Prolonged reaction time during episodes of elevated β-band corticomuscular coupling and associated oscillatory muscle activity

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1Graduate School of Science and Technology, Keio University, Kanagawa, Japan; 2Department of Rehabilitation Medicine, Keio University School of Medicine, Tokyo, Japan; and 3Department of Biosciences and Informatics, Faculty of Science and Technology, Keio University, Kanagawa, Japan

Matsuya R, Ushiyama J, Ushiba J. Prolonged reaction time during episodes of elevated β-band corticomuscular coupling and associated oscillatory muscle activity. J Appl Physiol 114: 896–904, 2013. First published February 7, 2013; doi:10.1152/japplphysiol.00942.2012.—Oscillatory activity in the sensorimotor cortex is coherent with 15–35 Hz band (β-band) muscle activity during tonic isometric voluntary contractions. In human subjects with higher corticomuscular coherence, prominent group discharge associated with a significant silent period was observed in electromyographic (EMG) signals. We examined the potential effects of β-band corticomuscular coupling on new ballistic movement as assessed by reaction time (RT). First, we quantified the coherence between electroencephalographic (EEG) signals over the sensorimotor cortex and rectified EMG signals from the tibialis anterior muscle during tonic isometric voluntary dorsiflexion at 30% of maximal effort in 15 healthy subjects. Subjects were divided into 2 groups (i.e., those with significant EEG-EMG coherence (COH+, n = 8) and those with no significant coherence (COH−, n = 7)). Next, subjects performed ballistic contractions from a preliminary state of sustained contractions in reaction to auditory signals. RT was defined as the interval between the signal and the response onset measured by force. There were no intersubject differences in RT between COH+ and COH−. However, when the trials performed by COH+: subjects were divided into 2 groups depending on whether clear group discharge in the β-band was observed in the EMG (GD+ or GD−) just prior to the reaction, RT was significantly longer in the GD+ than in the GD− trials. We found that the magnitude of EEG-EMG coherence just before the reaction was significantly greater in the GD+ than in the GD− trials. These results suggest that generation of a new movement is delayed when corticomuscular coupling is elevated.

EEG-EMG coherence; β-band oscillation; motor function

Recently, we reported that the magnitude of EEG-EMG coherence varies among individuals, even within the same population (i.e., healthy young adults) (28, 55, 56). Furthermore, it has been quantitatively demonstrated that the stronger the magnitude of EEG-EMG coherence, the more prominent the β-band group discharge in EMG signals (55). These data lead us to expect that differences in motor performance among individuals are the result of variation in EMG activation patterns depending on the strength of corticomuscular coupling. However, further electrophysiological and kinematic analyses are needed to clarify the functional role of corticomuscular coupling in motor function.

It has recently been estimated that β-oscillations in the corticospinal system affect new ballistic movements. Indeed, Pogosyan et al. (45) demonstrated that transcranial alternating-current stimulation at 20 Hz enhances β-band corticomuscular coherence and slows velocity when initiating voluntary movements. Considering this phenomenon along with our recent data showing a relationship between the magnitude of EEG-EMG coherence and EMG β-oscillation (55), it is possible that the magnitude of corticomuscular coherence is a determinant of the variation in the kinesiological index related to the initiation of movement among individuals. Thus, we hypothesize that individual differences in corticomuscular coherence produce variations in the generation of new ballistic movements from the steady contraction state. Furthermore, it seems likely that the β-oscillation in the periphery is not constant throughout the task, even during steady contractions (19). Because moment-to-moment changes in the magnitude of corticomuscular coupling would vary the strength of oscillation in the periphery, we hypothesized that ballistic reaction performance is interrupted when the magnitude of β-band corticomuscular coupling is naturally elevated.

The present study aimed to test the two hypotheses mentioned above. First, we examined the intersubject differences in reaction time (RT) depending on the magnitudes of EEG-EMG coherence. Second, in subjects who showed significant EEG-EMG coherence, we examined the intrasubject differences in RT depending on the magnitudes of β-band oscillation during preliminary contraction. We used the tibialis anterior (TA) muscle as the recorded muscle, because we previously reported that the distally located lower limb muscles show the greatest EEG-EMG coherence among various upper and lower limb muscles (56). Furthermore, the TA is widely used to determine neuromuscular activation characteristics (4, 5, 24, 32, 36, 44, 52, 55), because it is the primary muscle involved in ankle dorsiflexion (accounting for ~60% of the physiological cross-sectional area of all ankle dorsiflexors; Ref. 18), and is a flat, straight, superficial muscle, making it amenable to surface EMG recording.

