Coupling of Oscillatory Activity Between Muscles Is Strikingly Reduced in a Deafferented Subject Compared With Normal Controls

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INTRODUCTION

Neurons within the sensorimotor cortex of monkeys and humans have been demonstrated to exhibit synchronous oscillatory activity in the 15- to 30-Hz range (Baker et al. 1997; Donoghue et al. 1998; Gastaut 1952; Jasper and Penfield 1949; Murthy and Fetz 1992, 1996a,b; Salmelin and Hari 1994; Sanes and Donoghue 1993). Such oscillatory activity is known to influence descending motor commands to the contralateral hand muscles, with power in the 15- to 30-Hz range of the cortical and electromyographic (EMG) activity showing a constant phase relationship (Baker et al. 1997; Conway et al. 1995; Hari and Salmelin 1999; Kilner et al. 1999, 2000, 2003; Murthy and Fetz 1992; Salmelin et al. 1997). This phase difference between the cortex and the periphery is consistent with the hypothesis that fast corticomotoneuronal connections mediate some of this coherence (Gross et al. 2000). This has led to the hypothesis that 15- to 30-Hz oscillations within the cortico-muscular network are generated in efferent, motor pathways.

Coherence in the 15- to 30-Hz range between activity recorded from sensorimotor cortex and EMG from contralateral hand muscles is thought to be at least partly responsible for coherence between EMGs recorded from different hand muscles (Kilner et al. 1999). Both cortico-muscular and muscle-muscle coherence in the 15– to 30-Hz range exhibit task-dependent modulations: coherence is abolished during finger movements and strongest during steady hold periods just after movement (Baker et al. 1997; Feige et al. 2000; Kilner et al. 1999, 2000, 2003). We have also shown that coherence is modulated by the degree of compliance in a precision-grip task (Kilner et al. 2000) with increased coherence observed when subjects gripped more compliant objects. We speculated that levels of coherence in the hold phase of this task might reflect important changes in sensorimotor state encompassing alterations in both grip force and digit position and hypothesized that rather than being a purely motor, effenter phenomenon, the level of coherence in the 15- to 30-Hz range could be modulated by sensory afferent inputs from the hand.

The current study tested the hypothesis that the oscillatory coupling between EMG activity recorded from different hand muscles in the 15- to 30-Hz frequency range is dependent on sensory inputs from the periphery. We recorded EMG activity of four hand muscles in 10 healthy control subjects and in a single deafferented patient while they performed a dynamic precision-grip task similar to the one we have used in previous studies (Fisher et al. 2002; Kilner et al. 1999, 2000, 2003). The coupling between the muscles as a function of the task was subsequently estimated using standard power and coherence spectral analysis. The study demonstrates a significant difference in the degree of EMG-EMG coherence between control subjects and the deafferented subject, with the deafferented subject having very low levels of coherence. Furthermore, the deafferented subject had a significantly lower level of EMG power in the 15- to 30-Hz bandwidth than the control subjects. These results are discussed in terms of the role of sensory feedback in the modulation and generation of oscillations within the motor system.

METHODS

Subjects

Experiments were performed on a single female patient, GL (51 yr) and on 10 healthy volunteers, aged 22–54 yr (5 female). All subjects were right-handed, each gave informed consent, and the recordings

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had local ethical committee approval. GL has had two severe episodes of extensive polyneuropathy at ages 27 and 31 (for an extensive clinical description see Forget and Lamarre 1987; further details are available at http://jacquespaillard.apinc.org/deafferented/index.htm).

In brief, clinically she has a total loss of touch, vibration, pressure, and kinesthetic senses below the neck and she has no tendon reflexes in the four limbs. Pain and temperature sensations are present that indicate selective impairment of the large-diameter peripheral sensory myelinated fibers. The motor fibers are not affected. Motor nerve conduction velocities and needle EMG investigation in the muscles of the arms are normal. H reflexes are absent in the legs. No sensory potentials could be recorded from the hands or the feet, and no sensory evoked potentials were evoked in cortical recordings in response to electrical stimulation of the upper limb peripheral nerves on either side. The results of a sural nerve biopsy revealed a severe demyelination affecting particularly the large fibers: the density of the myelinated fibers, 2,496 fibers/mm², was much lower than normal values (>6,000 fibers/mm²). The percentage of myelinated fibers >9 μm in diameter was also very small (0.31%) as compared with normal values (>18%).

