Coherent Motor Unit Rhythms in the 6–10 Hz Range During Time-Varying Voluntary Muscle Contractions: Neural Mechanism and Relation to Rhythmic Motor Control

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Erimaki S, Christakos CN. Coherent motor unit rhythms in the 6–10 Hz range during time-varying voluntary muscle contractions: neural mechanism and relation to rhythmic motor control. J Neurophysiol 99: 473–483, 2008. First published December 5, 2007; doi:10.1152/jn.00341.2007. In quasi-sinusoidal (0.5–3.0 Hz) voluntary muscle contractions, we studied the 6- to 10-Hz motor unit (MU) firing synchrony and muscle force oscillation with emphasis on their neural substrate and relation to rhythmic motor control. Our analyses were performed on data from 121 contractions of a finger muscle in 24 human subjects. They demonstrate that coherent 6- to 10-Hz components of MU discharges coexist with carrier components and coherent modulation components underlying the voluntary force variations. The 6- to 10-Hz synchrony has the frequency of the tremor synchrony in steady contractions and is also widespread and in-phase. Its strength ranges from very small to very large (MU/MU coherence >0.50) among contractions; moreover, it is not related to the contraction parameters, in accord with the notion of a distinct 6– to 10-Hz synaptic input to the MUs. Unlike the coherent MU modulations and the voluntary force variations, the in-phase 6- to 10-Hz MU components are suppressed or even eliminated during ischemia, while the respective force component is drastically reduced. These findings agree with the widely assumed supraspinal origin of the MU modulations, but they also strongly suggest a key role for muscle spindle feedback in the generation of the 6- to 10-Hz synaptic input. They therefore provide important information for the study of generators of the 6- to 10-Hz rhythm which subserves the postulated rhythmical control and is manifested as force and movement components. Moreover, they argue for a participation of oscillating spinal stretch reflex loops in the rhythm generation, possibly in interaction with supraspinal oscillators.

INTRODUCTION

In a previous study (Erimaki and Christakos 1999), we observed a tremor-like oscillation riding on top of the voluntary variations (≈2 Hz) of the force produced by a human finger muscle. This oscillation had its frequency in the range 6–10 Hz and was accompanied by corresponding motor unit (MU) firing synchrony. In parallel to the 6- to 10-Hz rhythmic synchrony, a slower synchrony of MU firing modulations acted as the basis for the voluntary force variations.

Slow finger and wrist movements are also known to exhibit a rhythmic component within the 6- to 10-Hz range (Kakuda et al. 1999; Vallbo and Wessberg 1993). This component is accompanied by corresponding coherent rhythms in the discharge of the MUs (Kakuda et al. 1999) and the spindles (Wessberg and Vallbo 1995) of the participating muscles. The 6- to 10-Hz movement component is believed to have a supraspinal origin and to be a peripheral manifestation of rhythmical motor control in humans (Farmer 1999; Vallbo and Wessberg 1993).

More generally, 6- to 10-Hz coherent rhythms attributed to network coupling at different supraspinal levels are thought to be involved in rhythmical motor control (Evans and Baker 2003; Gross et al. 2002; McAuley and Marsden 2000; McAuley et al. 1999; Pollok et al. 2005; Raethjen et al. 2004; Welsh and Lináš 1997). The basis for such hypotheses has often been the observation of weak 6- to 10-Hz coherence of electromyograms (EMGs) to electroencephalograms (EEGs) or magnetoencephalograms (MEGs)—i.e., coherence of synchronous MU firing rhythms to activities in cortical neuron populations. Notably, in other studies where such coherences were uncommon, subcortical generators were assumed (Conway et al. 1995; Marsden et al. 2001). Overall, however, there are no specific demonstrations of the mechanism that generates the basic rhythm in the postulated rhythmical control or of the way such control is actually performed.

In the various hypotheses involving central generators, the synchronous 6- to 10-Hz MU rhythms were clearly assumed to manifest peripherally the postulated rhythmical control. However, there exist no systematic studies of this synchrony and its dependencies, e.g., on movement parameters or, equivalently, on the parameters of the muscle forces causing movements. Yet, the question of the neural substrate of this synchrony is of particular interest because it is directly related to the issue of the generator and the functional relevance of the 6- to 10-Hz rhythm.

Importantly, in steady muscle contractions, the 6- to 10-Hz MU synchrony and tremor component seem to critically depend on the feedback from muscle spindles and to likely result to some extent from rhythmical action in the spinal stretch reflex loop (Christakos et al. 2006a). Analogously, the 6- to 10-Hz synchrony and force oscillation in time-varying contractions could also depend on spindle feedback.

In the present study, we systematically examined the above questions for quasi-sinusoidal voluntary contractions of the first dorsal interosseus (FDI) muscle of the hand, having wide ranges of frequency and amplitude. We performed extensive
analyses of the 6- to 10-Hz MU synchrony using a sensitive and efficient technique (Christakos 1994, 1997), to study its characteristics (extent, strength, and MU phases) and their relation to the parameters of the voluntary contractions. We also used ischemia tests to examine the involvement of muscle spindle feedback in the generation of the particular rhythmical synchrony and force oscillation. On the basis of our results, we therefore considered possible underlying neural mechanisms, also in relation to rhythmical motor control.

Preliminary reports have been presented in abstract form (Christakos and Erimaki 2000; Christakos et al. 2006b; Papadimitriou et al. 2003).

