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

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Abstract

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 (EEG) 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), 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 spectral power, stronger task-related desynchronization, higher EMG spectral power 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 to a worse performance.

Key words: coherence, human, predictable, oscillations, unpredictable
Introduction

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. 2006; Baker et al. 1997; Bressler 2009; Brown 2000; Conway et al. 1995; Cheyne et al. 2008; Engel and Fries 2010; Feige et al. 2000; Gross et al. 2000; Halliday et al. 1998; Houweling et al. 2010; Kristeva-Feige et al. 1993; Murthy and Fetz 1992; 1996a; b; 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 (Conway et al. 1995; Baker et al. 2003). However, a large body of evidence was accumulated that the CMC also represents sensory feedback from the moving part of the body (Baker et al. 2006). We have reported that the beta CMC is not specific for static forces only. The sensorimotor system may resort to stronger and also broader beta CMC to generate stable corticospinal interaction at higher force levels than 4% 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 with beta- and in other ones with 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 RT and therefore proposed the neuronal coherence as a mechanism for effective corticospinal interaction. The effect of predictability on the coherence was investigated also by Van Wijk et al. (2009) who also reported modulation of both beta power and corticomuscular coherence 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 Omlor et al. (2011) we showed that corticospinal beta-range 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 as compared to predictable frequency-modulated forces.

During forces with predictable frequency-modulated (PF), a sensorimotor memory trace is built up and anticipation can occur. In contrast, forces with unpredictable frequency modulation (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).
Based on the non-stationarity in motor output and the large number of corrective movements we predicted lower CMC in the UF than in the PF condition. Further, on the basis of the lower cortical motor spectral power during UF in Omlor et al. (2011) we predicted stronger cortical motor desynchronization during UF, which would be reflected in smaller cortical motor spectral power (SP). We expected also a stronger cortical activation, as measured by the task-related desynchronization (TRD) computed by the spectral power 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 EEG spectral power, TRD, 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 females and 6 males, mean age 27.7 ± 10.3 years) 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
case we can 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).

(Please insert Figure 1 about here)

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 compensate isometrically this target force and maintain the ring in its initial position (Fig. 1A).

Visual feedback about the position of the ring was provided to the subject via a 19" monitor placed 100 cm in front of him/her and displaying two concentric circles (Fig. 1B). The green outer circle (radius 6 mm including the thickness of 2 mm) was fix and represented the ring’s reference position while the inner solid white circle (radius 2 mm) moved together with the ring’s actual position. When a target force was applied to the ring, the subject had to compensate it by applying a force in the opposite direction (here flexion) and thereby to 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 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. 1C, D): a ramp phase (rising cosine function) ensuring 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, D):

- *Predictable force (PF condition):* the frequency of the modulated force was 1 Hz (Fig. 1C).

- *Unpredictable force (UF condition):* the modulated force consisted of 16 full cycle oscillations of three different frequencies (8 oscillations at 0.6 Hz (W1), 5 at 1 Hz (W2) and 3 at 1.6 Hz (W3)), which were intermingled at a random fashion to produce unpredictable force (Fig. 1D).
The three frequencies $W_1$, $W_2$, and $W_3$ were carefully selected so that they were equidistant on a logarithmic scale, holding the following relations: $W_2 = \frac{5}{3} \times W_1$ and $W_3 = \frac{8}{5} \times W_2$, where $\left( \frac{5}{3} = 1.67 \right) \approx \left( \frac{8}{5} = 1.6 \right)$. Therefore, $W_2$ was approximately the geometric mean of $W_1$ and $W_3$. This selection is in line with the notion that signal discrimination in humans is usually following logarithmic rules (Green and Swets 1966). Besides, any single stimulus frequency would not overlap with the frequency spectrum of another stimulus frequency including its harmonics in order to reduce unwanted crosstalk (Scharf 1990). During UF, the randomization of the three frequencies was so that no learning was possible.