**Behavioral task**

Subjects gripped two perspex levers of a spring-loaded manipulandum between the thumb and index finger of their right hand. Each lever was 110 mm long, 25 mm wide, and 5 mm thick. The tip of each lever was 65 mm from the shaft on which it rotated. The distance between the levers at rest was 50 mm. The index finger lever was free to rotate whereas the thumb lever was fixed. The index finger lever was attached by a steel spring to the manipulandum, such that moving the finger lever toward the thumb lever required an increasing force. The displacement of the finger lever was measured by potentiometers attached to the shaft. A card mounted on the manipulandum adjacent to the finger lever was marked with three lines, indicating the target positions for the finger lever, and these were clearly visible to the subject. The lines were marked at 0, 12, and 24 mm, where the 0 mm marker was aligned to the position of the finger lever at rest.

Subjects performed a hold-move-hold task (HMH). The level of compliance, ~0.0167 N/mm, of the finger lever was adjusted to be similar to the degree of compliance that had given maximal coherence values in the second of the two hold periods in a previous study (Kilner et al. 2000). Each trial of the HMH task was signaled by a computer beep which cued subjects to displace the index finger lever to the 12-mm target line and hold it there; this required a grip force of 1.35 N. Three seconds later a second computer beep cued subjects to further displace the index finger to the 24-mm target line and hold it there. This required a grip force of 1.55 N. A third computer beep, 5 s later, indicated to the subject that the trial was over. Control subjects performed four consecutive blocks of 25 trials in a single session. GL performed the same task in two sessions in each of which she performed four consecutive blocks of 25 trials. There was a 2-h break between the sessions. However, only data from the first session were used for any statistical comparison with the control groups. This was to ensure that all subjects had equivalent data sets obtained with the same experimental protocol. The data from the second session was used to confirm that the results obtained in the first session were reproducible (see Fig. 2, E–G).

**Recordings**

Surface EMGs were recorded using bipolar electrodes from four hand muscles: two intrinsic hand muscles [abductor pollicis brevis (AbPB), first dorsal interosseous (1DI)] and two extrinsic [Flexor digitorum superficialis (FDS) and extensor digitorum communis (EDC)]. Surface EMG activity was amplified (gain: 0.5–10 K), high-pass filtered at 30 Hz, and then sampled at 5 kHz by a PC computer fitted with a 1401+ interface (CED, Cambridge, UK). Finger lever position was also recorded (sampling rate: 5 kHz).

**Analysis**

Off-line, finger position signals were examined by eye; trials in which subjects did not perform the task correctly were rejected before further analysis.

EMG activity was rectified and then all channels were down sampled to an effective sampling rate of 200 Hz, after first low-pass filtering the data at 80 Hz. These signals were subsequently used for spectral analysis.

Power spectra and estimates of the coherence between all the rectified and downsampled EMG signals were calculated over a sliding 1.28-s time window with a 256-point FFT. These were then averaged across trials aligned to trial onset (as in Kilner et al. 2000). The time window was moved through the task in 0.1-s steps. As between-subject variance can be large for the spectral power measure, we were averaging across subjects the power spectra were transformed such that the value at each time-frequency bin was expressed as a percentage of the total power.

The current study tested the null-hypothesis that the patient GL would have the same level of coherence between EMGs in the 15- to 30-Hz frequency range as control subjects. Our previous studies have shown that 15- to 30-Hz coherence between muscles is greatest during the second hold period after movement (Kilner et al. 1999, 2000, 2003) and we therefore concentrated the analysis on this period of interest. To this end, we have tested the null hypothesis that coherence estimates and spectral power in the second hold period of the HMH task, between 4 and 6 s after trial onset, would be the same in control subjects and in GL. As there was only a single deafferented subject, we were unable to use standard statistical tests to test for differences between the control subjects and the single deafferented subject. Unlike previous studies however we were unable to use the general linear model approach (Crawford and Garthwaite 2002) as coherence data are not normally distributed because it is a bounded measure (0–1). Therefore all statistical tests were limited to a nonparametric binomial test of the hypothesis that differences between GL and healthy controls are equal to zero with a 50% probability (Howell 1997).

