The strength of the corticospinal coherence depends on the predictability of modulated isometric forces

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Mendez-Balbuena I, Naranjo JR, Wang X, Andrykiewicz A, Huethe F, Schulte-Mönting J, Hepp-Reymond M, Kristeva R. The strength of the corticospinal coherence depends on the predictability of modulated isometric forces. J Neurophysiol 109: 1579–1588, 2013. First published December 19, 2012; doi:10.1152/jn.00187.2012.—Isometric compensation of predictably frequency-modulated low forces is associated with corticomuscular coherence (CMC) in beta and low gamma range. It remains unclear how the CMC is influenced by unpredictably modulated forces, which create a mismatch between expected and actual sensory feedback. We recorded electroencephalography from the contralateral hand motor area, electromyography (EMG), and the motor performance of 16 subjects during a visuomotor task in which they had to isometrically compensate target forces at 8% of the maximum voluntary contraction with their right index finger. The modulated forces were presented with predictable or unpredictable frequencies. We calculated the CMC, the cortical motor alpha-, beta-, and gamma-range spectral powers (SP), and the task-related desynchronization (TRD), as well as the EMG SP and the performance. We found that in the unpredictable condition the CMC was significantly lower and associated with lower cortical motor SP, stronger TRD, higher EMG SP, and worse performance. The findings suggest that due to the mismatch between predicted and actual sensory feedback leading to higher computational load and less stationary motor state, the unpredictable modulation of the force leads to a decrease in corticospinal synchrony, an increase in cortical and muscle activation, and a worse performance.

coherence; human; predictable; oscillations; unpredictable

THE BETA AND GAMMA OSCILLATIONS over the sensorimotor cortex are known to synchronize with oscillations in the contralateral motoneuronal pool that can be computed by coherence. Previous primate and human studies showed that beta-range corticomuscular coherence (CMC) is mainly associated with isometric compensation of steady-state forces (Baker and Baker 2003; Baker et al. 1997, 2006; Bressler 2009; Brown 2000; Cheyne et al. 2008; Conway et al. 1995; Engel and Fries 2010; Feige et al. 2000; Gross et al. 2000; Halliday et al. 1998; Houlweling et al. 2010; Kristeva-Feige et al. 1993; Murthy and Fetz 1992, 1996a, 1996b; Perez et al. 2006; Riddle and Baker 2006; Salenius et al. 1997; Sanes and Donoghue 1993; Tecchio et al. 2006; Witham et al. 2010). The CMC is most likely mediated by monosynaptic connections to the motoneurons (Baker et al. 2003; Conway et al. 1995). However, a large body of evidence was accumulated indicating that the CMC also represents sensory feedback from the moving part of the body (Baker et al. 2006). We have reported that the beta-range CMC is not specific for static forces only. The sensorimotor system may resort to stronger and also broader beta-range CMC to generate stable corticospinal interaction at higher force levels than 4% maximum voluntary contraction (MVC) when compensating for dynamic predictable frequency-modulated forces (from 8 to 16 and to 24% MVC) (Chakarov et al. 2009). Interestingly, predictable frequency-modulated forces at 8% MVC are accompanied in some subjects by beta-range and in others by gamma-range CMC (Naranjo et al. 2010).

A very important feature of the CMC is its variation with predictability. Schoffelen et al. (2005) used a reaction-time paradigm in which the hazard rate of the go cue determines the subjects’ readiness to respond, as reflected in reaction times. They showed higher gamma-range corticospinal coherence with shortened reaction time and therefore proposed the neuronal coherence as a mechanism for effective corticospinal interaction. The effect of predictability on the coherence also was investigated by Van Wijk et al. (2009), who also reported modulation of both beta power and CMC when information on the response was given in advance. This is well in line with Doyle et al. (2005).

But how is the CMC modulated by predictability during frequency-modulated forces? In a previous study (Omlor et al. 2011), we showed that beta-range corticospinal coherence during isometric compensation of static force is highly dependent on the prestationary motor state: the beta-range CMC was higher after unpredictable frequency- and amplitude-modulated forces. These modulated forces induce higher computational load as reflected in the stronger cortical motor desynchronization (i.e., lower cortical motor spectral power) than predictable frequency-modulated forces. However, this study did not address how the oscillatory activity in the sensorimotor area is synchronized with the motoneuronal pool during unpredictable frequency-modulated forces (UF), which represent most of the forces required in our everyday life compared with predictable frequency-modulated forces (PF).

