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RESEARCH ARTICLE

Cortical representation of different motor rhythms during bimanual movements

M. Muthuraman · K. Arning · R. B. Govindan · U. Heute · G. Deuschl · J. Raethjen

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Abstract The cortical control of bimanual and unimanual movements involves complex facilitatory and inhibitory interhemispheric interactions. We analysed the part of the cortical network directly related to the motor output by corticomuscular (64 channel EEG–EMG) and cortico-cortical (EEG–EEG) coherence and delays at the frequency of a voluntarily maintained unimanual and bimanual rhythm and in the 15–30-Hz band during isometric contractions. Voluntary rhythms of each hand showed coherence with lateral cortical areas in both hemispheres and occasionally in the frontal midline region (60–80 % of the recordings and 10–30 %, respectively). They were always coherent between both hands, and this coherence was positively correlated with the interhemispheric coherence ($p < 0.01$). Unilateral movements were represented mainly in the contralateral cortex (60–80 vs. 10–30 % ipsilateral, $p < 0.01$). Ipsilateral coherence was more common in left-hand movements, paralleled by more left–right muscle coherence. Partial corticomuscular coherence most often disappeared ($p < 0.05$) when the contralateral cortex was the predictor, indicating a mainly indirect connection of ipsilateral/frontomesial representations with the muscle via contralateral cortex. Interhemispheric delays had a bimodal distribution (1–10 and 15–30 ms) indicating direct and subcortical routes. Corticomuscular delays (mainly 12–25 ms) indicated fast corticospinal projections and musculocortical feedback. The 15–30-Hz corticomuscular coherence during isometric contractions (60–70 % of recordings) was strictly contralaterally represented without any peripheral left–right coherence. Thus, bilateral cortical areas generate voluntary unimanual and bimanual rhythmic movements. Interhemispheric interactions as detected by EEG–EEG coherence contribute to bimanual synchronization. This is distinct from the unilateral cortical representation of the 15–30-Hz motor rhythm during isometric movements.

Keywords Bimanual movements · Corticomuscular coherence · Motor rhythms

Introduction

Coordinated bimanual movements are among the most important motor functions in everyday life. Synchronized timing of the movements in both hands is indispensable to effective interlimb coordination in these movements (Wiesendanger et al. 1994; Serrien 2008). Interactions and activation of bilateral cortical motor centres have been hypothesized to be the basis of such an intermanual coupling (Kazennikov et al. 1999; Swinnen 2002). On the other hand, in strictly unimanual tasks it is necessary to suppress the tendency of the motor system to involve both hands which can be seen in the case of physiological and

M. Muthuraman (✉) · K. Arning · G. Deuschl · J. Raethjen
Department of Neurology, University of Kiel,
Schittenhelmstrasse 10, 24105 Kiel, Germany
e-mail: m.muthuraman@neurologie.uni-kiel.de

R. B. Govindan
Division of Fetal and Transitional Medicine,
Children's National Medical Center,
Washington, DC, USA

U. Heute
Institute for Circuit and System Theory,
University of Kiel, Kiel, Germany

pathological movements (Ziemann et al. 1999, 2004; Armatas and Summers 2001; Addamo et al. 2009). Inhibition of ipsilateral motor centres (e.g. transcallosal inhibition) is an important mechanism enabling purely unilateral motor activity (Cincotta and Ziemann 2008). How these counteracting synchronizing and desynchronizing mechanisms are controlled and interact during bilateral and unilateral hand movements remains an open question. Many previous studies dealing with the cortical mechanisms of bimanual motor control have used functional imaging or EEG/MEG approaches. They have mainly looked at the activation of correlation/coherence between different cortical areas in different frequency bands during bimanual task performance (Gross et al. 2005; Mayville et al. 2005; Pollok et al. 2005; Liuzzi et al. 2011); these measures alone leave the direct relation of these cortical activities to the peripheral movement unclear. There are specific frequency bands, however, at which the cortical activity is directly coupled with the peripheral muscles. In the physiological situation, such a cortical representation of the peripheral muscle activity is well established for the 15–30-Hz band (Conway et al. 1995; Halliday et al. 1998; Brown 2000) during isometric muscle contractions and has been shown also for voluntarily produced rhythmic movements of the hand at lower frequencies (Pollok et al. 2004a; Muthuraman et al. 2012). We know that the cortical activity in the 15–30-Hz band is only coupled to the contralateral hand's muscles even during bimanual isometric contraction (Kilner et al. 2003). With respect to voluntary bimanual rhythmic hand movements, there are a number of studies looking at changes in oscillatory EEG/MEG activity during this motor behaviour (Gerloff and Andres 2002; Serrien and Brown 2002; Koeneke et al. 2004; Pollok et al. 2004b, 2006, 2007). In the present study we specifically concentrate on the part of EEG activity that is coherent with the rhythmic muscle activity resolving the cortical network in which these movements are actually represented and look at the difference between isometric holding and isotonic repetitive finger movements. It is well established that bimanual voluntary movements are typically coupled between both hands (Peters 1977; O'Suilleabhain and Matsumoto 1998; Brown and Thompson 2001). We hypothesize that this synchronization between both hands during bilateral rhythmic movements is reflected in the topography and connectivity of this cortical network representing these movements. Therefore, we analyse the nature of the interactions between left and right cortical representations by coherence, partial coherence and delay analysis. On the basis of these results, we develop a hypothesis on the organization of the contra- and ipsilateral network components for bimanual hand movements.