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MATERIALS AND METHODS

Subjects

Fifteen healthy young adults (age 21–33 years; 11 men, 4 women) with no history of neurological disorders voluntarily participated in this study. All subjects provided informed consent for the study after receiving a detailed explanation of the purpose, potential benefits, and risks involved. The experimental procedures were approved by the local ethics committee of the Faculty of Science and Technology, Keio University.

Recordings

EEG was recorded from the region of the scalp overlying the sensorimotor cortex using 5 Ag/AgCl electrodes that were 10 mm in diameter, placed at Cz (defined by the international 10–20 system) and 20 mm frontal, back, left lateral, and right lateral positions. The reference electrode was placed at A2 (right earlobe). The ground electrode for both EEG and EMG was placed on the right patella. EEG signals were derived using the Hjorth transformation (29). This is a popular method for deriving local electric fields, which consisted of subtracting the averaged signals of the 4 surrounding electrodes from the monopolar-derived signals recorded from a center electrode. Surface EMG was recorded from the TA, over the muscle belly, using bipolar Ag/AgCl electrodes that were 10 mm in diameter with an interelectrode distance of 20 mm. Impedance of the EEG and EMG electrodes was kept below 5 kΩ and 20 kΩ, respectively, during the recording. All analog EEG and EMG signals were amplified and band-pass–filtered (EEG, 0.5–100 Hz; EMG, 5–500 Hz) using a standard EEG/EMG recording system (Neuropack MEB-4308; Nihon Kohden, Tokyo, Japan). Force signal was recorded with a custom-ordered ankle–dynamometer (MK-808052; ME Incorporated, Nagano, Japan) and low-pass–filtered at 50 Hz. All signals were converted to digital signals at a sample frequency of 1 kHz by an analog-to-digital converter with 12-bit resolution (DAQCard-6062E, National Instruments, Austin, TX) controlled by data logger software originally designed using MATLAB software (The MathWorks, Natick, MA).

Experimental Protocol

Each subject was comfortably seated on a chair connected to the dynamometer. Before experimentation, subjects were instructed to practice maximal voluntary contractions (MVCs). Each MVC lasted ~3 s and subjects completed 3 to 5 practice trials. Our aim was to confirm that the differences in peak force values over periods of stable force output were smaller than 5% in the last 3 trials. After this was confirmed, subjects performed the MVC task once, and we used the peak force from this trial as a measure of MVC force. We also confirmed that the obtained MVC force value was within the range of the practice trials. After a rest period of 90–120 s, subjects performed a steady contraction task requiring sustained isometric voluntary contraction of the TA at 30% of MVC for 60 s to evaluate whether they had significant EEG–EMG coherence. As in our recent studies (28, 55, 56), we used 30% of MVC as the contraction level for measuring EEG–EMG coherence for the following reasons: 1) the magnitude of β-band corticomuscular coherence is not affected by the contraction levels of weak to moderate isometric contraction of the TA (7, 53); 2) compared with lower contraction levels, we can observe the β-band oscillations in EMG signals more clearly; and 3) we can avoid the effects of muscle fatigue on EEG–EMG coherence because it takes much longer than 60 s to induce muscle fatigue in the TA by sustained isometric dorsiflexion at 30% of MVC (3, 21). During the task, visual feedback about the level of dorsiflexion force was given via a level meter on a computer screen positioned 1.2 m in front of the subjects. The subjects were instructed to maintain their exerted force as close as possible to a line corresponding to 30% of their MVC force.

Following a rest period that took place after the steady contraction task, subjects performed a ballistic contraction task. The RT paradigm was constructed on the basis of previously described methods (13). It is common for a ballistic movement from a tonic contraction to be preceded by a 40- to 50-ms period of EMG silence accompanying a clear drop in force (40). To eliminate the potential effects of this period of EMG silence on the present data, we gave the subjects a sufficient practice period (i.e., producing ballistic contractions from a tonic contraction state for 10–20 repetitions). This occurred to ensure that they would be able to achieve ballistic dorsiflexion without the preceding EMG silence and associated force drop. After sufficient practice, the subjects performed isometric dorsiflexion at 30% of MVC for 4–6 s. During this preliminary contraction trial, subjects were given 2 computer-generated auditory signals meaning “ready” and “go” (frequency, 250 Hz; duration, 400 ms). The go signal followed the ready signal after a randomized period between 1.0 and 2.0 s. Subjects were required to perform ballistic dorsiflexion as quickly as possible in response to the go signal. After one ballistic contraction, subjects were asked to rest for ~4–5 s while relaxing the TA, and then restarted the next preliminary contraction. This task was repeated 100 times with a 2- to 3-min rest period once every 10 trials.

