Modulation of human corticomuscular beta-range coherence with low-level static forces

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Summary

Although corticomuscular synchronization in the beta range (15–30 Hz) was shown to occur during weak steady-state contractions, an examination of low-level forces around 10% of the maximum voluntary contraction (MVC) is still missing. We addressed this question by investigating coherence between electroencephalogram (EEG) and electromyogram (EMG) as well as cortical spectral power during a visuomotor task. Eight healthy right-handed subjects compensated isometrically static forces at a level of 4% and 16% of MVC with their right index finger. While 4% MVC was accompanied by low coherence values in the middle to high beta frequency range (25–30 Hz), a significant increase of coherence mainly confined to low beta frequencies (19–20 Hz) was observed with force of 16% MVC. Furthermore, this increase was associated with better performance, as reflected in decreased relative error in force during 16% MVC. We additionally show that periods of good motor performance within each condition were associated with higher values of EEG–EMG coherence and spectral power. In conclusion, our results suggest a role for beta-range corticomuscular coherence in effective sensorimotor integration, thus stabilizing corticospinal communication.

Introduction

It has been known for a long time that oscillatory activity over a range 15–35 Hz occurs in the primate sensorimotor cortex (Adrian & Matthews, 1934; Murthy & Fetz, 1992, 1996; Sanes & Donoghue, 1993). These oscillations are synchronized to activity in motor units (Farmer *et al.*, 1993; Conway *et al.*, 1995; Baker *et al.*, 1997; McAuley *et al.*, 1997; Gross *et al.*, 2000). This synchronization can be assessed by calculation of coherence between electroencephalogram (EEG) and electromyogram (EMG) (Nunez *et al.*, 1997). The strong coupling to muscles also implies the view of the sensorimotor cortex as an integrative operator which controls force output (Ashe, 1997). It is therefore not surprising that different force levels are associated with different oscillations in the motor system. While gamma corticomuscular coherence (CMC) was found during maximal and submaximal contraction levels (Brown *et al.*, 1998), CMC in the beta range (15–30 Hz) is restricted to periods of weak to moderate maintained contractions (Conway *et al.*, 1995; Baker *et al.*, 1997; Salenius *et al.*, 1997; Brown *et al.*, 1998; Halliday *et al.*, 1998; Kilner *et al.*, 1999; Mima & Hallett, 1999; Gross *et al.*, 2000; Kristeva-Feige *et al.*, 2002).

Interestingly, many previous studies in humans investigated these low-level forces around a fixed value of 1.6 N (Baker *et al.*, 1997; Kilner *et al.*, 2000; Fisher *et al.*, 2002; Riddle & Baker, 2005) not considering interindividual differences in maximum force production. Although a normalized approach has already been undertaken in a range of 10–60% of maximum voluntary contraction (MVC) (Brown *et al.*, 1998; Mima *et al.*, 1999; Stancak *et al.*, 2005), we sought to analyse CMC during steady-state forces below and just above 10%

MVC. This refers to the observation that neuronal activity in the monkey motor cortex best correlates with fine force output over a narrow range during precision grip tasks (Hepp-Reymond *et al.*, 1978, 1989; Maier *et al.*, 1993). Based on this high sensitivity of the motor cortex neurons to fine forces, we investigated CMC during low-level static forces of 4 and 16% MVC. For the first time we provide evidence that an increase of force within the low-level range is associated with enhanced coupling between sensorimotor cortex and muscle, as reflected by increased magnitude of beta-CMC.

Methods

We investigated eight healthy subjects (mean age 24 ± 2 years, three men) whose right-handedness was confirmed using the Oldfield questionnaire (Oldfield, 1971). In accordance with the declaration of Helsinki all subjects gave written informed consent prior to the experiment, which was approved by the local ethics committee of the University of Freiburg.