METHODS

Experiments

The experiments were conducted on 24 neurologically normal volunteers (age 21–48) who gave informed consent. Approval for this study was obtained from the Ethics Committee of the University of Crete Medical School.

In the recording sessions, the subjects assumed a comfortable sitting position; their dominant hand and arm were secured on the laboratory bench in front of a force transducer (WPI-Fort1000).

The subjects exerted nearly isometric abduction force on a vertical plane with the lateral side of the horizontally extended index finger by contracting the FDI muscle against the transducer. The thumb and fingers 3–5 were constrained in flexion. Therefore the force on the transducer in the direction of index abduction was caused only by the FDI muscle because this is the sole agonist (Stephens and Taylor 1972).

The subjects were instructed to have the FDI contraction force follow a target curve displayed on the oscilloscope. This curve was a sine wave (frequency between 0.5 and 3 Hz) around a horizontal line representing a constant force level. Clearly, the subjects had continuous visual feedback of their actual force curve and, indirectly, their mean force level. Wide ranges of values were used for the mean force level [3–30% of maximal voluntary contraction (MVC); mean 15.4%, SD 7.1%] and the relative amplitude of the voluntary force variations (3–42% of mean contraction level; mean 20.4%, SD 8.7%).

Simultaneous 2-min records were obtained of the muscle force and the filtered (0.25–2.5 kHz) surface EMG (using Ag/AgCl disk electrodes) and intramuscular EMG (using bifilar nichrome wire electrodes, 40 μm) of the FDI muscle. The data were digitized at 5 kHz and stored using the program LabView.

Discrimination of single-MU spike trains in the intramuscular electrical activity, performed by a combination of a threshold operation and manual sorting, provided usually one and sometimes two MUs per recording. Spike trains were represented as sequences of zeroes and ones. All recorded signals, including the discrete sequences, were low-pass filtered at 250 Hz and resampled at 500 Hz for analysis (Christakos et al. 1984). The filtering was digital and introduced no time shifts.

Ischemia

Ischemia of the arm was used to examine the possible involvement of the feedback from muscle spindles in the generation of the 6- to 10-Hz MU synchrony and muscle force oscillation. During ischemia, a decline, or even practical interruption, of such feedback is known to occur and is related to one or both of the following.

1) A suppression of the force oscillation, in association with an increase in interstitial potassium concentration (Lakie et al. 2004), or, equivalently, a suppression of the impact of the internal-length input on muscle spindle discharges (see Fig. 4 of Matthews and Stein 1969).

2) A reduction in spindle sensitivity (Matthews 1933; see also Burke et al. 1984; Lippold 1970) and/or a partial blockade of the conduction of spindle output via group Ia afferents (Cody et al. 1987; Cresswell and Loescher 2000; Fellows et al. 1993; Haque and Burke 2003).

Such effects limiting spindle feedback are present after an interval ranging from a few to about 10 min after ischemia onset.

Our ischemia experiments were therefore conducted as follows: A sphygmomanometer cuff applied to the upper arm was inflated to 200 mmHg. The subjects had paresthesias immediately after inflation of the cuff. Within the next 5 min they reported increasing numbness, which was verified using the two-point discrimination test. After about 8 min, they showed complete loss of touch and deep sensation for the hand and forearm. Thus the recordings usually started after 10 min from initiation of the ischemia procedure and lasted 2 min.

However, in certain cases, the start of the recordings was 5–8 min after ischemia onset because the subjects reported some discomfort. In all recording periods, no pain was reported by the subjects.

Data analysis

Analyses were performed in both the frequency and the time domains using MATLAB (The MathWorks, Natick, MA). The analysis methods, including those regarding measurement of the MU synchrony, are briefly presented here, but were previously described in more detail (Christakos 1997; Christakos et al. 2006a).

Frequency-domain analysis, performed via the Fast Fourier transform on pairs of recorded activities, included (Wang et al. 2004): 1) segmentation of the 2-min time series into 60, 2-s-long segments; 2) mean removal and windowing (Hanning) for each data segment; 3) computation of the auto-spectra and the cross-spectrum from each segment; and 4) final estimation of the auto-spectra and the cross-spectrum of the activity pair by averaging the estimates from the individual segments. The coherence spectrum was subsequently estimated as the squared modulus of the cross-spectrum divided by the product of the individual auto-spectra.

Amplitudes of the voluntary variations and the 6- to 10-Hz oscillations of the force in the different contractions were estimated as the square root of the total power (integral) within the frequency bands of the corresponding auto-spectral deflections. For each contraction, these values were subsequently presented as a percentage of mean contraction level.

Time-domain analysis consisted of cross-correlation computations for pairs of activities over the 2-min time records.

In the study of the synchrony of both the MU modulations and the 6- to 10-Hz MU rhythms, we used a combination of unit-to-aggregate (UTA) coherence and cross-correlation analyses (Christakos 1994, 1997; Christakos and Giatroudaki 1998; Christakos et al. 2006a; see also Christakos et al. 1994; Iyer et al. 1994, where certain principles of this technique were used). The unitary signal was MU activity and the aggregate signal was the muscle force waveform (or the rectified surface EMG).