Methods

Subjects

Eighteen healthy subjects, 8 females and 10 males, were recruited. All subjects were examined by a neurologist (J.R.), and only those without any signs or history of neurological disease or orthopaedic problems of the hands and arms or centrally acting medications were included in the study. Age ranged from 20 to 52 years (mean: 29 ± 5). Sixteen of them were right-handed and 2 left-handed. All of them gave informed consent prior to the experiments, and the experimental protocol was approved by the local ethics committee.

Behavioural paradigm and data recording

Subjects were seated in a comfortable chair in a slightly supine position. Both forearms were supported by firm arm rests up to the wrist joints. All subjects were then asked to move both index fingers to flex and extend in a rhythmical fashion. In the first two recordings, they had to move each finger individually; in the third recording, they were instructed to perform rhythmical movements with both index fingers at the same time. A subgroup of 6 subjects was asked to perform the same movements with the hands, and another subgroup (6 subjects) was instructed to perform the bilateral finger movements again but then in a strictly reciprocal (anti-phase) manner. All subjects were allowed to practice for 5–10 min before each recording. Those who had difficulties to produce a regular rhythmic movement were helped by different acoustic metronome rhythms in this period. During the actual recordings the movements were self-paced in all the subjects. The difficulties with these tasks varied in a percentage scale (60 %) across our subjects but were neither age nor sex dependent in our sample. The maximum frequencies reached were between 2 and 5 Hz and did not differ significantly between the different tasks. Nevertheless, all the subjects who performed rhythmic hand and finger movements reported that they had more difficulties in keeping up the hand than the finger rhythm. The duration of the recordings ranged between 1 and 2 min. In 12 of the subjects who did not manage to keep up the movement for longer than 1 min, each task was recorded twice.

In a second set of experiments (isometric condition), the same subjects were asked to hold their hands parallel to the horizontal plane (floor) with the resting forearm with and without an extra weight (1,000 g) fixed on the dorsum of the hand. Again, the subjects first had to hold each hand individually while the other was relaxed, and then both hands were held together.

The subjects were asked to keep their eyes open and fix their eyes on a point about 2 m away during each of the recordings. The order of the different recording conditions was randomized.

The muscle activity underlying the different movements was recorded by surface EMG from the forearm flexors and extensors using silver chloride electrodes. In recordings with hand movements, EMG electrodes were placed on the ulnar portion of the forearm muscles as described previously (Raethjen et al. 2000). In the finger tasks the optimal recording sites for EMG activity related to index finger movements were determined prior to the experiments. It typically was more radially and distally on both forearm sides. EEG was recorded in parallel with a standard 64-channel recording system (Neuroscan, Herndon, VA, USA) using a linked mastoid reference. EEG and EMG were sampled at 1,000 Hz and band-pass filtered (EMG 30–200 Hz; EEG 0.05–200 Hz). Data were stored in a computer and analysed offline.