Data Analyses

Steady contraction task. To assess the data for the steady contraction task, we evaluated the magnitude of EEG–EMG coherence for each subject. EMG signals were rectified because full wave rectification is known to emphasize the temporal pattern of grouped firing motor units (26, 27). Raw EEG and rectified EMG signals were segmented into artifact-free epochs 1,024 ms in duration with no overlap (58 epochs). Each 1,024-ms data epoch was Hanning-windowed to reduce spectral leakage (2, 16, 22). Correlations between EEG and rectified EMG [C(f)] were calculated by coherence using the following equation (27):

$$C(f) = \frac{|P_{xy}(f)|^2}{P_{xx}(f) \cdot P_{yy}(f)}$$

(Eq.1)

where $P_{xy}(f)$ and $P_{yy}(f)$ are the averaged power-spectral density functions (PSDs) of the EEG and the rectified EMG signals throughout the epochs for a given frequency f, respectively, and $P_{xx}(f)$ is the averaged cross-spectral density function between EEG and rectified EMG signals throughout the epochs. The coherence function provides a normative measure of linear correlation on a scale of 0 to 1, where 1 indicates a perfect linear correlation.

To confirm whether maximal peaks of the coherence spectrum actually exist within the β-band (15–35 Hz), we set the frequency range for the latter quantitative analyses at 3–50 Hz (including α, β-, and γ-bands), and then defined the 95% confidence limit of EEG–EMG coherence according to the equation reported in previous studies (27, 48). To eliminate the possibility that the resulting coherence value is judged to be significant due to a statistical error, a Bonferroni correction for multiple comparisons across the 48 frequency bins (i.e., between 3 and 50 Hz) was applied to the equation defining the significant level coherence (SL) (31, 55). Thus, when the confidence limit is α%, the SL is estimated as follows:

$$SL(\alpha) = 1 - \left[ \frac{1}{N} \left( 1 - \frac{\alpha}{100} \right) \right]^{1/(L-1)}$$

(Eq.2)

where N is the number of frequency bins and L is the number of epochs. Because an N of 48, L of 58, and α of 95 were chosen, the SL was determined to be 0.114.

Ballistic contraction task. As mentioned above, subjects practiced ballistic contractions before measurements were taken. This occurred to reduce the chance of obtaining ballistic contractions that had brief periods of EMG silence and associated drops in force before the
reaction. Despite this, we still observed this drop in force in a few trials from several subjects. To address this, we conducted an off-line analysis wherein we carefully checked the EMG and force signals before the reaction in every trial, and omitted the trials with apparent periods of EMG silence (40–50 ms) and associated drops in force. Similarly, we also omitted the trials in which acceleration of ballistic contraction was clearly slower than in the other trials. RT was defined by reference to Duclos et al. (13), as follows: the time when the force level exceeded mean ± 3 standard deviations (SDs) of the force data for the 3-s period prior to the go signal was determined as the reaction onset. We measured the interval between the go signal and the reaction onset, and defined this interval as RT.

First, we divided the subjects into 2 groups on the basis of data from the steady contraction task [i.e., those subjects showing significant EEG-EMG coherence in the β-band (COH+, n = 8) and those subjects showing no significant coherence within any frequency range for our analyses (COH−, n = 7)]. As previously reported (55), the rhythmic grouped discharge in EMG within the β-band was observed in all COH+ subjects, but not in all COH− subjects (Fig. 1). We determined the mean value of RT for each subject, and examined group differences in RT between COH+ and COH− subjects by conducting a 2-sample t-test. In addition, to compare the difference in intertrial variance of RT between COH+ and COH− groups, we also calculated pooled variance in each group, and tested the difference in variance between COH+ and COH− groups by an F-test.