Experimental paradigm

Prior to the experiment, the MVC of each subject was determined using an isometric force transducer. During the task itself, subjects had to isometrically compensate upwards directed static forces of 4 and 16% MVC that were produced by a custom-built manipulandum (Fig. 1A and C). The right index finger had to keep the ring in its initial reference position (flexion of the right index finger at the metacarpophalangeal joint) for 12 s under feedback of both target and actual position displayed on a computer screen (Fig. 1B). This was accomplished by keeping a fixed green circle (reference position of the ring) and a moving white circle (actual ring position) congruent on the screen at any time, indicating that an applied vertical force was
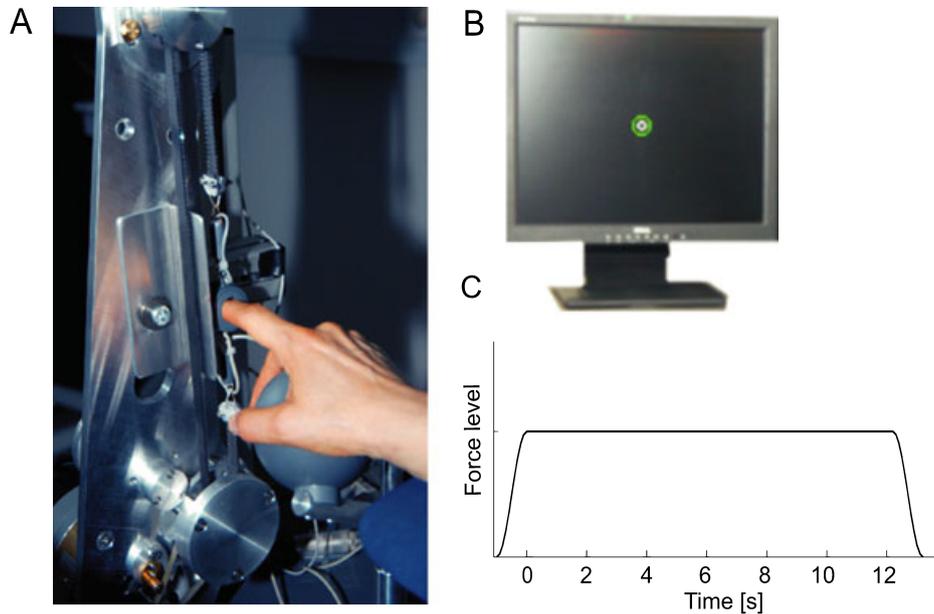
FIG. 1. (A) Custom-built manipulandum with tooth-belt-driven ring and synthetic sphere. (B) Visual feedback of actual (inner white circle) and reference (outer green circle) position of the ring. An applied force is perfectly compensated when both circles remain congruent. (C) Force profile of the static forces generated by the manipulandum. After a smooth increase in force up to 4 or 16% MVC, the subject has to maintain this force level for 12 s by keeping the ring in its central position.

compensated by the same force exerted in the opposite direction. The sensitivity of the visual feedback with respect to the finger position was 2.85 mm for 1 mm of ring displacement.

After a training session each subject performed a series of 35 trials per condition, with 5–10 s of resting time in-between to avoid muscle fatigue. The target position of the index finger was always the same in order to differentiate between finger displacement and force (Riddle & Baker, 2006).

Recordings

We used 20 Ag–AgCl electrodes to record electrical potentials over the left sensorimotor cortex referenced to Cz with ground at FzA (international 10–20 system; Synamps 2, NeuroScan, El Paso, TX, USA). The EEG data were filtered online (0–200 Hz) and sampled at a rate of 1000 Hz. Bipolar surface EMG from first dorsal interosseus (FDI) and pars indicis of flexor digitorum superficialis of the right forearm were recorded (same filter and sampling rate as for EEG). To avoid contamination of the data with eye movement artefacts, the electrooculogram (EOG) was also recorded (same filter and sampling rate as for EEG). Electrode impedances were kept stable under 5 kΩ. As behavioural data, the set point of force, indicated by the applied target force (TF), and the actual exerted force (EF) were stored along with the actual position of the ring.

Data analysis

To eliminate transient effects due to the force ramp phase, a marker was set semi-automatically at the beginning of the hold period and the following 9.728 s of continuous EEG data were further divided into 19 segments of 512 ms length. This resulted in a frequency resolution of 1.96 Hz. Segments were visually inspected trial-by-trial to exclude those contaminated by eye movements or muscle artefacts. For each subject 300 artefact-free segments were used for averaging.

A transformation into the reference-free current source density distribution (CSD) was performed to avoid smearing effects and to obtain the underlying cortical activity (Nunez et al., 1997). The CSD algorithm was calculated using spherical spline interpolation (Perrin et al., 1989). Subsequently, the discrete 512-point Fourier transform was calculated for each segment in a frequency range from 1 to 500 Hz. The EMG signal was rectified because full wave rectification reflects the temporal firing pattern of grouped motor units (Halliday et al., 1995). Additionally, the muscle signal was band pass filtered offline at 5–200 Hz before rectification.