During PF, a sensorimotor memory trace is built up and anticipation can occur. In contrast, UF require a continuous adjustment of the force output because of the constant mismatch between predicted and actual sensory feedback. It has been already shown that the brain also processes random stimuli by applying predictive strategies, which implicates higher computational load (Schubotz et al. 2004; Schubotz and von Cramon 2002).
On the basis of the nonstationarity in motor output and the large number of corrective movements, we predicted lower CMC in the UF than in the PF condition. Furthermore, on the basis of the lower cortical motor spectral power (SP) during UF described in Omlor et al. (2011), we predicted stronger cortical motor desynchronization during UF, which would be reflected in smaller cortical motor SP. We also expected a stronger cortical activation, as measured by the task-related desynchronization (TRD) computed by the SP during the task with reference to a baseline (Pfurtscheller 1992; Pfurtscheller and Andrew 1999; Pfurtscheller and Aranibar 1977). We also expected higher muscular activation under the unpredictable frequency-modulation condition.

To test these predictions, we compared CMC, cortical motor electroencephalography (EEG) SP, TRD, electromyography (EMG), and motor performance in the two force conditions: the one with predictable frequency-modulated forces and the other in which the frequency modulation was unpredictable.

**MATERIALS AND METHODS**

**Subjects**

Sixteen healthy right-handed subjects (10 women and 6 men, mean age 27.7 ± 10.3 yr) without any history of neurological disease took part in the study. To exclude cyclic ovarian effects on the cortical excitability and oscillatory cortical activity, the female subjects were in different lunar phases (Smith et al. 2002). The handedness was tested with the Oldfield questionnaire (Oldfield 1971). All subjects had previously participated in a similar study investigating CMC. All subjects were preselected on the basis that they showed corticomuscular coherence. Only in such cases can we find whether there is a difference in CMC amplitude between predictable and unpredictable force condition. All subjects participated according to the Declaration of Helsinki from 1964, with informed consent and approval of the local ethics committee.

**Experimental Paradigm**

During the experimental session, the subject sat in an electrically shielded, dimly lit room. The right arm was supported by a splint, and the subject was instructed to place the right hand over a sphere and the index finger in the ring of a home-made manipulandum (see Fig. 1A).

The manipulandum was designed for applying vertical forces on the finger at the level of the metacarpophalangeal joint. A computer-controlled tooth belt drive with two sensors to measure vertical forces and displacements produced a defined force on the ring, called target force. The subject had to isometrically compensate this target force and maintain the ring in its initial position (Fig. 1A).

Visual feedback about the position of the ring was provided via a 19-in. monitor placed 100 cm in front of the subject and displaying
two concentric circles (Fig. 1B). The green outer circle (radius 6 mm including the thickness of 2 mm) was fixed and represented the ring’s reference position, whereas the inner solid white circle (radius 2 mm) moved along with the ring’s actual position. When a target force was applied to the ring, the subject had to compensate for it by applying a force in the opposite direction (in this case, flexion) and thereby maintain the small white circle inside the green one, thus keeping the ring in its central position. A finger displacement of 1 mm corresponded to 2.85 mm of visual feedback. The tolerance for the positional errors was the green circle. Sections of the trials in which the white circle was outside of the green circle were excluded from further analysis. The tolerance for the positional errors was the same for the PF and UF.

Force Profile

The target force had a trajectory consisting of four different phases (Fig. 1, C and D). A ramp phase (rising cosine function) ensured a smooth start of the generated force. This 1-s ramp phase was followed by a 3-s period of static force (between markers T1 and T2) that gave time to stabilize the force in the “0” position. In the two experimental conditions, this force was 8% MVC. After the static period, the sinusoidally modulated force period (between markers T2 and T3), with 8% MVC peak-to-peak amplitude and lasting 15 s, was followed by a downward ramp phase to ensure a smooth force decrease to baseline.

Experimental Conditions

Two experimental conditions were investigated in each recording session (Fig. 1, C and D): 1) the predictable force (PF) condition, in which the frequency of the modulated force was 1 Hz (Fig. 1C); and 2) the unpredictable force (UF) condition, where the modulated force consisted of 16 full-cycle oscillations of 3 different frequencies [8 oscillations at 0.6 Hz (W1), 5 at 1 Hz (W2), and 3 at 1.6 Hz (W3)], which were intermingled in a random fashion to produce unpredictable force (Fig. 1D).

