Bourguignon, Mathieu; Piitulainen, Harri; Smeds, Eero; Zhou, Guangyu; Jousmäki, Veikko; Hari, Riitta

MEG insight into the spectral dynamics underlying steady isometric muscle contraction

Published in:
JOURNAL OF NEUROSCIENCE

DOI:
10.1523/JNEUROSCI.0447-17.2017

Published: 25/10/2017

Please cite the original version:
Bourguignon, M., Piitulainen, H., Smeds, E., Zhou, G., Jousmäki, V., & Hari, R. (2017). MEG insight into the spectral dynamics underlying steady isometric muscle contraction. JOURNAL OF NEUROSCIENCE, 37(43), 10421–10437. https://doi.org/10.1523/JNEUROSCI.0447-17.2017
MEG Insight into the Spectral Dynamics Underlying Steady Isometric Muscle Contraction

Mathieu Bourguignon,1,2,3 Harri Piitulainen,1 Eero Smeds,1 Guangyu Zhou,1,4 Veikko Jousmäki,1,5,6 and Riitta Hari1,7

To gain fundamental knowledge on how the brain controls motor actions, we studied in detail the interplay between MEG signals from the primary sensorimotor (SM1) cortex and the contraction force of 17 healthy adult humans (7 females, 10 males). SM1 activity was coherent at ~20 Hz with surface electromyogram (as already extensively reported) but also with contraction force. In both cases, the effective coupling was dominant in the efferent direction. Across subjects, the level of ~20 Hz coherence between cortex and periphery positively correlated with the “burstiness” of ~20 Hz SM1 (Pearson r ≈ 0.65) and peripheral fluctuations (r ≈ 0.9). Thus, ~20 Hz coherence between cortex and periphery is tightly linked to the presence of ~20 Hz bursts in SM1 and peripheral activity. However, the very high correlation with peripheral fluctuations suggests that the periphery is the limiting factor. At frequencies <3 Hz, both SM1 signals and ~20 Hz SM1 envelope were coherent with both force and its absolute change rate. The effective coupling dominated in the efferent direction between (1) force and the ~20 Hz SM1 envelope and (2) the absolute change rate of the force and SM1 signals. Together, our data favor the view that ~20 Hz coherence between cortex and periphery during isometric contraction builds on the presence of ~20 Hz SM1 oscillations and needs not rely on feedback from the periphery. They also suggest that effective cortical proprioceptive processing operates at <3 Hz frequencies, even during steady isometric contractions.

Key words: cortex-muscle coherence; corticokinematic coherence; isometric contraction; magnetoencephalography; motor control; primary sensorimotor cortex

Significance Statement
Accurate motor actions are made possible by continuous communication between the cortex and spinal motoneurons, but the neurophysiological basis of this communication is poorly understood. Using MEG recordings in humans maintaining steady isometric muscle contractions, we found evidence that the cortex sends population-level motor commands that tend to structure according to the ~20 Hz sensorimotor rhythm, and that it dynamically adapts these commands based on the <3 Hz fluctuations of proprioceptive feedback. To our knowledge, this is the first report to give a comprehensive account of how the human brain dynamically handles the flow of proprioceptive information and converts it into appropriate motor command to keep the contraction force steady.

Introduction
Steady muscle contraction is maintained by a continuous drive from the cortex to spinal motoneurons and by fine motor adjustments according to proprioceptive feedback (Scott, 2012). Still, we do not know how the brain integrates this proprioceptive feedback to affect motor control.

During steady contraction, the sensorimotor cortical rhythms and the muscle activity, as measured with surface EMG, are...
pled at ~20 Hz, a phenomenon known as cortex–muscle coherence (Conway et al., 1995; Salenius et al., 1996, 1997). Some authors suggested that cortex–muscle coherence reflects cortical drive to the muscles (Salenius et al., 1997; Gross et al., 2000), whereas others argued for the existence of a reafferent contribution (Riddle and Baker, 2005; Baker, 2007; Witham et al., 2011) used for sensorimotor control (Baker, 2007). According to this latter view, ~20 Hz sensorimotor oscillations could represent a cortical state that promotes the maintenance of steady motor output (Gilbertson et al., 2005; Androulidakis et al., 2006, 2007; Baker, 2007; Witham et al., 2011). Alternatively, according to a hypothetic mechanism, the sensorimotor system could send pulses at ~20 Hz and monitor the resulting afferent signal to probe the state of the periphery for continuous sensorimotor recalibration (MacKay, 1997; Baker, 2007). Still, these accounts of the functional role of ~20 Hz reafferent signals are highly speculative.

During transient limb movements, cortex–muscle coherence disappears (Küller et al., 2000) and primary sensorimotor (SM1) activity is coupled with movement kinematics (Kelso et al., 1998; O’Suilleabhain et al., 1999; Jerbi et al., 2007; Bourguignon et al., 2011, 2012; Piitulainen et al., 2013a, b). This coupling is known as the corticothalamokinematic coherence (CKK). When the movement is regular, CKK mainly peaks at movement frequency and its first harmonic (Bourguignon et al., 2011, 2012; Piitulainen et al., 2013a, b). Irregular movements lead to CKK at frequencies <8 Hz (Jerbi et al., 2007). The slow brain activity underpinning CKK is typically strong and reliable enough for brain machine interfaces to use them to detect some features of the movement (Hammon et al., 2008; Waldert et al., 2008; Bradberry et al., 2010; Jerbi et al., 2011). However, CKK appears to reflect the processing of proprioceptive feedback generated by the movements. Indeed, voluntary and passive movements elicit similar CKK level (Piitulainen et al., 2013a), and directionality analyses revealed that the afferent component dominates over the efferent one (Bourguignon et al., 2015).

CKK also unfolds during slow tracking movements. Indeed, the kinematics of slow tracking movements is characterized by fluctuations at frequencies of 1–4 Hz (Craik, 1947), regardless of movement speed (Miall et al., 1986; Roitman et al., 2004; Pasalar et al., 2005), and these fluctuations synchronize with SM1 activity (Dipietro et al., 2011; Hall et al., 2014). In that context, rhythmic fluctuations in movement position are termed submovements (Craik, 1947).

Here, we tested the hypothesis that CKK also manifests itself during isometric steady muscle contractions. To that aim, we analyzed the coupling between MEG signals (Harri and Puce 2017) and natural force fluctuations in an isometric contraction task. First, we expected to uncover significant coupling at ~20 Hz since a previous study revealed the existence of ~20 Hz coherence between MEG and acceleration signals recorded from the index finger in an isometric wrist extension task (Airaksinen et al., 2015). We expected that coupling to dominate in the afferent direction, as is the case during voluntary movements.

in the afferent direction, as is the case during voluntary movements.
Measurements

MEG. The MEG measurements were performed in a three-layer magnetically shielded room (Imedco AG at the MEG Core of Aalto Neuroimaging; http://ami.aalto.fi), Aalto University, with a 306-channel whole-scalp neuromagnetometer (Elekta Neuromag, Elekta Oy). The recording passband was 0.1–330 Hz, and the signals were sampled at 1 kHz. Subjects' head position inside the MEG helmet was continuously monitored by feeding current into four head-tracking coils located on the scalp: the locations of the coils and at least 200 head–surface points (scap and nose) with respect to anatomical fiducials were determined with an electromagnet tracker (Fastrak, Polhemus).

EMG and force. Surface EMG was measured from the first dorsal interosseous and the flexor carpi ulnaris of the right hand, which are both recruited during a pinch grip task. EMG electrodes were placed on the muscle bulk, and signals were measured with respect to an electrode placed over the distal radial bone. Recording passband was 10–330 Hz for EMG signals and DC–330 Hz for the force signal. EMG and force signals were then sampled at 1 kHz and recorded time-locked to MEG signals.

MRI. 3D-T1 MRIs were acquired with Signa 3.0 T whole-body MRI scanner (Signa VH/i, General Electric) or with 3T MAGNETOM Skyra whole-body MRI scanner (Siemens Healthcare) at the AMI Centre, Aalto Neuroimaging, Aalto University School of Science.