Prior to the experiment, we recorded rest EEG for 5 minutes 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. Then subjects 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. 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 pseudo-randomised fashion within the 18 trials, so that both PF and UF trials appeared 9 times. To avoid muscle fatigue, rest intervals of 7 to 12 s were included between the trials and ca. 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 1000 Hz) was recorded (SynAmps 2, NeuroScan, El Paso, TX, USA) from 62 scalp positions referenced to Cz with ground at FzA, accordingly to the 10/10 system (Fig. 1A). Electrode impedances were under 5 kOhm. The electrooculogram (EOG, same bandpass and sampling rate as for EEG) was recorded to exclude trials contaminated with eye movements for further analysis. Electromyographic activity (EMG, bandpass DC-200 Hz; sampling rate 1000 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 interosseus (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 analysed 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 was taken corresponding to the markers T2-T3 (Fig.1C, D). PF and UF data from all trials were concatenated. Then, within each of these conditions, data was further cut into non-overlapping segments of 512 ms length allowing a frequency resolution of 1.96 Hz. Artefact 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” (München, Germany). EMG signals were rectified, as 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 points Fourier transform was computed for each segment for the whole 0 to 200 Hz frequency range. 300 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, spectral power (SP), performance, and the task-related desynchronization (TRD).
Calculation of EEG and EMG spectral power (SP) and EEG-EMG coherence (CMC)

The maximum EEG SP was found in 9 subjects over C3 and in 7 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 one subject with FDS. The EMG SP was calculated exactly for these muscles with the highest coherence.

Spectral power (SP) for a given channel \( c \) was calculated according to the following equation

\[
SP_c(f) = \frac{1}{n} \sum_{i=1}^{n} C_i(f) C_i^*(f), \quad (1)
\]

where \( C_i \) represents the Fourier transformed in channel \( c \) for a given segment number \( (i=1,\ldots,n=300) \) and \( ^* \) 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) in order to calculate the synchronization between the two signals. Coherence values were calculated on the basis of the following formulae:

\[
Coh_{c1,c2}(f) = \frac{|S_{c1,c2}(f)|^2}{|SP_{c1}(f)||SP_{c2}(f)|}, \quad (2)
\]

where
Thus \( S_{c_1,c_2}(f) \) is the cross-spectrum for the EEG signal channel \( c_1 \) and the rectified EMG signal in channel \( c_2 \) at a given frequency \( f \) and \( SP_{c_1}(f) \) and \( SP_{c_2}(f) \) are the respective spectral power for \( c_1 \) and \( c_2 \) at the same frequency. For frequency \( f \), the coherence value, \( Coh_{c_1,c_2}(f) \) thus corresponds to the squared magnitude of a complex correlation coefficient. The function \( Coh_{c_1,c_2}(f) \) 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)

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

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 active right index finger movement and the rectified EMG. This procedure may account for the different location of the maximum CMC peak (C1 or C3) due to inter-individual differences in brain morphology.
Analysis of Centre of Mass (CoMf)

To detect shifts in the frequency of the coherence, we also calculated the Centre of Mass for the frequency (CoMf), i.e. the frequency at which all CMC activity could in theory be concentrated; around this point the CMC is balanced. This was done according to:

\[
\text{CoM}_f = \frac{\sum_{i=1}^{n} f_i \times \text{Coh}_i}{\sum_{i=1}^{n} \text{Coh}_i}
\]  

(5)

where \( i = 1, \ldots, n \) indicates the number of significant bins with its respective frequency value \( f \) and coherence amplitude \( \text{Coh} \).

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

\[
\text{Mean}_{\text{coh}} = \frac{1}{n} \sum_{j=1}^{n} \text{Coh}_j
\]  

(6)

where \( \text{Coh} \) is the coherence amplitude and \( j = 1, \ldots, n \) indicates the number of significant bins.

Analysis of position error (PE) and error estimate based on phase (PhE)

To estimate a possible relationship between CMC, spectral power and performance, we calculated the mean of the rectified finger position magnitude (\(|E_i|\)). A global measure was obtained by computing the mean of position over all segments (\(n=300\)). We define this measure as the position error (PE), computed as:
\[ PE = \frac{1}{s \cdot n} \sum_{i=1}^{s} \left( \sum_{k=1}^{n} |E_{k,i}| \right) \] (7)

where \( E_{k,i} \) is the value of sample point \( k \) in the segment \( i \) \((k=1, \ldots, 512 \text{ and } i=1, \ldots, 300)\)

whereas \( k \) is an arbitrary variable for the points and \( i \) for the segments.

