 0.1$).

Coherence spectra in the deafferented patient

Previous neurophysiological investigation of this patient has revealed that there is an extensive loss of the large, myelinated peripheral afferent fibres below the neck (Cole *et al.* 1986). This was confirmed by demonstrating an absent sensory volley recorded from the median nerve during electrical stimulation of a digital nerve at 3 stimuli/s. It was also demonstrated that, in contrast to healthy subjects, there are no short- or long-latency muscle responses in 1DI to either percussion of its muscle belly or following electrical stimulation of the digital nerves of the index finger.

Figure 7A shows a peak in the cross-intensity constructed between the firing of two motor units recorded from within the patient's 1DI during a steady voluntary abduction of the index finger. Figure 7B shows the corresponding coherence spectra for the data used to construct the cross-intensity in A; significant coherence peaks are present in the frequency ranges 1–9 and 20–32 Hz. The maximum sizes of the observed peaks were 0.31 at 1 Hz and 0.04 at 30 Hz. For a further two 1DI:1DI motor unit pairs recorded from this patient, significant coherence peaks of similar size to those illustrated were detected in the typical low- (1–12 Hz) and high- (16–32 Hz) frequency ranges. The mean size of peak coherence in the low-frequency range was 0.18; in the high-frequency range it was 0.04 ($n = 3$). The corresponding values obtained from sixteen healthy subjects were 0.206 ± 0.1 and 0.084 ± 0.07 respectively ($n = 49$). The mean firing rate of the three motor unit pairs recorded in this patient was 10.0 Hz for the reference motor units and 11.0 Hz for the response motor units; these firing rates were similar to those of normal subjects. These results suggest that large-fibre peripheral afferent feedback is not necessary for generation of central cross-intensity peaks or coherence in either the 1–12 or 16–32 Hz frequency ranges.

Coherence spectra in stroke patients

Motor unit spike train data recorded from within the affected 1DI of eleven stroke patients were analysed in the time and frequency domains. The studies of Datta *et al.* (1991) and Farmer *et al.* (1993) have described a variety of changes in the strength and time course of motor unit synchronization that follow central nervous lesions in man. In the present study these data have been analysed in the frequency domain in order to illuminate the findings obtained from healthy subjects; therefore data in which broad-peak synchronization was present have been excluded, as it has been argued that this phenomenon largely reflects processes that differ from those

involved in the production of short-term synchronization in healthy subjects (Farmer *et al.* 1993). In addition, no attempt has been made to formally study the relation between coherence and the changes in the time course of central cross-intensity peaks described by Farmer *et al.* (1993) that may be associated with CNS

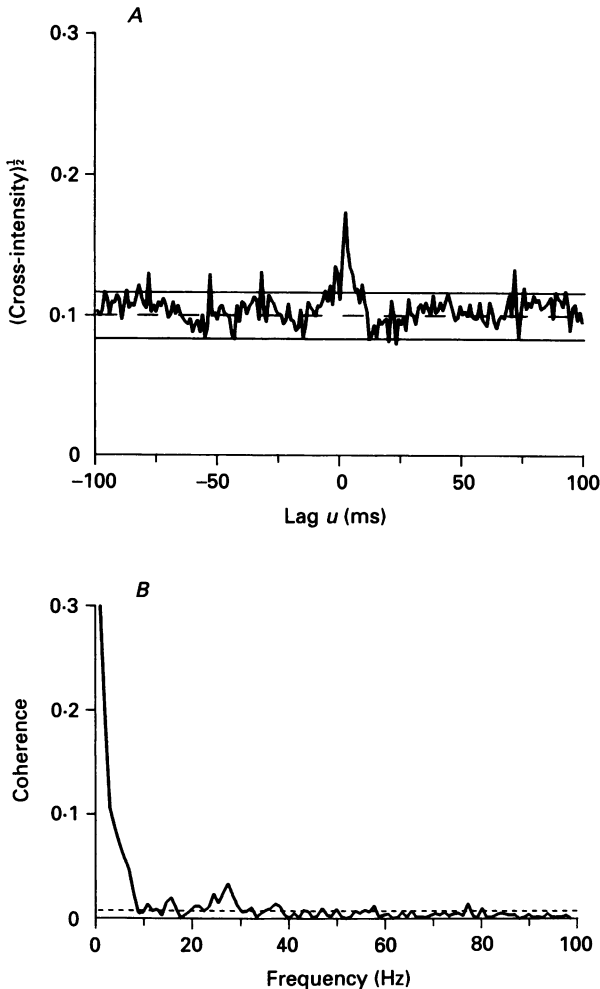


Fig. 7. *A*, cross-intensity (bin width 1 ms; 3642 reference spikes) constructed between the discharges of two motor units recorded from within 1DI in the deafferented patient. *B*, coherence spectra (frequency resolution 1 Hz) for the data used to construct the cross-intensity in *A*. The cross-intensity (*A*) contains a central peak and significant coherence is present in both low- and high-frequency ranges (*B*).

lesions. Neither have we studied any possible relations between coherence and the timing, site or clinical effects of the CNS lesions.