Specifically, UTA coherence computations on a sample of pairs of simultaneously recorded MU/force activities were used for: 1) identification of correlated MUs, given that a significant such coherence indicates the presence of a correlated subset to which the given unit belongs; 2) estimation of the extent of the MU synchrony (proportion of the correlated units within the active population) as the fraction of nonzero coherences in the sample; 3) obtaining information on the strength of the synchrony and its distribution within the population; moreover, 4) MU/force cross-correlation computations for the coherent MUs in the sample were used for estimation of phases of the MUs in terms of delays of the MUs relative to the force signal (common reference signal). It is noteworthy that such cross-correlograms represent spike-triggered averages with the spikes at zero delay. They thus provide straightforward information on the time relation between MU spikes and muscle force signals, even when the MU/force
coherence is too low for reliable phase estimation from the cross-spectrum.

Compared with traditional MU/MU analysis, this technique requires a much smaller sample of easily recorded activity pairs, it shows higher sensitivity in detecting synchrony, and it provides information in a compact form (Christakos 1994). Moreover, the use of a reference signal (muscle force) enables one to estimate the individual MU phases, compared with the MU phase differences that are provided by MU/MU analyses. Overall, this technique of analysis of population synchrony is thus both sensitive and efficient.

For the 60 segments used in the spectral analyses, and for the smooth data tapering used for leakage suppression, the threshold for a significant coherence at the 99% confidence level is about 0.08 (Rosenberg et al. 1989; Wang et al. 2004).

In the contractions where the 6- to 10-Hz MU/force coherence(s) was(were) not statistically significant by this criterion, we performed additional computations of coherence between the rectified EMG and the muscle force signal. This is an aggregate-to-aggregate (ATA) coherence and is widely used in the analysis of neural population synchrony (e.g., Grosse et al. 2002), including sometimes assessment of the strength of such synchrony. In our study, we used the EMG/force coherence only for detection of synchrony and determination of its frequency, by taking advantage of properties that make it much higher than the MU/MU and the MU/force coherence.

Specifically, for a large extent of population synchrony and high concentration of units’ phases, the ATA coherence has large values and represents a great overestimation of the true UTU and UTA coherences (Christakos 1997). Examples of such overestimation have been presented in various experimental studies (e.g., Christakos et al. 1994, 2006a; Hamm et al. 1999). One example can also be seen in our Fig. 4, as the 6- to 10-Hz MU synchrony was found to be both widespread and in phase (RESULTS). In addition, the ATA coherence may exhibit saturation effects, particularly in cases where the UTU coherence is not very low.

Consequently, ATA coherence analysis can provide an easy and sensitive means of detection of population synchrony, but needs to be used with great caution in assessing the strength of such synchrony. Therefore in all cases where the 6- to 10-Hz MU/force coherence was not statistically significant with 99% confidence, whereas the EMG/force coherence was significant, the synchrony was considered present but minimal, with a very limited influence on the corresponding force oscillation (Christakos et al. 2006a).

Statistical tests

All data were analyzed using the SPSS v12.0 statistical package. Estimates of the Spearman rank-order correlation coefficient were used to examine possible relationships between such variables as mean level of contraction, frequency and amplitude of voluntary force variations, and 6- to 10-Hz MU/force coherence. The independent-samples t-test was used to compare the frequencies of the 6- to 10-Hz force oscillation in time-varying contractions and the tremor of steady contractions. Finally, to compare the conditions in the ischemia tests and to assess the effects of ischemia on the 6- to 10-Hz MU synchrony and force oscillation, Friedman ANOVA by ranks was used for multiple within-subjects comparisons (preischemia, ischemia, and posts ischemia). All tests were performed at the P < 0.05 level.

RESULTS

In agreement with previous observations (Erimaki and Christakos 1999; Iyer et al. 1994), under conditions of quasi-sinusoidally varying voluntary muscle force (0.5- to 3.0-Hz range), the force auto-spectrum displayed a dominant component at the frequency of the voluntary force variations. In all 121 contractions studied, the auto-spectra of MU activities exhibited a corresponding component, indicative of the presence of MU firing modulations. These modulations were correlated to the force variations and among themselves, as was indicated by corresponding components in the MU/force coherence spectra (METHODS).

In the example of Fig. 1, for a quasi-sinusoidal muscle contraction at 2 Hz (middle column), a large and sharp peak is seen at this frequency in the force auto-spectrum (left vertical dotted line). The corresponding peak in the MU1 auto-spectrum represents the modulation component of the MU’s discharge. This component is coherent to the 2-Hz force variations (MU1/force coherence = 0.61) and thus to the modulation components of other MUs (METHODS). The component at 6 Hz (arrow) represents the carrier of the modulated discharge of MU1, where the carrier rate equals the intrinsic firing rate of a unit for a steady contraction at the same force level (Iyer et al. 1994).

In the example of Fig. 2, for a second, simultaneously recorded unit (MU2), a modulation component is again seen at 2 Hz, showing coherence to the respective force (0.75) and MU1 component (0.44; left vertical dotted line). In this case the carrier rate of the unit is 11 Hz (arrow), i.e., MU2 is smaller than MU1 (Milner-Brown et al. 1973).

These MU firing patterns consisting of carrier and coherent modulation components were typical of our sample of 133 randomly selected MUs during the time-varying contractions of the 24 subjects of this study. The estimated MU/force coherence at the modulation frequency varied from contraction to contraction. This is seen in Fig. 3, where data of mean and SD of this coherence in the different contractions, grouped according to the frequency of the voluntary force variations, are presented. Notably, statistical analysis did not reveal a relationship between the particular frequency and the corresponding MU/force coherence (Spearman rank-correlation coefficient = 0.05, P > 0.50).