In addition to the position error, 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, \( \text{PhE} \)). This error is produced by the delayed reaction of the subject to the force phase changes or by failed anticipation of these phase changes. This error was computed as the mean angle phase error \( (\text{PhE}) \) according to the formula

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

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

Statistical analysis of CMC, performance error (PE), and error based on phase (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 the \( A_{\text{coh}} \) 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:
The first factor has been selected following two claims to be fulfilled as far as possible: a) homogeneity of variance, and b) 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 paired non-parametric test because the distances between values play an important role.

The data for the CMC mean amplitude ($Mean_{coh}$) were also transformed logarithmically to yield symmetric distributions according to the formula:

$$Mean_{coh}' = \log_{10}(0.001 + Mean_{coh}) + 3$$  \hspace{1cm} (10)

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

$$PE' = \log_{10}(0.01 + PE) + 1$$  \hspace{1cm} (11)

The data for phase error were not logarithmically transformed since raw data were apt for shift hypothesis (Wilcoxon test).
To compare values for the $CoG_f$, $Mean_{coh}$, $A_{coh}$, and PhE we performed Wilcoxon signed-rank test with the null hypotheses that the differences of the means between PF and UF were zero.

Statistical analysis of the EEG spectral power (SP)

To test for any statistical difference on cortical spectral power between PF and UF, we measured the individual areas under the EEG SP curve, $A_{pow}$. The frequency windows for EEG $A_{pow}$ 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:

$$A'_{pow} = \log_{10}(1 + A_{pow})$$

(12)

A repeated measure 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 the EMG spectral power (EMG SP)

To test for any statistical difference between PF and UF on EMG spectral power, individual EMG SP values were measured as the area under the rectified EMG SP curve ($A'_{Pow}$) for the frequency window 0-200 Hz. To prepare data for statistical
analysis, data was logarithmically transformed to yield symmetric distributions according to the formula:

\[ A'_{pow} = \log_{10}(90 + A'_{pow}) - \log_{10}(90) \] (13)

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:

\[ A'_{pow} = \log_{10}(3 + A_{pow}) - \log_{10}(3) \] (14)

A repeated measure 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 the task-related desynchronization (TRD)**

It has been shown that an increased cellular excitability in the thalamo-cortical 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 the Event Related
Desynchronization (ERD) (Pfurtscheller and Aranibar 1977; Pfurtscheller and Lopes
da Silva 1999). To perform such analysis we previously filtered the EEG in the range
10-12 Hz with a slope of 48 dB/octave and then we defined the Task-Related
Desynchronization as

\[
TRD = \left( \frac{SP_{\text{Task}} - SP_{\text{Rest}}}{SP_{\text{Rest}}} \right) \times 100, \tag{15}
\]

where \(SP_{\text{Task}}\) is the \(SP\) of the EEG where significant CMC was calculated (during
predictable or unpredictable force) and \(SP_{\text{Rest}}\) 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 in beta- (15-30) and gamma-range (31-45 Hz) was
calculated using the same formula.

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

\[
TRD = \log_{10}(300 + TRD) - \log_{10}(300) \tag{16}
\]
To test for any statistical difference in the task-related desynchronization between PF and UF we performed repeated measures 2-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: Force Condition (PF, UF) and Frequency Range (alpha, beta, gamma).

**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 (E) 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 here 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.

Fig. 1G shows the better behavioural performance measured as lower position error (PE) for PF than for UF. The statistical analysis revealed a highly significant difference ($p<0.0004$, Wilcoxon paired test $n=16$). The better behavioural performance can be seen also in the smaller error based on phase (PhE) for PF shown in Fig. 1H: The statistical analysis revealed significantly higher PhE during PF than during UF ($p=0.0001$, Wilcoxon paired test $n=16$).