Central peaks were absent in 33/91 (36%) of the cross-intensities obtained from the affected hand of the eleven patients. Examples of a cross-intensity from a normal subject and one from a stroke patient in which the central peak is absent are shown

in Fig. 8A and D. Figure 8B and E shows the corresponding coherence spectra. In the stroke patient significant coherence was present at low frequencies (1–3 Hz); however, significant peaks were altogether absent from the high- (16–32 Hz) frequency band in which coherence between motor unit discharges can usually be detected in recordings from healthy subjects.

The percentage of motor unit pairs ($n = 91$) recorded from the affected 1DI of the stroke patients that displayed significant coherence peaks at each frequency between 1 and 100 Hz is shown Fig. 8F. For comparison, a similar graph (Fig. 8C) was constructed from recordings obtained from sixteen healthy subjects ($n = 49$ motor unit pairs). At low frequencies (1–3 Hz), the incidence of significant coherence peaks was similar for the two groups; however, at frequencies in excess of 4 Hz the stroke patients showed a much lower incidence of coherence. The incidence of coherence above 56 Hz was similar in the two groups. The most striking difference between the two groups was the complete loss of the high-frequency (16–32 Hz) band of coherence in the stroke patients.

In the healthy subjects, the mean \pm s.d. peak coherence in the frequency range 1–12 Hz was 0.206 ± 0.1 ; for the frequency range 16–32 Hz the mean peak coherence was 0.084 ± 0.07 ($n = 49$). In the stroke patients, the mean peak coherence in the frequency range 1–12 Hz was 0.153 ± 0.12 ; for the frequency range 16–32 Hz the mean value was 0.029 ± 0.032 ($n = 91$). The mean values of peak coherence in both low- and high-frequency ranges differed significantly between the two groups (unpaired t test, $P < 0.02$ and $P < 0.0001$, respectively). The mean firing rates of reference and response motor units recorded from the affected 1DI in the stroke patients were 9.2 ± 2.4 and 9.6 ± 2.4 ($n = 91$) respectively. The mean firing rates of reference and response motor units recorded from the control subjects were 9.3 ± 1.7 and 9.3 ± 1.6 ($n = 49$) respectively; these did not differ significantly from those of the stroke patients (unpaired t test, $P > 0.7$). The mean size (E/M) of cross-intensity peaks detected between motor unit discharges from the affected 1DI of the stroke patients was 6.1 ± 5.6 ($n = 91$), which was significantly smaller than the mean value of 12.3 ± 5.8 ($n = 49$) obtained from the normal subjects (unpaired t test, $P < 0.0001$).

In the subgroup of stroke patients from whom bilateral EMG recordings were obtained, data from the unaffected 1DI contained a narrow central peak in the cross-intensity function in all cases. The mean size (E/M) of these peaks was 7.6 ± 4.7 ($n = 40$). Central peaks were absent in 43% of cross-intensities in data from the patients' stroke-affected 1DI. The mean size (E/M) of these peaks was 2.9 ± 3.5 ($n = 37$). The mean size of cross-intensity peak from the affected and unaffected hands differed significantly (unpaired t test, $P < 0.01$). Coherence analysis of data from the unaffected 1DI revealed significant peaks in the ranges 1–7 and 11–22 Hz; the most frequently occurring values of coherence in the two ranges were 2 Hz (90% of cases) and 15 Hz (38% of cases). Analysis of data from the stroke-affected 1DI revealed significant coherence in the range 1–3 Hz (maximum incidence 80% at 1 Hz); very little significant coherence was detected at frequencies in excess of 3 Hz. When expressed in terms of the mean value of maximum coherence for the low- and high-frequency ranges there was a clear difference between the affected and unaffected hands for the higher frequency band of coherence. The mean peak coherences for the unaffected 1DI were 0.153 ± 0.15 and 0.042 ± 0.041 for the 1–7 and 11–22 Hz

