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Impaired corticomuscular coherence during isometric elbow flexion contractions in humans with cervical spinal cord injury

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Abstract

After spinal cord injury (SCI), the reorganization of the neuromuscular system leads to increased antagonist muscles' co-activation—that is, increased antagonist vs. agonist muscles activation ratio—during voluntary contractions. Increased muscle co-activation is supposed to result from reduced cortical influences on spinal mechanisms inhibiting antagonist muscles. The assessment of the residual interactions between cortical and muscles activity with corticomuscular coherence (CMC) in participants with SCI producing different force levels may shed new lights on the regulation of muscle co-activation. To achieve this aim, we compared the net joint torque, the muscle co-activation and the CMC ~ 10 and ~ 20 Hz with both agonist and antagonist muscles in participants with SCI and healthy participants performing actual isometric elbow flexion contractions at three force levels. For all participants, overall CMC and muscle co-activation decreased with the increase in the net joint torque, but only CMC ~ 10 Hz was correlated with muscle co-activation. Participants with SCI had greater muscle co-activation and lower CMC ~ 10 Hz, at the highest force levels. These results emphasize the importance of CMC as a mechanism that could take part in the modulation of muscle co-activation to maintain a specific force level. Lower CMC ~ 10 Hz in SCI participants may reflect the decreased cortical influence on spinal mechanisms, leading to increased muscle co-activation, although plasticity of the corticomuscular coupling seems to be preserved after SCI to modulate the force level. Clinically, the CMC may efficiently evaluate the residual integrity of the neuromuscular system after SCI and the effects of rehabilitation.

Introduction

After spinal cord injury (SCI), the intensive reorganization of the neuromuscular system leads to increased antagonist muscles co-activation (Thomas *et al.*, 1998; Cremoux *et al.*, 2016). Muscle co-activation refers to the simultaneous activation of agonist and antagonist muscles, respectively, acting in and against the direction of the net joint torque (Kellis *et al.*, 2003). It takes an active part in joint stabilization according to the exerted force level (Baratta *et al.*, 1988; Solomonow *et al.*, 1988; Gribble *et al.*, 2003; Rao *et al.*, 2009; Amarantini & Bru, 2015). After SCI, increased muscle co-activation may be caused by reduced influence of the cortical structures on the spinal mechanisms inhibiting antagonist muscles (Boorman *et al.*, 1996; Xia & Rymer, 2005), and especially altered reciprocal inhibition (Cremoux *et al.*, 2016). Therefore, the residual interactions between cortical and muscles' activities may play a major role in the regulation of muscle co-activation.

Interestingly, the corticomuscular coherence (CMC) can be taken to investigate motor cortex-to-muscle interactions. CMC is the spectral relationship between the electroencephalographic activity (EEG) recorded over the primary motor cortex (M1) and the electromyographic (EMG) activity of the muscles involved in the motor performance (Salenius & Hari, 2003). Significant CMC is found in the frequency band ~ 10 and ~ 20 Hz (Mima & Hallett, 1999). The CMC ~ 20 Hz is supposed to reflect the direct implication of the M1 neurons in muscle activations (Conway *et al.*, 1995). The modulation of the magnitude of the CMC ~ 20 Hz is thought to be specifically related to the task performance (Kristeva-Feige *et al.*, 2002) and has functional relevance for the modulation of the net joint torque (Chakarov *et al.*, 2009; Ushiyama *et al.*, 2010, 2012). The neurophysiological processes underlying CMC ~ 10 Hz are still object of debates in the literature. On the one side, some authors

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proposed that CMC ~ 10 Hz could reflect some integrative cortical processing of sensory afferent inputs (Vecchio *et al.*, 2008; Budini *et al.*, 2014). For example, Budini *et al.* (2014) revealed CMC between EEG channels over the sensorimotor cortex and the EMG from biceps brachii (BB) muscle in healthy individuals performing sustained elbow contractions against a spring load and in isometric conditions. CMC ~ 10 Hz was found in some participants during isometric contractions and in all but one participants during contractions against the spring load. These results were interpreted as enhanced afferent activity from muscle spindles during contractions against the spring load. On the other side, based on the systematic phase difference between cortex and muscles activation, Raethjen *et al.* (2002) interpreted CMC ~ 10 Hz as a transmission of information from the supraspinal structures to the muscles. Both of these interpretations are supported by Williams & Baker (2009a,b) who modeled that a reduction in CMC ~ 10 Hz can be understood by spinal inhibitory mechanisms, enhanced by sensory afferent inputs. It is well known that reciprocal inhibition mechanism, inhibiting antagonist muscles activation, is under the influence of both sensory and cortical information (Schomburg, 1990; Jankowska, 1992). A modulation of the CMC ~ 10 Hz with antagonist muscles could thus reflect an alteration of the cortical control on spinal reciprocal inhibition after SCI.

This study aimed to test whether the CMC ~ 10 and ~ 20 Hz are linked to the level of co-activation in healthy people and following SCI. All participants performed elbow flexion contractions at different force levels. We hypothesized differences in the magnitude of CMC with both agonist and antagonist muscles with the modulation of force level between participants. An alteration of CMC ~ 10 Hz especially with antagonist muscles, correlated with the level of muscle co-activation, was expected in participants with cervical SCI. Such an alteration could reflect the reduced cortical influences on spinal inhibitory mechanisms controlling muscle co-activation.