To exclude fatigue effects also objectively we compared the performance between the first and second part of the experiment using 2-way ANOVA with factors...
Predictability (Predictable vs. Unpredictable) and Experimental Part (1\textsuperscript{st} vs. 2\textsuperscript{nd} 150 segments). The difference in performance between 1\textsuperscript{st} and 2\textsuperscript{nd} 150 segments was not significant for both position error and error based on phase. No significant differences between 1\textsuperscript{st} and 2\textsuperscript{nd} 150 segments were found also for the EMG amplitude and EMG mean power frequency. Further, the performance difference between PF and UF remains the same in the 1\textsuperscript{st} and 2\textsuperscript{nd} 150 segments. Thus fatigue effects can be excluded.

Corticomuscular coherence (CMC)

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 at 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. Fig. 2B shows the individual centres of mass ($CoM_f$) of CMC (x-axis) and the individual Mean Coherence ($Mean_{coh}$) (y-axis) for PF (black) and UF (gray) for all subjects. The triangles (black for PF and gray for UF) in Fig. 2B present the mean values for all subjects. In this figure, the qualitative differences between PF and UF are obvious, in particular the larger CMC in the PF compared to the UF trials while the CMC frequency ranges in PF and UF were similar.
This was confirmed by the outcome of the statistical analysis which disclosed significant lower mean CMC amplitude during UF as compared to PF ($p<0.0004$, Wilcoxon paired test $n=16$) while the average shift of the Centre of Mass for all subjects from PF to UF was $0.83\pm3.02$ Hz. This shift was not statistically significant ($p=0.37$, Wilcoxon paired test $n=16$).

Cortical motor EEG spectral power (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. Fig. 3A and 3B present original curves of EEG SP for two representative subjects. In both subjects, a 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 significant main effect for the factor Frequency Band (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 which is frequency-unspecific.
Fig. 3C shows also grand average of the rest EEG. One can immediately see that predictable and unpredictable force conditions are characterized with stronger desynchronization as compared to the rest EEG.

*Electromyographic spectral power (EMG SP)*

The EMG SP was also modulated by PF and UF. Figures 3E and 3F present rectified curves of EMG SP for two representative subjects. In both subjects, a 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 significant main effect for the factor Frequency Band (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 (7-14 Hz), beta (15-30 Hz) and gamma (31-45 Hz) EMG SP were higher for UF than for PF. This means that the stronger EMG SP during UF is frequency-unspecific.

*Cortical activation as reflected in the Task-related desynchronization (TRD)*

The cortical motor activation as reflected in the TRD was also modulated by PF and UF. Fig. 4 displays the grand average for all subjects (in A) and the individual values (in B, C, D) for alpha, beta and gamma ranges respectively. One can see the stronger cortical activation as reflected in the stronger TRD in UF than in the PF, confirmed by the two-way ANOVA which revealed 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 grey zone (between 5 and 10%). This means
that the stronger TRD during UF is frequency-unspecific and can be deduced from Fig. 3C where the rest EEG spectral power is shown.

(Please insert Fig. 4 about here)

Discussion

The present study was designed to compare the corticomuscular coherence (CMC) under two experimental conditions differing only in the predictability of the frequency modulation of a force which had to be isometrically compensated. We show that the CMC is reduced in the unpredictable condition as compared to the predictable one 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 show the stronger activation of the thalamo-cortical network, as reflected in the higher cortical task-related desynchronization during unpredictable force control. Further, 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 non-random 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, as 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. Due to 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 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 are the larger number of correction movements which 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 spectral power, as well as a stronger alpha, beta and gamma task-related desynchronization (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).
Up to now, neuronal correlates of a mismatch were found in fMRI experiments and evidence was accumulated that mismatch strongly activates several networks and brain regions: cerebellum (Nitschke et al. (2003), cerebello-thalamo-parietal network (for a review cf. Blakemore and Sirigu (2003)), fronto-parietal network (Schmitz et al. 2005), hippocampus (Kumaran and Maguire (2006). In the present study, using the task-related desynchronization as a measure of the increased cellular excitability in the thalamocortical network (Steriade and Llinas 1988), we show for the first time to our knowledge the stronger activation of this network during unpredictable as compared to predictable force control. At the peripheral level the mismatch during unpredictable frequency changes induces stronger muscular co-contraction reflected in the higher EMG spectral power in all frequency ranges (cf. Fig. 3E-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 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). Further, 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). Due to 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 this produces a more efficient communication which is reflected in the higher CMC, the better performance and less desynchronized state of the cortical and thalamo-cortical motor network. This interpretation would support the view that the
CMC itself is a mechanism for effective communication (Fries 2009; Kristeva et al. 2007; Schoffelen et al. 2008; van Elswijk et al. 2010). However, it is unlikely that during unpredictable behaviour the brain uses a less effective way of communication with the periphery. Therefore, we favour 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 non-oscillatory mode, which permits more freedom to represent and process information (Baker 2007; Baker et al. 1999). Further, Brown and co-workers provided evidence that beta-band oscillations represent a cortical state which 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 show 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. The behavior performance (in our study the position error and the phase error) is the output of this less stationary network. It is related to the activity of some of the muscles activated in the motor task: pars indicis of the flexor digitorum superficialis (FDS), first dorsal interosseus (FDI), and extensor digitorum communis (EDC). Our task requires the co-contraction of these muscles which work synergistically and have intermingled cortical representations (Schieber 2002; Spinks et al. 2008). Unlike in the isometric contraction of one single muscle, the motor performance in our task is not influenced by the EMG activation level of the individual muscles. Therefore, we propose that the reduced CMC in the unpredictable condition is related to a less stationary motor control.