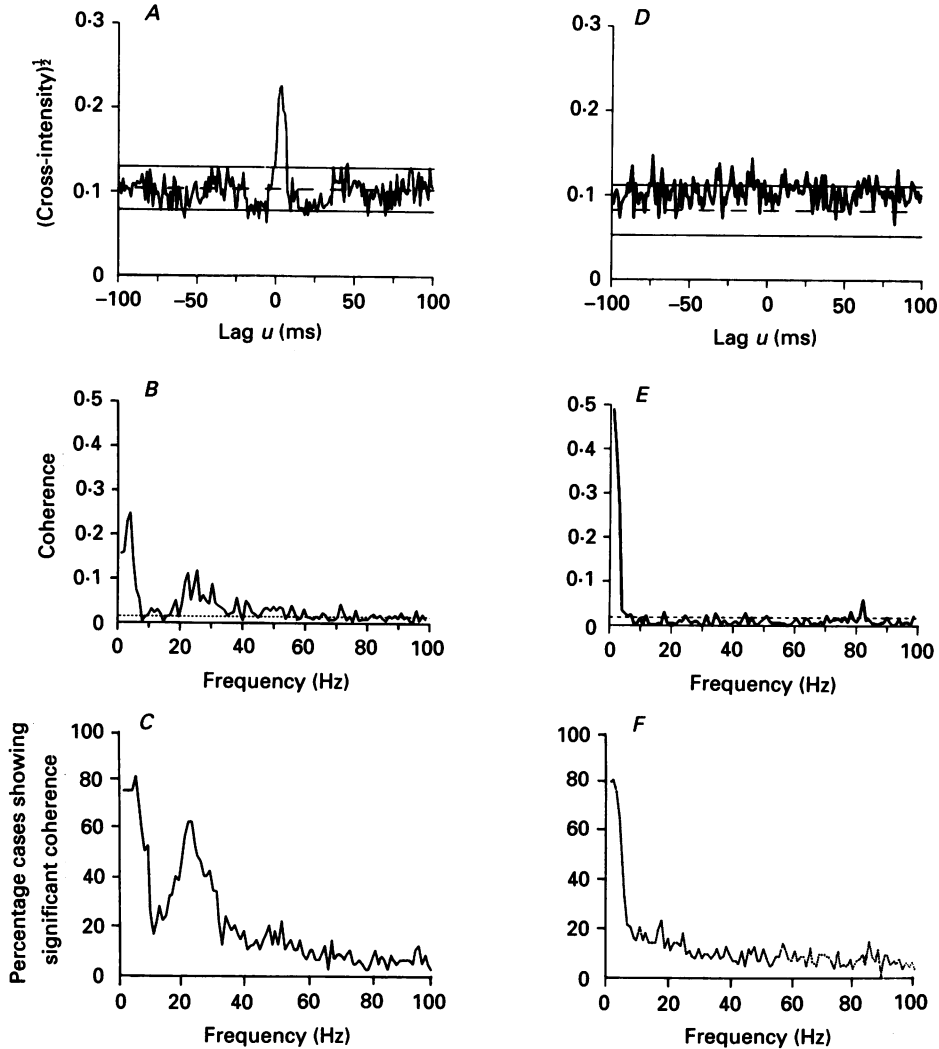


Fig. 8. *A*, cross-intensity constructed between the discharges of two motor units from within 1DI in a healthy subject (1551 reference spikes). *B*, coherence spectra for the data used to construct the cross-intensity in *A*. *D*, cross-intensity constructed between the discharges of two motor units recorded from within the affected (left) hand of a patient who had suffered an infarct of the right internal capsule approximately 4 months previously (1168 reference spikes). *E*, coherence spectra for the data used to construct the cross-intensity in *D*. The central cross-intensity peak is absent in the data recorded from the stroke patient. Significant coherence can only be detected at low frequencies in the recordings from the stroke patient. Bin width *A* and *D*: 1 ms; frequency resolution *B* and *E*: 1 Hz. *C* and *F*, the percentage of 1DI motor unit pairs that show significant coherence at each frequency between 1 and 100 Hz. *C*, data from 1DI of sixteen healthy subjects ($n = 49$ motor unit pairs); *F*, data from the affected 1DI of eleven stroke patients ($n = 91$ motor unit pairs).

frequency bands, respectively ($n = 40$). The corresponding values obtained for the stroke-affected 1DI were 0.149 ± 0.144 and 0.017 ± 0.021 ($n = 37$). There was no significant difference between the values in the low-frequency band (unpaired t test, $P > 0.9$); the values in the high-frequency band differed significantly (unpaired t test, $P < 0.01$).

DISCUSSION

Mechanisms of generation of motor unit coherence

This study demonstrates that pairs of human motor unit spike trains recorded during isometric contraction both from within and between muscles share certain frequency components that are quite different from the intrinsic firing rate of the motoneurons (approximately 10 impulses/s). The coherence between a pair of motor unit discharges is a measure in which components attributable to the autospectra of the two contributory spike trains have been removed (see eqn (1), Methods); therefore, the 1–12 and 16–32 Hz coherence spectra must either reflect periodicities in the firing of common presynaptic inputs to motoneurons or be generated by the synaptic processes that are common and which produce correlated motor unit discharges.