Materials and methods

Participants

Eighteen volunteers participated in this study. Prior to any procedure, all participants signed informed consent to participate after receiving explicit information about the experimental design. The study protocol followed the local ethic guidelines from the Faculty of Sport Sciences and Human Movement, Paul Sabatier University (Toulouse 3) in Toulouse, France. All participants were right-handed as assessed by the Edinburgh handedness inventory (mean laterality quotient: 69.3 ± 23.8%; Oldfield, 1971). Two groups of participants, matched for age, mass and height (*t*-tests; all $P > 0.05$), were distinguished. The SCI group included eight participants (age: 32.5 ± 6.2 years; mass: 61.5 ± 13.3 kg; height: 174.7 + 9.7 cm). Seven participants (one female) had a complete SCI located from C5-C6 to C8-T1 vertebrae, and one participant had an incomplete SCI located at the C5-C6 vertebrae (graded D on the American Spinal Injury Association Impairment Scale). The able-bodied (AB) group included 10 healthy participants with no neuromusculoskeletal or sensory disorders (27.0 ± 4.0 years; 69.6 ± 8.0 kg; 175.3 ± 4.5 cm).

Materials

The net moment was recorded around the right elbow joint at 1 kHz using a calibrated dynamometer (System 4 Pro, Biodex Medical Systems, Shirley, NY, USA).

Electromyographic was recorded from four muscles of the right upper limb at 1000 Hz with Ag-AgCl EL503 surface electrodes connected to MP 150 amplifiers (Biopac Systems Inc., Goleta, USA). Electrodes were placed with a 2-cm inter-electrode distance on the belly of each muscle following suitable skin preparation (Hermens *et al.*, 2000). The BB and brachioradialis (BR) were chosen as representative of elbow flexors, and the long and lateral heads of the triceps brachii (TBlh and TBlt, respectively) were chosen as representative of elbow extensors (Bouisset *et al.*, 1976; Buchanan *et al.*, 1989). The reference electrode was placed on the left ulna styloid process.

Electroencephalography was recorded at 1024 Hz from 64 electrodes mounted on a 10–20 system cap (Active II, Biosemi Inc., Amsterdam, the Netherlands). Electro-oculogram was recorded from the left eye to detect any eye movements or blinks.

Time synchronization of data acquisitions was achieved offline using a TTL pulse.

Experimental setup

Participants were seated on the chair of the dynamometer with their trunk firmly strapped to the back of the chair. The right arm was positioned along the trunk, and the right forearm was supinated and 90° flexed relative to the arm before being strapped to the limb support of the dynamometer. Participants were asked to place the left arm at rest on the left thigh.

Protocol

Prior the experimental session, participants performed 3 so-called relative Maximum Voluntary Contractions (rMVC) around the right elbow joint in flexion. The rMVC was determined as the highest net moment reached while keeping at rest all the muscles not involved in the task, especially face and neck muscles, to avoid muscles artifact in EEG recordings (Dal Maso *et al.*, 2012; Cremoux *et al.*, 2013a,b). The experimental protocol consisted of 21 elbow isometric flexion contractions at 25, 50 and 75% rMVC randomized in seven sets of contractions. Each contraction lasted 6 s and was followed by a 6 s rest. Each set of contractions was followed by a 3-min rest period. The required force level was presented with a visual feedback (Presentation program, NeuroBehavioral Systems Inc. Albany, USA) appearing on a screen located 1 m in front of the participants. A full description of the experimental protocol is given in Cremoux *et al.* (2013a).

Data analysis

The continuous data were reduced into [-0.5 + 8] s trials from the appearance of the visual feedback. Each trial was visually inspected through the EEGLAB Matlab toolbox (Delorme & Makeig, 2004) to remove trials where EEG signals were contaminated by muscle artifacts. Whatever the force level, the number of trials used for further analysis was similar for all participants (18.01 ± 2.29; $P > 0.05$).

All filters mentioned below were fourth-order, zero-lag Butterworth-type filters.

Net torque production

The net torque signal was low-pass filtered at 10 Hz (Nordez *et al.*, 2008). For each trial, the net torque production was averaged over a [+3 + 6] s period, considered as a relevant period of interest.

Muscle co-activation

Raw EMG data were [10–400] Hz band-pass filtered, full-wave rectified and 9 Hz low-pass filtered to obtain the linear envelope (Shiavi *et al.*, 1998). As recommended by Kellis *et al.* (2003), the muscle co-activation between elbow agonist/antagonist muscle pairs, expressed as a percentage, was calculated over the [+3 + 6] s period of interest from MVC-normalized linear envelopes of antagonist (TBlt and Tblh) and agonist (BB and BR) muscles (Falconer & Winter, 1985; Winter, 2005; Amarantini & Bru, 2015).

$$\text{Muscle Co-activation} = \frac{2 \times \text{EMG}_{\text{ANTAGO}}}{\text{EMG}_{\text{AGO}} + \text{EMG}_{\text{ANTAGO}}} \times 100\% \quad (1)$$

Corticomuscular coherence

Corticomuscular coherence was calculated in the time-frequency domain using the *WaveCrossSpec* software for wavelet coherence analysis (Bigot *et al.*, 2011; http://www.math.u-bordeaux1.fr/~jbigot/Site/Software_files/WavCrossSpec.zip) between the signal from the C3 EEG electrode and each of the four EMG signals. Previous methodological studies revealed that time-frequency transformation was most suitable to conventional frequency domain analysis for analyzing coherence in non-stationary electrophysiological signals (Zhan *et al.*, 2006; Allen & MacKinnon, 2010; Bigot *et al.*, 2011), even though the quantification of corticomuscular interactions is subsequently quantified over a specified time period of interest. C3 EEG electrode was taken as the optimal location for studying cortical activity dedicated to right elbow muscle contractions, in accordance with previous investigations (Siemionow *et al.*, 2000; Caviness *et al.*, 2006; Tuncel *et al.*, 2010; Cremoux *et al.*, 2013a,b).