The three frequencies W1, W2, and W3 were carefully selected so that they were equidistant on a logarithmic scale, holding the following relations: W2 = 5/3 × W1 and W3 = 8/5 × W2, where 5/3 ≈ 1.67 and 8/5 = 1.6. Therefore, W2 was approximately the geometric mean of W1 and W3. This selection is in line with the notion that signal discrimination in humans is usually following logarithmic rules (Green and Swets 1966). In addition, any single stimulus frequency would not overlap with the frequency spectrum of another stimulus frequency, including its harmonics, to reduce unwanted cross talk (Scharf 1990). During UF, the randomization of the three frequencies was such that no learning was possible.

Before the experiment, we recorded rest EEG for 5 min while subjects were attending to the small white circle and their right hand was resting over the sphere with the right index finger in the ring of the manipulandum. During this rest period, no force was applied on the manipulandum so that the right index finger remained stable in its initial position (with the white circle in the center of the green one). After that, the force corresponding to the individual MVC was measured. Subjects then performed a few trials with predictable and unpredictable force to get familiarized with the task and to learn “what” to do and “how” to do it. The experiment started when the task was learned.

An experimental session consisted of five recording series of 18 trials each. The two experimental conditions, PF and UF, were presented in a pseudorandomized fashion within the 18 trials so that both PF and UF trials appeared 9 times. To avoid muscle fatigue, rest intervals of 7–12 s were included between the trials and ~5 min between the series.

To optimize performance, the subjects were requested to concentrate on the temporal structure of the exerted force. At the end of each trial, they had to verbally report the type of force trial using the labels “predictable” or “unpredictable.” The subjects were instructed to avoid any movements and to fix their gaze on the concentric circles displayed on the screen.

Recordings

The EEG (bandpass DC 200 Hz, sampling rate 1,000 Hz) was recorded (SynAmps 2; NeuroScan, El Paso, TX) from 62 scalp positions referenced to Cz with ground at FzA, accordingly to the 10/10 system (Fig. 1A). Electrode impedances were under 5 kΩ. The electrooculogram (EOG; same bandpass and sampling rate as for EEG) was recorded to exclude trials contaminated with eye movements for further analysis. EMG activity (bandpass DC-200 Hz, sampling rate 1,000 Hz) was recorded with surface electrodes using a belly-tendon montage from pars indicis of the right flexor digitorum superficialis (FDS), the right first dorsal interosseous (FDI), and the right extensor digitorum communis (EDC). Our task requires co-contraction of these three muscles, which work synergetically and have intermingled cortical representations (Schieber 2002; Spinks et al. 2008).

The force and displacement of the finger were recorded in parallel with the electrophysiological data (same bandpass and sampling rate as for EEG). Data were stored and analyzed off-line.

Data Analysis

EEG-EMG coherence analysis. Data related to the force ramp phase and to the static force (T1–T2) were not taken into the analysis. In each trial for data analysis, data were taken corresponding to the markers T1–T2 (Fig. 1, C and D). PF and UF data from all trials were concatenated. Within each of these conditions, data were then further cut into nonoverlapping segments of 512 ms in length, allowing a frequency resolution of 1.96 Hz. Artifact rejection was visually performed off-line trial by trial to exclude segments contaminated with eye movements. The EEG signal was then transformed into the reference-free current source density (CSD) distribution, which approximates the underlying cortical activity (Nunez et al. 1997). The CSD algorithm was estimated using the spherical spline interpolation method (Perrin et al. 1989) implemented in the commercial software Brain Vision 2.0.1 (Munich, Germany). EMG signals were rectified, because it is known that full-wave rectification, providing the temporal pattern of grouped firing motor units (Halliday et al. 1995), is an appropriate procedure for power and coherence analysis (Yao et al. 2007). The discrete 512-point Fourier transform was computed for each segment for the whole 0- to 200-Hz frequency range. Three hundred artifact-free segments per condition were analyzed for each subject. For all subjects, data were pooled separately for both conditions, and we compared the CMC, SP, performance, and TRD.

Calculation of EEG and EMG SP and EEG-EMG CMC. The maximum EEG SP was found in 9 subjects over C3 and in 7 subjects over C1. It was located where the maximum value of the EEG-EMG coherence was obtained with one of the following three muscles: FDS, FDI, and EDC. In 8 subjects the maximum coherence was found with EDC muscle, in 7 subjects with FDI, and in 1 subject with FDS. The EMG SP was calculated exactly for these muscles with the highest coherence.

SP for a given channel c was calculated according to the following equation:

\[
SP(c) = \frac{1}{n} \sum_{i=1}^{n} C_i(c)C_i^*(c),
\]

where \(C_i(c)\) represents the Fourier transformed in channel c for a given segment number (\(i = 1,...,n = 300\)) and the asterisk indicates the complex conjugate.