Data preprocessing

Continuous MEG data were preprocessed off-line with MaxFilter 2.2.10 (Elekta Oy), including head movement compensation. The SSS preprocessing was applied with a correlation limit of 0.9 and segment length equal to the recording length (Taulu and Kajola, 2005; Taulu and Simola, 2006). Independent component analysis was then applied to MEG signals filtered through 1–25 Hz, and 1–3 components corresponding to eye-blink and heartbeat artifacts were visually identified based on their topography and time-series. The corresponding components were subsequently subtracted from raw MEG signals.

Functional (nondirectional) coupling

We used coherence analysis to estimate the functional coupling between MEG and all peripheral (2 EMGs, force) signals, and to identify the optimal MEG sensor and muscle for further analyses. Time periods coinciding with visual feedback (i.e., when the force level was not properly kept between 2 and 4 N) were marked as bad to exclude periods during which contraction was intentionally corrected. Time periods for which MEG signals exceeded 5 pT (magnetometers) or 1 pT/cm (gradiometers) which contraction was intentionally corrected. Time periods for which MEGSM1 signals exceeded 5 pT (magnetometers or 1 pT/cm (gradiometers); and to avoid edge effects, further analyses were based on timepoints at least 2 s away from artifacts and appearance of visual feedback. The analytical signals were then created by means of the Hilbert transform. From these analytical signals (s1(f, t); k = 1, 2 indexing the MEG and the peripheral signal respectively), amplitude spectra were estimated as follows:

$$A_k(f) = \sqrt{|\mathcal{I}[s_k(f, \cdot)]|^2},$$

where |·| denotes the absolute value and ⟨·⟩ the average across time. Coherence was then estimated as follows:

$$\text{Coh}(f) = \frac{\langle |\mathcal{I}[s_1(f, \cdot)]| \cdot |\mathcal{I}[s_2(f, \cdot)]\rangle^2}{\langle |\mathcal{I}[s_1(f, \cdot)]|^2 \cdot |\mathcal{I}[s_2(f, \cdot)]|^2 \rangle},$$

where a superscript * denotes the complex conjugate. This procedure consistently enhanced the coherence with the force signal while it left the coherence with EMG signals virtually unchanged.

Finally, we also estimated envelope correlation. To avoid contamination by very slow envelope variations, both envelope signals (\(s_k(f, t)\), k = 1, 2) were divided by their low-pass filtered version at 0.1 Hz (squared-sine transition from 0.05 to 0.15 Hz). This procedure is illustrated in Figure 2. Such normalization ensured that the correlation was blind to changes slower than 0.1 Hz that could be linked to, for example, changes in contraction strategy (which induces substantial changes in EMG amplitude). Hence, the envelope coupling was estimated as follows:

$$R(f)^\text{lp} = \text{corr}\left(\frac{\mathcal{I}[s_1(f, \cdot)]}{\mathcal{I}[s_1(f, \cdot)]^\text{lp}}, \frac{\mathcal{I}[s_2(f, \cdot)]}{\mathcal{I}[s_2(f, \cdot)]^\text{lp}}\right)^2,$$

where the subscript “lp” stands for “low pass filtered at 0.1 Hz.”

The same analysis was repeated with a finer spectral resolution for the force signal only. In this analysis, amplitude and coherence spectra were computed based on MEG and force signals filtered through 0.6-Hz-wide frequency bands centered on 0.4–40 Hz by steps of 0.2 Hz.

Effective (directional) coupling

We used renormalized partial directed coherence (rPDC) (Schelter et al., 2000, 2009) to estimate the causal influence of force and MEGSM1 signals on one another. The estimation of the rPDC requires fitting a multivariate autoregressive model of order 100 to the data low-pass filtered at 50 Hz and resampled at 100 Hz with the ARfit package (Schneider and Neumaier, 2001). Across subjects and conditions, the optimal model order range was 17–34 (mean ± SD, 21 ± 4) according to Schwartz’s Bayesian criterion and 46–376 (166 ± 97) according to Akaike’s final prediction error, both implemented in the ARfit package (Schneider and Neumaier, 2001). Adopting a model order of 100 therefore represented a good compromise between the two criteria. The chosen parameters (resampling and model order) enabled us to explore frequencies up to 50 Hz with a 1 Hz frequency resolution. Finally, to achieve a frequency smoothing similar to that of coherence spectra, rPDC was smoothed with a square
Figure 2. Illustration of the procedure used to obtain envelopes of band-limited signals corrected for slow drifts. A, Raw MEG signal recorded over the primary sensorimotor cortex (MEGSM1). B, Band-limited MEGSM1 envelope. That is, the Hilbert envelope (black trace) of MEGSM1 signal filtered through a narrow band (gray trace). In the present illustration, the band was 5 Hz wide and centered on 20 Hz (hence the ~20 Hz MEGSM1 envelope). The same procedure was repeated for center frequencies from 5 to 40 Hz by steps of 1 Hz (data not shown on the figure). C, ~0.1 Hz fluctuations of the envelope displayed in B. D, Envelope corrected for slow drifts. That is, the envelope (displayed in B) divided timepoint by timepoint by its slow fluctuations (displayed in C). The coefficient of variation (CoV) of that envelope (CoV-E; computed over 10 min) is indicated in the top right corner. E–H, Same as A–D for the EMG signal. I–L, Same as A–D for the force signal. M–P, Same as A–D for a white noise. All corrected envelopes fluctuate around 1, but qualitatively less so for the white noise, leading to a lower CoV.
kernel wide of 5 frequency bins, following the approach proposed by Sommerlade et al. (2009). The ensuing spectral smoothing was ±2.5 Hz. This procedure yielded for each subject one rPDC spectrum in the efferent direction (MEGSM1 → force) and one in the afferent direction (force → MEGSM1).

**Link between cortex–muscle coherence and burstiness of brain and peripheral signals**

We performed additional analyses to clarify the causal influence of ~20 Hz fluctuations in SM1 and peripheral signals on one another. We know that activities of both the SM1 cortex and periphery (EMG, force) are characterized by bursts of ~20 Hz cycles often followed by ~1-s-long silent periods (Jasper and Penfield, 1949; Murthy and Fetz, 1992, 1996; Baker et al., 1997; Gilbertson et al., 2005). We also know that the ~20 Hz cortex–muscle coherence is tightly linked to the presence of these ~20 Hz bursts in both SM1 and peripheral signals (McAuley et al., 1997; Kilner et al., 2000, 2003; Gilbertson et al., 2005; Kristeva et al., 2007; Ushiyama et al., 2011; Matsuya et al., 2013). Accordingly, we here quantify the “burstiness” of MEGSM1 and peripheral signals, and strive to ascribe the interindividual variability in this burstiness to that in ~20 Hz coherence between MEGSM1 and peripheral signals. Of note, the magnitude of the cortex–muscle coherence is widely known for its great interindividual variability, from values below the detection limit afforded by even 10-min-long recordings (i.e., ~<0.003) up to values of 0.3 (Pohja et al., 2005; Bayraktaroglu et al., 2013).

Figure 2 illustrates the processing procedure we used (detailed below) to estimate the “burstiness” of MEGSM1 and peripheral signals. The coefficient of variation (CoV; ratio between the SD and the mean) of the envelope (CoV-E) of a bursting signal is higher than that of white noise filtered similarly (in our setting, the CoV-E of a filtered white noise is ~0.51). Accordingly, we filtered MEGSM1 and peripheral signals through 15–25 Hz (gray trace), following the approach proposed by Faes et al. (2004). This procedure yielded for each subject one rPDC spectrum in the ~20 Hz MEGSM1 and peripheral signals (maximum across 10–30 Hz) with Spearman and Pearson correlation (across the 17 subjects). Pairs of Pearson correlation coefficients were compared with the Steiger test (Steiger, 1980).