Over the entire sample, such coherences were generally high (range 0.13–0.97; mean 0.70, SD 0.18). Accordingly, a widespread and strong synchrony of modulated MU discharges underlies the generation of time-varying muscle force. Detailed examination of other characteristics of the MU modulation synchrony in sinusoidal contractions has been performed in our previous studies (Erimaki and Christakos 1999; Iyer et al. 1994). Here the analysis is restricted to MU firing patterns in time-varying contractions because they provide a necessary basis for studying the 6- to 10-Hz MU rhythms and synchrony that constitute the main focus of the present investigation.

6- to 10-Hz oscillation and synchrony in quasi-sinusoidal muscle contractions

One characteristic feature of the 0.5- to 3.0-Hz quasi-sinusoidal contractions was the presence of a more or less clear superimposed oscillation on the voluntary variations of the muscle force. This force oscillation had its frequency in the 6- to 10-Hz range and was accompanied by corresponding rhythms in MU activities, which were coherent to it and thus to one another (METHODS). This 6- to 10-Hz synchrony was identified as significant MU/force coherence(s) per contraction or was at least detected as significant EMG/force coherence (METHODS).
In the example of Fig. 1, the time records of the raw and high-pass-filtered (4-Hz cutoff) force signal in the middle column show a superimposed involuntary oscillation at 6 Hz. In the left column, this oscillation is represented by a local peak in the force auto-spectrum (right vertical dotted line and figure insert), which represents a superimposed involuntary oscillation. According to the time records, most of the spikes of the simultaneously recorded MU1 tend to occur rhythmically at, or near, the local minima of the 6-Hz force oscillation, in a one-to-one relation on average. This is represented by the 6-Hz component in the MU1 auto-spectrum (left column) obtained from the entire 2-min time series. A corresponding large one-to-one relation on average. This is represented by the 6-Hz component in the MU1 auto-spectrum (left column) obtained from the entire 2-min time series. A corresponding large component is also evident in the MU1/force coherence spectrum at 6 Hz. It is worth noting that even though the carrier rate of MU2 (11 Hz) is higher than the frequency of the fast force oscillation (6 Hz), the time record of the high-pass-filtered force and the corresponding MU1/force cross-correlogram (not shown) again revealed that some MU2 spikes tended to occur rhythmically near the local minima of the 6-Hz oscillation, whereas the remaining spikes were interspersed. This explains the observed MU2/force coherence at 6 Hz.

Overall, a 6- to 10-Hz MU component showing coherence to the muscle force, such as in Figs. 1 and 2, characterized MU firing in the 121 time-varying contractions studied in the 24 subjects. The observed frequency (Hz) of synchrony had a mean value of 7.8 and SD 1.1.

The MU/force coherence was reliably identified with 99% confidence (value ≥0.08) in 106 of the 121 contractions. In these contractions, a locking of spikes to the local minima of the 6- to 10-Hz oscillation was indicated by MU1/force cross-correlograms. Both cross-correlograms show a 6-Hz oscillation, whereas the one for the high-pass-filtered force signal also verifies the locking of the MU1 spikes to the minima of the 6-Hz force oscillation.

Interestingly, for all 117 MUs recorded in the 106 contractions, the MU carrier rates were higher than, or equal to, the frequency of synchrony (observed range 6.0–19.5 Hz; mean 11.7, SD 2.5). In other words, among the randomly selected MUs in this sample, there existed last-recruited, relatively large ones that fired at (11%), or just above, the frequency of
and a very small (0.07) but distinct peak at 6.5 Hz (right dotted line). The latter was the frequency of the 6- to 10-Hz synchrony in the particular contraction, as is indicated by the corresponding clear peak (0.54) at 6.5 Hz in the EMG/force coherence spectrum. Such contractions were observed in 6 of the 24 subjects who, however, showed significant MU/force coherence in other contractions irrespective of conditions.

Finally and importantly, the 6- to 10-Hz synchrony for each of the 24 subjects had the frequency (Hz) of the subject’s tremor synchrony in steady contractions, as this frequency was estimated in a preceding study (Christakos et al. 2006a) (mean 7.8 vs. 7.6, SD 1.1 vs. 1.1; \(t = -1.211; P > 0.20\)).

**Characteristics of the 6- to 10-Hz MU firing synchrony**

As described earlier, in 106 of the 121 muscle contractions of this study, significant 6- to 10-Hz coherence to the force was exhibited by all 117 analyzed MUs, including 11 pairs of simultaneously recorded units. This is a very high incidence (88%), considering the strict criterion of 99% confidence, and reveals a large extent of the particular synchrony within the active MU population. It should be stressed that in the remaining 15 contractions that showed minimal such synchrony, all 16 analyzed MUs, including one pair, did exhibit small coherence peaks at the frequency of the synchrony (e.g., Fig. 4). These coherences were in the range 0.05–0.07 and were therefore significant by the usually assumed 95% confidence criterion (0.04 in the case of 60 segments).

Accordingly, since there was practically no exception in the entire sample of 133 randomly selected MUs regarding the presence of coherence to the force, it can be concluded that the 6- to 10-Hz MU synchrony was widespread in the time-varying contractions of this study.