Coherence between pairs of motor unit spike trains at a particular frequency is likely to reflect periodicities in the discharges of common motoneurone inputs. It can be demonstrated that highly periodic motoneurone inputs, generated by vibrational stimulation of human Ia afferents, have a marked common modulatory effect on the firing of pairs of motor units, detectable as coherence between motor unit discharges at frequencies corresponding to those of the vibrational stimulus (Farmer, Farmer, Halliday, Rosenberg & Stephens, 1990a). The coherence spectra detected between motor unit discharges recorded during isometric finger abduction in man may reflect periodicities in the firing of branched monosynaptic inputs to motoneurons or alternatively they may reflect activity in presynaptic inputs that are themselves periodically correlated. Central peaks in the cross-correlogram can be modelled using the equations of Kirkwood & Sears (1978) on the assumption that they are generated by common unitary EPSPs from branched monosynaptic inputs. Datta & Stephens (1990) have argued that similar mechanisms may be involved in the production of central cross-correlogram peaks detected from 1DI:1DI motor unit pairs in man. The time courses of the central peaks detected in the present study were similar to those described by Datta & Stephens (1990). These considerations suggest that the dominant contribution to the central cross-correlogram peaks is from branched monosynaptic inputs to motoneurons. However, a contribution made by other types of correlated input that may or may not branch to form monosynaptic connections with motoneurons cannot be excluded. The evidence presented here suggests that the central peak in the cross-intensity and coherence in the frequency range 16–32 Hz reflect activity in the same presynaptic pathways.

While we suppose that periodicities in the firing of motoneurone inputs must exert a powerful influence on the frequencies at which significant coherence is detected between motor unit discharges, it is recognized that the time course of the central cross-correlogram peak is related to the time course of the motoneurone EPSP and the spike-generating properties of the motoneurone (Kirkwood & Sears, 1978). Given

the correspondence between the cross-intensity peaks detected in the present study and the coherence spectra, one might expect that the frequency characteristics of common motoneurone EPSPs will influence the frequencies at which coherence is detected between the motor unit spike trains. Thus, rather than representing periodicities in the firing of motoneurone inputs, the coherence spectra may contain components that reflect the frequency content of the common EPSPs evoked in the motoneurones. For motoneurone EPSPs to be responsible for either 1–12 or 16–32 Hz coherence they would have to introduce spectral peaks exclusively within the narrow frequency bands of 1–12 and 16–32 Hz, either by adding in or filtering out specific frequency components.

We have addressed the question of the contribution made by EPSP frequency characteristics through the use of a conductance-based model of the motoneurone. The results are discussed in an appendix to this paper, in which it is demonstrated that the effect of common motoneurone EPSPs on the coherence between two motor unit spike trains is similar to that of a low-pass filter. The highest frequency at which the coherence is no longer significant depends on the shape indices of the EPSP. The more slowly rising the EPSP, the lower the frequency beyond which the coherence is no longer significant. It is shown in the Appendix that the time course of EPSPs with realistic shape indices has little effect on the magnitude of coherence at frequencies of less than 250 Hz (see Fig. 9). More significantly, no discrete components are introduced into or subtracted from the frequency ranges in which motor unit coherence is detected experimentally (see Fig. 9*A* and *B*). The results from modelling suggest that in the experimental situation, the time courses of motoneurone EPSPs simply constrain values of coherence that may be detected at high frequencies (in excess of 250 Hz for the EPSP shape indices used). The spectral content of motoneurone EPSPs cannot be held responsible for the discrete bands of coherence detected at 1–12 and 16–32 Hz. These frequency components are likely, therefore, to reflect periodicities in the firing of common motoneurone inputs.

Comparison of 1–12 and 16–32 Hz coherence spectra

Several sources of evidence suggest that the mechanisms underlying 1–12 Hz coherence differ from those that generate 16–32 Hz coherence. Given that periodicities in the firing of common motoneurone inputs are the most likely cause of the coherence spectra between motoneurone firing, there are two likely mechanisms for generation of coherence in the range 1–12 Hz. First, the 16–32 Hz periodic component of common motoneurone inputs may be a carrier frequency which can be modulated at a lower frequency, producing coherence in the range 1–12 Hz. Second, significant values of coherence in the range 1–12 Hz may be generated by activity in inputs separate from those generating 16–32 Hz coherence. The majority of the experimental evidence points towards there being two separate sources of common input. Furthermore, compared with the mechanisms responsible for generating 1–12 Hz coherence, those underlying 16–32 Hz coherence are more intimately related to the synaptic processes that produce central peaks in the cross-intensity function.