Upon detailed visual observation of the data from the steady contraction task, we found that the extent of the grouped discharge changed from moment to moment in the COH+ subjects (i.e., the grouped discharge in EMG did not always occur but occurred at random on the order of a few hundred milliseconds; Fig. 2). Similarly, in the ballistic contraction tasks performed by COH+ subjects, we found that the extent of grouped discharge during preliminary contractions differed on a trial-by-trial basis. To examine the hypothesis that RT is influenced by the presence or absence of grouped discharge in EMG just before the reaction, which may be associated with corticomuscular coupling, we selected trials with rhythmic β-band grouped discharge associated with a significant short silent period (10–20 ms) (GD+) and those with no grouped discharge (GD−) from all the trials for each subject, as follows: first, from the data for the steady contraction task we determined the characteristic frequency band (CFB) of PSD for the rectified EMG for each COH+ subject by defining the frequency band at which EMG-PSD exceeded its mean value within 3–50 Hz (Fig. 3). We here note that the CFB was determined from a broad range of frequencies (3–50 Hz) to avoid arbitrary assessments of the CFB of grouped discharges on individual EMG traces. The result confirmed that the CFB included the β-band [and not any higher components (35–50 Hz)] in all COH+ subjects. Next, using the data for the ballistic contraction task, we calculated EMG-PSD for the period 512 ms before the onset of ballistic activities in the EMG for each trial and determined the ratio of the sum of PSD within CFB to that of the entire frequency range (3–256 Hz). Note that the onset of ballistic EMG activities was defined as the point 31 ms before reaction was detected in the force signals, according to the duration of electromechanical delay reported by Corcos et al. (12). We sorted the data for all analyzed trials in ascending order on the basis of the above-mentioned ratios, and defined the top 25 trials as GD+ and the bottom 25 trials as GD− trials. For all of the COH+ subjects, the top 25 trials clearly showed the grouped discharge, whereas the bottom 25 trials did not, according to careful visual inspection. A t-test confirmed a significant difference in the mean value of the ratio of PSD within CFB between GD+ and GD− for all COH+ subjects (GD+, 0.161 ± 0.041; GD−, 0.105 ± 0.035; P = 0.011). We determined the mean RT values for both the GD+ and GD− trials for each subject, and examined group differences in RT between the GD+ and GD− trials by conducting a paired t-test. For each subject, differences in mean RT values between the GD+ and GD− trials were tested via a 2-sample t-test. Note that we focused on the differences in RT between the GD+ and GD− trials in COH+ subjects only. This was because the number of trials showing a clear

Fig. 1. Representative samples of raw EEG signals, raw EMG signals, power spectral density functions (PSDs) for EEG and rectified EMG signals, and coherence spectra between EEG and rectified EMG signals during tonic isometric voluntary contraction of the tibialis anterior muscle (TA). Data for a subject who showed significant EEG-EMG coherence (COH+.), and data for a subject who did not show significant EEG-EMG coherence (COH−) are shown, respectively. In the coherence spectra, the estimated significance levels of coherence (SLs, 0.114) are shown as horizontal dashed lines.
grouped discharge in COH− subjects was insufficient for a statistical comparison in RT between the GD+ and GD− trials.

To confirm whether the magnitude of corticomuscular coupling differed statistically between the GD+ and GD− trials, we also calculated EEG-EMG coherence by gathering data from a time point 512 ms before the reaction. We then compared the magnitude of EEG-EMG coherence between the GD+ and GD− trials for each COH+ subject. We tested for differences in the peak values of Fisher’s transformed EEG-EMG coherence between the GD+ and GD− trials using a paired t-test. In addition, we calculated the pooled coherence for all COH+ subjects. This allowed us to compare the averaged tendency of the EEG-EMG coherence between the GD+ and GD− trials.

Additionally, to make sure that there were no temporal changes in the RT and magnitude of EEG-EMG coherence on the basis of time-dependent changes in several factors such as attention and muscle fatigue, we compared the RT and peak value of EEG-EMG coherence between the first and last 25 trials. Note that the EEG-EMG coherence calculation included data from 512 ms before each reaction.

An α level of 5% was chosen to indicate statistical significance. All statistical analyses were performed using PASW statistics software (SPSS Japan, Tokyo, Japan).

RESULTS

We compared the group RT data (mean ± SD) between the COH+ and COH− subjects. A 2-sample t-test detected no significant intersubject differences in RT (COH+, 730 ± 29 ms; COH−, 744 ± 42 ms; P = 0.646). In addition, as a result of a statistical comparison of the pooled variance, there was no significant difference in SD between the COH+ and COH− groups (COH+, 45 ms; COH−, 45 ms; P = 0.418).