Coherence values were calculated between the rectified EMG and the EEG channels overlying the sensorimotor area contralateral to the
active hand (SM1c) to calculate the synchronization between the two signals. Coherence values were calculated on the basis of the following formulas:

\[ \text{Coh}_{i,1,2}(f) = \frac{|S_{i,1,2}(f)|^2}{|S_{\text{P}}(f)|^2 |S_{\text{SP}}(f)|^2}, \]  

where

\[ S_{i,1,2}(f) = \sum_{n=1}^{n} C_{1}(f)C_{2}^*(f), \]

thus \( S_{i,1,2}(f) \) is the cross-spectrum for the EEG signal channel 1 and the rectified EMG signal in channel 2 at a given frequency \( f \), and \( S_{\text{P}}(f) \) and \( S_{\text{SP}}(f) \) are the respective spectral power values for channel 1 and 2 at the same frequency. For frequency \( f \), the coherence value \( \text{Coh}_{i,1,2}(f) \) thus corresponds to the squared magnitude of a complex correlation coefficient. The function \( \text{Coh}_{i,1,2}(f) \) is a real number between 0 and 1.

Coherence is considered to be significant if the resulting value lies above the confidence level (CL) (Rosenberg et al. 1989):

\[ \text{CL}(\alpha) = 1 - (1 - \alpha)^{1/n}, \]

where \( n \) is the number of segments and \( \alpha \) is the desired level of confidence. We considered coherence to be significant above the 95% confidence limit.

We focused on the strongest coherences obtained between the EEG channels (C1 or C3) over the left sensorimotor area contralateral to the respective frequency value and coherence amplitude \( \text{Coh} \).

For the coherence values, the individual means were calculated according to

\[ \text{Mean}_{\text{coh}} = \frac{1}{n} \sum_{i=1}^{n} \text{Coh}_i, \]

where \( j = 1,...,n \) indicates the number of significant bins.

Analysis of position error and the error estimate based on phase. To estimate a possible relationship between CMC, SP, and performance, we calculated the mean of the rectified finger position magnitude (\( |E_k| \)). A global measure was obtained by computing the mean of the deviations of the segments (\( n = 300 \)). We define this measure as the position error (PE), computed as

\[ \text{PE} = \frac{1}{s \cdot n} \sum_{(k,i)=1}^{n} \left( \sum_{j=1}^{s} |E_{kj}| \right), \]

where \( E_{kj} \) is the value of sample point \( k \) in the segment \( i \) (\( k = 1,...,512 \) and \( i = 1,...,300 \)), where \( k \) is an arbitrary variable for the points and \( i \) for the segments.

In addition to the PE, we calculated the error based on the phase differences between the temporal changes of the force and the temporal changes of the subject’s position (phase error, PhE). This error is produced by the delayed reaction of the subject to the force phase changes or by failed anticipation of these phase changes. PhE was computed as the mean angle phase error according to the formula

\[ \text{PhE} = \frac{1}{s \cdot n} \sum_{(k,i)=1}^{n} \left( \sum_{j=1}^{s} \text{arctg} \left( \frac{H(E_{kj})}{E_{kj}} \right) \right), \]

where the operator HT denotes the discrete Hilbert transform of the finger position value \( E_{kj} \) at sample point \( k (k = 1,...,512) \) corresponding to the segment \( i (i = 1,...,300) \), as calculated by the algorithm introduced by Marple (1999) and implemented by the commercial software MATLAB. Importantly, the phase angles calculated with \( \text{arctg} \) are restricted to \( \pm \pi \) radians.

Statistical analysis of CMC, PE, and PhE. To test for any statistical difference in CMC between PF and UF, we measured the individual area under the coherence curve and above the significance level, \( A_{\text{coh}} \). The frequency window for \( A_{\text{coh}} \) was 5–45 Hz. To prepare these data for the statistical analysis, individual values for \( A_{\text{coh}} \) were first transformed logarithmically to yield symmetric distributions according to the formula

\[ A_{\text{coh}} = \log_{10}(0.01 + A_{\text{CMC}}) + 2. \]

The first factor has been selected following two claims to be fulfilled as far as possible: 1) homogeneity of variance and 2) symmetry of distribution. The second factor was defined in such a way that any transformation maps 0 to 0. Normalizing transformations are advisable even in the case of a paired nonparametric test, because the distances between values play an important role.