Coherence values (Coh) between EEG signals and rectified EMG were calculated according to the following equations:

$$\text{Coh}_{c1,c2}(f) = \frac{|S_{c1,c2}(f)|^2}{|SP_{c1}(f)| \times |SP_{c2}(f)|} \quad (1)$$

where

$$S_{c1,c2}(f) = \frac{1}{n}\sum_{i=1}^{n} C1_i(f)C2_i^*(f) \quad (2)$$

thus $S_{c1,c2}(f)$ is the cross-spectrum for the EEG signal channel c_1 and the rectified EMG signal in channel c_2 at a given frequency f with C_1 and C_2 representing the respective Fourier-transformed data. $SP_{c1}(f)$ and $SP_{c2}(f)$ are the respective power spectra for c_1 and c_2 at the same frequency.

According to these equations, coherences between all EEG electrodes and rectified EMG of the two muscles were calculated. For further analysis we concentrated on the EEG–EMG electrode pair showing the highest degree of synchronization.

To test for significant values the confidence level (CL) was considered (Rosenberg et al., 1989) as indicated by

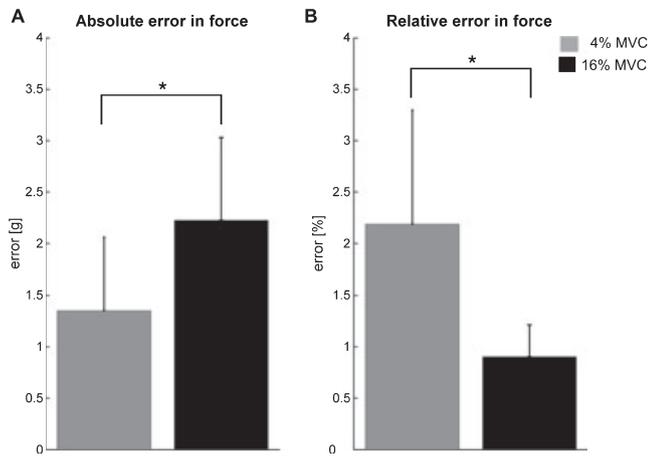$$CL(\alpha) = 1 - (1 - \alpha)^{\frac{1}{n-1}} \quad (3)$$

FIG. 2. (A) Mean absolute error in force (eight subjects) for both conditions, 4% and 16% MVC. (B) Corresponding mean relative error (see Results). Asterisks denote significant group differences ($P < 0.05$, $n = 8$, Wilcoxon signed rank test). Note the decrease in relative error of approximately 50% from 16 to 4% MVC.

where n is the number of segments and α is the desired level of confidence. Significant coherence was represented by values above the 95% confidence limit.

The spectral power (SP) for a given channel (c) was derived using

$$SP_c(f) = \frac{1}{n}\sum_{i=1}^{n} C_i(f)C_i^*(f) \qquad (4)$$

where C_i represents the Fourier transformed channel c for a given segment i and '*' indicates the complex conjugate. To demonstrate changes in the SP associated with CMC we analysed values for the same electrode which yielded peak coherence.

For analysis of motor performance, TF and EF were off-line filtered at 0.5–30 Hz to eliminate artefacts and offsets. Then the error in force (E) was evaluated according to