For CMC calculation, the following steps were used. The EEG and EMG data were first band-pass filtered at [3–100] Hz and notched at [45–55] Hz (Sabri & Campbell, 2002; Baker & Baker, 2012; Dal Maso *et al.*, 2012; Cremoux *et al.*, 2013b). Channels visually identified as 'bad' channels were removed, and EEG signals were average referenced (Delorme *et al.*, 2007; note that the C3 EEG channel has never been identified as 'bad' channel during this step; see Fig. 1A and B after these processing steps). The wavelet power spectrum of centered C3 EEG signal (Fig. 1C) and each unrectified EMG signals (Fig. 1D) was then obtained with parameters 'nvoice' (scale resolution of the wavelet), 'J1' (number of scales) and 'wavenumber' (Morlet mother wavelet parameter) set, respectively, to 0.125, 871 and 7 to yield accurate identification of oscillatory activity from 0.13 Hz to 114.39 Hz in 1.07 Hz step. EMG signals were not rectified to properly model EMG time series as centered Gaussian processes (Bigot *et al.*, 2011; Charissou *et al.*, 2016) and not to lose important information contained in the EMG signal spectrum (Neto & Christou, 2010; McClelland *et al.*, 2012; Yang *et al.*, 2016). The wavelet cross-spectrum (Fig. 1E), that is, the common power spectrum between the centered C3 EEG signal and each unrectified EMG signal, was calculated using the following equation.

$$\boldsymbol{S}_{\mathbf{EMG,EEG}}(\boldsymbol{\omega}, \boldsymbol{u}) = \mathbb{E}\left(\boldsymbol{W}_{\mathbf{EMG}}(\boldsymbol{\omega}, \boldsymbol{u})\overline{\boldsymbol{W}_{\mathbf{EEG}}(\boldsymbol{\omega}, \boldsymbol{u})}\right) \quad (2)$$

where $\boldsymbol{S}_{\mathbf{EMG}}(\boldsymbol{\omega}, \mathbf{u})$ and $\boldsymbol{S}_{\mathbf{EEG}}(\boldsymbol{\omega}, \boldsymbol{u})$ are the wavelet auto-spectrum of each **EMG** and **EEG** signal, respectively, which are defined as

$$\boldsymbol{S}_{\mathbf{EMG}}(\boldsymbol{\omega}, \boldsymbol{u}) = \mathbb{E}|\boldsymbol{W}_{\mathbf{EMG}}(\boldsymbol{\omega}, \boldsymbol{u})|^2 \quad (3)$$

$$\boldsymbol{S}_{\mathbf{EEG}}(\boldsymbol{\omega}, \boldsymbol{u}) = \mathbb{E}|\boldsymbol{W}_{\mathbf{EEG}}(\boldsymbol{\omega}, \boldsymbol{u})|^2 \quad (4)$$

The values of the wavelet cross-spectrum between EEG and EMG signals that were above the significant threshold $\hat{\boldsymbol{\lambda}}_{\boldsymbol{\alpha}}$ (with $\boldsymbol{\alpha} = 0.05$) were considered as significant interactions (Bigot *et al.*, 2011). The significance threshold was calculated using the following equation.

$$\hat{\boldsymbol{\lambda}}_{\boldsymbol{\alpha}} = \frac{\hat{\boldsymbol{\rho}}\mathbf{EMG}\hat{\boldsymbol{\rho}}\mathbf{EEG}}{\left(1 + \sqrt{\frac{\mathbf{T}}{\mathbf{n}}}\right)^2}\left(-\frac{\log(\boldsymbol{\alpha}/\mathbf{2})}{\mathbf{n}} + \sqrt{-\frac{\mathbf{2}\log(\boldsymbol{\alpha}/\mathbf{2})}{\mathbf{n}}}\right) \quad (5)$$

With $\hat{\boldsymbol{\rho}}_{\mathbf{EMG}}$ and $\hat{\boldsymbol{\rho}}_{\mathbf{EEG}}$ being the largest eigenvalue of the empirical covariance matrix of the EMG and the EEG signal, respectively. The computation of the threshold is thus data-based as it includes an estimation of the variance of the two time series. This procedure is particularly adapted for signals having different magnitude of covariance.

Finally, the wavelet magnitude-squared coherence (Fig. 1F), that is, the cross-spectrum normalized by the power spectrum of each signal, was calculated using the following equations.

$$\boldsymbol{R}^2_{\mathbf{EMGEEG}}(\boldsymbol{\omega}, \boldsymbol{u}) = \frac{|\boldsymbol{S}_{\mathbf{EMG,EEG}(\boldsymbol{\omega},\boldsymbol{u})}|^2}{\boldsymbol{S}_{\mathbf{EMG}}(\boldsymbol{\omega}, \mathbf{u})\boldsymbol{S}_{\mathbf{EEG}}(\boldsymbol{\omega}, \mathbf{u})}, \quad (6)$$

where $\mathbf{S}_{\mathbf{EEG,\ EEG}}(\boldsymbol{\omega},\ \boldsymbol{u})$ is the wavelet cross-spectrum between **EMG** and **EEG** signals (Eqn 2), and $\mathbf{S}_{\mathbf{EMG}}(\boldsymbol{\omega},\ \boldsymbol{u})$ and $\mathbf{S}_{\mathbf{EEG}}(\boldsymbol{\omega},\ \boldsymbol{u})$ are the wavelet auto-spectrum of each **EMG** and **EEG** signal (Eqns 3 and 4).

The magnitude of the CMC was calculated from 0 to 1 bounded corticomuscular values as the volume under the time-frequency map of magnitude-squared coherence only where the wavelet cross-spectrum between the EEG and EMG signals was detected as significant (Charissou *et al.*, 2016; Yoshida *et al.*, 2017). Over the [+3 + 6] s period of interest, the magnitude of the CMC was computed in two frequency bands of interest: [8–13] Hz ($CMC_{8\text{-}13}$) (Christou *et al.*, 2007) and [13–31] Hz ($CMC_{13\text{-}31}$) (Mima *et al.*, 1999). For each frequency band, the magnitude of the CMC was finally averaged for two elbow flexor muscles, BB and BR, and for two elbow extensor muscles, TBlh and TBlt.

Figure 2 illustrates more precisely the modulation of the magnitude of the CMC depicted in Fig 1E over frequency in the period of interest (left panel) and time in the frequency bands of interest (bottom panel).