The data for the CMC mean amplitude (\( \text{Mean}_{\text{coh}} \)) were also transformed logarithmically to yield symmetric distributions according to the formula

\[ \text{Mean}’_{\text{coh}} = \log_{10}(0.001 + \text{Mean}_{\text{coh}}) + 3. \]

To account for the intersubject variability and to render the distribution symmetric, the performance data measured as PE values were also first logarithmically transformed according to the formula

\[ \text{PE}’ = \log_{10}(0.01 + \text{PE}) + 1. \]

The data for PhE were not logarithmically transformed, since raw data were appropriate for shift hypothesis (Wilcoxon test).

To compare values for the CMC, Mean_{\text{coh}}, A_{\text{coh}}, and PhE, we performed the Wilcoxon signed-rank test with the null hypothesis that the differences of the means between PF and UF were zero.

Statistical analysis of the EMG SP. To test for any statistical difference on cortical SP between PF and UF, we measured the individual areas under the EEG SP curve, \( A_{\text{pow}} \). The frequency windows for EEG \( A_{\text{pow}} \) were 7–14 Hz (alpha), 15–30 Hz (beta), and 31–45 Hz (gamma). To prepare data for statistical analysis, data were logarithmically transformed to yield symmetric distributions according to the formula

\[ A’_{\text{pow}} = \log_{10}(1 + A_{\text{pow}}). \]

A repeated-measures two-way ANOVA was performed under the null hypothesis that the dependent variable \( A_{\text{pow}} \) was the same across the factors force condition (PF, UF) and frequency range (alpha, beta, gamma). The interaction effects were calculated.

Statistical analysis of the EMG SP. To test for any statistical difference between PF and UF on EMG SP, individual EMG SP values were measured as the area under the rectified EMG SP curve (\( A’_{\text{pow}} \)) for the frequency window 0–200 Hz. To prepare data for statistical analysis, data were logarithmically transformed to yield symmetric distributions according to the formula

\[ A’_{\text{pow}} = \log_{10}(90 + A_{\text{pow}}) - \log_{10}(90). \]

In addition to the 0–200 Hz, we measured the EMG SP in the three frequency ranges: alpha, beta, and gamma. The frequency windows

\[ \text{Mean}_{\text{coh}} = \log_{10}(0.001 + \text{Mean}_{\text{coh}}) + 3. \]

To account for the intersubject variability and to render the distribution symmetric, the performance data measured as PE values were also first logarithmically transformed according to the formula

\[ \text{PE}’ = \log_{10}(0.01 + \text{PE}) + 1. \]

The data for PE were not logarithmically transformed, since raw data were appropriate for shift hypothesis (Wilcoxon test).

To compare values for the CMC, Mean_{\text{coh}}, A_{\text{coh}}, and PhE, we performed the Wilcoxon signed-rank test with the null hypothesis that the differences of the means between PF and UF were zero.

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A repeated-measures two-way ANOVA was performed under the null hypothesis that the dependent variable \( A_{\text{pow}} \) was the same across the factors force condition (PF, UF) and frequency range (alpha, beta, gamma). The interaction effects were calculated.

Statistical analysis of the EMG SP. To test for any statistical difference between PF and UF on EMG SP, individual EMG SP values were measured as the area under the rectified EMG SP curve (\( A’_{\text{pow}} \)) for the frequency window 0–200 Hz. To prepare data for statistical analysis, data were logarithmically transformed to yield symmetric distributions according to the formula

\[ A’_{\text{pow}} = \log_{10}(90 + A_{\text{pow}}) - \log_{10}(90). \]

In addition to the 0–200 Hz, we measured the EMG SP in the three frequency ranges: alpha, beta, and gamma. The frequency windows
for EMG $A_{pow}$ were 7–14 Hz (alpha), 15–30 Hz (beta), and 31–45 Hz (gamma). To prepare data for statistical analysis, data were logarithmically transformed to yield symmetric distributions according to the formula

$$A'_{pow} = \log_{10}(3 + A_{pow}) - \log_{10}(3). \quad (14)$$

A repeated-measures two-way ANOVA was performed under the null hypothesis that the dependent variable $A'_{pow}$ was the same across the factors force condition (PF, UF) and frequency range (alpha, beta, gamma). The interaction effects were calculated.

**Statistical analysis of TRD.** It has been shown that an increased cellular excitability in the thalamocortical system results in a low-amplitude desynchronized EEG (Steriade and Llinas 1988). Therefore, the stronger desynchronization during a task, the higher the TRD, i.e., the stronger cortical activation.