**RESULTS**

**Task performance**

Figure 1, A and B, shows the index finger lever positions of the 25 trials of the first block of the HMH task for a single healthy subject (SI) and GL, respectively. Although there was a slight increase in the variance of finger lever position during the initial movement to target in the first 0.5 s for GL compared with SI, there was no qualitative difference in the variance of the finger lever position during either of the steady hold periods. Indeed during both steady hold periods, GL had a slightly reduced, although not significant, degree of variance than the healthy controls. Figure 1C show the mean rectified EMG activities of the four hand muscles for SI and Fig. 1D for GL. Although in general there was a good correspondence between the modulation of each of the EMGs with respect to the task demands in both GL and the representative control, SI, there was a slight increase in the overall amplitude of EMG activity for GL compared with SI. This was particularly clear for the extrinsic finger muscles FDS and EDC.

**Analysis of single-subject data**

Figure 2A shows the time-frequency map of the coherence between the 1DI and AbPB muscles collected from a single
control subject, S1. As expected from previous studies, the coherence was restricted to the 15- to 30-Hz range and showed clear task-dependent modulation. Coherence was abolished during the movement but was present during both hold periods and was greatest during the second hold period after the movement. This is in complete contrast to the corresponding and was greatest during the second hold period after the movement but was present during both hold periods clear task-dependent modulation. Coherence was abolished coherence was restricted to the 15- to 30-Hz range and showed cant coherence was weak and showed no clear modula-

Figure 2 shows coherence spectra between EMGs from 1DI and AbPB for S1 (solid) and for GL (dotted lines). Figures 2F and G show the power spectra for the two muscles. The coherence and power spectra were averaged over the 2-s time window during the second hold period shown in Fig. 2, A and B. Compared with S1, GL showed no clear significant coherence peaks in the 15- to 30-Hz range (compare dark solid with dotted and light solid lines in Fig. 2E). S1 also had clear peaks in the 15- to 30-Hz range in the power spectra of both 1DI and AbPB (Fig. 2, F and G, dark solid lines). The power spectra of the corresponding EMGs from GL showed no obvious peaks in the 15- to 30-Hz range (Fig. 2, F and G, dotted and light solid lines).

Analysis of grouped data

Figure 3, A–F, shows the difference in EMG-EMG coherence during the second hold period between control subjects (—) and GL (···) for the six EMG-EMG pairs. In all plots, the level of EMG-EMG coherence in GL was visibly smaller than in the control subjects. This was particularly marked for estimates of coherence in the 15- to 30-Hz range. These data are summarized in Fig. 3G. In all EMG-EMG pairs, coherence was on average greater for healthy controls than for GL in the 15- to 30-Hz range (~20-Hz mid-range) this was significant for four out of the six muscle pairs (P < 0.05 binomial test with P = 0.5). Coherence was also significantly reduced in the 7.8–12.5 Hz (~10 Hz) bandwidth for the 1DI-FDS and 1DI-EDC pairs. In contrast, GL had significantly higher coherence than normals in the 7.8- to 12.5-Hz bandwidth for the AbPB-EDC pair. No EMG-EMG pair showed a significant difference in coherence between GL and healthy controls in the 30.5- to 45.5-Hz (~40 Hz). Similar results were obtained for the first hold period, averaged over a time window from 0.5 to 2 s (data not shown). Coherence in the 15- to 30-Hz bandwidth was again significantly greater in healthy controls than for GL in three of the six muscle pairs: 1DI-FDS, AbPB-FDS, and EDC-FDS (P < 0.05 binomial test with P = 0.5) and was significantly greater in controls than GL in the 7.8- to 12.5-Hz bandwidth in two of the six muscle pairs (P < 0.05 binomial test with P = 0.5). In no muscle pair was GL’s coherence greater than that for the controls.