We also computed the sensor topography for the CoV-E of ~20 Hz MEG signals. Practically, for each gradiometer pair, we retained the 95th percentile of the distribution of the maximum CoV-E, across 10–30 Hz, of white noise signals (1000 repetitions) (Faes et al., 2004).

We searched for an association between (1) the magnitude of ~20 Hz cortex–muscle coherence (maximum across 10–30 Hz) and (2) the CoV-E of ~20 Hz MEGSM1 and peripheral signals (maximum across 10–30 Hz) with Spearman and Pearson correlation (across the 17 subjects). Pairs of Pearson correlation coefficients were compared with the Steiger test (Steiger, 1980).

**Coupling at lower frequencies**

Figure 3 presents representative samples of the slow fluctuations of MEGSM1 and force signals considered here.

We estimated the coherence at lower frequencies (<5 Hz) between MEG signals (Fig. 3B) and force fluctuations (Fig. 3E). The analysis was identical to that described in Coherence analysis, except that epochs were 5000 ms long, affording a finer spectral resolution of 0.2 Hz and 3 tapers were used (yielding a spectral smoothing of ±0.3 Hz). In addition, MEG and force signals were high-pass filtered at 0.2 Hz to avoid spectral leakage from near to DC components. Another difference was that the threshold for statistical significance (p < 0.05 corrected for multiple comparisons) was obtained for the mean coherence across 0.5–3 Hz.
The same analysis was repeated to evaluate the coupling between MEG signals and fluctuations in the absolute change rate of the force (Fig. 3). The absolute change rate of the force was obtained as the absolute value of the time derivative of the force signal band-passed through 0.5–10 Hz. It is relevant to seek coupling with this signal given that some proprioceptive receptors (e.g., Golgi tendon organs) are sensitive to the force itself, whereas others (e.g., the primary endings of muscle spindles) are sensitive to the change rate of muscle stretch.

The same analysis was repeated also to evaluate the coupling between the envelope of MEG signals filtered through 15–25 Hz (Fig. 3) and the slow fluctuations of both the force signal and its absolute change rate. In what follows, the envelope of MEG signals filtered through 15–25 Hz will be referred to as the ∼20 Hz MEG envelope. This envelope signal fluctuates at frequencies <10 Hz.

We used rPDC to quantify the causal influence of the following: (1) the envelope of ∼20 Hz MEG SM1 signals, (2) the MEG SM1 signals as such, and (3) the force on one another. A multivariate autoregressive model of order 50 was fitted to the data low-pass filtered at 5 Hz and resampled at 10 Hz, enabling us to explore frequencies up to 5 Hz with a 0.2 Hz frequency resolution. Across subjects and conditions, the optimal model order range was 2–6 (mean ± SD, 4 ± 1.5) according to Schwarz’s Bayesian criterion and 59–147 (96 ± 25) according to Akaike’s final prediction error. To achieve a frequency smoothing similar to that of coherence, rPDC was smoothed with a square kernel wide of 3 frequency bins, leading to a spectral smoothing of ±0.3 Hz. This procedure yielded, for each subject, 6 rPDC spectra: one for each possible combination of directions (2 possibilities) and signal pairs (3 possibilities).
The same procedure was repeated to quantify the causal influence of the following: (1) the envelope of ~20 Hz MEGSM1 signals, (2) the MEGSM1 signals as such, and (3) the absolute change rate of the force on one another.

Finally, we used temporal response functions (TRFs) to model how force signals affect the temporal dynamics of ~20 Hz MEGSM1, envelope and MEGSM1 signals. A similar approach has been used previously to model brain responses to continuous speech sounds (Lalor and Foxe, 2010; Zion Golumbic et al., 2013; Lawler et al., 2015). TRFs are the direct analog of evoked responses in the context of continuous stimulation.

Practically, we used the mTRF toolbox (Crosse et al., 2016) to estimate the TRF of MEGSM1, and of ~20 Hz MEGSM1 envelope associated with force signals, all signals being filtered through 0.5–5 Hz and down-sampled to 20 Hz. For each subject, the TRFs were modeled from ~1.5 to 2.5 s, for a fixed set of ridge values (red from 1 at 2 to 0.5 s) to dampen regression artifacts. We next used these windowed TRFs to predict the 10% of data left out, and estimated the Pearson correlation coefficient between predicted and measured signals. These correlation values in the 10 runs were tested against 0 with a Wilcoxon signed rank test. Finally, the square of the mean correlation value across the 10 runs provided an estimate of the proportion of variance explained by the signals imputable to force fluctuations. In the final analysis, we used the ridge value maximizing the mean explained variance across our 17 subjects (sum of the logarithm across the 2 signals considered: MEGSM1, ~20 Hz MEGSM1 envelope; 2)

The same procedure was repeated to estimate the TRFs to the absolute change rate of the force of MEGSM1, and ~20 Hz MEGSM1 envelope, all signals being filtered through 0.5–5 Hz.

Impact of heartbeats on low-frequency coupling

Heartbeats transiently increase blood pressure in all blood vessels of the body, leading to changes in the pressure measured at the fingertips (Parati et al., 1989). Such transient pressure changes in the fingertips are thus expected to slightly impact the contraction force at frequencies matching cardiac rhythm and its harmonics, and they also produce some thus expected to slightly impact the contraction force at frequencies 20 Hz with the surface EMG (Cohforce; Fig. 4A; Table 1) as is widely known in the literature (Conway et al., 1995; Salenius et al., 1996, 1997) but also with the fluctuations of the contraction force (Cohforce; Fig. 4B; Table 1). Cohforce and Cohforce were statistically significant in all subjects (p values <0.05; surrogate-data-based statistics), and their maximum values were highly correlated (r = 0.90, p < 0.0001; Spearman correlation). The peak frequencies and maximum values of Cohforce and Cohforce did not differ statistically significantly from each other (p = 0.11 and p = 0.068, respectively; Wilcoxon test). These results are in line with a previous finding that, during static extension of the wrist, SM1 activity is coherent at 20 Hz with finger vibrations recorded with an accelerometer (Airaksinen et al., 2015).
The existence of ~20 Hz Coh_force implies that steady contractions inherently involve ~20 Hz force fluctuations that are coherent with ~20 Hz SM1 oscillations. A close inspection of the force amplitude spectra (Fig. 4B) revealed clear peaks at ~10 Hz, the typical frequency of physiological tremor (McCaulley et al., 1997; Gilbertson et al., 2005), but not at ~20 Hz (for amplitude values, see Table 2). The existence of genuine ~20 Hz tremor has nonetheless been demonstrated previously by showing its synchronization with ~20 Hz MEG_SMI signals (Airaksinen et al., 2015), which was evident also in the current study, and by relating finger ~20 Hz tremor to impairment in motor performance (McCaulley et al., 1997; Gilbertson et al., 2005).

A natural question to ask is whether the sensorimotor system is sensitive enough to detect refferent signals associated with the nonsalient ~20 Hz force fluctuations (Fig. 4B, C). Our response is a definitive yes because the Golgi tendon organs can detect stretches as low as 30–90 μN during active muscle contraction (Binder et al., 1977) and thus are sensitive enough to detect the force fluctuations of 2900 ± 1200 μN we observed in the current study (values integrated over a 5 Hz band from 17.5 to 22.5 Hz). Nevertheless, the directional coupling strength was 5.6 times stronger in the efferent than in the afferent direction, as quantified by rPDC (mean across 10–30 Hz; Fig. 4D, p = 0.00035, Wilcoxon test), implying that ~20 Hz Coh_force mainly reflects effects of the efferent cortical drive, similarly to what has been demonstrated for cortex–muscle coherence (Salenius et al., 1997; Gross et al., 2000; Witham et al., 2011; Lim et al., 2014).

**Link between cortex-muscle coherence and burstiness of brain and peripheral signals**

Here we relate the interindividual variability in the burstiness of brain and peripheral signals (quantified with CoV-E) to that in Coh_force and Coh_EMG to draw conclusions about the causal influence of ~20 Hz brain and peripheral signals on one another. The CoV-E of MEG_SMI (CoV-E_SM1), EMG (CoV-E_EMG), and force (CoV-E_force) peaked for carrier signal at ~20 Hz, as was observed in all subjects for CoV-E_SM1 (Figs. 5A, 6A) and in the majority of the subjects for CoV-E_force (Fig. 5B) and CoV-E_EMG (Fig. 6B).