In what follows the analyses are performed on the sample of 117 MUs for which the coherence to the force was \(\geq 0.08\).
because this allows direct comparisons to the data of our preceding study concerning tremor synchrony in steady contractions. For these 117 MUs, the range of estimated MU/force coherences was 0.08–0.78 (mean 0.32, SD 0.16). Notably, the MU/EMG coherences had values similar to those of MU/force coherences over the entire sample of 117 MUs (but also over the sample of the 16 MUs from contractions showing minimal synchrony).

Interestingly, in each of the 11 pairs of simultaneously recorded MUs, the individual MU/force coherences had similar values (usually within 10% of their mean), as in the examples of Figs. 1 and 2. A scatter diagram constructed from the differences between coherences in such MU pairs and the corresponding differences of firing rates did not show any obvious trend (Spearman r = 0.04, P > 0.90).

Because the sample of 11 MU pairs was too small to allow for any conclusions, we examined the possible relation between MU coherence and MU firing rate over the entire sample of 117 MUs since the rate characterizes an MU (size, type; Milner-Brown et al. 1973). This statistical analysis did not reveal a significant relationship either (Spearman rank-correlation coefficient −0.12, P > 0.20). It thus seems that the 6- to 10-Hz MU synchrony had a fairly uniform strength in each contraction, as it also did in the steady contractions of the same subjects (Christakos et al. 2006a).

Figure 5 summarizes across subjects the 6- to 10-Hz MU/force coherence data from the 106 contractions (117 MUs), plotted versus the corresponding frequencies of synchrony. Accordingly, the strength of the 6- to 10-Hz synchrony varied widely among subjects and contractions.

Since the observations on this strength were obtained for broad ranges of values for the parameters of the varying contractions, its possible dependence on such parameters was examined. Statistical analyses did not reveal a relationship in the 106 contractions between the MU/force coherence and: 1) the mean force level (Spearman rank-correlation coefficient −0.137; P > 0.15); 2) the amplitude of the voluntary force variations (Spearman rank-correlation coefficient −0.05; P > 0.60); 3) the frequency of the latter (Spearman rank-correlation coefficient 0.025; P > 0.80); and 4) the product of amplitude and frequency, representing the contraction speed (Spearman rank-correlation coefficient 0.028; P > 0.50).

Finally, in all 117 cases, MU/force cross-correlation analysis revealed a clear tendency for some MU spikes to occur rhythmically near the local minima of the 6- to 10-Hz oscillation (mean delay 2.79 ms, 95% confidence interval 2.32–3.26 ms). This was the case irrespective of the MUs’ carrier rates. Thus the MUs had in-phase components at the frequency of the 6- to 10-Hz oscillation, which coexisted with the components at the MU intrinsic carrier rates and those at the modulation frequency.

Therefore the strength of the widespread, in-phase, and uniform 6- to 10-Hz synchrony can be estimated in terms of MU/MU coherences by squaring the estimates of the respective MU/force coherences (Christakos 1997). Thus the MU/MU coherences are found to be in the range 0.0064–0.61, i.e., the strength of the 6- to 10-Hz synchrony in the time-varying contractions ranged from very small to very large, as it did in the steady contractions of the same subjects in our preceding study (Christakos et al. 2006a).

It is worth noting that the values of the MU1/force, MU2/force, and MU1/MU2 coherences in Figs. 1 and 2 verify this square relationship, and this was also the case for the other 10 pairs of simultaneous MUs. It is also noteworthy that, according to this relationship: 1) the MU/force coherence is much higher than the MU/MU coherence, and thus facilitates the identification of correlated MUs; and 2) in the 15 contractions with MU/force coherences <0.08, the MU/MU coherences were <0.0064, i.e., the synchrony detected by EMG/force analysis was indeed minimal.

**Effects of ischemia on the 6- to 10-Hz synchrony and force oscillation**

Ischemia of the arm was used as a means of blocking muscle spindle feedback (METHODS) during 16 sinusoidal contractions of the FDI muscle in eight of our subjects.

The general, clear effect of ischemia was the suppression, even close to elimination, of the 6- to 10-Hz MU components and synchrony. This effect was accompanied by a drastic reduction of the amplitude of the corresponding force oscillation. Furthermore, removal of the occlusion reinstated the coherent MU rhythms and the initial oscillation.

In the example of Fig. 6 (left column), for a 0.5-Hz muscle contraction, the force and MU auto-spectra initially show a distinct component at 8.5 Hz (right vertical dotted line), whereas the MU has its carrier at 12 Hz (arrow). The 8.5-Hz component is accompanied by a 0.41 MU/force coherence. As seen in the middle column, 10–12 min of ischemic occlusion did not significantly change the firing rate of the MU. However, it largely suppressed the 8.5-Hz MU and force component and it practically eliminated the respective MU/force coherence. Finally, removal of the occlusion led to a situation similar to that before ischemia (right column). Notably, in Fig. 6, the 8.5-Hz coherence component after ischemia is larger than that in the preischemia phase (0.65 vs. 0.41), but in other tests the opposite was the case (Table 1).
Table 1 summarizes the conditions and effects in the ischemia tests. Accordingly, the mean force level and the amplitude of the voluntary force variations did not change in the three phases of the tests; the same applies to the firing rates of the MUs. However, during ischemia the 6- to 10-Hz MU synchrony was much weaker and the amplitude of the corresponding force oscillation was much smaller. Finally, the return to the initial values in the postischemia phase indicates that the effects of ischemia were transient. It should be emphasized that in 7 of the 16 tests, the 6- to 10-Hz synchrony was practically eliminated (as in Fig. 6), irrespective of its initial strength (initial MU/force coherence in the range 0.11–0.50). Overall, these observations thus strongly suggest an involvement of muscle spindle feedback in the generation of the 6- to 10-Hz synchrony.