To illustrate the effect of trial-by-trial changes in β-band oscillatory EMG activity on RT, representative examples of raw EMG and force signals from GD+ and GD− trials, respectively, are shown in Fig. 4A. Not surprisingly, GD+ trials produced more prominent grouped discharge in EMG. RT seemed to be prolonged on the order of a few dozen millisecond compared with GD− trials (the vertical dashed line compares the onset of the reaction in the GD+ trials with that of GD− trials, shown in Fig. 4A). We plotted pooled SDS for the raw EEG signals and the rectified EMG signals and pooled coherence spectra between raw EEG and rectified EMG signals in Fig. 4B, that were determined using the shaded time range shown in Fig. 4A. The magnitude of pooled coherence was clearly larger in GD+ trials than in GD− trials. The peak value of the pooled coherence spectrum in GD+ was greater than SL, but not in GD−. We included data obtained 512 ms before the reaction onset when calculating EEG-EMG coherence for each COH+ subject, and compared the peak values of the coherence spectrum between the GD+ trials and GD− trials. Figure 5A illustrates the group EEG-EMG coherence data from the GD+ and GD− trials. According to an earlier mathematical study, if coherence is determined from a small number of data epochs (for example, 30 epochs, then the estimated magnitude of coherence is potentially biased from the true value (10). Despite this, a statistical t-test detected a significant group difference in the transformed peak value of coherence between the GD+ and GD− trials (GD+, 0.34 ± 0.15; GD−, 0.21 ± 0.10; P = 0.011, Fig. 5A). In addition, the peak values of the coherence spectrum were observed within the β-band in all of the COH+ subjects.
trials indicate no significant temporal differences were
EMG coherence between the first and last 25 ballistic contrac-
significant in 3 of 8 subjects. trials for 7 of 8 subjects, and this difference was statistically
subject 6
back-averaged rectified EMG triggered by the reaction onset in
GD trials, as described for subject 6. However, in the other 6 subjects, oscillatory activity was not observed in the
back-averaged rectified EMG (as for subject 1, shown in Fig. 6,
right), although grouped discharge was observed in each trial. This finding indicates that for most subjects, the reaction was not
time-locked to the timing of grouped discharge.

**DISCUSSION**

The present study was designed to examine the influence of
β-band corticomuscular coupling during a preliminary isomet-
tractions; and 2) there were significant intrasubject differences
in RT that were dependent on the extent of β-band oscillatory
activity in EMG during a preliminary contraction.

Potential Mechanisms Underlying Intrasubject Differences in
RT between GD+ and GD− Trials

Several recent studies have attempted to examine the influ-
ence of the β-oscillation on reaction movements. For example,
was reported that new movements are slowed when
β-band microtremor (as recorded by an accelerometer) is elevated
tonic extension of the index finger (19). On the basis of
this finding, we divided the trials performed by the COH
subjects into either GD+ or GD− trials by quantifying the
extent of grouped discharge in EMG. This allowed us to

Figure 5B illustrates the group data for RT values from the
GD+ and GD− trials. Note that each plot indicates the mean
RT value in GD+ or GD− trials for each COH+ subject. A
statistical t-test detected a significant group difference in RT
between GD+ and GD− trials (GD+, 744 ± 24 ms; GD−,
728 ± 26 ms; P = 0.005, Fig. 5A). Table 1 shows the mean ±
SD of the RT values from the GD+ and GD− trials for each
COH+ subject. The RT was longer in GD+ than in GD−
trials for 7 of 8 subjects, and this difference was statistically
significant in 3 of 8 subjects.

Results of statistical comparisons of RT and peak EEG-
EMG coherence between the first and last 25 ballistic contrac-
tion trials indicate no significant temporal differences were
detected in terms of RT (first 25 trials, 738 ± 33 ms; last 25
trials, 737 ± 29 ms; P = 0.45) and peak EEG-EMG coherence
(first 25 trials, 0.251 ± 0.088; last 25 trials, 0.276 ± 0.076;
P = 0.32).