Data analysis

EMG was full wave rectified, and the EEG was made reference free by constructing Laplacians (Hjorth 1975). The combination of band-pass filtering and rectification is the common demodulation procedure for EMG during rhythmic movements (Journee 1983). Only 49 EEG electrodes were used. The boundary electrodes were used only for the Laplacian construction and not for the subsequent analysis. Each record was segmented into a number of 1-s high-quality epochs discarding all those data sections with visible artefacts. Depending on the length of the recording and the quality of the data, between 40 and 120 segments of 1 s were used for the analysis of one record. Following Halliday et al. (1995), we calculated the periodogram of the power spectra and the cross-spectrum for each of the 1-s segments independently using a Hanning window. These periodograms were then averaged over all the segments to get a reliable spectral and cross-spectral estimate with a frequency resolution of 1 Hz (Halliday et al. 1995). The coherence between the EEG signals and active muscles and between the muscles on both sides was then calculated as the ratio of the squared magnitude of the cross-spectrum to the product of the power spectra. Coherence is a normalized linear measure, taking on a value of one in the case of a perfect linear dependence and zero in case of complete independence between the two processes. The statistical significance of coherence is assessed by the 99 % confidence limit, which is derived under the hypothesis of linear independence (Halliday et al. 1995; Timmer et al. 1998) and is given by

$$1 - (0.01)^{1/(L-1)}$$

where L is the number of disjoint 1-sec. sections (segments) used in the spectral estimation. The estimated values of coherence lying below this confidence limit are taken as an indication of a lacking (linear) dependence between the two processes. A typical example of an EEG and contralateral EMG recording during voluntary rhythmic movements, the power spectra and the coherence spectrum is displayed in Fig. 1. In recordings with a significant coherence between the activity of the left and right forearm muscles, the phase spectrum was calculated as the argument of the cross-spectrum.

The localization of the corticomuscular coherence on the scalp was determined by calculating isocoherence maps taking into account all the electrodes. For this purpose the 99 % confidence limit was subtracted from the coherence at the tremor frequency for each of these electrodes, thereby setting the level of significance to zero. These coherence differences were grey-scale-coded with black indicating the maximal corticomuscular coherence found in the respective recording and white indicating coherence values below the confidence level. In case of a mechanical transmission of the hand or finger movements to the head inducing rhythmic movement artefacts in the EEG, we found a characteristic pattern of widespread bilateral coherence especially marked in the posterior electrodes. Those recordings were excluded from further analysis. This is in line with the observations and the procedure for movement artefact detection described in earlier work (Timmermann et al. 2003).

In recordings with two or three separate coherent cortical areas (hot spots) in the isocoherence maps (e.g. contralateral, ipsilateral, frontomesial), cortico-cortical coherence between these areas was calculated for all combinations of the 1–3 electrodes showing maximal coherence with the muscle in the respective hot spots. For each hot spot the electrode that displayed significant corticomuscular coherence was arranged in the descending order based on the magnitude of coherence at the tremor frequency. Of them, the top three electrodes were chosen for cortical–cortical coherence analysis. Partial corticomuscular coherence was calculated for each of the hot spots with the other hot spot(s) as predictor(s) for all electrode combinations. Similarly, in recordings showing all three hot spots, partial cortico-cortical coherence was calculated for all three combinations of hot spots with the remaining hot spot as the predictor. In a network of three different interconnected sites, partial coherence allows us to distinguish between direct connections (partial coherence remains significant) and indirect connections via the third recording site (partial coherence with this third signal as predictor becomes insignificant) (Rosenberg et al. 1998; Mima et al. 2000; Raethjen et al. 2004). In the biological situation the interpretation can be complicated by common independent (e.g. subcortical) influences that have not been recorded, and it has been shown that a difference in signal-