The cortical activation during PF and UF was quantified by the spectral power decrease of the high-frequency (8–12 Hz) alpha rhythm with reference to a baseline period as described in Babiloni et al. (2004). We analyzed the desynchronization in the alpha range using a variant of the method of event-related desynchronization (ERD) (Pfurtscheller and Aranibar 1977; Pfurtscheller and Lopes da Silva 1999). To perform such an analysis, we previously filtered the EEG in the range 10–12 Hz with a slope of 48 db/octave, and then we defined the TRD as

$$\text{TRD} = \left( \frac{S_{\text{peak}} - S_{\text{rest}}}{S_{\text{rest}}} \right) \times 100, \quad (15)$$

where $S_{\text{peak}}$ is the SP of the EEG where significant CMC was calculated (during PF or UF) and $S_{\text{rest}}$ is the SP of the baseline EEG.

To quantify the TRD in each subject, we calculated the areas under the curves in the alpha range (8–12 Hz). The TRD values in the beta (15–30) and gamma ranges (31–45 Hz) were calculated using the same formula.

Individual TRD values were measured as area under the TRD curve in the alpha, beta, and gamma ranges. To prepare data for statistical analysis, data were logarithmically transformed to yield symmetric distributions according to the formula

$$\text{TRD} = \log_{10}(300 + \text{TRD}) - \log_{10}(300). \quad (16)$$

To test for any statistical difference in TRD between PF and UF, we performed repeated-measures two-way ANOVA with the factors frequency range (alpha, beta, gamma) and force condition (PF, UF). The null hypothesis was that the dependent variable TRD was the same across the factors.

**RESULTS**

All subjects performed the task according to the instructions. None of them reported fatigue or anxiety during the experimental session. Figure 1 shows the grand average of the finger position (i.e., force) for PF ($F$) and UF ($F$) for the 16 subjects. For PF, 45 trials are shown for each participant. Although the randomization of the three frequencies during UF was presented in three different ways, we show only one of them (15 trials for each subject). The frequency of the force oscillations exerted by the subject corresponded to the target force frequency.

Figure 1G shows the better behavioral performance measured as lower PE for PF than for UF. The statistical analysis revealed a highly significant difference ($P < 0.0004$, Wilcoxon paired test; $n = 16$). The better behavioral performance also can be also in the smaller PH for PF shown in Fig. 1H. The statistical analysis revealed significantly higher PH during PF than during UF ($P = 0.0001$, Wilcoxon paired test; $n = 16$).

To also objectively exclude fatigue effects, we compared the performance between the first and second part of the experiment using two-way ANOVA with the factors predictability (predictable vs. unpredictable) and experimental part (1st vs. 2nd 150 segments). The difference in performance between the first and second 150 segments was not significant for either PE or PH or. Also, no significant differences between the first and second 150 segments were found for the EMG amplitude and EMG mean power frequency. Furthermore, the performance difference between PF and UF remains the same in the first and second 150 segments. Thus fatigue effects can be excluded.

**Corticospinal Coherence**

All subjects exhibited CMC for both PF and UF, with eight of them having CMC in the gamma range and four in the beta range. For the other four subjects, the maximum peak of CMC was at 30 Hz. The proportion of subjects showing beta and gamma CMC at 8% MVC was in line with a previous study of ours using a similar paradigm (Naranjo et al. 2010). For all the subjects, the strongest CMC occurred over the left sensorimotor cortex, particularly at C3 (9/16) and C1 (7/16). The highest CMCs occurred with the FDI (7/16), EDC (8/16), and FDS (1/16).

Figure 2A shows original CMC curves for PF (black line) and UF (gray line) for nine representative subjects. Figure 2B shows the individual centers of mass of CMC (CoM$_x$ x-axis) and the individual mean coherence (Mean$_{coh}$ y-axis) for PF (black symbols) and UF (gray symbols) for all subjects. The triangles in Fig. 2B represent the mean values for all subjects. In Fig. 2, the qualitative differences between PF and UF are obvious, in particular the larger CMC in the PF compared with the UF trials, whereas the CMC frequency ranges in PF and UF were similar.

This was confirmed by the outcome of the statistical analysis, which disclosed significantly lower mean CMC amplitude during UF compared with PF ($P < 0.0004$, Wilcoxon paired test; $n = 16$), whereas the average shift of CoM$_x$ for all subjects from PF to UF was $0.83 \pm 0.02$ Hz. This shift was not statistically significant ($P = 0.37$, Wilcoxon paired test; $n = 16$).