First, when the entire population of motor unit pairs was analysed there was found to be a positive relationship between the size of the central cross-intensity peak and

the magnitude of maximal coherence in both low- and high-frequency ranges. However, this positive relationship was weaker for 1–12 Hz coherence than for 16–32 Hz coherence. When successive sections of data from individual pairs of motor units were studied, only coherence in the high (16–32 Hz) range co-varied with the size of the central cross-intensity peak. Second, coherence in the frequency range 1–3 Hz was present in approximately 25% of cases in which the central cross-intensity peak and 16–32 Hz coherence were absent, suggesting that very low-frequency coherence can be generated in the absence of branched common synaptic input and the processes that produce 16–32 Hz coherence. Third, data from stroke patients and subjects in whom 1DI:1DI and Biceps:Biceps recordings were obtained, demonstrated that low-frequency (1–12 Hz) coherence was preserved in recordings in which central cross-intensity peaks and 16–32 Hz coherence were reduced. Finally, coherence at very low frequencies (≈ 1 Hz) could be produced by voluntary common modulation of the motor unit firing rate. Voluntary common rate modulation was not observed to affect either the size of the central cross-intensity peak or the magnitude of maximal coherence in the frequency range 16–32 Hz (see Fig. 5), suggesting that the mechanisms of voluntary firing rate modulation may be dissociated from those responsible for the generation of 16–32 Hz coherence and central peaks in the cross-intensity function. Taken together these considerations argue for there being two separate neural processes. The first provides a common input that is responsible for short-term motor unit synchronization and 16–32 Hz coherence. Activity in the second produces 1–12 Hz coherence but is not responsible for short-term synchronization of motor unit firing.

The nervous origins of motor unit coherence

The neural origin of the presynaptic fibres that give rise to motoneurone coherence is unknown. The Ia afferent system is known to branch extensively within homonymous and heteronymous motoneurone pools (Mendell & Henneman, 1971; Nelson & Mendell, 1978). It is known that during vibrational stimulation of the Ia afferent system, discrete coherence peaks can be detected between the on-going activity of motor unit pairs corresponding to the frequency of the stimulation (Farmer *et al.* 1990a). Activity in the Ia system may be responsible for at least some of the coherence in the frequency ranges described in this study. Typical discharge frequencies of human spindle afferents recorded during isometric contraction of the forearm flexors are approximately 25 Hz (Valbo, 1981).

In the monkey, branched corticospinal tract projections are known to form monosynaptic connections with different limb muscle motoneurons and to produce in them short-latency excitation (Asanuma, Zarzecki, Jankowska, Hongo & Marcus, 1979; Fetz & Cheney, 1980; Shinoda, Yokata & Futami, 1981; Buys, Lemon, Mantel & Muir, 1986; Lemon, Muir & Mantel, 1987). Analysis of spike-triggered averages and cross-correlograms between the firing of corticospinal tract neurones and motoneurons suggests that during the hold phase of a precision grip task, interspike intervals in the range 40–70 ms exert particularly strong facilitatory effects on motoneurone discharge (Lemon & Mantel, 1989). These firing rates correspond to corticomotoneuronal firing frequencies of 14–25 Hz. It has recently been shown in the monkey that during fine finger tasks periodic synchronization may occur between corticomotoneurons at a frequency of 25–35 Hz (Murthy & Fetz, 1991; see

also Engel, Konig, Kreiter, Schillen & Singer, 1992 for review). The task of index finger abduction used in the present study may reasonably be equated to the hold phase of a precision grip. The following considerations suggest that the generation of central cross-intensity peaks and 16–32 Hz coherence involves activity in presynaptic inputs that originate in the central nervous system.

In the deafferented patient, the median nerve sensory action potential was found to be absent, as were all forms of short- and long-latency reflex activity dependent on activity in both Ia and cutaneous afferents. In this patient maximal coherence was detected in both the low- and high-frequency ranges seen in healthy subjects. Coherence in the low-frequency range was particularly marked, probably due to the difficulty experienced by the patient in maintaining steady motor unit firing in the absence of peripheral afferent feedback. The mean size of coherence peaks in the high-frequency (16–32 Hz) band was within the range of values found for the normal subjects, although its value was somewhat less than the group mean. It was found by Baker *et al.* (1988) that the sizes of the central cross-intensity peaks observed in recordings from this patient were typical of those found for normal subjects. The peripheral deafferentation in this patient appears profound; this would suggest that the activity in afferent pathways is unlikely to have contributed to either the central cross-intensity peak or to the peaks in the coherence spectra. The similarity of the results of cross-correlation and coherence analysis to those found in normal subjects, suggests that during isometric abduction of the index finger in normals, common peripheral afferent fibres contribute little to correlation of 1DI motor unit discharges in either the time or frequency domain.

The above conclusion is supported by the observations concerning the size of cross-intensity and coherence peaks in proximal *versus* distal muscles in healthy subjects. The tendency for cross-intensity and 16–32 Hz coherence peaks to be larger and more prevalent in distal compared to proximal muscles is inconsistent with the hypothesis that they are generated by activity in branched Ia afferent fibres; for compared to distal muscles, segmental pathways are known to be more influential in producing motor unit firing in proximal muscles in which the cross-intensity and 16–32 Hz coherence peaks were found to be smaller.

Monosynaptic corticomotoneuronal inputs form stronger connections with distal as opposed to proximal muscle motoneurons (Phillips & Porter, 1964). Thus the finding of a proximal–distal gradient for both the size of the central cross-intensity peak and the incidence and magnitude of significant coherence peaks in the frequency band 16–32 Hz suggests that these phenomena are produced in part by activity in common corticospinal inputs to motoneurons. This assertion receives further support from the studies on stroke patients.