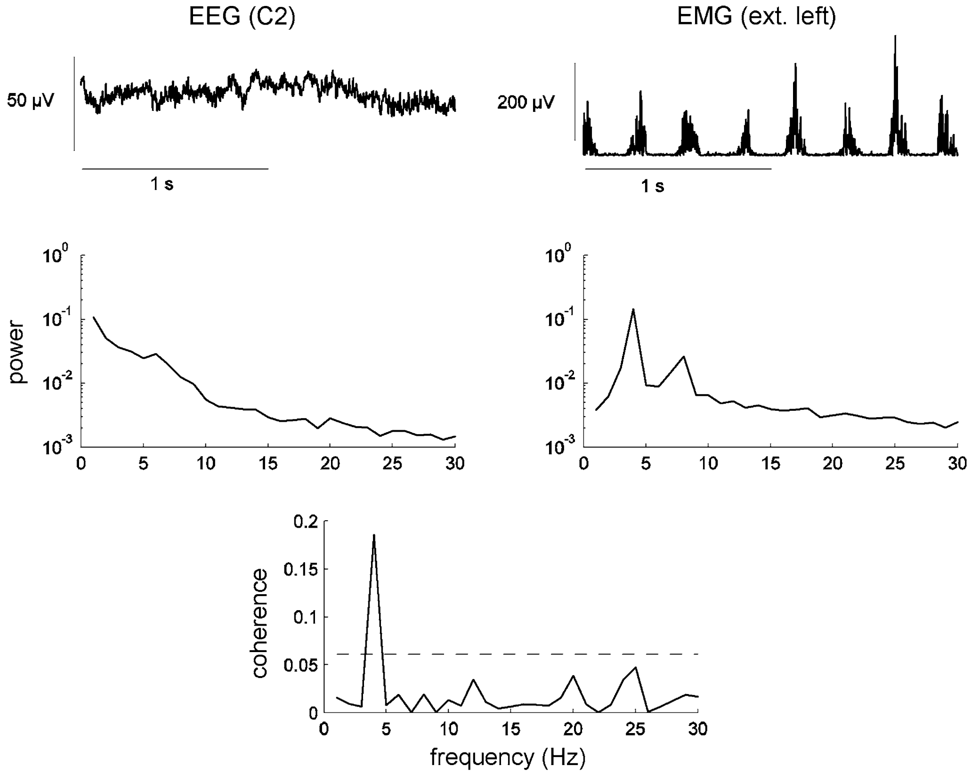

Fig. 1 Example of EEG and EMG raw data (*top row*), power spectra (*middle row*) and EEG–EMG coherence (*bottom*), recorded during bilateral rhythmic movements of the hand

to-noise ratios of the different recording sites can have an artificial influence on partial coherence results (Albo et al. 2004; Govindan et al. 2006).

A new method was used to determine the direction of interaction and delay between the different cortical areas and muscle. The traditional way of determining the direction of interaction and time delay between two time series by fitting a line or curve to the phase spectrum in the coherent frequency range (McAuley et al. 1997; Brown et al. 1998; Mima and Hallett 1999; Lindemann et al. 2001; Muller et al. 2003) fails in case of very narrow band signals like the strictly rhythmic movements in the present experiments. The new method is also based on spectral analysis but overcomes this problem. It takes advantage of the fact that a delay between two signals introduces a time misalignment which slightly reduces the estimated coherence (Carter 1987). In order to estimate the delay between the time series, one of them is time shifted backwards in time keeping the other constant. The coherence at the frequency of the rhythmic movement or at the frequency of maximal coherence in the 15–30-Hz band in the isometric conditions is estimated as a function of the shift. If there is a delay in this direction, coherence will increase and reach a maximum value at the shift corresponding to the delay. The analysis is repeated by shifting the other time series (which was held constant in time in the above analysis) to estimate the delay, if any, in the other direction. Thus, we can obtain the nature of coupling and the delay in both directions by this method. The level of significance and the standard deviation of the calculated delays were determined by surrogate analysis. The details of the procedure are given in Govindan et al. (2005, 2006). The delays and their standard deviations for all the coherent electrodes belonging to one hot spot were weighted according to the strength of their coupling with the periphery (coherence) at the respective frequency and then averaged. This weighted average was taken as a good approximation of the delay between the respective hot spot and the peripheral rhythms. To determine cortico-cortical delays between the different coherent hot spots, the intracortical delays for all the different combinations of the 1–3 electrodes with the strongest coupling to the peripheral muscle rhythm in each hot spot were calculated by maximizing the coherence at the movement frequency, weighted by the cortico-cortical coherence and averaged over all electrode combinations.

In order to compare the coherence estimates between different recording lengths, we performed a *z*-transformation (arctanh-transform) of the coherence and normalized the *z*-transformed values by the reciprocal of the pointwise confidence interval of the respective coherence spectrum (Kilner et al. 2000). This transformation can be considered an estimate of the 'true *z*-transformed coherence' and has been used to compare different recordings within the same or between subjects before (Kilner et al. 2000). It leads to values far above one and will be referred to as '*z*-transformed normalized coherence' in the following.

Possible differences between these normalized coherence values in different cortical hot spots and under different recording conditions were analysed statistically by the Friedman test and post hoc Wilcoxon tests. To compare the incidences of significant corticomuscular coherence between the different hot spots and between different recordings, the Cochran Q test with post hoc comparisons using the Mc-Nemar test was performed. For this purpose we first counted the number of cortical hot spots with respect to the muscle on each side during bilateral movements (maximal value 6: contralateral, ipsilateral and frontomesial representation for left and right muscle). The relationship between the pattern of corticomuscular coherence (number of cortical areas being coherent with left and right muscle) and the maximal *z*-transformed normalized coherence between the coherent central areas of the left and right hemisphere were correlated with the *z*-transformed normalized interlimb coherence (extensor EMG right–left) using the Spearman rank correlation. *p* values below 0.05 were considered to indicate statistical significance in these tests.