Figure 6 illustrates representative data from 2 subjects, with
back-averaged rectified EMG triggered by the reaction onset in
GD+ trials at top of the figure, and rectified EMG from each
trial in the other 25 plots. Figure 6 illustrates representative data from 2 subjects, with
back-averaged rectified EMG triggered by the reaction onset in
GD+ trials at top of the figure, and rectified EMG from each
trial in the other 25 plots. In subject 6, the reaction onset
seemed to be time-locked to the phase of grouped discharge in
some trials (see shaded areas in Fig. 6), resulting in an evident
β-oscillation in the back-averaged rectified EMG. In 2 out of 8
COH+ subjects, the β-oscillation was observed in the back-
averaged rectified EMG, as described for subject 6. However, in the other 6 subjects, oscillatory activity was not observed in the

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estimate the effects of β-band oscillatory EMG activity on motor performance as measured by RT. We found that RT was significantly prolonged in the GD+ compared with the GD− trials, although the observed difference was very small (~10–30 ms). Furthermore, using coherence analyses, we found that the magnitude of the EEG-EMG coherence just before the reaction was significantly stronger in the GD+ than the GD− trials. Thus, it is reasonable to assume that the β-oscillation observed in the raw EMG in the GD+ trials was generated during periods of elevated corticomuscular coupling. These data would provide supportive evidence that the occasional occurrences of β-band microtremor reported by Gilbertson et al. (19), which slowed new ballistic movements, were likely due to these moment-by-moment changes in the strength of corticomuscular coupling.

One might expect the magnitude of the EEG-EMG coherence and RT to vary in the later trials because of the potential effects of attention/stress, practice, fatigue, or a combination of these, resulting from the large number of ballistic contraction trials performed by the subjects. Indeed, previous studies have reported that β-band corticomuscular coherence is influenced by several factors such as attention (30, 33) and muscle fatigue (54). To address this, we statistically compared the RT and the magnitude of EEG-EMG coherence (i.e., peak coherence) between the first and last 25 trials. However, there was no significant difference between the first and last 25 trials in terms of RT or peak EEG-EMG coherence. These results indicate that factors such as attention/stress, practice, fatigue, or a combination of these had a limited impact on the present findings.

In 2 COH+ subjects, we found that β-oscillations before the reaction movement was observed in the back-averaged rectified EMG triggered by the reaction onset. In these subjects, the reaction onset might have been time-locked to the phase of the β-oscillation, which could explain the significant prolongation in RT in GD+ trials. This association between the phase of oscillatory activity and reaction onset is similar to that of resting tremor in patients with Parkinson’s disease (51, 58), essential tremor (14), and action tremor in patients with multiple sclerosis (62). However, a phase-dependent onset of reaction was observed in only 2 of 8 subjects. Thus, this explanation may apply only to some subjects. Another potential mechanism regarding the cause of β-oscillation-related prolongation of the reaction component of new ballistic movements is discussed below.

It is possible that the prolonged RT in GD+ trials was a result of delayed desynchronization of cortical neuron activity due to β-band corticomuscular coupling. Indeed, 20–40 Hz oscillatory synchrony in local field potentials (LFPs) in the motor cortex has been associated with clamping of motor cortical single unit firing rates in monkeys (41). Additionally, it has been well documented that elevation in β-synchrony at the level of the motor cortex contributes to the maintenance of a steady-state force output in healthy subjects (8, 11, 31). Thus, we suggest that although β-band corticomuscular coupling appears to play a role in clamping a rhythm of synchrony in motor neurons to efficiently maintain steady force output, it might take more time to desynchronize the coupled oscillatory neural activity in the corticospinal system that is needed to rapidly elevate the force level.

Using a brain-computer-interface technique, Boulay et al. (6) demonstrated that voluntary increases in the β-rhythm of the sensorimotor area with motor imagery are associated with longer reaction times than when the sensorimotor β-rhythm was decreased. Unlike this study, the trial-by-trial changes in β-band corticomuscular coupling observed in the present study were involuntary. However, taken together, it is suggested that the extent of β-synchrony in cortical cell populations within the sensorimotor cortex affects motor behavior as measured by RT. The nonprimary motor cortex or basal ganglia (or both) would be one of the candidates for a modulator of neural activity in the corticospinal tract. Indeed, Marsden et al. (38) found significant coherence between the LFP of the subthalamic nucleus and EEG recorded over the supplementary motor cortex or the sensorimotor cortex in term of both the β-band and γ-band during isometric wrist contractions. Moreover, in Parkinsonian patients, β-band activity in LFP recorded from the subthalamic nucleus has been found to decrease prior to movement, and there is a positive correlation between the latency of onset of the β-power reduction in LFP and RT.