Statistical analysis

A two-factor group (between-subjects factor: AB vs. SCI) × force level (within-subjects factor: 25% vs. 50% vs. 75%) mixed analysis of variance (ANOVA) was conducted on the mean net torque, muscle co-activation and magnitude of CMC. For the latter, independent ANOVA was performed for $CMC_{8\text{-}13}$ and $CMC_{13\text{-}31}$ magnitude with elbow flexors and extensors with η_p^2 reported to represent effect size. Huynh & Feldt (1976) correction for degrees of freedom was used where applicable. For each force level, Spearman's correlation coefficients were calculated to test the strength of correlation between muscle co-activation and $CMC_{8\text{-}13}$ and $CMC_{13\text{-}31}$ magnitude with elbow flexors and extensors. For all statistical tests, the level of significance was set at $P < 0.05$.

Results

Net torque

The ANOVA performed on the mean net torque revealed only a main force level effect ($F_{2,32} = 208.77$; $P < 0.01$; $\eta_p^2 = 0.93$). For

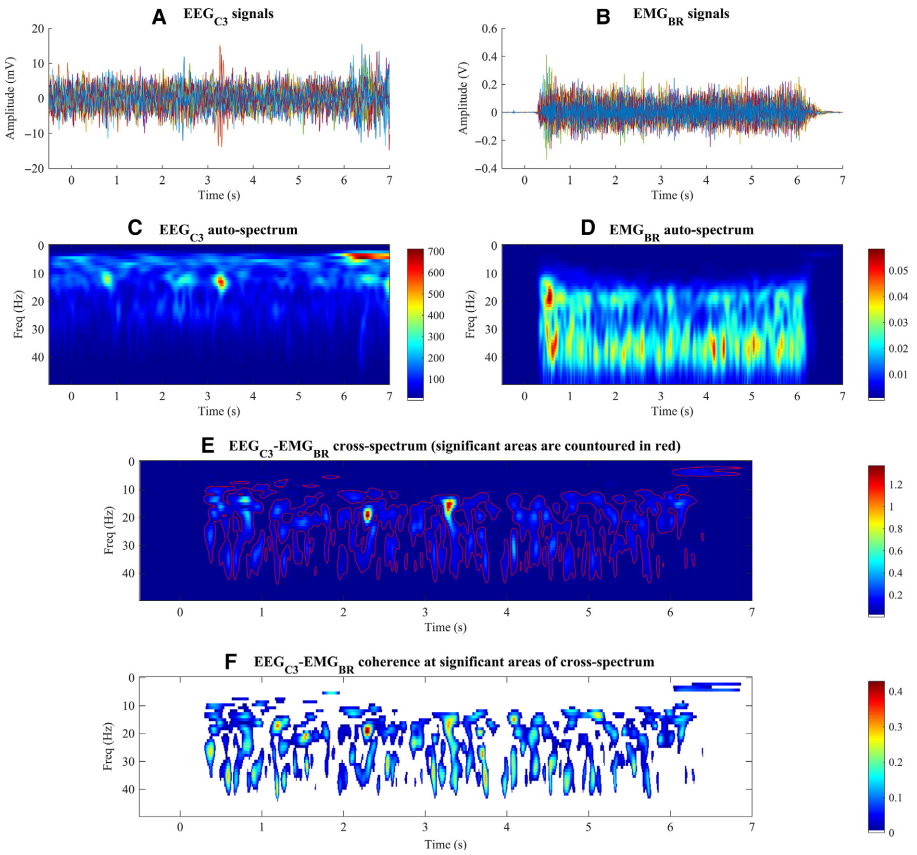

FIG. 1. Illustration of the processing steps used for time-frequency analysis of corticomuscular coherence from one representative able-bodied participant. First row: typical recordings of C3 electroencephalography (EEG) signals (A) and brachioradialis (BR) electromyographic (EMG) signals (B) obtained during contractions at 25% relative Maximum Voluntary Contraction after filtering and C3 EEG signals normalization. Second row: auto-spectra of the C3 EEG (C) and BR EMG (D) time series. Third row (E): wavelet cross-spectrum between the C3 EEG and the BR EMG time series; the red contours identify the time-frequency areas where the correlation between the C3 EEG and BR EMG time series is significant. Fourth row (F): significant wavelet magnitude-squared coherence between the C3 EEG and BR EMG signals in the time-frequency domain. All non-significant values are whitened. [Colour figure can be viewed at wileyonlinelibrary.com].

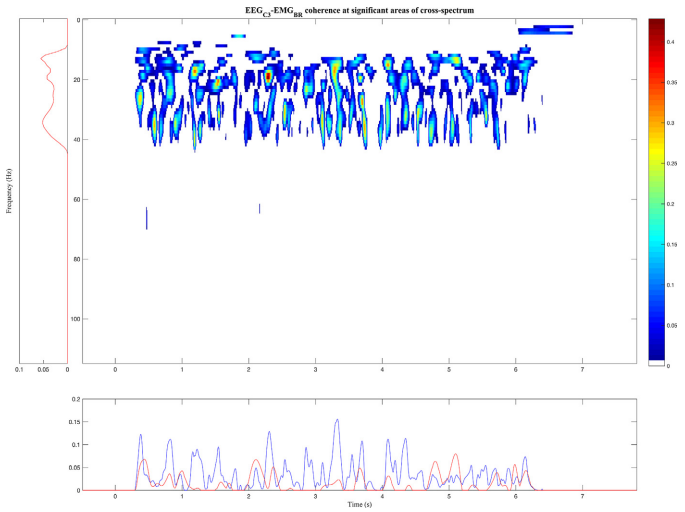

FIG. 2. Significant wavelet magnitude-squared coherence between the C3 electroencephalography and brachioradialis electromyographic signals in the time-frequency domain (also depicted in Fig. 1F). All non-significant values are whitened. Left panel: average corticomuscular coherence in the period of interest. Bottom panel: average corticomuscular coherence in the 8–13 Hz (red line) and 13–31 Hz (blue line) frequency bands of interest over time. [Colour figure can be viewed at wileyonlinelibrary.com].

all participants, the mean net torque increased from 10.63 ± 3.25 Nm at 25% rMVC to 30.89 ± 8.59 Nm at 75% rMVC (Fig. 3A).