In contrast, according to Table 1, the modulation components of the force and MU signals, and the corresponding synchrony, were preserved during ischemia. Therefore their generation does not seem to depend on spindle feedback, i.e., their mechanism is likely different from that of the 6- to 10-Hz synchrony and oscillation. It should be noted that because of the difficulty of the task, the size of the slow force component sometimes differed between the preischemia and the ischemia conditions (e.g., in Fig. 6, the amplitude of the 0.5-Hz force variation was about 75% of that in the preischemia contraction). However, it could be larger in either case.

DISCUSSION

The results of this study, obtained from a large sample of subjects and muscle contractions under various conditions of contraction level and speed:

1) demonstrate the presence of 6- to 10-Hz firing synchrony of MUs, coexisting with the synchrony of the MU firing modulations that underlie the voluntary force variations;

2) provide a broad view of the characteristics of the 6- to 10-Hz synchrony and oscillation. It should be noted that because of the difficulty of the task, the size of the slow force component sometimes differed between the preischemia and the ischemia conditions (e.g., in Fig. 6, the amplitude of the 0.5-Hz force variation was about 75% of that in the preischemia contraction). However, it could be larger in either case.

Different types of MU firing synchrony in time-varying muscle contractions

The existence of synchronous MU firing modulations during sinusoidal voluntary variations of the muscle force has been reported before (Erimaki and Christakos 1999; Iyer et al. 1994;...
see also DeLuca and Mambrito 1987; Farmer et al. 1993; Knight and Kamen 2007; Sosnoff et al. 2005; van Bolhuis et al. 1997). The here-demonstrated widespread and generally strong modulation synchrony is in accord with the notion of a common drive to the α-motoneuron (MN) pool (DeLuca and Erim 1994; see also Farmer et al. 1993; Henneman and Mendell 1981; Semmler et al. 1997). In the present case, the activities composing the drive presumably are coherent, quasi-sinusoidally modulated spike trains (see, e.g., the behavior of pyramidal tract neurons in the study of Baker et al. 2001, their Fig. 5). They thus cause, through synaptic action, coherent waves in the membrane potential of the MNs and hence coherent MU firing modulations.

In parallel to the modulation synchrony, there exists a 6- to 10-Hz firing synchrony of MUs and a corresponding muscle force oscillation. According to our results, the active MUs exhibit 6- to 10-Hz rhythms that are in-phase (i.e., coherent at zero lag), irrespective of the MUs’ intrinsic (carrier) discharge rates.

Importantly, the MU firing rates in the contractions of our subjects were usually higher than the frequency of the 6- to 10-Hz synchrony, but in 11% of the cases, contrary to the observations of Wessberg and Kakuda (1999), they were equal to it. This reveals that the recruitment rate of MUs coincides with the frequency of the 6- to 10-Hz synchrony, as it does in the case of the tremor of steady contractions (Christakos et al. 2006a). Last-recruited, relatively large MUs firing at minimal rates thus tend to show rhythmical spikes near the minima of the 6- to 10-Hz force oscillation in a one-to-one relation; smaller MUs firing at higher rates tend to show spikes near such minima as well as additional interspersed spikes.

The in-phase MU rhythms in the 6- to 10-Hz range presumably reflect in-phase oscillations in the membrane potential of α-MNs, caused by a common, rhythmical synaptic input. Importantly, the strength of the 6- to 10-Hz synchrony was here found to vary widely among contractions, but not to depend on either the mean level and other parameters of the contractions or the MU firing rates. The 6- to 10-Hz synaptic input seems therefore to be a distinct one, additional to the common drive that underlies the voluntary force variations through the MU recruitment and rate-coding mechanisms (DeLuca and Erim 1994; Freund 1983).

Such 6- to 10-Hz membrane oscillations ride on top of the coherent slower waves that underlie the MU modulations. Thus within the frequency-modulation pattern of cell firing, grouped MN spikes from different MUs tend to occur rhythmically near the local maxima of the 6- to 10-Hz membrane oscillations. [Analogous behaviors have been shown in intracellular studies of respiratory high-frequency oscillations (Huang et al. 1996; Parkis et al. 2003), where MNs fired at local peaks of the membrane oscillations.] Each time, superposition of the corresponding grouped twitches forms a cycle of a 6- to 10-Hz force oscillation.

Importantly, for each of our subjects, the 6- to 10-Hz synchrony had the frequency of the tremor synchrony in steady muscle contractions. It also shared other important characteristics with the tremor synchrony (Christakos et al. 2006a), being widespread, in-phase and of fairly uniform strength, and showing great variability in strength and lack of strength dependence on the mean force level. Furthermore, this synchrony also seems to depend on spindle feedback.