**Cortical Motor EEG SP**

The cortical motor synchrony as reflected in the cortical motor SP over the left sensorimotor cortex was also modulated by PF and UF. Figure 3, A and B, presents original curves of EEG SP for two representative subjects. In both subjects, an SP amplitude decrease occurred during UF, particularly in the alpha range. That the UF is related to stronger desynchronization; i.e., smaller SP, can be seen in the SP grand average (Fig. 3C). The two-way ANOVA revealed a significant main effect for the factor frequency range (alpha, beta, gamma) ($F = 18.33, P < 0.0001$) and for the factor force condition (PF, UF) ($F = 12.94, P < 0.0026$) but without significant interaction effects. Thus alpha, beta, and gamma SP were smaller for UF, meaning that the UF generated stronger desynchronization that is not frequency specific.

Figure 3C shows also the grand average of the rest EEG. One can immediately see that PF and UF conditions are characterized with stronger desynchronization compared with the rest EEG.
Electromyographic SP

The EMG SP was also modulated by PF and UF. Figure 3, E and F, presents rectified curves of EMG SP for two representative subjects. In both subjects, an SP amplitude increase occurred during UF. That the UF is related to stronger EMG SP can be seen in the SP grand average (Fig. 3G). The two-way ANOVA revealed a significant main effect for the factor frequency range (alpha, beta, gamma) (F = 58.29, P < 0.0001) and for the factor force condition (PF, UF) (F = 37.53, P < 0.0001) but without significant interaction effects. Thus alpha, beta, and gamma EMG SP were higher for UF than for PF. This means that the stronger EMG SP during UF is not frequency specific.

Cortical Activation as Reflected in the TRD

The cortical motor activation as reflected in the TRD was also modulated by PF and UF. Figure 4 displays the grand average for all subjects (A) and the individual values for alpha, beta, and gamma ranges (B–D, respectively). One can see the stronger cortical activation as reflected in the stronger TRD in UF than in PF, confirmed by the two-way ANOVA, which revealed a significant main effect for the factor force condition (PF, UF) (F = 55.23, P < 0.0001) for alpha, beta, and gamma ranges. The frequency range effect (F = 2.75, P < 0.08) and the interaction effect (F = 3.3, P < 0.051) were in the statistical gray zone (between 5 and 10%). This means that the stronger TRD during UF is not frequency specific and can be deduced from Fig. 3C, where the rest EEG SP is shown.

DISCUSSION

The present study was designed to compare the CMC under two experimental conditions differing only in the predictability of the frequency modulation of a force that had to be isometrically compensated. We have shown that the CMC is reduced in the UF compared with the PF condition without any effect on the CMC frequency range and topography of the networks. This suggests that similar neuronal networks or two highly overlapping networks are involved in both predictable and unpredictable force conditions, but to a different degree. We also have shown the stronger activation of the thalamocortical network, as reflected in the higher cortical TRD during unpredictable force control. Furthermore, the predictability leads to more economic resources, revealed here in the lower cortical and muscular activation and better performance in the predictable condition.

Anticipation During Predictable Forces

A prerequisite for prediction is that events occur in a nonrandom fashion, allowing the brain to extract regularities in the relationship between the events and to use this knowledge (Bubic et al. 2010). Even when the brain processes random stimuli, it applies predictive strategies to recognize a pattern within a random input. This implicates a higher computational load (Schubotz et al. 2004; Schubotz and von Cramon 2002).

Both force conditions required the same force (8% MVC) and general attention demand, because the subjects had to report after each trial whether the force was predictable or unpredictable. The only difference was in the predictability of its frequency modulation. Because of the repetitive similar force cycles during predictable force, a sensorimotor memory trace can be built up and the force output can be anticipated. The sensorimotor memory is used in advance to specify the appropriate motor commands (Johansson 1998; Macefield et al. 1996; Schmitz et al. 2005). In parallel, an efference copy of the frequency coherence plots (A) and center of mass (CoM) for the corticomuscular coherence (CMC) frequency and mean coherence amplitude (B). A: individual frequency-coherence plots for CMC in 9 representative subjects during PF (black line) and UF (gray line). Note the larger CMC during PF than during UF. B: CoM for frequency (f) and mean coherence. X-axis represents CoM for the frequency of CMC for the range 5–45 Hz; Y-axis represents mean coherence amplitude. Each subject is represented with a number. Black and gray circles are the values for PF and UF, respectively. The black and gray triangles represent the means for all 16 subjects for PF and UF, respectively.
the motor command is generated and the sensory consequence of the motor action are predicted (Von Holst and Mittelstädt 1950; Wolpert et al. 1995). Predicted and actual sensory inputs are then compared. During the unpredictable condition, a continuous adjustment of the force output is required by the randomized frequency changes. Therefore, the mismatch between predicted and actual sensory feedback triggers all the time update of the sensorimotor representation. This implicates a higher computational load (Schmitz et al. 2005). Another possible reason for the higher computational load is the larger number of correction movements that have to be processed. The higher computational load during the unpredictable condition is reflected in the stronger cortical activation revealed by the more desynchronized cortical motor network with lower alpha, beta, and gamma EEG SP, as well as a stronger alpha, beta and gamma TRD. This interpretation is also in line with the memory-prediction framework, which postulates stronger activation of the neocortical, thalamic, and hippocampal networks during mismatch (Hawkins 2004).