$$E = TF - EF \qquad (5)$$

Finally, the root mean square error (RMSE) was calculated using

$$RMSE_i = \sqrt{\sum_{k=1}^{s} \frac{(E_{k,i})^2}{s}} \qquad (6)$$

where $i = 1 \ldots n$ is the segment number, $k = 1 \ldots s$ is the sampled point in the actual segment i and $s = 512$ is the number of sampled points in each segment. To compare the motor performance between the two force conditions, the resultant absolute error values were related to the individual desired TF of each subject for 4 and 16% MVC, respectively.
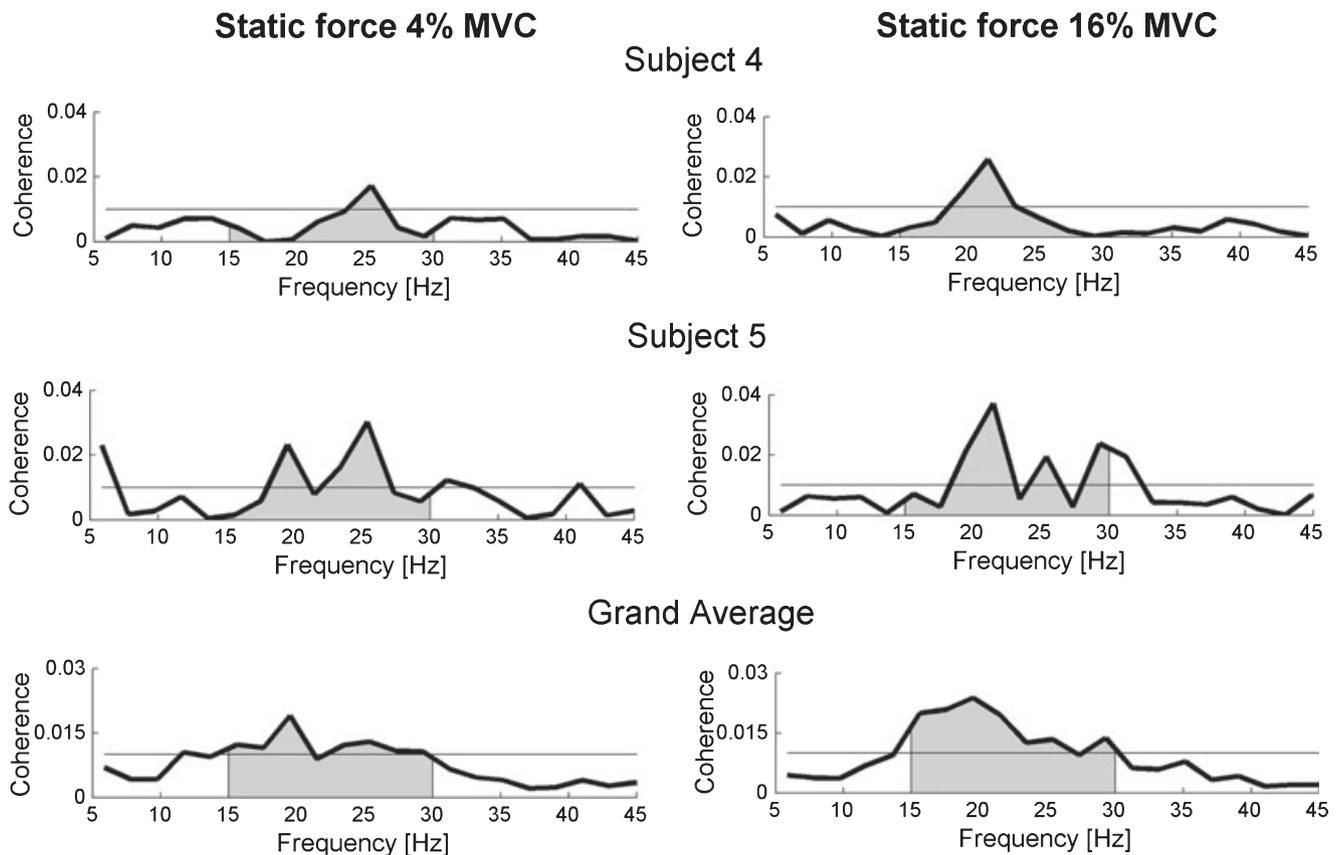