These behaviors, which point to a common neural mechanism under static and dynamic conditions, seem to contradict the conclusion of Kakuda et al. (1999) that 6- to 10-Hz synchrony characterizes slow movement and is absent or weak under steady conditions. The existence of significant such synchrony during steady muscle contractions has been demonstrated in many previous studies (e.g., Elble and Randall 1976; Erimaki and Christakos 1999; Farmer et al. 1993; Halliday et al. 1999; Raethjen et al. 2000; Semmler et al. 2003). Moreover, the strength of the 6- to 10-Hz synchrony (MU/force coherence) in our present sample of varying contractions and the preceding sample of steady contractions, from the same subjects, had similar ranges (0.08–0.78 vs. 0.08–0.90) and nearly identical means (0.32 vs. 0.34) as well as SDs (0.16 vs. 0.17).

It is noteworthy that Vallbo and Wessberg (1993) argued that the 6- to 10-Hz movement “discontinuities” they observed were not tremor because of their nonsymmetric appearance. However, rhythms in movement velocity and acceleration, which show coherence to MU activity, necessarily result through complex transformations from coherent muscle force oscillations. Therefore the 6- to 10-Hz synchrony during movement could not be of a nature and origin different from those of the synchrony underlying the 6- to 10-Hz force oscillation in time-varying contractions or, equivalently, the tremor in steady contractions. Both the force and the movement rhythms could thus be classified as action tremors.

Regarding the role of MU synchrony in the generation of the 6- to 10-Hz force oscillation, it should be stressed that such an oscillation was present in a fraction of the present contractions, where the synchrony was practically absent. This was also the case for about one half of the contractions studied during ischemia. In analogy to tremor (Allum et al. 1978; Christakos 1982a,b; Taylor 1962) and, contrary to the conclusion of Kakuda et al. (1999), a distinct force component is expected at, or just above, the MU recruitment rate, even in the absence of synchrony. It reflects the intrinsic rhythmicity and the relatively large sizes of the last-recruited MUs. In the presence of MU synchrony, the component caused by the in-phase rhythms of all active MUs is additional (Christakos 1986) and prevails or dominates, except when the synchrony is weak (Christakos et al. 2006a).

Finally, our MU/force and EMG/force coherence analyses also revealed the presence of a third type of MU synchrony, in the range 15–30 Hz (Erimaki and Christakos 2006). Our results on this type of synchrony will be reported elsewhere.

Origins of the modulation and the 6- to 10-Hz MU synchrony

In view of our ischemia observations on the synchrony of MU modulations, the underlying common drive to MNs seems not to depend on spindle feedback (see also Kamen and DeLuca 1992). Since, in addition, the FDI muscle lacks recurrent inhibition (Katz and Pierrot-Deseilligny 1999), this drive is with high likelihood of supraspinal origin (see also DeLuca and Erim 2002). This view is supported by observations regarding cortical influences on MNs (Gibbs et al. 1999; McKiernan et al. 2000) and also by the ability of our subjects to determine by volition the frequency and amplitude of the force variations in their contractions.
The situation is quite different with respect to the 6- to 10-Hz synchrony of MUs. Specifically, in about one half of our ischemia tests, the suppression of this synchrony was practically complete (MU/force coherence <0.08, or MU/MU coherence <0.0064), whereas in the ones showing measurable residual synchrony the ischemic block may have only been inadequate. At the same time, during our recording intervals (starting at 10 min, or sometimes 5–8 min, after ischemia onset), spindle feedback was limited because of reduced 1) length input to spindles, 2) spindle sensitivity, and 3) conduction of spindle output by group Ia fibers (methods). Moreover, a further limitation of the synaptic impact of Ia on MNs probably occurred due to enhanced Ia presynaptic inhibition. This rise is expected from action in group III–IV afferents (Avela et al. 2001; Kaleziec et al. 2004) because increases in other metabolic substances accompany the increase in interstitial potassium concentration that was described by Lakie et al. (2004).

Therefore the observed suppression, or even practical elimination, of the 6- to 10-Hz MU synchrony strongly suggests that muscle spindle feedback is actually necessary for the generation and/or maintenance of this synchrony.

With respect to point 3), it should be noted that in the H-reflex studies by Hayashi et al. (1987) and Pierrot-Deseilligny et al. (1981), the conduction block of Ia afferent fibers occurred after about 15 min of ischemia. However, in experiments performed by us on the FDI muscle, an H-reflex decline was sometimes evident before 10 min of ischemia. The great difficulty in obtaining a consistent H-reflex in the case of this phasic muscle (Schieppati 1987) prevented us from reaching definitive conclusions, but we nevertheless consider a relatively early Ia blockade to be a possible effect of ischemia (see also Cresswell and Loscher 2000).

Given the likely critical role of spindle feedback in the generation of the 6- to 10-Hz synchrony, there exist two obvious possibilities related to mechanisms that were previously considered in isolation or in combination:

The first possibility is that group Ia afferent signals provide a necessary bias or trigger input to a central oscillator that independently causes the 6- to 10-Hz MU synchrony. This possibility is worth examining in relation to hypotheses implicating supraspinal oscillators, such as the olivo-cerebellar system exhibiting intrinsic 5- to 12-Hz rhythms (Welsh and Llinás 1997), the cerebellathalamo-cortical network generating 8-Hz oscillatory drive on spinal MNs (Schnitzler et al. 2006), and the cortico-cortical interactions in the 6- to 15-Hz range (Raethjen et al. 2004). The consideration of Ia central projections could facilitate such investigations.

The second possibility is that an oscillating spindle-feedback loop generates the 6- to 10-Hz synchrony of MUs, possibly alone or in interaction with a supraspinal oscillator. This question is presently easier to approach because there are well-known facts on the signal flow around, and the rhythmical action within, the spinal stretch reflex loop (Durba et al. 2005; Hagbarth and Young 1979; Lippold 1970; Stein and Oguztoreli 1976).