Figure 4 shows the corresponding data for the normalized spectral power. Figure 4, A–D, shows that power in the 15- to 30-Hz bandwidth was significantly reduced in GL compared with control subjects for all muscles (P < 0.05 binomial test with P = 0.5; Fig. 4E). In addition for 1DI, AbPB, and FDS muscles GL had significantly smaller percentage of total power in the 7.8- to 12.5-Hz range, and for 1DI, GL had a significantly smaller percentage of power in the 30.5- to 45.5-Hz range (P < 0.05 binomial test with P = 0.5; Fig. 4E).

DISCUSSION

In the current study, we compared the level of EMG-EMG coherence in the 15- to 30-Hz range between different hand muscles during the steady hold period of a precision-grip task.
performed by control subjects and by a deafferented patient, GL. The results show that there was a clear and significant difference between the level of EMG-EMG coherence in the 15- to 30-Hz range between controls and GL. The deafferented subject showed very low levels of between-muscle coherence that rarely reached significance. Furthermore, in GL, there were significantly smaller amounts of EMG power both in the 15- to 30-Hz range and the 7.8- to 12.5-Hz range compared with healthy controls. Analysis of the power and coherence spectra in the Piper frequency range, 35–60 Hz (Brown et al. 1998), revealed that in none of the comparisons between GL and controls were GL’s percentage of total power or amplitude of EMG-EMG coherence significantly greater than in controls ($P < 0.05$ binomial test with $P = 0.5$; data not shown).

These results are particularly interesting in the light of a previous study that showed that when cutaneous input from the digits was blocked by digital anesthesia, the level of EMG-EMG coherence was significantly reduced although not abolished (Fisher et al. 2002). In this study, the authors also found that subjects showed a significant decrease in their ability to perform the precision-grip task under the conditions of reduced somatosensory input (also cf. Monzée et al. 2003). It is important to stress that this was not the case in the current study. Although GL has virtually no large-fiber peripheral sensory feedback, she had no difficulties in performing the task under visual control, and her task performance was comparable with that of the normal subjects investigated (compare Fig. 1, A and B).

In contrast to the results of Fisher et al. (2002), the decrease in EMG-EMG coherence in the 15- to 30-Hz range in GL was accompanied by a significant decrease in EMG power in the same range. This difference may reflect the extent and nature of the sensory loss in the two studies. The digital nerve block, as used by Fisher et al. (2002), interrupted inputs from digit joint and cutaneous receptors but did not affect muscle or tendon afferents. It is known that proprioceptive acuity is more impaired by the absence of muscle afferent inputs than by the absence of joint and cutaneous inputs (Gandevia et al. 1983), and clearly the deafferention in GL is far more extensive than in the subjects investigated by Fisher et al. (2002).

We are aware of only one previous study that has reported oscillatory activity in muscle activity recorded from a deafferented subject. Farmer et al. (1993) reported that there were no clear differences between a deafferented patient, IW, and

![FIG. 2. Single subject data: time-frequency maps of coherence between first dorsal interosseous (1DI) and abductor pollicis brevis (AbPB). A and B: the time-frequency maps of coherence between 1DI and AbPB for S1 and GL, respectively, estimated over 100 and 95 trials, respectively. In these plots frequency is on the y axis and time is on the x axis. The greyscale of each image indicates the degree of coherence, with white indicating higher coherence as in the scalebar to the right of B. The dotted white square describes the time and frequency bins used for further analysis. C and D: the average position of the index finger lever for S1 and GL and alignment to the time-frequency coherence maps shown in A and B. E: the coherence spectra between 1DI and AbPB averaged over the time window indicated by the white dotted box in A and B for S1, dark solid line and for both of GL’s sessions, the dotted and light solid lines. The solid horizontal line shows the 95% confidence level (Kilner et al. 1999). F and G: the corresponding power spectra for 1DI and AbPB, respectively. To allow comparison of power spectra, they have been normalized such that the power in each frequency bin is expressed as a percentage of the total power.](http://jn.physiology.org/doi/10.1152/jn.00197.2004)
healthy controls in the degree of short-term and oscillatory synchrony in the 15- to 30-Hz range between single motor units belonging to the same intrinsic hand muscle. At first glance, therefore it would appear that the results of the current study are at odds with those reported in Farmer et al. (1993). However, the studies differ at the level of investigation. The results presented here concern synchrony between EMGs from different hand muscles recorded with surface electrodes, whereas Farmer et al. (1993) reported synchrony between single motor units within the same hand muscle. In light of these differences the two sets of findings are not necessarily inconsistent. Thus it would appear that although there may oscillatory drives synchronizing motor-unit activity within GL’s motor pools, there is no significant common drive coupling 15- to 30-Hz oscillations across muscles.