Indeed, CoV-E_SM1, CoV-E_EMG, and CoV-E_force peak values in 10–30 Hz exceeded significantly the ~0.51 level expected for white noise for all subjects (p < 0.05), except for 2 subjects for CoV-E_EMG. Importantly, the ~20 Hz peak of individual subjects’ CoV-E_SM1, CoV-E_force, and CoV-E_EMG tightly matched in all subjects, except in these 2 subjects lacking significant CoV-E_EMG therefore supporting physiological rather than artifact origins of these envelope modulations.

Moreover, the spatial pattern of the 20 Hz CoV-E_SM1 agreed with the origin of the signal variations in theRolandic region (Figs. 5A, 7A). Of note, the corresponding topography obtained with task-free MEG data was similar (Fig. 7B), and so were the
As last confirmation of the physiological origin of ~20 Hz envelope fluctuations, the ~20 Hz bursts in MEGSM1 and peripheral signals occur in synchrony. This can be appreciated from the raw envelope traces displayed in Figure 2D, H, L. More quantitatively, MEGSM1–Peripheral envelope correlation peaked for carrier frequencies of ~20 Hz in the majority of our subjects (Fig. 8). This was expected since significant envelope correlation was previously reported for ~20 Hz MEGSM1 and EMG signals (Bayraktaroglu et al., 2013).

Across subjects, the maximum CoV-EMEG across the 10–30 Hz range correlated with the maximum coherence across the same range (Spearman correlation; Cohforce $r = 0.75$, $p = 0.0008$, see Fig. 5A; CohEMG, $r = 0.73$, $p = 0.0012$, see Fig. 6A), but the association was not strong (Pearson correlation; Cohforce $r =$

![Figure 7](image_url)

**Figure 7.** Sensor topography of the CoV of the envelope of ~20 Hz MEG signals (CoV-EMEG) during the isometric contraction task (A) and during the task-free session (B). Subjects are ordered according to their maximum coherence between MEG and force signals (Cohforce) across 10–30 Hz.

![Figure 8](image_url)

**Figure 8.** Envelope squared-correlation of MEGsm1 with peripheral signals (EMG and force; one trace per subject; $n = 17$). The correlation was computed between the envelopes of the signals filtered through a 5-Hz-wide bands centered on frequencies from 5 to 40 Hz by steps of 1 Hz.
0.66, \( p = 0.004 \); \( \text{Coh}_{\text{EMG}} \), \( r = 0.61, \ p = 0.01 \); some subjects with almost identical CoV–ESM1 had coherence values differing by a factor of \( \approx 10 \). The maximum CoV–E\(_{\text{force}}\) and CoV–E\(_{\text{EMG}}\) across the 10–30 Hz range correlated with the corresponding maximum coherences across the same range (Spearman correlation; \( \text{Coh}_{\text{force}} \), \( r = 0.93, \ p < 0.0001 \), see Fig. 5B; \( \text{Coh}_{\text{EMG}} \), \( r = 0.81, \ p = 0.0001 \), see Fig. 6B), and the association was strong (Pearson correlation: \( \text{force}, \ r = 0.92, \ p < 0.0001; \ EMG, \ r = 0.86, \ p < 0.0001 \)). Indeed, the association with the coherence magnitude was significantly stronger with CoV–E\(_{\text{force}}\) than with CoV–E\(_{\text{EMG}}\) (Fig. 8C, \( z = 2.47, \ p = 0.013; \) Steiger test), and marginally stronger with CoV–E\(_{\text{EMG}}\) than with CoV–E\(_{\text{SM1}}\) (\( z = 1.87, \ p = 0.061 \)).

These results confirm that \( \approx 20 \) Hz cortex–muscle coherence is tightly linked to the presence of \( \approx 20 \) Hz bursts in MEGSM1 and peripheral signals; but ultimately, the periphery appears to be the limiting factor. Indeed, some subjects with elevated magnitude of MEGSM1 bursts had lower coherence, whereas, in contrast, subjects with low (respectively high) CoV–E\(_{\text{force}}\) had systematically low (respectively high) \( \text{Coh}_{\text{force}} \). This relationship is illustrated in Figure 9 where two subjects with similar \( \approx 20 \) Hz MEGSM1 have strikingly different \( \approx 20 \) Hz \( \text{Coh}_{\text{force}}\) while their CoV–E\(_{\text{force}}\) and \( \text{Coh}_{\text{force}} \) vary hand in hand. We take these findings as evidence that, in \( \approx 20 \) Hz cortex–muscle coherence, the bursting SM1 activity drives the periphery and the \( \approx 20 \) Hz bursts are transmitted with a subject-dependent efficiency.

<3 Hz coupling with force
Although peaking at \( \approx 20 \) Hz, \( \text{Coh}_{\text{force}} \) was also salient <3 Hz (Fig. 4C). This frequency range corresponds to the strongest bulk of force fluctuations. Indeed, the power of force fluctuations is \( \approx 35 \) times stronger at 1 Hz than at 20 Hz (Fig. 4G; Table 2). A dedicated coherence analysis revealed that both (1) \( \approx 20 \) Hz MEGSM1 envelope and (2) MEGSM1 signals were significantly coherent with both force (Fig. 10A) and its absolute change rate (Fig. 10B) in 13–16 subjects of 17 (\( p < 0.05; \) mean coherence across 0.5–3 Hz; Table 3).

The MEG signals related to these four investigated couplings originated from the SM1 cortex, as was confirmed by individual coherence maps (Figs. 11, 12) and by group-level source-space maps (Fig. 10A,B). At the SM1 sensor with highest mean coherence, the coherence peaked at frequencies between 0.6 and 2.4 Hz (Fig. 10A,B; Table 3).

Directionality analyses revealed a significantly stronger afferent than efferent coupling (quantified with the mean rPDC across 0.5–3 Hz) between (1) force fluctuations and the \( \approx 20 \) Hz MEGSM1 envelope (\( p = 0.0023; \) Wilcoxon test; Fig. 10C), and (2) the absolute change rate of the force and the MEGSM1 signals (\( p = 0.013; \) Wilcoxon test; Fig. 10D). No statistically significant differences in the mean rPDC were found for the other pairs of signals (\( p \) values >0.05).

We further characterized the dynamics of brain signals with respect to changes in force using the TRFs (Fig. 10E,F). Table 4 shows the percentage of variance explained by TRFs. TRFs of the \( \approx 20 \) Hz MEGSM1 envelope associated with force consistently decreased within 100 ms following the force signal (group-level minimum at 60 ms) and showed weaker, although still prominent, increase peaking \( \approx 200 \) ms before the force signal. Individual TRFs of MEGSM1 signals associated with force consistently showed their highest values around time 0, but the phase of the oscillations was inconsistent across subjects. Similar observations can be made on TRFs associated with the absolute change rate of the force, but this time, the maximum decrease of \( \approx 20 \) Hz MEGSM1 envelope occurred later (peak at 220 ms).