Results

Intermuscular, corticomuscular and partial coherence

In all the recordings in which the subjects were asked to produce bilateral fast rhythmic movements, we found significant coherence between left and right muscle activity at the frequency of the movement (Fig. 2c). This was the case for finger as well as hand movements (Fig. 3). The *n* in Fig. 3 represents the number of recordings for a particular task and is followed in all the figures where n is used. Phase spectra (Fig. 2c) revealed that during the rhythmic movements without any prior instruction, the phase difference scatters around zero with a narrow distribution (Fig. 3a, b bottom). Thus, subjects tended to synchronize the oscillations between both hands or fingers (in-phase) although the instruction was only to move both sides rhythmically and as fast as possible. In those recordings in which a subgroup of subjects were asked to maintain a reciprocal alternating pattern between both fingers (anti-phase), we found phase differences close to pi as expected (Fig. 3a bottom). The magnitude of the *z*-transformed normalized intermuscular coherence did not differ between hand and finger movements or in-phase and anti-phase movements (Fig. 3 middle).

In those recordings in which subjects moved only on one side, left–right muscle coherence was only rarely found (Fig. 2a), and the *z*-transformed normalized coherence in the few coherent cases was significantly lower than with bilateral movements ($p < 0.05$). When only the right finger (or hand) was moved alone, we found coherent EMG activity only in one (2) (Fig. 3) recording, whereas left–right muscle coherence was clearly more common when only the left finger or hand was moved (Fig. 2b). In unilateral left-hand movement recordings, we found coherent activity in the right muscles in almost 50 % of the recordings (Fig. 3). This proportion was considerably higher than in the finger movements although this difference did not reach statistical significance. Phase differences between the homonymous muscles on both sides were more widely scattered than in bilateral movements but also tended to cluster around 0 (synchronized activity) (Figs. 2b, 3).

In none of the unilateral or bilateral holding (isometric) trials did we find a significant coherence between the left and right muscles at any frequency between 0 and 40 Hz.

Taking all the recordings and conditions together, we found significant corticomuscular coherence at the voluntary movement frequency or its first higher harmonic in all subjects. By contrast, only in 60 % of them there was corticomuscular coherence in the 15–30-Hz band in at least one of the recordings with isometric muscle contraction. The 15–30-Hz coherence was restricted to the central area of the hemisphere contralateral to the muscle under study, and this did not differ between unilateral and bilateral innervation in any of the subjects (Fig. 4). The incidence and the magnitude (*z*-transformed normalized) of this contralateral 15–30-Hz coherence did differ significantly neither between the holding condition with and without additional weight nor between unilateral and bilateral innervation (Fig. 5). It tended to be slightly more common for the right hand than for the left, but this did not reach the level of significance (Fig. 5).

In the case of voluntary rhythmic movements, we found corticomuscular coherence mainly in the same contralateral central region as in the 15–30-Hz band as long as the rhythm was maintained unilaterally (Fig. 4). However, when the subjects performed bilateral rhythmic movements, both hemispheres also were coherent with the voluntary rhythm of the ipsilateral muscles (Fig. 4). As can be seen in Fig. 4, the electrodes showing the maximal corticomuscular coherence sometimes were slightly different between the left and right muscles. Occasionally, there was also another coherent hot spot in the frontal-mesial region the location of which was slightly more variable. The incidence of the ipsilateral coherence in bilateral movements did not differ from the incidence of contralateral coherence (Fig. 6c/d). This situation was different in unilateral movements, in which the ipsilateral coherence was only seen in a minority of recordings for most of the muscles ($p < 0.01$, Fig. 6a/b). Only when the rhythm was maintained with the left hand alone, the situation was different ($p < 0.05$) in that the ipsilateral cortex was