In comparison to results obtained from the healthy subjects, far fewer motor unit pairs recorded from the affected 1DI of stroke patients showed significant coherence peaks. In addition, the narrow central cross-intensity peak was absent in 36% of recordings from the affected hand of the stroke patients. The deviation between the graph of the incidence of coherence peaks obtained from normal subjects and that obtained from the stroke patients commenced at 3 Hz and continued until 58 Hz, whereupon the incidence of significant peaks in normals fell to that of the stroke patients (compare Fig. 8C and F). A similar result was obtained when data from the affected and unaffected hands in the same patients were compared. These results

strongly suggest that the detection of coherence between motor unit discharges in the frequency range 16–32 Hz depends largely on the integrity of supraspinal pathways that contralaterally innervate the motoneurons of intrinsic hand muscles.

Concluding comments

The findings of the present study demonstrate well-defined frequency bands of coherence between the firing of pairs of motor units recorded during isometric contraction in man. Evidence from healthy subjects and from patients with neurological lesions suggests that similar presynaptic processes are responsible for both the central cross-intensity peak and 16–32 Hz motor unit coherence. On the basis of theoretical modelling we further suggest that the main determinant of discrete frequencies of coherence between a pair of motor unit spike trains is the presence of a periodically discharging common input to the motoneurone pair. The presynaptic inputs responsible for motor unit coherence in the frequency range 16–32 Hz are likely to arise centrally rather than peripherally and may be of corticospinal tract origin. An intriguing possibility is that the results described in the present study represent the human correlate of the types of corticomotoneuronal discharge behaviour described by Lemon & Mantel (1989) and Murthy & Fetz (1991) in the monkey. Further work is in progress to investigate this possibility.

APPENDIX

The narrow peak that may be observed in the cross-intensity between the discharges of pairs of motor units has been attributed to the joint increase in motoneurone firing probability brought about by activity in branches of presynaptic fibres that commonly innervate the motoneurone pair (Sears & Stagg, 1976; Kirkwood & Sears, 1978). On the basis of a theoretical framework proposed by P. A. Kirkwood (Kirkwood & Sears, 1978), the time course of the central peak in the cross-correlation histogram can be related to the time course of the common postsynaptic potentials generated by presynaptic fibres.

The cross-intensity may be related to the cross-spectrum through the Fourier transform. The magnitude of the cross-spectrum, when normalized by the product of the autospectra of the two processes, gives an estimate of the coherence (see Methods, eqn (1)). It might be expected, therefore, that values of the coherence computed between a pair of motor unit discharges will be influenced by characteristics of the EPSPs arising from inputs shared by the two motoneurons.

Using a conductance-based model we have examined the relation between the characteristics of the EPSPs arising from activity in branches of common presynaptic fibres and the coherence between two motor unit spike trains resulting from this shared input. In this the pair of model neurones receive a large number of common synaptic inputs as well as a number of independent inputs.

The basic equation describing the membrane current for a single neurone, incorporating multiple synaptic inputs and after-hyperpolarization, may be written as

$$C_m \frac{dV_m}{dt} = -I_{\text{leak}}(V_m) - \sum_{j=1}^n I_{\text{syn}}^j(V_m, t) - \sum_{i=1}^m I_{\text{AHP}}^i(V_m, t), \quad (A1)$$

where C_m is the membrane capacitance, V_m the membrane potential, and $I_{\text{leak}}(V_m)$ the leakage current given by $(V_m - V_r)/R_m$ (cf. Getting, 1989). V_r and R_m represent the resting potential and membrane resistance, respectively. In our simulations $C_m = 4 \times 10^{-9}$ F, $R_m = 1.5 \times 10^6$ Ω and $V_r = -70$ mV, giving a membrane time constant of $\tau = 6$ ms.

The synaptic current due to the j th synaptic input to the neurone is $I_{\text{syn}}^j(V_m, t)$, with the summation in eqn (A1) over the total number of synaptic currents denoted by n . The synaptic current in response to a single input spike at $t = 0$ was modelled by $I_{\text{syn}} = G_{\text{syn}} g_{\text{syn}}(t)(V_m - V_{\text{syn}})$, where G_{syn} is the maximum synaptic conductance, $g_{\text{syn}}(t)$ the time-dependent conductance change and V_{syn} the synaptic reversal potential. The time course of a single synaptic conductance change was represented by the α -function $(At/\tau) \exp(-t/\tau)$ (cf. Jack, Noble & Tsien, 1975). The constants A and τ were chosen to give EPSPs with rise times and half-widths, in relation to a membrane time constant of $\tau_m = 6$ ms, that approximate to those found in animal experiments (cf. Jack, Miller, Porter & Redman, 1971) and encompass the range of values found by Bremner *et al.* (1991a) to best describe the time course of the central cross-correlogram peaks detected between the firing of motor unit pairs recorded from within the first dorsal interosseous muscle in man (EPSP 10–90% rise times and half-widths in the ranges 0.5–5.0 and 4.7–15.1 ms).