Muscle co-activation

The ANOVA performed on the muscle co-activation revealed a force level effect ($F_{2,32} = 14.94$; $P < 0.01$; $\eta_p^2 = 0.48$) and a group effect

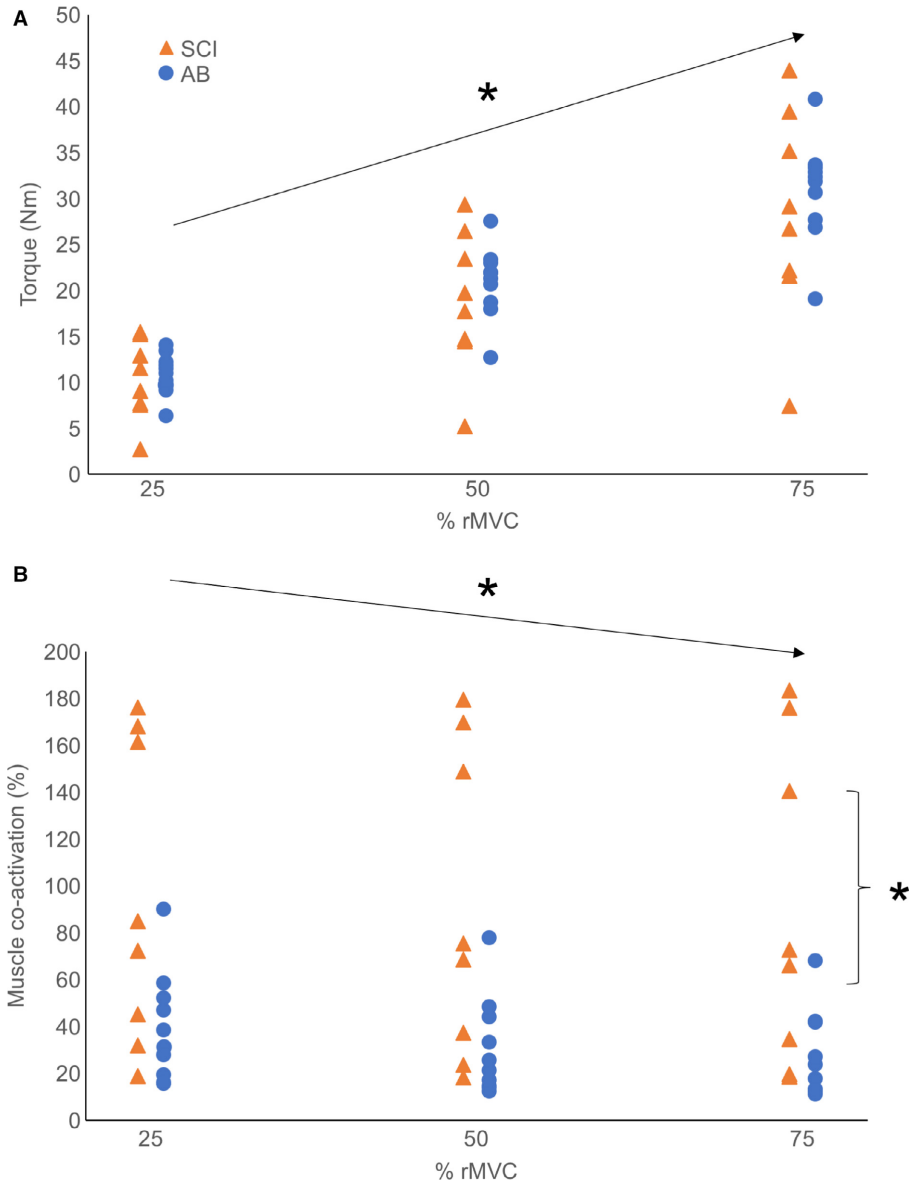

FIG. 3. Net joint torque (A) and muscle co-activation (B) for the participants with spinal cord injury (orange triangle) and healthy participants (blue square). * next to a curly bracket represents a significant group effect; * above an arrow represents significant force level effect. [Colour figure can be viewed at wileyonlinelibrary.com].

($F_{1,16}$ = 7.12; P = 0.02; η_p^2 = 0.31). For all participants, the muscle co-activation decreased from 64.11 ± 52.93% at 25% rMVC to 54.44 ± 55.72% at 75% rMVC. All force levels combined, and the muscle co-activation was higher for the SCI group (91.23 ± 63.53%) in comparison with that of the AB group (32.40 ± 20.94%) (Fig. 3B).

Magnitude of $CMC_{8\text{-}13}$

The ANOVA performed on the magnitude of the $CMC_{8\text{-}13}$ with elbow flexors only revealed a force level effect ($F_{2,32}$ = 21.98; P < 0.01; η_p^2 = 0.58). For all participants, the magnitude of the $CMC_{8\text{-}13}$ with elbow flexors decreased by 72.25 ± 29.43% from 25% rMVC to 75% rMVC (Fig. 4A).

Concerning the magnitude of the $CMC_{8\text{-}13}$ with elbow extensors, the ANOVA revealed a force level ($F_{2,32}$ = 21.29; P < 0.01; η_p^2 = 0.57) and a group effect ($F_{1,16}$ = 124.38; P = 0.04; η_p^2 = 0.24). For all participants, the magnitude of the $CMC_{8\text{-}13}$ with elbow extensors decreased by 46.94 ± 27.06% from 25% rMVC to 75% rMVC (Fig. 4A). All force levels combined, and the magnitude of the $CMC_{8\text{-}13}$ with elbow extensors was smaller for the SCI group in comparison with that of the AB group (Fig. 4B).