<table>
<thead>
<tr>
<th>Subject</th>
<th>GD+ (ms)</th>
<th>GD− (ms)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>741 ± 51</td>
<td>711 ± 54</td>
<td>0.048*</td>
</tr>
<tr>
<td>2</td>
<td>739 ± 36</td>
<td>718 ± 27</td>
<td>0.019*</td>
</tr>
<tr>
<td>3</td>
<td>756 ± 52</td>
<td>735 ± 57</td>
<td>0.172</td>
</tr>
<tr>
<td>4</td>
<td>723 ± 40</td>
<td>710 ± 36</td>
<td>0.222</td>
</tr>
<tr>
<td>5</td>
<td>776 ± 58</td>
<td>760 ± 63</td>
<td>0.353</td>
</tr>
<tr>
<td>6</td>
<td>759 ± 48</td>
<td>726 ± 40</td>
<td>0.011*</td>
</tr>
<tr>
<td>7</td>
<td>699 ± 29</td>
<td>694 ± 31</td>
<td>0.508</td>
</tr>
<tr>
<td>8</td>
<td>760 ± 41</td>
<td>769 ± 52</td>
<td>0.512</td>
</tr>
</tbody>
</table>

Values are mean ± SD of reaction time (RT) of GD+ and GD− trials for each COH+ subject. *Differences between GD+ and GD− trials are statistically significant (P < 0.05).
Reaction

hance the size of GABAA inhibitory postsynaptic potentials reported that the administration of benzodiazepines that en-

GD/H11001 be responsible for the intrasubject variance in RT between the sensorimotor cortex from moment to moment. These could

loop, play a key role in generating/modulating some central mechanisms, such as the basal ganglia-cortex necessary for the reaction movement. Thus, it is possible that and that elevated synchrony may antagonize the processing

subcortical areas modulate β-band corticomuscular coupling, and that elevated synchrony may antagonize the processing necessary for the reaction movement. Thus, it is possible that some central mechanisms, such as the basal ganglia-cortex loop, play a key role in generating/modulating β-synchrony in the sensorimotor cortex from moment to moment. These could be responsible for the inrasubject variance in RT between GD+ and GD− trials.

It has recently been suggested that not only central oscillations cause corticomuscular coupling. Baker and Baker (1) reported that the administration of benzodiazepines that enhance the size of GABA_A inhibitory postsynaptic potentials increased the β-power of EEG over the sensorimotor cortex, but did not change the magnitude of EEG-EMG coherence. Thus, they suggested that corticomuscular coupling is not just a phenomenon that simply reflects the propagation of central oscillations to the periphery through the corticospinal tract. Additionally, it was found that peripheral sensory input from muscles affects corticomuscular coherence by evaluating the modulation of MEG-EMG coherence after induction of ischemic sensory deafferentation (46), and the phase of coherence between EEG and EMG following arm cooling (47). Moreover, Witheram et al. (60) demonstrated that directed coherence between EEG and EMG during a precision grip task was significant in both descending (EEG→EMG) and ascending (EMG→EEG) directions within the β-band. Thus, in addition to the descending central drive, ascending sensory inputs may also contribute to the generation/modulation of corticomuscular coherence. It is possible that the gain of afferent information such as visual or proprioceptive feedback (or a combination of these) momentarily varies in response to force fluctuation, and is then integrated into a motor command. Thus we suggest that the extent of β-band corticomuscular coupling changes in the process of sensorimotor coupling, and therefore affects the performance of new movements.

Potential Mechanisms Behind the Lack of Intersubject Difference in RT between COH+ and COH−

Contrary to our hypothesis, there was no significant difference in RT between COH+ and COH−. One might expect that intersubject differences in RT were caused by physical factors such as the distance from the cortex to the muscle due to height, rather than by the magnitude of corticomuscular coherence. However, variance in the latency of motor-evoked potentials (MEPs) induced by transcranial magnetic stimulation (TMS) is known to be in the range of several milliseconds for the TA of healthy subjects (~32 ± 3 ms) (9). By contrast, the RT in our study varied on a time scale of several tens of milliseconds among subjects. Thus, it seems that the variance in time required for a neural transmission to travel from the primary motor cortex to a muscle is too small to be a main contributor to the variance in RT. Thus, it is unlikely that the length of the corticospinal tract caused the intersubject variance in RT.