FIG. 3. Frequency–coherence plots of EEG − EMG coherence for 4% (left panel) and 16% (right panel) MVC for subjects 4 and 5, as well as for all eight subjects (Grand Average). Beta range (15–30 Hz) is marked in light grey; horizontal lines indicate the 95% significance level. During 4% MVC moderate coherence values occur at middle to high beta-frequencies. During 16% MVC the maximum coherent peak is significantly increased ($P < 0.05$, $n = 6$, Wilcoxon signed rank test), predominantly at lower frequency.
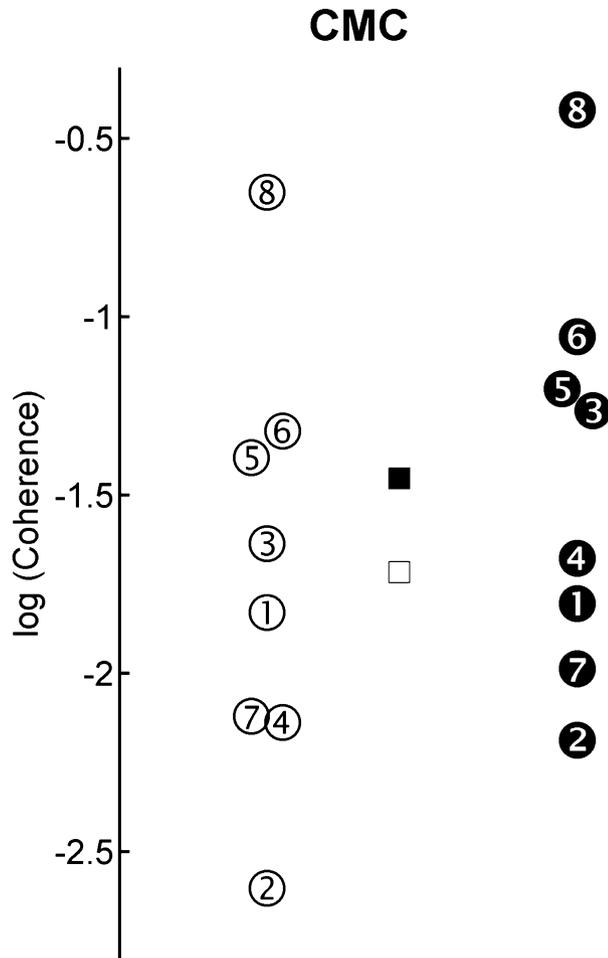
CMC

FIG. 4. Individual values of coherent area above the significance level of 95% for all eight subjects (1–8). Empty circles highlight the 4% MVC, filled circles the 16% MVC condition, and squares are the respective mean values for each condition. Note that each subject showed a clear increase of CMC with 16% MVC except for subject one.

The position values of the moving ring within each segment were evaluated in an analogous manner, with

$$RMSE_i = \sqrt{\sum_{k=1}^{k=512} \frac{(P_{k,i} - mean(P)_{k,i})^2}{512}} \qquad (7)$$

where P represents the respective position value of sample point k in segment number i.

To investigate any possible link between performance and CMC we then divided the total set of 300 segments per condition into two halves based on RMSE, one corresponding to 150 segments with low errors ('good' segments) and one containing 150 segments with high errors ('bad' segments). CMC and SP were then calculated for these groups for each subject. This method was applied because the relationship between the continuous numerical values of CMC and performance error cannot be compared between subjects, i.e. a low CMC value in one subject may be a high one in another subject.

Statistical analysis

The changes in CMC, SP and performance were tested for significance using the non-parametric paired Wilcoxon signed-rank test.

A probability value of $P < 0.05$ was considered significant. The null hypothesis that a distribution symmetric around zero is responsible for the differences between the matched samples of 4 and 16% MVC was tested. To compare the two conditions, the area under the coherence curve and above the significance level, as well as the area under the power curve were calculated in the beta-range. To account for the skewed distribution of CMC values observed, the individual area values were transformed using

$$\log(0.0001 + Area_{Coherence}) \qquad (8)$$

before changes in CMC were tested. This procedure allows avoiding overestimation of large CMC values during application of Wilcoxon's signed-rank test where pairwise subtractions are ranked.

Results

Behavioural performance

The absolute error in force, indicated by the RMSE of the difference TF − EF, was higher for 16% than for 4% MVC (Fig. 2A; $P = 0.0078$, Wilcoxon signed-rank test; $n = 8$ throughout the text). We then normalized the absolute errors to the TF individual values computed on the MCV of each subject and obtained a mean of 63 ± 15 g for 4% MVC and 250 ± 59 g for 16% MVC. As shown in Fig. 2B this normalization yielded a significant decrease of the relative error with increase in force ($P = 0.0078$, Wilcoxon signed-rank test).

The RMSE of the ring's position averaged over eight subjects revealed significantly lower values for 4% (0.13 ± 0.06 mm) than for 16% MVC (0.18 ± 0.05 mm; $P = 0.0391$, Wilcoxon signed-rank test).

Corticomuscular coherence and spectral power with 4 and 16% MVC

Overall significant broad-band beta-range CMC was found for both conditions. The maximal coherent activity was generally confined to electrode pairs C1/FDI or C3/FDI. Original coherence spectra of two individuals and the pooled data (Grand Average) are displayed in Fig. 3.