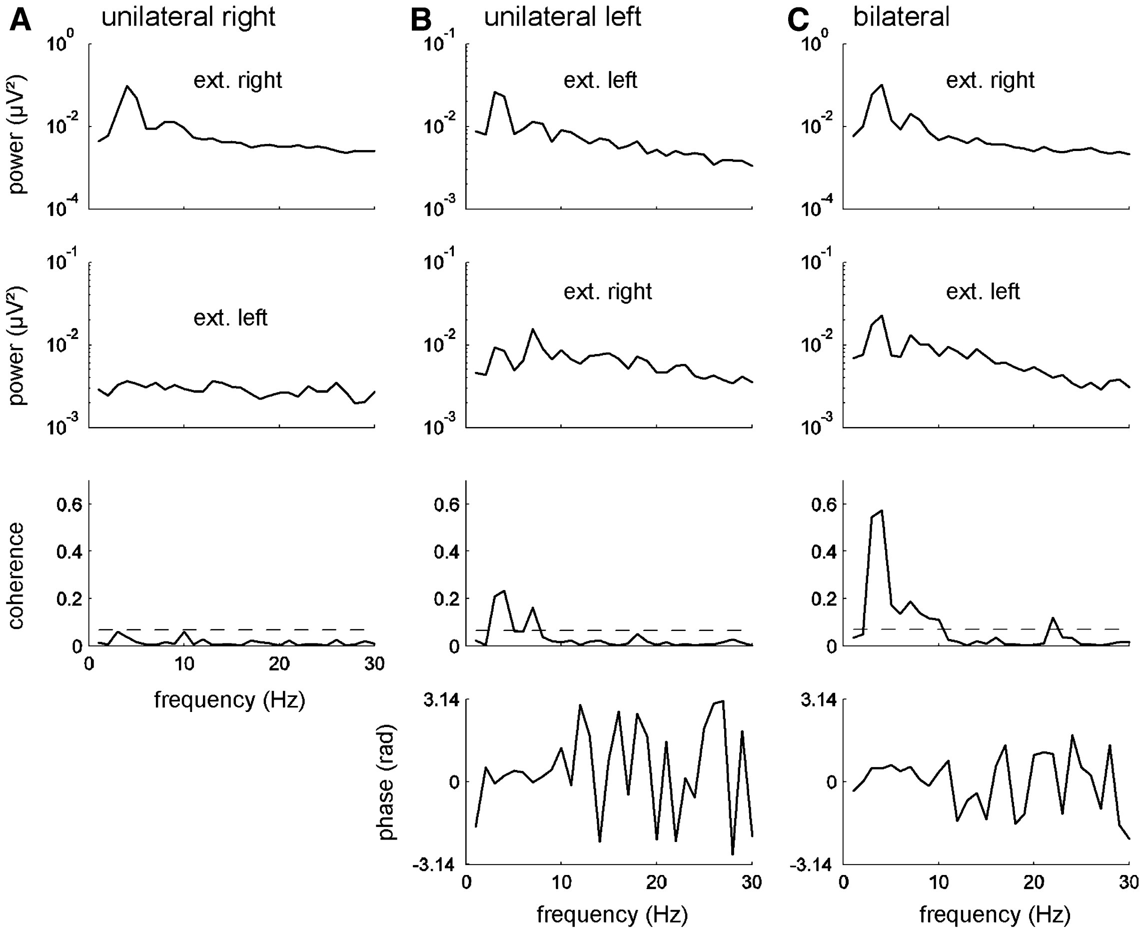

Fig. 2 Example of EMG power spectra of the extensor muscle (ext.) and left–right coherence. The EMG power spectra of the left- and right-hand extensors (*upper two rows*) and the coherence spectra (*third row*) are displayed for unilateral rhythmic movements of the right-hand (**a**), unilateral left-hand movements (**b**) and bilateral movements in one subject. In case of a significant coherence, the phase spectra are displayed at the bottom. **a** During unilateral movements of the right hand, we saw a spectral peak only in the moving hand muscle, and there was no left–right coherence. **b** During unilateral movements of the left hand, we saw a spectral peak on both the muscles, and there was left–right coherence. In bilateral movements the typical bilaterally coherent rhythm appears (**c**). The phase spectra indicate that the muscles on the two sides are close to synchronized (phase shift of zero)

coherent to a similar extent as in the bilateral hand movements (Fig. 6b). Interestingly, this relatively higher incidence of ipsilateral coherence in left-hand movements was paralleled by the higher incidence of left–right muscle coherence under this condition (see above and Fig. 3b). The separate coherent hot spot in the frontal midline region was seen only in a minority of recordings under all conditions (Fig. 6). The magnitude of significant corticomuscular coherence as measured by the z-transformed normalized coherence did not differ between the different cortical regions, movement conditions and muscles under study (Fig. 6). The distribution of the corticomuscular coherence in those recordings in which six of the subjects performed bilateral reciprocal finger movements did not differ significantly from the synchronous movements.