The existence of both EMG-EMG coherence and corticomuscular coherence in the 15- to 30-Hz range are now well established and have been extensively reported as have task-dependent modulations in such coherence estimates (Baker et al. 1997; Conway et al. 1995; Feige et al. 2000; Fisher et al. 2002; Kilner et al. 1999, 2000, 2002; Mima et al. 2000; Salenius et al. 1997). There is now also a consensus that the oscillatory activity that can be recorded in the EMGs of the hand and forearm muscles mainly originates in the hand area of the primary motor cortex (Hari and Salenius 1999; Kilner et al. 1999, 2000; Salemelin and Hari 1994), and there is evidence that fast corticomotoneuronal connections may mediate some of this coherence (Gross et al. 2000). As far as we are aware, GL has an intact motor cortex, and TMS studies have shown that she has normal conduction delays from cortex to muscle (Forget 1986), suggesting a functionally normal corticospinal pathway. However, she has a greatly reduced level of 15- to 30-Hz oscillatory activity in her EMG activity and has virtually no EMG-EMG coherence, suggesting that the generation of this activity in the motor cortex and/or its propagation within the motor system might be critically dependent on the presence of afferent inputs.

In previous studies, we have shown that the level of both corticomuscular coherence, EMG-EMG coherence and coherence between individual motor units of the same muscle (Kilner et al. 2000, 2002) in the 15- to 30-Hz range were all modulated by the compliance of the object being manipulated. Coherence in the 15- to 30-Hz range was always greatest during steady hold periods after manipulation of compliant objects and was significantly reduced during steady hold periods after manipulation of noncompliant objects. To hold and manipulate compliant objects, precise coordinated control of both grip force and grip aperture (i.e., digit position) is needed.
and the need for such control becomes more demanding when very compliant objects are handled as small changes in grip force will lead to large changes in digit position with increased risk of loosing a secure grasp of the object (Monzé et al. 2003; Westling and Johansson 1984). In the context of the current study, it is interesting to note that in the book “Pride and a Daily Marathon” (Cole 1991) which is a biographical account of the life of another deafferented patient, IW, Cole describes IW’s increased difficulty in manipulating compliant objects over noncompliant ones. “He held cups and mugs by their body, not by their handle. ... Plastic or polystyrene cups weren’t easy to drink from because of their lack of rigidity. It was too difficult to judge how to put enough force into a grasp to hold an object without crushing it.” Likewise, GL uses a cigarette holder to avoid crushing her cigarettes between her fingers.

We have previously argued that oscillatory synchrony may characterize a low-level control system that engages and then maintains the particular level of activity in the large number of synergistic muscles that are needed to exert efficient grip between the digits (Kilner et al. 2002). Such a control system would be highly sensitive to changes in finger position signaled by cutaneous, joint, and muscle afferents as well as other inputs from the hand. The present results suggest that this oscillatory control system cannot exist in the complete absence of somatosensory afferent inputs. These afferent inputs may normally serve to modulate or even be involved in the generation of 15- to 30-Hz oscillations in the motor system. Such a hypothesis is consistent with the reduced level of EMG-EMG coherence after digital nerve block (Fisher et al. 2002) and is further supported by the well-documented observation that there is a large burst of such oscillatory activity in the hand area of M1 after median nerve stimulation (Hari and Salenius 1999; Salenius et al. 1997).

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REFERENCES