For the 4% MVC condition, the predominant peak of coherence was found in the middle to high beta-range (24.6 ± 3.6 Hz). In contrast, for 16% MVC maximum coherent activity was significantly shifted to lower beta (20.5 ± 4.1 Hz; $P = 0.0313$, Wilcoxon signed-rank test). While two subjects showed single peaks (see example in the upper panel) the remaining six displayed several, although smaller, maxima in the beta-range (see example in the middle panel). The crucial difference between the two conditions was an amplitude increase of beta CMC with 16% MVC for all eight subjects. This proved to be true for the size of the dominant peak as well as for CMC area. Figure 4 displays the area values for 4% (mean, 0.045; range, 0.002–0.221) and for 16% MVC (mean, 0.079; range, 0.006–0.377). The difference between both was significant ($P = 0.0078$, Wilcoxon signed-rank test). Correspondingly, the relative area increase, i.e. the absolute difference in CMC divided by the CMC value of 4% MVC, was doubled ($192 \pm 164\%$ on average). In contrast to these changes in coherence, the statistical analysis revealed no significant differences in SP between the two conditions.

Relationship between performance, corticomuscular coherence and spectral power

For 'good' segments during 16% MVC, significantly higher CMC and SP amplitude in the beta-range were obtained when compared with
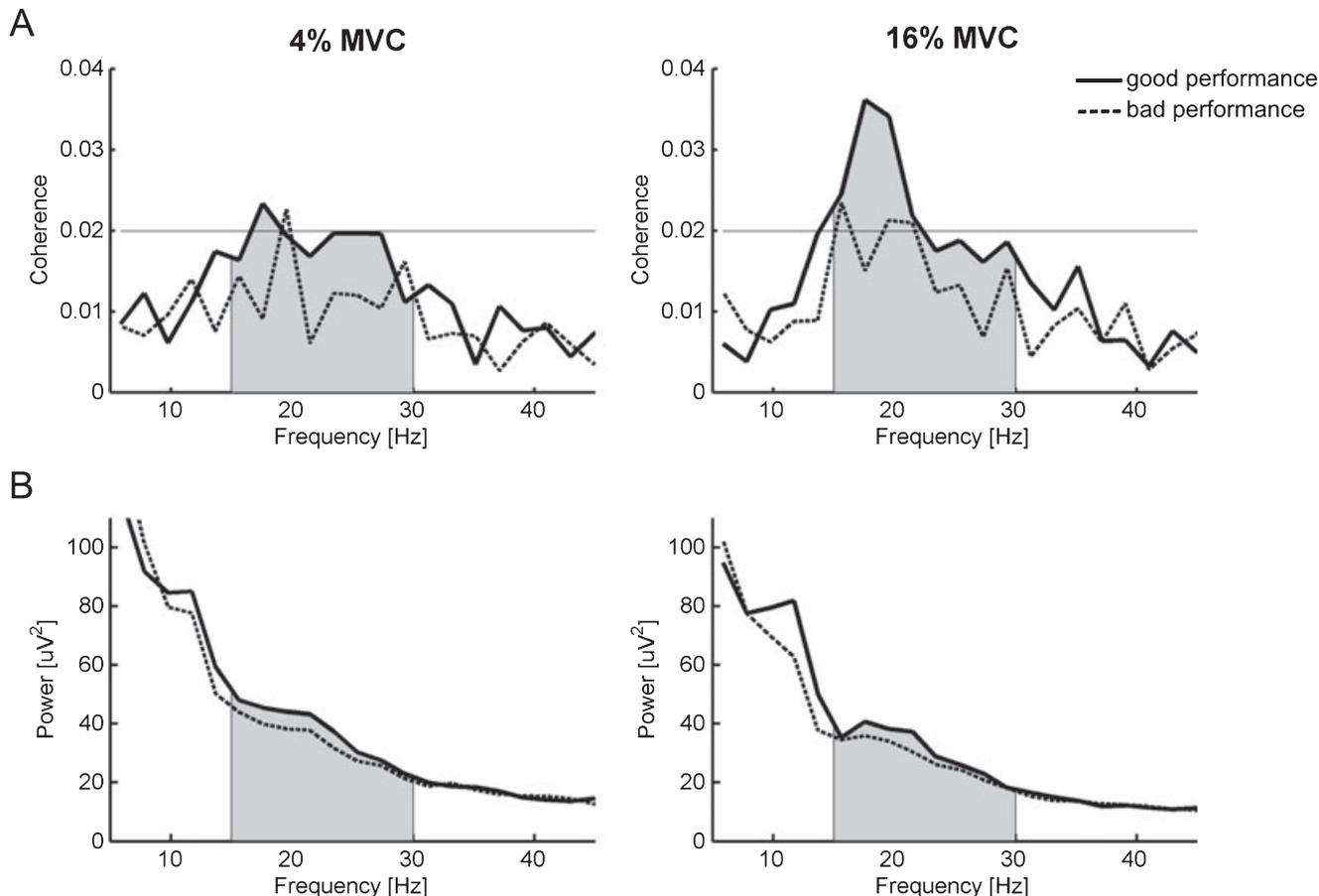
FIG. 5. (A) EEG–EMG coherence and (B) EEG spectral power during 150 segments of 'good' performance (solid line) and 150 segments of 'bad' performance (dashed line) for 4 and 16% MVC. The beta-range (15–30 Hz) is marked in grey and 95% significance level is indicated by horizontal lines.