Furthermore, one might question whether differences in electromechanical delay (EMD), such as the duration between the onset of EMG activity and the reaction onset detected via force signals, are a contributing factor in the intersubject variance of RT. Certainly, differences in EMD among subjects seemed to be observed. However, similar to a previous report (12), the observed EMD in the present study was ~30 ms. The EMD was short compared with the RT in our study, as is expected considering that it represents the amount of time required for a neural transmission to travel from the cortex to muscle. Thus although we cannot deny the potential influence

among subjects (35) and within subjects (59). In light of these findings, we suggest that neural loops between cortical and subcortical areas modulate β-band corticomuscular coupling, and that the variance of RT.

Difference in RT between COH+ and COH−

On the other hand, in subject 1 (right), although grouped discharge was observed in each trial, the timing of the grouped discharge was not synchronized. Thus, oscillatory activity was not observed in the back-averaged rectified EMG.

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of EMD variance, we suggest that this was not a major contributing factor in the intersubject variance in RT.

Rather, variance in the central processing time required for ballistic reactions could be a factor in the observed intersubject differences in RT, rather than the extent of β-band corticomuscular coupling. The neural signal processing related to the ballistic reaction performed in this study can be divided into the following steps: 1) cognition of auditory input; 2) central processing such as planning of movement; 3) motor command in the primary motor cortex; and 4) firing of spinal motor neuron populations. Considering the latency of MEP induced by TMS, it is reasonable to assume that the processing time required prior to involvement of the primary motor cortex is greater than the time for the transmission of the motor command from the primary motor cortex to the muscle, and therefore differs greatly among individuals. Thus variance in the time required for central processing, such as planning of a movement, is likely to be the main cause of intersubject variance in RT, masking the effects of elevated β-band corticomuscular coupling on RT. This assumption would be supported by the results that difference in the pooled variance of RT between COH⁺ and COH⁻ groups also was not detected. We suggest that enhanced corticomuscular coupling does slow the reaction of new movements, whereas no significant differences between COH⁺ and COH⁻ subject groups were detected because the RT was more affected by intersubject differences in central processing. We speculate that the time required for central processing was not particularly variable among trials within each subject, and it followed the present detection of the intersubject differences in RT based on the magnitude of β-band corticomuscular coupling.

One might claim that the subjects were not divided into 2 groups depending on the real magnitude of corticomuscular coherence (this might be due to technical limitations of EEG recording), and that this prevented us from detecting significant intersubject difference in RT between COH⁺ and COH⁻ trials. Indeed, the electric field measured by EEG depends on several factors, including the direction of electrical current flow, which is affected by the orientation of the corticospinal neurons relative to the electrodes, the depth of corticospinal neurons relative to the scalp, and the thicknesses of the scalp and skull (37, 42, 43, 63). Thus there were potentially some cases in which cortical activity actually did oscillate within the β-band, but was not recorded correctly from the EEG electrodes. In our previous study of 100 healthy individuals (55), some subjects had clear β-band oscillations in EMG but not in EEG, resulting in a lack of EEG-EMG coherence. In the present study, however, no COH⁻ subjects had clearly observable β-oscillations in EMG, whereas β-oscillations were visible in all COH⁺ subjects (although it changed moment-to-moment). Thus we cannot entirely refute the possibility that the above-mentioned technical limitations regarding EEG recordings affected the measurement of EEG-EMG coherence, but this would not have a considerable impact on the interpretation of the present data.

CONCLUSION

In the present study, we have demonstrated that there were no intersubject differences in RT that were conditional on the magnitude of EEG-EMG coherence. Within subjects, RT was significantly delayed relative to β-band oscillatory muscle activity during the preliminary contraction. In addition, the magnitude of corticomuscular coupling was significantly elevated when grouped discharge was present. These results suggest that generation of a new movement is delayed when corticomuscular coupling is elevated.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

Author contributions: R.M., J. Ushiyama, and J. Ushiba conceived and designed research; R.M. performed experiments; R.M. and J. Ushiyama analyzed data; R.M., J. Ushiyama, and J. Ushiba interpreted results of experiments; R.M. prepared figures; R.M. and J. Ushiyama drafted manuscript; R.M., J. Ushiyama, and J. Ushiba edited and revised manuscript; R.M., J. Ushiyama, and J. Ushiba approved final version of manuscript.

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