Magnitude of $CMC_{13\text{-}31}$

The ANOVA performed on the magnitude of the $CMC_{13\text{-}31}$ with elbow flexors only revealed a force level effect ($F_{2,32}$ = 8.69; P < 0.01; η_p^2 = 0.35). For all participants, the magnitude of the $CMC_{13\text{-}31}$ with elbow flexors decreased by 22.20 ± 27.19% from 25% rMVC to 75% rMVC (Fig. 5A).

Concerning the magnitude of the $CMC_{13\text{-}31}$ with elbow extensors, the ANOVA only revealed a force level ($F_{2,32}$ = 5.54; P < 0.01;η_p^2 = 0.26). For all participants, the magnitude of the $CMC_{13\text{-}31}$ with elbow extensors decreased by 5.34 ± 53.97% from 25% rMVC to 75% rMVC (Fig. 5B).

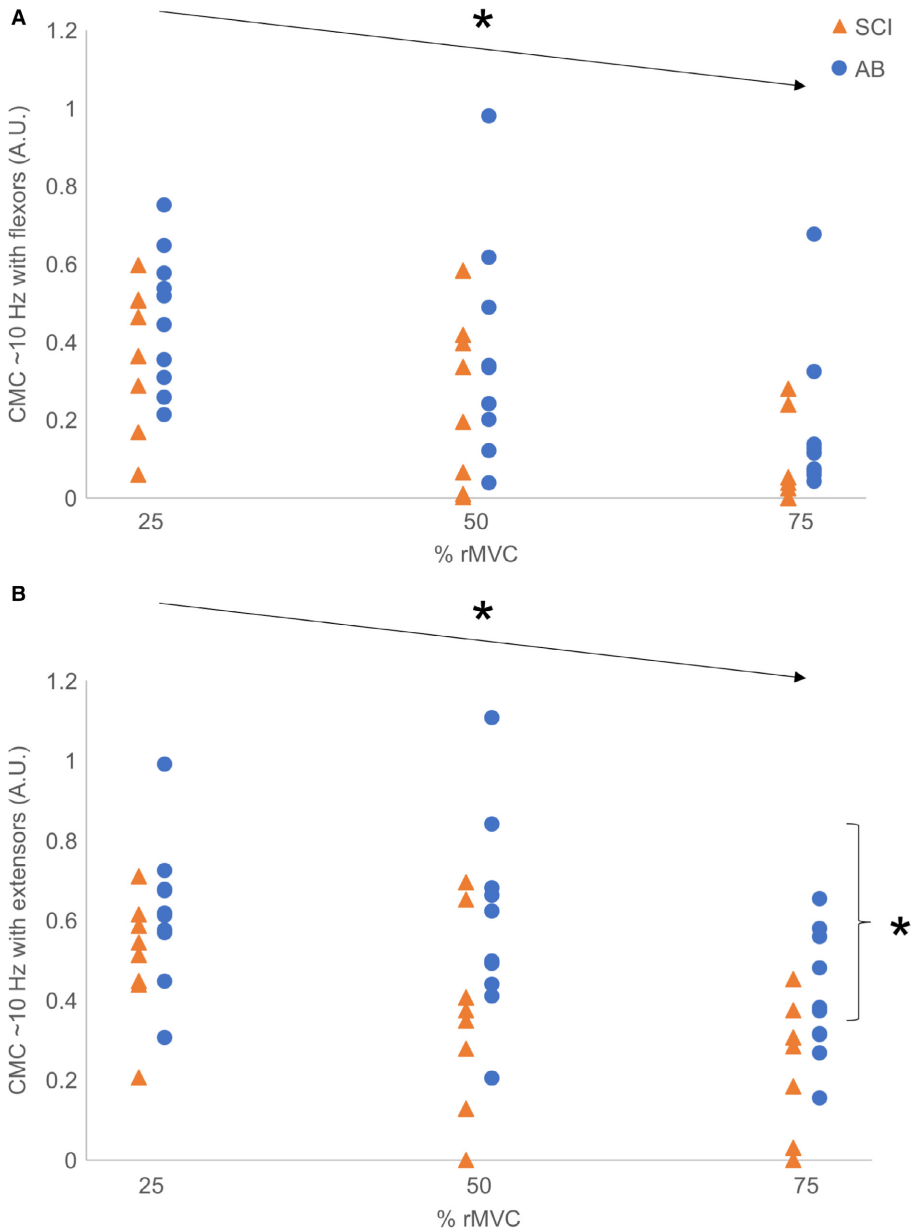

FIG. 4. Corticomuscular coherence ~ 10 Hz with elbow flexors (A) and elbow extensors (B) for the participants with spinal cord injury (orange triangle) and healthy participants (blue square). * next to a curly bracket represents a significant group effect; * above an arrow represents significant force level effect. [Colour figure can be viewed at wileyonlinelibrary.com].

Correlation between muscle co-activation and CMC

The modulation of muscle co-activation was significantly negatively correlated with the levels of $CMC_{8\text{-}13}$ with both elbow flexors and extensors at 50% rMVC (r_s = -0.42, P = 0.04 and r_s = -0.57, P = 0.01, respectively) and 75% rMVC (r_s = -0.46, P = 0.03 and r_s = -0.58, P = 0.01, respectively).

Discussion

This study aimed to evaluate the modulation of muscle co-activation in people with cervical SCI compared to healthy participants by evaluating the corticomuscular coupling with agonist and antagonist muscles. All participants were able to perform voluntary isometric elbow flexion contractions at different submaximal force levels. For all participants, CMC ~ 10 Hz was significantly correlated with muscle co-activation level, and participants with cervical SCI presented increased muscle co-activation and decreased CMC ~ 10 Hz with elbow extensors in comparison with healthy participants. The increase in the force level was associated with a decrease in the magnitude of the CMC ~ 10 and ~ 20 Hz with both elbow flexors and extensors.