$I_{\text{AHP}}(t)$ represents the output spike-triggered after-hyperpolarization current, where the summation term in eqn (A1) is over the number of output spikes. The after-hyperpolarization potential was modelled as a conductance change in the manner of Baldissera & Gustafsson (1974), where membrane potential changes associated with the after-hyperpolarization were modelled to have the same magnitude and time course as for cat motoneurones.

The input spike trains were all Poisson processes and thus had exponentially distributed interspike intervals. The mean rates of the input spike trains were set at 30 impulses/s. The magnitudes of the EPSPs were set in the range 50–100 μ V. Each motoneurone received a total of 850 inputs (thus producing a total drive of 25500 EPSPs/s); of these inputs, 820 were common to both motoneurones. The output firing rate of the two motoneurones was kept constant for differing EPSP time course parameters at approximately 12 impulses/s; this was achieved by reducing the amplitude of the EPSP as the time course increased. However, repeating the simulations with a constant magnitude of EPSP (100 μ V), and thus differing motoneurone firing rates, did not affect the results as illustrated in Fig. 9.

Figure 9C illustrates the spectral decomposition of three EPSPs with differing time courses; the time courses of these EPSPs (scaled to 1 mV) are shown in Fig. 9D. The coherences estimated between the two output spike trains associated with each of the EPSPs in Fig. 9D are illustrated in Fig. 9A and B.

The spectral decomposition for the EPSP with the fastest rise time and shortest half-width is shown in Fig. 9C by the curve labelled 1. The coherence between the output spike trains associated with common input EPSPs with this spectral composition is significant for frequencies in excess of 500 Hz (see Fig. 9A, plot 1).

As EPSP rise times become slower and half-widths longer, there is a decrease in the magnitude of the high-frequency content of their spectrum (Fig. 9C). This change in spectral content of the EPSP brings about a decrease in the highest frequency at