In this study we demonstrate 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; Engel and Fries 2010; Engel et al. 2001; Fell and Axmacher 2011; Fell et al. 2001; Fries 2009; Singer and Gray 1995; Tallon-Baudry 2009; Schoffelen et al. (2005); Doyle et al. 2005; van Wijk et al. 2009).

Figures

**Figure 1**

**Experimental setup.** (A) High-resolution EEG recorded from 62 scalp positions together with electrooculogram (EOG), home-made manipulandum and EMG recorded from FDI, FDS and EDC muscles during the experiment. (B) Visual feedback of the ring position displayed on a monitor in front of the subject. The green outer circle had a radius 6 mm. (C) Target force profile: Predictable frequency-modulated force (PF) in black and (D) unpredictable frequency-modulated force (UF) in gray at 8%MVC. PF consists of sinusoidal waves of 1.0 Hz. UF consists of sinusoidal waves of randomly intermingled frequencies of 0.6, 1.0 and 1.6 Hz. The modulation for both forces has a peak-to-peak amplitude of 8% MVC. T2-T3 is the interval considered for the data analysis. (E) and (F) Grand average across 16 subjects of finger position for PF and UF respectively. For UF due to the three different ways of intermingling three frequencies, only one third of the trials are averaged. (G) Individual Position Error (PE) for all 16 subjects for PF and UF, circles in black and gray respectively. Each subject is represented with a number. (H) Individual Phase Error (PhE) for all 16 subjects for PF and UF, circles in black and gray respectively. Each subject is represented with a number.
Figure 2

Frequency-coherence plots (A) and Centre of Mass for the CMC frequency and mean coherence amplitude (B). Left panel (A): Individual frequency-coherence plots for CMC in 9 representative subjects. PF as black line, UF as gray line. Note the larger CMC during PF than during UF. Right panel (B): Centre of Mass (CoM) for frequency and mean coherence. X-axis: the Center of Mass for the Frequency of CMC for the range 5-45 Hz. Y-axis: the 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 triangle represents the means for all 16 subjects for PF and UF, respectively.

Figure 3

EEG and EMG Spectral Power for PF (black) and UF (gray). (A, B) Cortical motor EEG spectral power (SP) for two subjects, (C) grand average for 16 subjects. The grand average for rest EEG SP is given in dotted line. Note the highest SP during rest. (D) EEG SP for alpha -, beta -, and gamma–range. Note the higher SP for PF than for UF. (E, F) EMG SP for two subjects, (G) the grand average for EMG SP for 16 subjects for the frequency range 0 - 200 Hz, and (H) EMG SP for PF and UF for alpha-, beta- and gamma-range. Note the significantly higher EMG SP for UF than for PF.
Figure 4.

Task-Related Desynchronization (TRD). Mean TRD values in upper panel (A) and individual values in lower panel (B). (A) Black and gray lines for PF and UF respectively. (B, C, D) Individual TRD values for 16 subjects in black and gray circles for PF and UF respectively, and for alpha (B), beta (C) and gamma (D) range.

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References