For this loop such a role seems to some extent inevitable (Christakos et al. 2006a), considering: 1) the fairly fixed time relation between the Ia bursts and the decaying phase of the cycles of the 6- to 10-Hz force oscillation (velocity component); and 2) the self-oscillatory tendencies exhibited by this loop due to signal transmission delays, where the muscle delay (primarily) and the conduction delay compose a loop delay corresponding to a frequency in the 6- to 10-Hz range. In this case, in-phase Ia activities reflecting the ongoing force oscillation or tremor (Hagbarth and Young 1979; Koehler et al. 1984; Windhorst 1978) constitute a common 6- to 10-Hz synaptic input to the MNs.

In the case of antagonistic muscles acting around a joint, an involvement of coupled such loops is expected. Mechanical coupling is effected through the segment to which the two antagonists are attached, and neural coupling is also present through action in spinal circuits, such as those of reciprocal Ia inhibition. Longer loops (e.g., transcortical; Stein and Oguztoreli 1976) could also be responsible for rhythmical synchrony (at somewhat lower frequencies because the muscle delay is much longer than the conduction delay).

Regarding the possible interaction with a supraspinal oscillator, Gross et al. (2002) observed a flow of the above-mentioned 8-Hz signal from the level of MU activity (EMG) to those of the cerebellum and the somatosensory cortex. Muscle spindles with their tremor-related rhythmical activity thus seem to be part of the 6- to 10-Hz rhythm generator. This fact is in favor of the possibility of loop action, or interaction with a central oscillator, underlying the 6- to 10-Hz synchrony. Clearly, for such interactions, the degree of the involvement of the spinal stretch reflex loop in any given contraction will depend on the loop gain.

In general, a high sensitivity of primary spindle endings to minute length changes is known to exist (Christakos and Windhorst 1986; Kakuda 2000; Matthews and Stein 1969; Wessberg and Valbo 1995). On the other hand, evidence and arguments disputing 1) the adequacy of the loop gain in causing MU synchrony and 2) the appropriateness of the timing of the neural and mechanical events associated with loop tremor have been presented (Durba et al. 2005; Valbo and Wessberg 1996). However, in both our present study and our preceding study (2006a), the strength of the 6- to 10-Hz synchrony ranged from minimal to very large, sometimes being low and difficult to measure. The apparent absence of synchrony could therefore reflect differences in spindle sensitivity and Ia synaptic efficacy (i.e., in loop gain) among different contractions. Moreover, the above-assumed sequence of events during loop action (Christakos et al. 2006a) is based on well-known facts.

More generally, the frequency of the tremor synchrony within subjects is known to differ among different muscles, further arguing for an important role for loop action, even if a central generator is also involved. This view is in accord with the more general belief that central rhythms result from interactions between central and peripheral systems, or even reflect the action of peripheral generators (see review by McAuley and Marsden 2000; see also Sowman et al. 2006).

Functional relevance of the coherent 6- to 10-Hz rhythms

In line with Bernstein’s (1967) view, oscillations such as tremors have been considered in various studies advantageous in regard to linearization of muscle properties, execution and timing of movements, etc. (see review by Windhorst 2007). However, there is uncertainty with respect not only to such
issues, but also to the issue of rhythmic motor control, in spite of the existence of attractive hypotheses.

Thus the relevance of the coherent 6- to 10-Hz rhythms is unknown according to certain studies (e.g., Evans and Baker 2003), whereas McAuley et al. (1999) consider rhythmic control as one of many alternatives. At the same time, the hypothesis of Llinás and collaborators (1997, 2005) considers that intrinsic 5- to 12-Hz rhythms in the inferior olive act as a timing mechanism for complex movements and secure temporally coherent activities in motor circuits. Similarly, the hypothesis of Wessberg and Valbo (1993) assumes the 6- to 10-Hz movement rhythm to represent a series of bipolar pulses in motor command, effecting intermitted control. In line with this, Schnizler and Gross (2005) consider finger movements as a series of micromovements controlled by the cerebellothalamo-cortical loop. Notably, in a modeling study by Kistemaker et al. (2006), an intermittent control signal did provide faster movement and better agreement with experimental data.

According to our results, the 6- to 10-Hz neural rhythm that is manifested as force and movement components may to some extent reflect action in coupled spinal stretch reflex loops. This rhythm is projected centrally via group Ia afferents, thus resulting in corticomuscular coherence. Even in the absence of an interacting central generator, the central projections of this rhythm could provide a basis for spatially restricted control of the contractions of muscles acting around a joint.

A more specific application of elementary rhythmic control at spinal levels is suggested by our observation of MUs being recruited at the frequency of the 6- to 10-Hz synchrony. Accordingly, the in-phase membrane oscillations of MNs, whether caused by a central generator or loop action, or both, determine the recruitment rate of MUs in each muscle (Henneman 1979). Indeed, in preliminary experiments (Christakos et al. 2006b), we induced transient pauses in MU firing by varying the level of the voluntary force of the FDI muscle around the recruitment threshold of MUs. After a pause, each MU resumed firing with spikes near the minima of the 6- to 10-Hz force oscillation in a one-to-one relation, thus joining the group of active MUs showing in-phase components in the 6- to 10-Hz range.

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