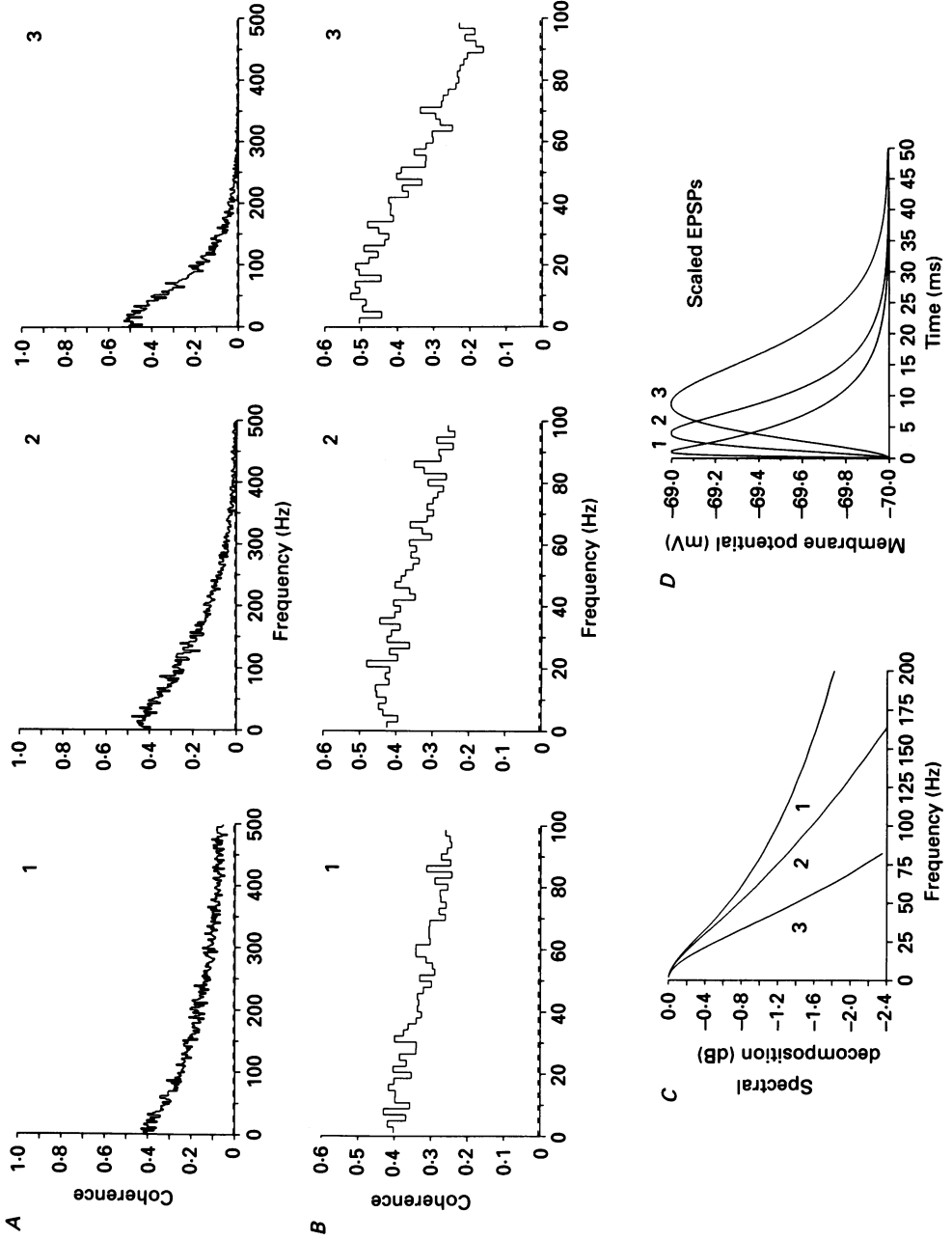


Fig. 9. For legend see facing page.

which coherence between the motor unit spike trains is significantly different from what one might expect for two independent processes. For example, if the EPSP rise time is increased from 0.5 to 2.3 ms, with a corresponding increase in half-width from 4.7 to 8.4 ms, the highest frequency in the coherence is decreased to approximately 400 Hz (Fig. 9A, plot 2). When the rise time and half-width are increased to 5.0 and 15.1 ms, respectively, the highest frequency in the coherence is decreased to approximately 250 Hz (Fig. 9A, plot 3). It is apparent, therefore, that the shape indices of the EPSP have an effect in limiting the linear transmission characteristics of the motoneurone for high input frequencies.

For realistic EPSP shape indices (cf. Jack *et al.* 1971) the highest frequency beyond which values of coherence are no longer significant is an order of magnitude greater than any of the frequencies for which coherence was shown to be significant in our experiments (compare Fig. 1B with Fig. 9A). The most extreme case with the slowest rise time and longest half-width still only brought the highest frequency to approximately 250 Hz, a value well in excess of the 1–12 and 16–32 Hz ranges of coherence we detected experimentally. Thus in the absence of any structure in the common input spike train, such as in our model where the inputs are a Poisson process, changes in the shape of EPSPs within the parameters selected here simply limit the detection of frequency components in the input spike trains for values in excess of 250 Hz.

It can be seen from Fig. 9A that different shapes of EPSPs influence the relative amount of coherence at low and high frequencies. However, despite these differences, the spectral decompositions of the EPSPs and the coherence spectra themselves approach their respective upper frequency limits as smooth functions. This is emphasized in Fig. 9B, where the coherences in Fig. 9A have been plotted between 1 and 100 Hz. It can be seen from Fig. 9B that the differing EPSP characteristics do not introduce any discrete structure into the coherence such as that detectable between human motor unit discharges in the frequency ranges 1–12 and 16–32 Hz. These considerations lead us to conclude that the effect of the time course of EPSPs on the coherence is similar to that of a low-pass filter and that the discrete bands of coherence described between the firing of human motoneurons are likely to be produced by periodicities in the firing of common motoneurone inputs.

Fig. 9. The relation between the time course of common EPSPs and the coherence estimated from a pair of model neurones receiving 820 common inputs with uncorrelated spike trains. *A*, coherence between the discharges of two model neurones for three different shapes of common input EPSP (*D*). The mean rate of each of the input spike trains was 30 impulses/s, with exponentially distributed interspike intervals. The record length for each simulation was 300 s. The frequency resolution in *A* and *B* is 2 Hz. The horizontal dashed line in *A* and *B* represents the 95% confidence interval under the assumption that the spike trains from the model neurones are independent processes. The numbers (1, 2, 3) in each of the coherence plots correspond to the three different EPSP time courses used. *B*, identical coherence spectra as in *A* shown with expansion of the 1–100 Hz frequency scale. *C*, the spectral decomposition for each EPSP time course shown in *D*. The 10–90% rise times (RT) and half-widths (HW) of the simulated EPSPs shown in *D* are: 1, RT = 0.5 ms, HW = 4.7 ms; 2, RT = 2.3 ms, HW = 8.4 ms; 3, RT = 5.0 ms, HW = 15.1 ms. The spectral decompositions of faster rising EPSPs contain more high-frequency components (*C*). Faster rising EPSPs allow higher frequencies to be detected in the coherence (*A*).

We gratefully acknowledge the help of J. W. N. Lau and E. Murray-Smith. S. F. F. was supported by a Wellcome Trust Clinical Research Training Fellowship. J. R. R.'s research is supported by grants from the SERC and the Cognitive Science/HCI initiative.

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