Impact of heartbeats on low-frequency coupling
As the coupling we have just outlined occurs at frequencies overlapping with heart rate and its harmonics, we studied in detail the impact of heartbeats on force and brain signals. Figure 13 presents the TRFs of force, MEGSM1, and \( \approx 20 \) Hz MEGSM1 envelope associated with heartbeats. Time-locked to magnetocardiographic R peak, subjects’ contraction force consistently reached a minimum at \( \approx 200 \) ms and was increased by, on average, 17 mN (which corresponds to a movement of \( \approx 1 \) μm) at \( \approx 400 \) ms. These timings are consistent with known delays between the electric and ballistocardiographic signals (Kim et al., 2016). No consistent trend was visible on subjects’ MEGSM1 and \( \approx 20 \) Hz MEGSM1 envelope responses to heartbeats. Overall, the TRFs explained only \( \approx 4\% \) of the variance of the 0.5–5 Hz content of force, and even less of that of MEGSM1 (\( \approx 1\% \)) and \( \approx 20 \) Hz MEGSM1 envelope (\( \approx 0.3\% \); Table 4). Importantly, the proportion of force variance explained by heart pulses was not predictive of the level of 0.5–3 Hz coherence between force and \( \approx 20 \) Hz MEGSM1 envelope (\( r = 0.16, \ p = 0.53; \) Spearman correlation) or between force and MEGSM1 signals (\( r = 0.076, \ p = 0.77; \) Spearman correlation). Finally, the coherence in the sensorimotor sensors was mainly preserved when coherence between force and brain signals was controlled for heartbeats (Fig. 14, in comparison with Fig. 11). Indeed, at the MEGSM1 sensor, the ratio of partial coherence controlled for heartbeats to regular coherence was 0.97 ± 0.12 (mean ± SD; range 0.59–1.08) for coherence between force and \( \approx 20 \) Hz MEGSM1 envelope, and 0.84 ± 0.20 (mean ± SD; range 0.21–1.02) for coherence between force and MEGSM1. Contrastingly, controlling for heartbeats led to strik-
Table 3. Mean Cohforce across 0.5–3 Hz and corresponding peak frequencies (mean, SD, and range across subjects)^a

| Coherence strength | Coherence frequency [Hz] | Force Mean ± SD | Range Mean ± SD | Absolute change rate of the force Mean ± SD | Range Mean ± SD |
|--------------------|-------------------------|----------------|-----------------|-------------------------------------------|-----------------|
|                    | 0.5–3 Hz MEGSM1 envelope | 0.023 ± 0.017 | 0.005–0.073 | 0.021 ± 0.015 | 0.006–0.055 |
|                    | Slow MEGSM1 activity     | 0.019 ± 0.008 | 0.007–0.032 | 0.017 ± 0.009 | 0.007–0.037 |
|                    | Peak frequency [Hz]       |                |                |                                           |                 |
|                    | 0.5–3 Hz MEGSM1 envelope | 1.27 ± 0.41   | 0.8–1.8        | 1.13 ± 0.27 | 0.6–1.6 |
|                    | Slow MEGSM1 activity     | 1.64 ± 0.67   | 0.8–2.6        | 1.26 ± 0.52 | 0.6–2.4 |

^aValues reported here were taken from the gradiometer pair of maximum mean Cohforce for each subject separately.

Figure 10. Coupling of MEGSM1 with <3 Hz force fluctuations. A, Coherence between force and MEGSM1 signals (left), and between force and ~20 Hz MEGSM1 envelope (right). Sub-blocks display the group-averaged coherence source map at 0.5–3 Hz (top) and the individual coherence spectra with the MEGSM1 signals. For indicative purpose, an orange dotted line indicates the significance level of the mean coherence across 0.5–3 Hz. B, Same as in A with the force replaced by its absolute change rate (|dF/dt|). C, D, Directional coupling quantified with renormalized partial directed coherence (rPDC). E, F, TRFs associated to force (E) and |dF/dt| (F) of <5 Hz MEGSM1 (left) and ~20 Hz MEGSM1 envelope (right). The plots display individual TRFs (black traces) as well as the mean TRF across subjects (red trace) ± 1 SEM (blue area) and ± 2 SEM (cyan area). Note that we reversed the polarity of TRFs of MEGSM1 signals (when the scalar product with the first principal component of sensor orientation was negative) to ensure that all TRFs were estimated in a compatible orientation. This was necessary to warrant the validity of the across-subjects averaging procedure.

Table 3. Mean Cohforce across 0.5–3 Hz and corresponding peak frequencies (mean, SD, and range across subjects)^a
Because heartbeats consistently modulated force signals, we next tackled the question of whether these modulations would play a prominent physiological role in the 0.5–3 Hz coherence between force and SM1 activity. To that aim, we compared the different coherence estimates at f_{heart-rate} and f_{off-heart-rate}. The mean coherence between force and MEGSM1 signals at f_{heart-rate} (0.021 ± 0.009) was ~20% higher than that at f_{off-heart-rate} (0.018 ± 0.007), but this difference did not reach statistical significance (p = 0.08; Wilcoxon test). This result is in contrast with the finding that coherence between heartbeat and MEGSM1 signals was ~3 times higher at f_{heart-rate} (0.025 ± 0.025) than at f_{off-heart-rate} (0.008 ± 0.010; p = 0.0006) and that the coherence between heartbeat and force signals was ~4 times higher at f_{heart-rate} (0.049 ± 0.049) than at f_{off-heart-rate} (0.013 ± 0.015; p = 0.0003). Hence, we can conclude that, beyond heartbeats, there exists a prominent and independent coupling between force and SM1 activity at 0.5–3 Hz.

Discussion

Our data favor the view that ~20 Hz cortex–muscle coherence observed during isometric contraction builds on the presence of ~20 Hz SM1 oscillations and needs not rely on feedback from the periphery. More importantly, our data suggest that effective cortical proprioceptive processing operates at lower, <3 Hz frequencies, even when the motor task does not involve voluntary movements. In other words, during steady isometric contraction, small fluctuations in muscle contraction are processed similarly as larger fluctuations occurring during continuous movements (Kelso et al., 1998; O’Suilleabhain et al., 1999; Jerbi et al., 2007; Bourguignon et al., 2011, 2012; Piitulainen et al., 2013a, b) and slow tracking movements (Dipietro et al., 2011; Hall et al., 2014).

Pervasiveness of <3 Hz SM1 fluctuations

Based on our findings, we suggest the following mechanism for the maintenance of stable muscle contraction: The summed ac-
tivity of proprioceptors sensitive to the force or its change rate (possibly in comparison with expected proprioceptive feedback) (Scott, 2012) modulates population-level SM1 excitability and the 20 Hz SM1 oscillations to compensate their cause. This homeostatic mechanism would directly account for how the brain gets informed about the low-frequency (≤3 Hz) content of force fluctuations, which is the strongest and most relevant feedback signal, and needs to be continuously regulated to maintain a stable contraction. This interpretation emphasizes the importance of somatosensory feedback to control motor actions, in line with the influential view that the brain acts as a feedback controller for motor actions (Todorov and Jordan, 2002; Scott, 2004, 2012). Moreover, our finding sheds light on the type of signals the brain relies on to operate the way feedback controllers do.

Our MEG results do not tell whether increases and decreases of force were processed by identical, overlapping, or distinct neurop-
ronal populations. On the basis of animal neurophysiology, however, it is likely that the situation is mixed and complex because SM1 neurons can either increase or decrease their firing rate in response to force increase, or even display a mixed response pattern of, for example, phasic increase followed by tonic decrease (Wannier et al., 1991). Nevertheless, our finding that, during static contraction, SM1 signals were driven by the absolute change rate of the force rather than by the force itself is in line with and generalizes the previous observation that SM1 signals are also phase-locked to the absolute wrist velocity during slow tracking movements (O’Suilleabhain et al., 1999). Furthermore, SM1 signals are also triggered by the proprioceptive information during continuous movements (Kelso et al., 1998; O’Suilleabhain et al., 1999; Jerbi et al., 2007; Bourguignon et al., 2011, 2012; Piitulainen et al., 2013a, b) and slow tracking movements (Dipietro et al., 2011; Hall et al., 2014). This observation underlines the perversiveness of <3 Hz SM1 fluctuations that appear to reflect the proprioceptive information not only during movements but also during steady contractions. Accordingly, these <3 Hz SM1 fluctuations may represent one of the necessary elements used by the brain to achieve accurate motor control. Direct cortical recordings (with, e.g., electrocorticography) are however needed in the future to clarify the respective contributions to the <3 Hz coupling within the different sensorimotor areas that we grouped here into an SM1 cortex.