Decreased CMC ~ 10 Hz is correlated with increased muscle co-activation

Even though all participants exerted comparable net joint torque, our results revealed increased muscle co-activation in the SCI group. This increase in muscle co-activation mainly arises from increased antagonist muscles activation, as previously shown in participants with SCI during both electrically evoked and voluntary contractions

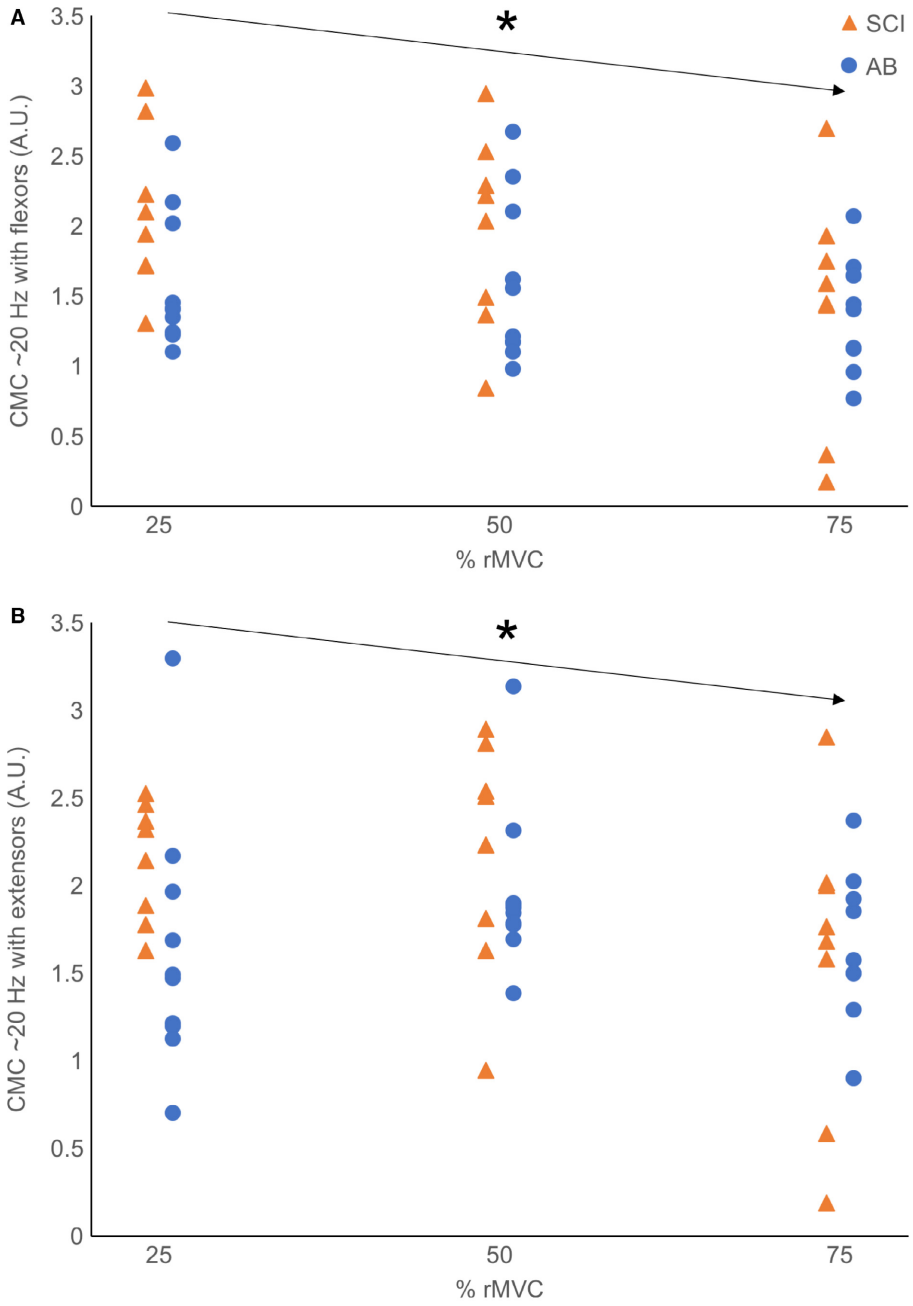

FIG. 5. Corticomuscular coherence ~ 20 Hz with elbow flexors (A) and elbow extensors (B) for the participants with spinal cord injury (orange triangle) and healthy participants (blue square). * above an arrow represents significant force level effect. [Colour figure can be viewed at wileyonlinelibrary.com].

(Thomas *et al.*, 1998; Cremoux *et al.*, 2016). Although necessary for data comparison, the normalization of EMG data revealed a supramaximal activation of elbow extensors when used as antagonist muscles (Cremoux *et al.*, 2012). Increased antagonist muscles activation is supposed to be due to the disruption of the descending pathways regulating spinal reciprocal inhibition mechanisms (Boorman *et al.*, 1996; Xia & Rymer, 2005; Knikou & Mummidisetty, 2011).

In the SCI group, CMC ~ 10 Hz with elbow extensors was lower in comparison with healthy participants. Higher CMC ~ 10 Hz was unexpected in healthy people given that CMC ~ 10 Hz is supposed to be either reduced or absent because of efficient spinal inhibitory mechanisms (Williams & Baker, 2009a,b). The detection of significant CMC ~ 10 Hz has been improved using a novel statistical procedure based on the EEG-EMG cross-spectrum (Bigot *et al.*, 2011). This statistical procedure is particularly relevant to detect truly significant corticomuscular interactions when the number of contractions is small (Lu *et al.*, 2013; Pedrosa *et al.*, 2014). In healthy people, CMC ~ 10 Hz is supposed to reflect complex two-way communication between cortical and muscles structures (Raethjen *et al.*, 2002, 2007; Budini *et al.*, 2014). The specific decrease in CMC ~ 10 Hz with antagonist muscles revealed in people with SCI may

highlight both concomitant decreased cortical integration of somatosensory afferent inputs and the decreased influence of cortical structures on spinal reciprocal inhibition mechanisms modulating antagonist muscles activation. Previous results also revealed altered EEG-EMG and EMG-EMG coherence ~ 10 Hz after SCI (Babiloni *et al.*, 2004; Hansen *et al.*, 2005). All of these results can be understood by the neurophysiological mechanisms underlying motor recovery following SCI. CMC ~ 10 Hz may efficiently evaluate the residual integrity of the neuromuscular system after SCI and the effects of rehabilitation.