'bad' segments (Fig. 5; CMC, $P = 0.0156$; SP, $P = 0.0078$, Wilcoxon signed-rank test). During the 4% MVC condition, a significant increase during 'good' segments was observed for SP ($P = 0.0156$, Wilcoxon signed-rank test) while an increase in CMC occurred in five subjects only ($P = 0.250$, Wilcoxon signed-rank test). Furthermore, a prominent SP peak in the alpha band (11–12 Hz) during good performance was markedly reduced in periods of bad performance for both 4 and 16% MVC (Fig. 5).

Discussion

The aim of our study was to investigate possible modulations of beta-range CMC during low-range static forces. Our results revealed three main findings. First, the CMC increased significantly in amplitude from 4 to 16% MVC without changes in the cortical location of the coherent activity. Furthermore, a significant shift of the CMC frequency to lower beta-range occurred with higher force. Second, the amplitude increase in CMC for 16% MVC as compared with 4% MVC was associated with a better motor performance, as revealed by the significantly smaller relative errors in force for 16% MVC. Third, within both conditions higher CMC was associated with 'good' segments, i.e. with better performance.

Only few studies have focused on the CMC modulation with force. Some of them have shown a discrete shift in the CMC frequency from beta (*c*. 25 Hz) to low gamma (*c*. 40 Hz) with increase from weak (20–40% MVC) to strong (above 60% MVC) steady-state contractions (Brown *et al.*, 1998; Brown, 2000). In another study, no changes in

CMC amplitude and frequency were reported within the force range from 10 to 60% MVC (Mima *et al.*, 1999). These studies did not consider forces under 10% MVC. Such low force ranges have been shown in primates to be a particular feature of primary motor cortex activity (Hepp-Reymond *et al.*, 1989; Maier *et al.*, 1993; Ashe, 1997). As with low-level forces, deviations from the desired TF occur easily, and rapid corrective reactions are required. This is incompatible with a rigid state or some kind of automatic process in the motor system. In fact, the higher CMC frequency for 4% compared with 16% MVC suggests that more focal activity in subpopulations of neurons is responsible. Based on the finding that the oscillation amplitude decreases with increasing frequency, rapidly oscillating cell assemblies are believed to comprise fewer neurons (Singer, 1993; Uhlhaas & Singer, 2006). Additionally, modelling studies (Lopes, 1991; Traub *et al.*, 1996) as well as physiological data (von Stein & Sarnthein, 2000) showed a confinement of synchronous high-frequency oscillations to local networks.

Three alternative interpretations can be considered for the higher CMC amplitude for 16% compared with 4% MVC. First, larger corrective movements in the 4% MVC condition may attenuate CMC. However, our statistical analysis proved the contrary, as for 16% MVC higher values of RMSE for the ring position were found and thus larger instabilities. Furthermore, we only found view segments characterized by outliers, suggesting a constant level of instabilities across trials. Second, the tuning of motor unit firing-rate to low beta-frequencies could theoretically boost CMC during 16% MVC. However, two findings argue against this hypothesis: (i) motor units