Still, the slow fluctuations of the ~20 Hz SM1 rhythm appeared to relate not only to somatosensory feedback, but also to activity that precedes changes in the force. Our results indeed revealed that the ~20 Hz SM1 rhythm increased ~200 ms before a change in the force, and that it was blocked ~100 ms after the change. Enhancement of the ~20 Hz SM1 rhythm has been suggested to indicate inhibition or deactivation of the motor cortex (Jasper and Penfield, 1949). The reason why the ~20 Hz SM1 rhythm is modulated with such dynamics can only be speculated. The possible associated effects include transient loss of fine-motor control (e.g., due to attentional reallocation), which generates proprioceptive feedback and/or correction of the ongoing motor plan.

Impact of heartbeats on force and brain signals

Heartbeats were associated with force changes of ~17 mN, which explained ~4% of the variance of slow force fluctuations (0.5–5 Hz). This finding is in line with a previous report that cardiovascular activity impacts contraction force during weak isometric finger contractions in the 0–6 Hz range among other frequencies (Sosnoff et al., 2011).

Still, heartbeats seemed to have only a limited impact on the coupling between <3 Hz force fluctuations and MEG signals. Indeed, using partial coherence to control for ECG signals attenuated the coupling with force at sensorimotor sensors by ~20% while it effectively removed heartbeat-related artifacts in the lowest sensors of the helmet; these planar sensors are typically the most contaminated by the cardiac artifacts (Joumasaki and Hari, 1996). Moreover, coherence at $f_{\text{off-heart-rate}}$ was ~<20% lower than coherence at $f_{\text{heart-rate}}$. These converging values indicate that heartbeats contributed to ~<20% of the magnitude of the coupling between <3 Hz force fluctuations and MEG signals. This percentage of coherence relates to both heartbeat artifacts in MEG signals and genuine physiological modulation of the force by the heartbeats.

Generation mechanism for the ~20 Hz cortex–muscle coherence

Previous studies have suggested a central role for the ~20 Hz SM1 oscillations in both encoding the motor command and processing the resulting proprioceptive feedback (Riddle and Baker, 2005; Baker, 2007; Witham et al., 2011; Aumann and Prut, 2015). Two action mechanisms have been hypothesized. First, the ~20 Hz cortex–muscle coherence could arise because the SM1 cortex sends pulsed output and monitors the resulting afferent signals to probe the state of the periphery (Mackay, 1997; Baker, 2007; Witham et al., 2011). The second proposed mechanism posits that the ~20 Hz cortex–muscle coherence reflects the integration of afferent information into motor commands to promote a stable motor state (Gilbertson et al., 2005; Androulidakis et al., 2006, 2007; Baker, 2007; Witham et al., 2011). However, our data challenge both these views and suggest that ~20 Hz cortex–muscle coherence builds on the presence of ~20 Hz SM1 oscillations and needs not rely on feedback from the periphery. We therefore propose below a hypothetical generation mechanism of ~20 Hz cortex–muscle coherence.

In monkeys maintaining isometric contraction, the spiking activity of pyramidal-tract neurons is coupled with local field potentials in the SM1 cortex at both ~10 and ~20 Hz (Baker et al., 2003). In other words, the excitability of the pyramidal neurons relates to the phase of the ~10 and ~20 Hz SM1 oscillations; and consequently, the common pyramidal output tends to structure according to these oscillations. However, cortex–muscle coherence seldom peaks at ~10 Hz, which speaks for the existence of a blocking mechanism that prevents the excitability of motoneuron pools from oscillating at ~10 Hz despite the presence of these frequencies in the corticospinal drive (Baker et al., 2003). Such a blocking was argued to be important to prevent excess
~10 Hz physiological tremor (Baker et al., 2003). Given the close-to-harmonic relationship between ~10 and ~20 Hz SM1 oscillations, we simply suggest that the same mechanism tends to block ~20 Hz oscillatory motor output as well. The ~20 Hz cortex–muscle coherence would then emerge due to nonperfect blocking of the ~20 Hz oscillatory input to the spinal α motoneurons.

**Perspectives for the ~20 Hz cortex–muscle coherence**

Abnormally high ~20 Hz cortex–muscle coherence has been observed in patients suffering from dysfunction of the sensorimotor system, especially of myoclonic disorders (Timmermann et al., 2001; Raethjen et al., 2002; Silén et al., 2002; Caviness et al., 2003; Grosse et al., 2003; Kristeva et al., 2004). Given the very strong association between the magnitude of cortex–muscle coherence and the burstiness of ~20 Hz force or EMG signals, we suggest that the observed abnormally high cortex–muscle coherence primarily reflects altered functioning at the level of the periphery, which would be seen (but has not yet been addressed) as high burstiness of both force and EMG due to the myoclonic disorder. Thus, a future alternative means to estimate the level of cortex–muscle coupling would be to quantify the burstiness (with the CoV-E) of both force and EMG; these signals are indeed easily accessible, as they only require measurement of contraction force or muscle activity, with no need to record brain activity.

Finally, our findings provide a novel insight into a so far unresolved puzzle about the cortex–muscle coherence, that is, its great interindividual variability, even in healthy subjects. It was reported that the maximum level of cortex–muscle coherence correlates positively with force CoV and force power in the α and β bands, but the Pearson correlation coefficients were <0.65 (Ushiyama et al., 2017). Here, we demonstrate a positive corre-

---

**Figure 14.** Sensor topography for the 0.5–3 Hz coherence of the force with (A) the envelope of 15–25 Hz MEG and (B) MEG signals controlled for heart pulses. Subjects are ordered as in Figure 7.
lation between maximal cortex–muscle coherence and CoV-E of ~20 Hz force and EMG fluctuations characterized by Pearson correlation coefficients of ~0.9. Accordingly, the present study considerably clarifies the situation by revealing that individual levels of ~20 Hz cortex–muscle coherence are strongly related to the “burstiness” of EMG and force signals at ~20 Hz. In other words, the questions “why is the ~20 Hz cortex-muscle coherence fraught with so high interindividual variability” and “why does the sensorimotor system of different individuals suppress differently the ~20 Hz content of the motor command” are equivalent.