Partial corticomuscular coherence was calculated separately for the right and left forearm muscles. It was computed for the contralateral hot spot with the ipsilateral coherent signal as predictor and for the ipsilateral hot spot partialized for the contralateral hot spot. In recordings with a frontal-mesial hot spot, the contralateral and ipsilateral partial corticomuscular coherence was also computed with the frontomesial hot spot as predictor and vice versa. A typical example of such an analysis for one EEG electrode from the contralateral and ipsilateral hot spots is given in Fig. 7a. The partial corticomuscular coherence of the ipsilateral electrode (C2) drops below the level of significance, whereas the contralateral coherence remains significant. This analysis was done for all the different combinations of EEG electrodes from the two hot spots, for the right and left muscle and for all recordings with a significant ordinary cortico-cortical coherence between at least one electrode pair from the two hot spots under study. In all analysed recordings we found unequivocal results for

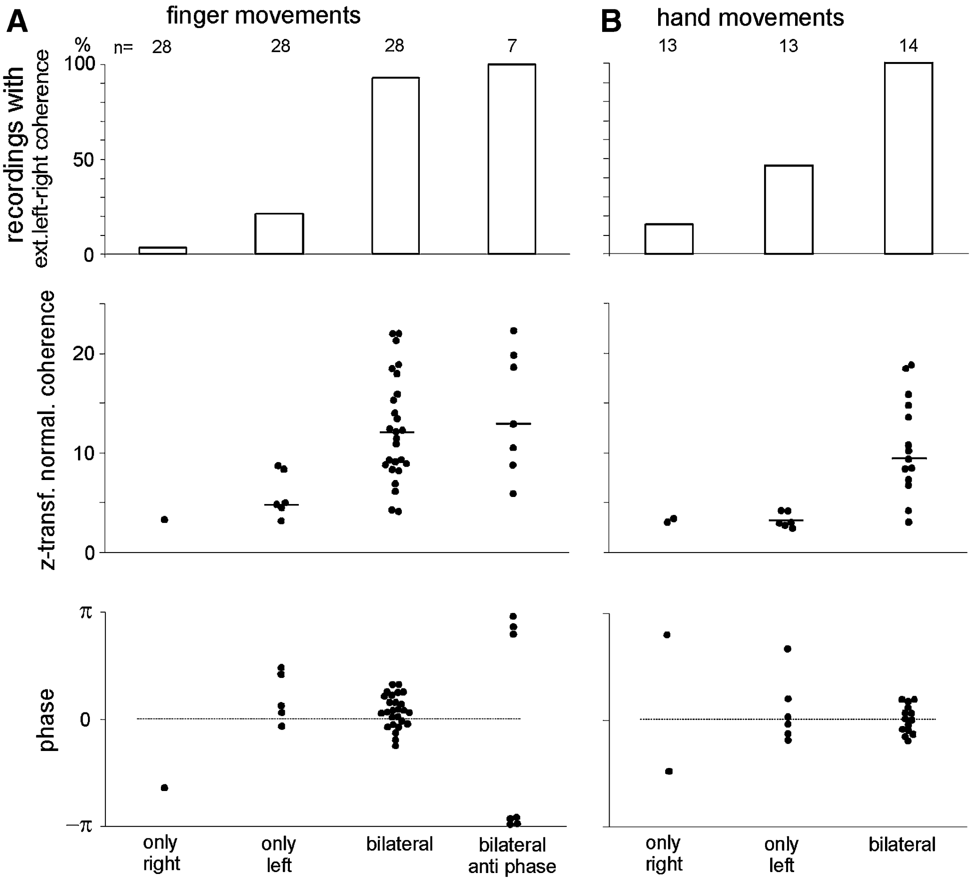

Fig. 3 Incidence and magnitude of intermuscular coherence during voluntarily maintained finger (**a**) and hand (**b**) rhythms. The n represents the number of recordings for a particular task. Only in a small proportion of unilateral movements did we see a left–right coherence, whereas the incidence of left–right coherence was significantly higher (nearly 100 %, $p < 0.01$) for all bilateral movement conditions, and there was a tendency towards a higher incidence of coherence in left-sided movements than in right-sided movements and in unilateral hand than in unilateral finger movements. The z-transformed normalized magnitude of the coherence was significantly higher in the bilateral than in the unilateral movements ($p < 0.05$). The phase shifts between left and right muscles typically scattered around zero, only when instructed to move in an anti-phase pattern subjects produced reciprocal alternating activation of the left and right muscles (phase shift of π)