An interesting finding is that for all participants, the increase in muscle co-activation was significantly correlated with the decrease in the magnitude of the CMC ~ 10 Hz with both elbow flexors and extensors. Even if further work is needed to reach a definitive conclusion, CMC ~ 10 Hz could then reflect a more general central mechanism controlling muscle co-activation through spinal inhibitory mechanisms. This would be in line with previous studies that inferred that the modulation of neurophysiological oscillations ~ 10 Hz could reflect complex corticospinal mechanisms modulating both agonist and antagonist muscles co-activation (Vallbo & Wessberg, 1993; Wessberg & Vallbo, 1996; Wessberg & Kakuda, 1999).

Both CMC ~ 10 and ~ 20 Hz decrease with the increase in the force level

For all participants, the increase in the force level was associated with a decrease in the muscle co-activation and in the magnitude of both CMC ~ 10 and ~ 20 Hz with elbow flexors and extensors. Previous studies indicated that the magnitude of the CMC ~ 20 Hz is modulated with the task performance (Kristeva-Feige *et al.*, 2002) and the force level (Mima *et al.*, 1999; Chakarov *et al.*, 2009; Ushiyama *et al.*, 2012). The scope of the aforementioned studies was, however, limited to the modulation of the CMC ~ 20 Hz with agonist muscles. Dal Maso *et al.* (2012) suggested that the cortical oscillations ~ 20 Hz recorded over the M1 might have a critical role in the modulation of antagonist muscle activations. The decrease in the magnitude of the CMC ~ 10 and ~ 20 Hz with the force level could thus reflect a functional neurophysiological mechanism that would take part in the control of the exerted force by modulating agonist and antagonist muscle activations. The overall decrease in the magnitude of the CMC with the increase in the force level and the specific decrease in the magnitude of the CMC ~ 10 Hz with the increase in muscles co-activation may thus shed new light on the 'common drive' principle (De Luca & Mambrito, 1987; Miles, 1987; De Luca & Erim, 1994, 2002; Mullany *et al.*, 2002). This principle supposes that the modulation of one master-driving cortical signal influences multiple antagonistic muscle activations. In such a context, the CMC ~ 10 Hz could represent the common drive influencing spinal inhibitory mechanisms that are degraded after cervical SCI, while CMC ~ 20 Hz could represent neurophysiological pathways exciting directly the motoneurons involved in the activation of both agonist and antagonist muscles during voluntary contractions. Both 10 Hz and 20 Hz frequency bands would be modulated in amplitude to adapt the level of agonist and antagonist muscles to the requested task. This interpretation would be in line with the influence of the cortical descending pathways on the spinal network as described in Duchateau & Baudry (2014). Despite the care taken to ensure the comparison across the conditions, results revealed in this study cannot rule out the implication of the other physiological systems that may influence motor output differently depending on the produced force level (Heroux & Gandevia, 2013; Farina *et al.*, 2014). To further investigate this interpretation about the neurophysiological mechanisms underlying CMC, it would be interesting to assess the relationship between the CMC and agonist and antagonist muscles activation using transcranial magnetic stimulation, which has direct access to the neuronal circuitry of the motor cortex (Hansen & Nielsen, 2004) in healthy and SCI participants.

Conclusion

Our results revealed that both force level and SCI modulate the muscle co-activation and the magnitude of the CMC during isometric elbow flexion contractions. On the one hand, the magnitude of the CMC ~ 10 and ~ 20 Hz, and muscle co-activation decreased with the increase in the force level for the two groups but only CMC ~ 10 Hz was correlated with muscle co-activation. These results emphasize the importance of corticomuscular coupling as a mechanism that could take part in the modulation of the muscle co-activation to maintain a specific force level. They also suggest a preserved plasticity of the corticospinal drive allowing to modulate force in participants with SCI. On the other hand, participants with cervical SCI had an increased muscle co-activation associated with a decreased magnitude of the CMC ~ 10 Hz with antagonist muscles. This result suggests that CMC ~ 10 Hz may reflect the alteration of the cortical mechanisms controlling muscle co-activation after a cervical SCI, especially through spinal reciprocal inhibition. Although further investigations are needed to complement these results, corticomuscular coupling appears to be a promising tool to explore the cortical mechanisms involved in the modulation of muscle co-activation. In a clinical environment, these results may have potential relevance to assess the integrity of the neurophysiological pathways of voluntary motor functions after SCI and its plasticity with rehabilitation.

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Conflict of interest

The authors of the manuscript declare no conflict of interest, including any financial, personal or other relationships with other people or organization.

Author contributions

Each author has been involved in the design of the study, collection, analysis and interpretation of data and writing of the manuscript.

Data accessibility

Raw data supporting this article can be received by e-mail upon request.

Abbreviations

AB, able-bodied; ANOVA, analysis of variance; BB, biceps brachii; BR, brachioradialis; CMC, corticomuscular coherence; EEG, electroencephalography; EMG, electromyography; M1, primary motor cortex; rMVC, relative Maximum Voluntary Contraction; SCI, spinal cord injury; TBlh, triceps brachii long head; TBlt, triceps brachii lateral head; TTL, transistor-transistor logic.

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