References
Airaksinen K, Lehti T, Nurminen J, Luoma J, Helle L, Taulu S, Pekkonen E, Mäkelä JP (2015) Cortico-muscular coherence parallels coherence of postural tremor and MEG during static muscle contraction. Neurosci Lett 602:22–26. CrossRef Medline
Androulidakis AG, Doyle LM, Gilbertson TP, Brown P (2006) Corrective movements in response to displacements in visual feedback are more effective during periods of 13–35 Hz oscillatory synchrony in the human corticospinal system. Eur J Neurosci 24:3299–3304. CrossRef Medline
Androulidakis AG, Doyle LM, Yarrow K, Litvak V, Gilbertson TP, Brown P (2007) Anticipatory changes in beta synchrony in the human corticospinal system and associated improvements in task performance. Eur J Neurosci 25:3758–3765. CrossRef Medline
Ashburner J, Friston KJ (1999) Nonlinear spatial normalization using basis functions. Hum Brain Mapp 7:254–266. CrossRef Medline
Ashburner J, Neelin P, Collins DL, Evans A, Friston K (1997) Incorporating prior knowledge into image registration. Neuroimage 6:344–352. CrossRef Medline
Aumann TD, Prut Y (2015) Do sensorimotor beta-oscillations maintain muscle synergy representations in primary motor cortex? Trends Neurosci 38:77–85. CrossRef Medline
Baker SN (2007) Oscillatory interactions between sensorimotor cortex and the periphery. Curr Opin Neurobiol 17:649–655. CrossRef Medline
Baker SN, Olivier E, Lemon RN (1997) Coherent oscillations in monkey motor cortex and hand muscle EMG show task-dependent modulation. J Physiol 501:225–241. CrossRef Medline
Baker SN, Pinches EM, Lemon RN (2003) Synchronization in monkey motor cortex during a precision grip task: II. Effect of oscillatory activity on corticospinal output. J Neurophysiol 89:1941–1953. CrossRef Medline
Bayraktarolu Z, von Carlswitz-Ghorii K, Curio G, Nikulin VV (2013) It is not all about phase: amplitude dynamics in cortical-muscular interactions. Neuroimage 64:496–504. CrossRef Medline
Birznieks I, Boonstra TW, Macefield VG (2012) Modulation of human muscle spindle discharge by arterial pulsations-functional effects and consequences. PLoS One 7:e35091. CrossRef Medline
Bortel R, Sovka P (2014) Approximation of the null distribution of the multiple coherence estimated with segment overlapping. Signal Process 96: 310–314. CrossRef
Bourguignon M, De Tiègue X, Op de Beeck M, Pirotte B, Van Bogaert P, Goldman S, Hari R, Jousmaäki V (2017) Functional motor-cortex mapping using corticokinematic coherence. Neuroimage 55:1475–1479. CrossRef Medline
Bourguignon M, Jousmaäki V, Op de Beeck M, Van Bogaert P, Goldman S, De Tiègue X (2012) Neuronal network coherence with hand kinematics during fast repetitive hand movements. Neuroimage 59:1684–1691. CrossRef Medline
Bourguignon M, Piitulainen H, De Tiègue X, Jousmaäki V, Hari R (2015) Corticokinematic coherence mainly reflects movement-induced proprioceptive feedback. Neuroimage 106:382–390. CrossRef Medline
Bradberry TJ, Gentili RJ, Contreras-Vidal JL (2010) Reconstructing three-dimensional hand movements from noninvasive electroencephalographic signals. J Neurosci 30:3432–3437. CrossRef Medline
Caviness VN, Adler CH, Sabaugh MN, Connor DJ, Hernandez JL, Lagerlund TD (2003) Abnormal corticomuscular coherence is associated with the small amplitude cortical myoclonus in Parkinson’s disease. Mov Disord 18:1157–1162. CrossRef Medline
Conway BA, Halliday DM, Farmer SF, Shahani U, Maas P, Wier AL, Rosenberg JR (1995) Synchronization between motor cortex and spinal motoneuronal pool during the performance of a maintained motor task in man. J Physiol 489:917–924. CrossRef Medline
Craik KJ (1947) Theory of the human operator in control systems: the operator as an engineering system. Br J Psychol 38:56–61. Medline
Crosby MJ, Di Liberto GM, Brown P, Bednar A, Lator EC (2016) The Multivariate Temporal Response Function (mTRF) Toolbox: a MATLAB toolbox for relating neural signals to continuous stimuli. Front Hum Neurosci 10: 604. CrossRef Medline
Dipietro L, Poizner H, Krebs HI (2011) EEG correlates of submovements. In: In: Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society, pp 7429–7432.
Faes L, Pinna GD, Porta A, Maestri R, Nollo G (2004) Surrogate data analysis for assessing the significance of the coherence function. IEEE Trans Biomed Eng 51:1156–1166. CrossRef Medline
Gilbertson TL, Lalo E, Doyle L, Di Lazzaro V, Cioni B, Brown P (2005) Existing motor state is favored at the expense of new movement during 13–35 Hz oscillatory synchrony in the human corticospinal system. J Neurosci 25:7771–7779. CrossRef Medline
Gramfort A, Luessi M, Larson E, Engemann DA, Stromheime D, Brodbeck C, Parkkonen L, Hamalainen MS (2014) MNE software for processing MEG and EEG data. Neuroimage 86:446–460. CrossRef Medline
Gross J, Tass PA, Salenius S, Hari R, Freund HJ, Schnitzler A (2000) Cortico-muscular synchronization during isometric muscle contraction in humans as revealed by magnetoencephalography. J Physiol 527:623–631. CrossRef Medline
Grosse P, Guerrini R, Parmeggiani L, Bonanni P, Poggyan A, Brown P (2003) Abnormal corticomuscular and intermuscular coupling in high-frequency rhythm myoclonus. Brain 126:326–342. CrossRef Medline
Hall TM, de Carvalho F, Jackson A (2014) A common structure underlies low-frequency cortical dynamics in movement, sleep, and sedation. Neuron 83:1185–1199. CrossRef Medline
Halliday DM, Rosenberg JR, Amjad AM, Breeze P, Conway BA, Farmer SF (1995) A framework for the analysis of mixed time series/point process data: theory and application to the study of physiological tremor, single motor unit discharges and electromyograms. Prog Biophys Mol Biol 64:237–278. CrossRef Medline
Hammon PS, Makeig S, Poizner H, Todorov E, de Sa VR (2008) Predicting reaching targets from human EEG. IEEE Signal Process Mag 25:659–77. CrossRef
Hari R, Puce A (2017) MEG-EEG primer. Oxford: Oxford University Press.
Jasper H, Penfield W (1949) Electroencephalograms in man: effect of voluntary movement upon the electrical activity of the precentral gyrus. Arch Psychol 183:163–174. CrossRef
Jerbi K, Lachaux JP, N’Diaye K, Pantazis D, Leahy RM, Garnero L, Baillet S (2007) Coherent neural representation of hand speed in humans revealed by MEG imaging. Proc Natl Acad Sci USA 104:7676–7681. CrossRef Medline
Jerbi K, Vidal JR, Mattout J, Maby E, Lecaignard F, Ossandon T, Hamamé CM, Davel SS, Bouter R, Lachaux JP, Leahy RM, Baillet S, Garnero L, Delpuech C, Bertrand O (2011) Inferring hand movement kinematics from MEG, EEG and intracranial EEG: from brain-machine interfaces to motor rehabilitation. IRBM 32:8–18. CrossRef
Jousmaäki V, Hari R (1996) Cardiac artifacts in magnetoencephalography. J Clin Neurophysiol 13:172–176. CrossRef Medline
Kelso JA, Fuchs A, Lancaster R, Holroyd T, Cheyne D, Weinberg H (1998) Dynamic cortical activity in the human brain reveals motor equivalence. Nature 392:814–818. CrossRef Medline
Kilner JM, Baker SN, Salenius S, Hari R, Lemon RN (2000) Human cortical muscle coherence is directly related to specific motor parameters. J Neurosci 20:8838–8845. Medline
Kilner JM, Salenius S, Baker SN, Jackson A, Hari R, Lemon RN (2003) Task-dependent modulations of cortical oscillatory activity in human subjects during a bimanual precision grip task. Neuroimage 18:67–73. CrossRef Medline
Kim CS, Ober SL, McMurtry MS, Finegan BA, Inan OT, Mukkamala R, Hahn JO (2016) Ballistocardiogram: mechanism and potential for unobtrusive cardiovascular health monitoring. Sci Rep 6:1–6. CrossRef Medline
Kristeva R, Patino L, Omlor W (2007) Beta-range cortical motor spectral power and corticomuscular coherence as a mechanism for effective cor-
ticosinal interaction during steady-state motor output. Neuroimage 36: 785–792. CrossRef Medline
Lalor EC, Foxe JJ (2010) Neural responses to uninterrupted natural speech can be extracted with precise temporal resolution. Eur J Neurosci 31:189–193. CrossRef Medline