Previously, neuronal correlates of a mismatch were found in functional MRI experiments, and evidence was accumulated that mismatch strongly activates several networks and brain regions: cerebellum (Nitschke et al. 2003), cerebellono-thalamic-parietal network (for a review, cf. Blakemore and Sirigu 2003), frontoparietal network (Schmitz et al. 2005), and hippocampus (Kumaran and Maguire 2006). In the present study, using the TRD as a measure of the increased cellular excitability in the thalamocortical network (Steriade and Llinas 1988), we have shown for the first time to our knowledge the stronger activation of this network during unpredictable compared with predictable force control. At the peripheral level the mismatch during unpredictable frequency changes induces stronger muscular co-contraction, reflected in the higher EMG SP in all frequency ranges (cf. Fig. 3, E–H), and a larger number of force corrections. The last finding supports the view that predictions made at different levels of processing save resources (Llinas 2002).

Why is the Corticomuscular Coherence Reduced with Unpredictable Forces Than With Predictable Ones?

Theoretical and experimental evidence has been accumulated showing that two groups of neurons have greater influence on each other when their temporal interaction windows are open at the same time. Synaptic input to an oscillating target neuronal network is maximally efficient if it arrives within a few milliseconds of the excitability peaks of the target (Volgushev et al. 1998). Furthermore, the neuronal interactions depend on the phase relationship between rhythmic activities, which modulate the gain of incoming synaptic input (Fries 2009; Womelsdorf et al. 2006). As a result of anticipation during predictable force, it is possible that the temporal interaction windows between the cortical motor and the spinal motoneuronal networks are “open” at the same time and that this produces a more efficient communication, which is reflected in the higher CMC, better performance, and less desynchronized state of the cortical and thalamocortical motor network. This interpretation would support the view that the CMC itself is a mechanism for effective communication (Fries 2009;
However, it is unlikely that during unpredictable behavior the brain uses a less effective way of communication with the periphery. Therefore, we favor an alternative interpretation. Baker et al. (2007) showed that the CMC is abolished during movements and claimed that movements require a disruption of oscillations and an entry into a nonoscillatory mode, which permits more freedom to represent and process information (Baker 2007; Baker et al. 1999). Furthermore, Brown and colleagues provided evidence that beta-band oscillations represent a cortical state that promotes the maintenance of steady motor output (Androulidakis et al. 2007; Pogosyan et al. 2009). We also showed that more desynchronized cortical motor network and/or more movements are associated with lower CMC (Kristeva et al. 2007). In the present study we have shown a higher number of correction movements and higher phase error for the unpredictable force condition. The latter is produced by the delayed reaction of the subject to the unpredictable force phase changes or by failed anticipation of these phase changes. Thus, by nature, due to the unpredictability of the force modulation, the EMG is less stationary. Therefore, we propose that the reduced CMC in the unpredictable condition is related to a less stationary motor control.

In this study we have demonstrated that anticipation during a predictable force condition is associated with higher corticomuscular coherence as well as saved resources in terms of lower cortical and muscular activation leading to better performance. Thus our findings are consistent with the current view that cognition optimizes the performance and that the pattern of large-scale synchronization covaries with specific predictions about forthcoming events (Buzsaki 2006; Doyle et al. 2005; Engel and Fries 2010; Engel et al. 2001; Fell and Axmacher 2011; Fell et al. 2001; Fries 2009; Schoffelen et al. 2005; Singer and Gray 1995; Tallon-Baudry 2009; van Wijk et al. 2009).

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

Fig. 4. Task-related desynchronization (TRD). A: mean TRD values for PF (black line) and UF (gray line). B–D: individual TRD values for 16 subjects during PF (black circles) and UF (gray circles) for alpha (B), beta (C), and gamma ranges (D).
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AUTHOR CONTRIBUTIONS


REFERENCES