in the FDI start firing at a mean rate of 8.4 ± 1.3 Hz and this rate increases by 1.4 ± 0.6 Hz for each 100 g force change (Milner-Brown et al., 1973); and (ii) as reported in the same study, recruitment of additional motor units was the major mechanism of force production in the low-level force range. Therefore, we assume that the mean force of 250 g during 16% MVC is most probably associated with firing rates lower than 15 Hz. Third, and most reasonable in our view, the amplitude increase of CMC in the low beta-range for 16% MVC as compared with 4% MVC suggests a stronger binding between cortical and motor neurons. Several studies favour this interpretation. Recently, we provided evidence that the beta-range corticomuscular coherence is a mechanism for effective corticospinal integration (Kristeva et al., 2007). Previous studies also found that low-frequency beta-oscillations during visuomotor tasks bind multiple cortical areas into a large-scale network and are particularly suitable to promote effective information processing (Classen et al., 1998; Brovelli et al., 2004).

In the framework of effective processing, it is important to emphasize that in our study higher CMC was accompanied by better motor performance. This proved to be true for 16% MVC, as reflected in the smaller relative error in force compared with 4% MVC (Fig. 2). Moreover, within each condition periods of lower absolute error tended to be associated with higher CMC. For 4% MVC this was only observed as a tendency because of statistical limitations occurring with generally low CMC values and with the division into sets of 150 segments, which yields higher confidence levels. However, we stress that low coherence values during steady-state forces are a frequently observed phenomenon (Kilner et al., 2000; Kristeva et al., 2007; Omlor et al., 2007). Regardless, the difference between 'good' and 'bad' segments becomes clearly evident in Fig. 5. This is in line with our recent study showing significantly higher values of beta-range CMC and SP with good performance (Kristeva et al., 2007). A similar connection between coherence and precise movements was recently reported by Perez et al. (2006) showing enhanced CMC after visuomotor skill learning. This relationship also proved to be true for the other extreme: lack of peripheral feedback, e.g. through anaesthesia of digital nerves (Fisher et al., 2002) or in a deafferented patient (Kilner et al., 2004), impaired coherence and performance. We therefore conclude that in our experiment the increased CMC amplitude in conjunction with the decreased performance error is a functional correlate of an effective communication between sensorimotor cortex and muscle. As suggested by other authors (Fries et al., 1997; Baker & Baker, 2003; Hummel & Gerloff, 2005), this sensorimotor loop may be at least partly independent of local cortical oscillations as indicated in our results by the unchanged SP between 4 and 16% MVC. On the other hand, the significant SP increase in alpha- and beta-band during good performance may indicate a moment to moment switch of cortical oscillatory activity coupled to CMC changes. These local cortical processes probably reflect fluctuations in the attentional involvement (Chen et al., 2003; Cooper et al., 2003), suggesting that high SP constitutes a focused state which results in more efficient sensorimotor integration and thus better corticospinal interaction (Lalo et al., 2006; Kristeva et al., 2007). In line with this is our result of significantly higher alpha-band SP with good performance, which suggests stronger attentional involvement (Kristeva et al., 2007). In the same way, Schoffelen et al. (2005) proposed that beta-range CMC and SP are not completely independent phenomena. The relationship between CMC and SP is complex and further investigations using intracortical recordings are in our view mandatory.

To conclude, the present study investigating CMC during steady-state forces in the low force range around 10% MVC reports a novel aspect of corticospinal interaction. In summary, we showed an increase of beta-range CMC from 4 to 16% MVC and likewise within each condition from periods of 'bad' to 'good' performance. This increased CMC amplitude is suggested to result in a more effective sensorimotor loop, which is reflected in better motor performance. An important implication of this view is that the definite contribution of motor commands and afferent feedback to CMC cannot be distinguished ad hoc. Instead, a functional role of CMC in sensorimotor integration, as proposed by others (MacKay, 1997; Classen et al., 1998; Brovelli et al., 2004; Riddle & Baker, 2005; Baker et al., 2006; Lalo et al., 2006) and by ourselves (Kristeva et al., 2007), seems to be reasonable. These integrative processes probably serve to adjust motor performance and therefore are highly relevant for appropriate motor control.

Acknowledgements

Abbreviations

CMC, corticomuscular coherence; CSD, current source density distribution; EEG, electroencephalogram; EMG, electromyogram; EOG, electrooculogram; EF, exerted force; FDI, first dorsal interosseus; MVC, maximum voluntary contraction; RMSE, root mean square error; SP, spectral power; TF, target force.

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