Lawler D, Begley C, Lalor J (2015) Reconstructing the process of transition to motherhood for women with a disability. J Adv Nurs 71: 1672–1683. CrossRef Medline
Lim M, Kim JS, Kim M, Chung CK (2014) Ascending beta oscillation from finger muscle to sensorimotor cortex contributes to enhanced steady-state isometric contraction in humans. Clin Neurophysiol 125:2036–2045. CrossRef Medline
Mackay WA (1997) Synchronized neuronal oscillations and their role in motor processes. Trends Cogn Sci 1:176–183. CrossRef Medline
Matsumoto Y, Ushiyama J, Ushiba J (2013) Protracted reaction time during episodes of elevated β-band corticospinal coupling and associated oscillatory muscle activity. J Appl Physiol 114:896–904. CrossRef Medline
Mcauley HJ, Rothwell JC, Marsden CD (1997) Frequency peaks of tremor, muscle vibration and electromyographic activity at 10 Hz, 20 Hz and 40 Hz during human finger muscle contraction may reflect rhythmicities of central neural firing. Exp Brain Res 114:525–541. CrossRef Medline
Miall RC, Weir DJ, Stein JF (1986) Manual tracking of visual targets by trained monkeys. Behav Brain Res 20:185–201. CrossRef Medline
Murthy VN, Fetz EE (1992) Coherent 25- to 35-Hz oscillations in the sensorimotor cortex of awake behaving monkeys. Proc Natl Acad Sci U S A 89:5670–5674. CrossRef Medline
Murthy VN, Fetz EE (1996) Synchronization of neurons during local field potential oscillations in sensorimotor cortex of awake monkeys. J Neurophysiol 76:3968–3982. Medline
Oldfield RC (1971) The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia 9:97–113. CrossRef Medline
O’Suilleabain PE, Lagerlund TD, Matsumoto YJ (1999) Cortical potentials at the frequency of absolute wrist velocity become phase-locked during slow sinusoidal tracking movements. Exp Brain Res 126:529–535. CrossRef Medline
Parati G, Casadei R, Groppelli A, Di Rienzo M, Mancia G (1989) Comparison of finger and intra-arterial blood pressure monitoring at rest and during laboratory testing. Hypertension 13:647–655. CrossRef Medline
Putasar S, Roitman AV, Ebner TJ (2005) Effects of speeds and force fields on submovements during circular manual tracking in humans. Exp Brain Res 163:214–225. CrossRef Medline
Pitulainen H, Bourguignon M, De Tiège X, Hari R, Jousmäki V (2013a) Corticokinemetic coherence during active and passive finger movements. Neuroscience 238:361–370. CrossRef Medline
Pitulainen H, Bourguignon M, De Tiège X, Hari R, Jousmäki V (2013b) Coherence between magnetoencephalography and hand-action-related acceleration, force, pressure, and electromyogram. Neuroimage 72:83–90. CrossRef Medline
Pohja M, Salenius S, Hari R (2005) Reproducibility of cortex-muscle coherence. Neuroimage 26:764–770. CrossRef Medline
Raether H, Lindemann M, Dümpelmann M, Wenzelburger R, Stolze H, Pfister G, Elger CE, Timmer J, Deuschl G (2002) Corticospinal coherence in the 6–15 Hz band: is the cortex involved in the generation of physiologic tremor? Exp Brain Res 142:32–40. CrossRef Medline
Reuter M, Schmansky NJ, Rosas HD, Fischl B (2012) Within-subject template estimation for unbiased longitudinal image analysis. Neuroimage 61:1402–1418. CrossRef Medline
Riddell CN, Baker SN (2005) Manipulation of peripheral neural feedback loops alters human corticospinal coherence. J Physiol 566:625–639. CrossRef Medline
Rotman AV, Masaquio SG, Takahashi K, Ebner TJ (2004) Kinematic analysis of manual tracking in monkeys: characterization of movement inter-mittencies during a circular tracking task. J Neurophysiol 91:901–911. CrossRef Medline
Salenius S, Salminen R, Neuper C, Pfurtscheller G, Hari R (1996) Human cortical 40 Hz rhythm is closely related to EMG rhythmicity. Neurosci Lett 213:75–78. CrossRef Medline
Salenius S, Portin K, Kajola M, Salminen R, Hari R (1997) Cortical control of human motoneuron firing during isometric contraction. J Neurophysiol 77:3401–3405. Medline
Schelter B, Winterhalder M, Eichler M, Peifer M, Hellwig B, Guschlbauer B, Lucking CH, Dahlhaus R, Timmer J (2006) Testing for directed influences among neural signals using partial directed coherence. J Neurosci Methods 152:210–219. CrossRef Medline
Schelter B, Timmer J, Eichler M (2009) Assessing the strength of directed influences among neural signals using renormalized partial directed coherence. J Neurosci Methods 179:121–130. CrossRef Medline
Schneider T, Neumaier A (2001) Algorithm 808: ARfit: a matlab package for the estimation of parameters and eigenmodes of multivariate autoregressive models. ACM Trans Math Softw 27:58–65. CrossRef
Scott SH (2004) Optimal feedback control and the neural basis of volitional motor control. Nat Rev Neurosci 5:532–546. CrossRef Medline
Scott SH (2012) The computational and neural basis of voluntary motor control and planning, Trends Cogn Sci 16:541–549. CrossRef Medline
Silén T, Fors N, Salenius S, Karjalainen T, Hari R (2002) Oscillatory cortical drive to isometrically contracting muscle in Unverricht-Lundborg type progressive myoclonus epilepsy (ULD). Clin Neurophysiol 113:1973–1979. CrossRef Medline
Sommerlade L, Eichler M, Jachan M, Henschel K, Timmer J, Schelter B (2009) Estimating causal dependencies in networks of nonlinear stochastic dynamical systems. Phys Rev E Stat Nonlin Soft Matter Phys 80(5):5128. CrossRef Medline
Sosnow JF, Jae SY, Heffernan K, Fernhall B (2011) Cardiovascular impulse and fluctuations in isometric force output. Motor Control 15:221–231. CrossRef Medline
Steiger JH (1980) Tests for comparing elements of a correlation matrix. Psychol Bull 87:245–251. CrossRef
Taulu S, Kajola M (2005) Presentation of electromagnetic multichannel data: the signal space separation method. J Appl Physiol 97:12940. CrossRef
Taulu S, Simola J (2006) Spatiotemporal signal space separation method for rejecting nearby interference in MEG measurements. Phys Med Biol 51: 1759–1768. CrossRef Medline
Theiler J, Eubank S, Longtin A, Galdrikian B, Doyne Farmer J (1992) Testing for nonlinearity in time series: the method of surrogate data. Phys D Nonlinear Phenom 58:77–94. CrossRef
Thomson DJ (1982) Spectrum estimation and harmonic analysis. Proc IEEE 70:1055–1096. CrossRef
Timmermann L, Gross J, Schmitz F, Freund HJ, Schnitzler A (2001) Involvement of the motor cortex in pseudochoreoathetosis. Mov Disord 16:876–881. CrossRef Medline
Todorov E, Jordan MI (2002) Optimal feedback control as a theory of motor coordination. Nat Neurosci 5:1226–1235. CrossRef Medline
Ushiyama I, Suzuki T, Masakado Y, Hase K, Kimura A, Liu M, Ushiba J (2011) Between-subject variance in the magnitude of corticospinal coherence during tonic isometric contraction of the tibialis anterior muscle in healthy young adults. J Neurophysiol 106:1379–1388. CrossRef Medline
Ushiyama I, Yamada J, Liu M, Ushiba J (2017) Individual difference in β-band corticospinal coherence and its relation to force steadiness during isometric voluntary ankle dorsiflexion in healthy humans. Clin Neurophysiol 128:303–311. CrossRef Medline
Van Veen B, Drongelen W, Yuchtman M, Suzuki A (1991) Localization of brain electrical activity via linearly constrained minimum variance spatial filtering. IEEE Trans Biomed Eng 44:867–880. CrossRef Medline
Waldert S, Preisil H, Demantd E, Braun C, Birbaumer N, Aertsen A, Mehring C (2008) Hand movement direction decoded from MEG and EEG. J Neurosci Methods 177:3401–3405. Medline
Wannier TM, Maier MA, Hepp-Reymond MC (1991) Contrasting properties of monkey somatosensory and motor cortex neurons activated during the control of force in precision grip. J Neurophysiol 65:572–589. Medline
Watanabe CL, Riddle CN, Baker MR, Baker SN (2011) Contributions of descending and ascending pathways to corticospinal coherence in humans. J Physiol 589:3789–3800. CrossRef Medline
Zion Golumbic EM, Ding N, Bickel S, Lakatos P, Schevon CA, McKhann GM, Goodman RR, Emerson R, Mehta AD, Simon JZ, Poeppel D, Schroeder CE (2013) Mechanisms underlying selective neuronal tracking of attended speech at a “cocktail party.” Neuron 77:980–991. CrossRef