the vast majority of electrode combinations. The results for the right muscle are summarized in Fig. 7b. The cortico-muscular coherence between ipsilateral (right) hemisphere and right muscle became insignificant in more than half of the recordings when it was partialized for the contralateral (left) hemisphere, whereas the partial coherence between contralateral (left) hemisphere and right muscle and between the two hemispheres remained significant for almost all the recordings ($p < 0.01$). Thus, the connection between right (ipsilateral) hemisphere and right muscle seems to be mostly indirect via the left (contralateral) hemisphere. The coherence between the right muscle and the frontal-mesial hot spot similarly disappeared after partialization for the left (contralateral) hemisphere in more than 40 % of the recordings ($p < 0.05$) (Fig. 7b, second histogram). When the frontomesial corticomuscular coherence was partialized for the ipsilateral hemisphere, however, it became insignificant in only about 25 % of the recordings. This relatively small reduction in coherent recordings was similar for the ipsilateral hemisphere when the frontal-mesial signal was used as predictor (Fig. 7b, third histogram), and it did not reach the level of significance. Thus, not only the ipsilateral hot spot but also the frontal-mesial area seems to be connected to the right muscle largely via the contralateral cortex. Between the different cortical areas being coherent with the left muscle, there often was no significant ordinary cortico-cortical coherence (maximally coherent cortical electrodes often slightly differed between right and left muscle). Therefore, there were less recordings in which we could perform a partial coherence analysis, but there were similar trends, indicating that the connection of the frontal-mesial and the ipsilateral (left) hot spots with the left muscle also seems to be largely via the contralateral (right) cortex.

In 12 recordings from 11 subjects in which we found three mutually coherent cortical hot spots, we also

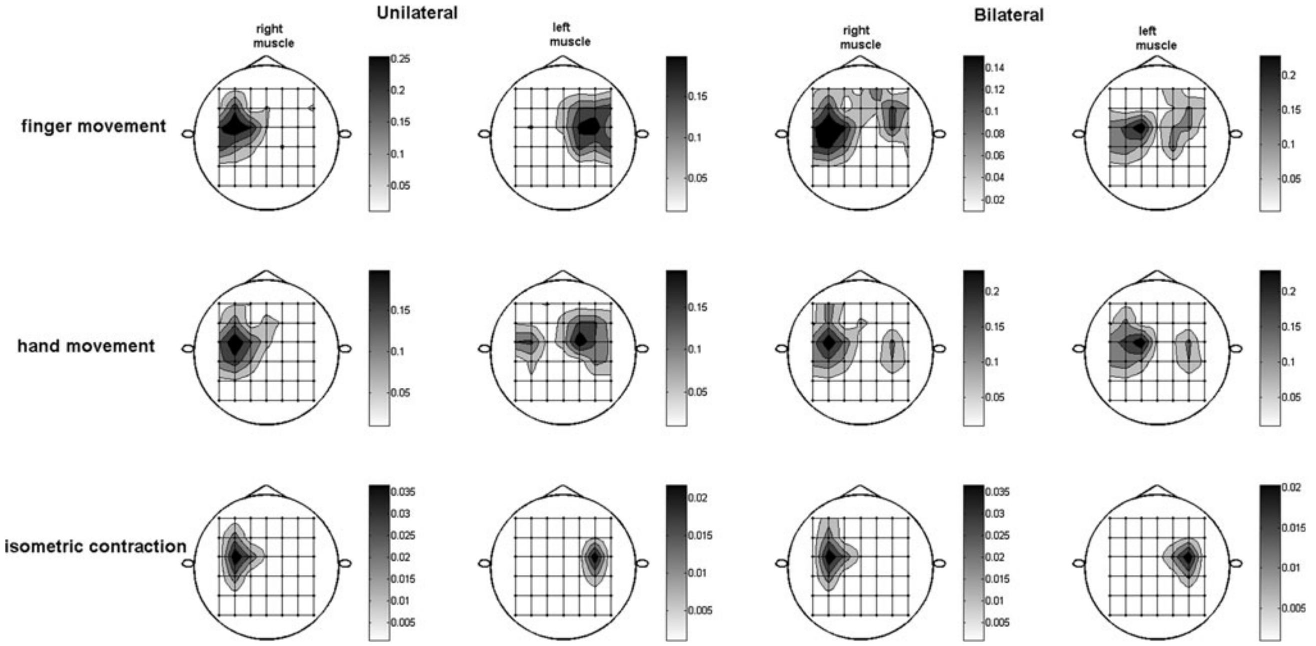

Fig. 4 The grand average isocoherence maps of all the subjects who showed significant coherence for different movement conditions. The schematic EEG electrode grids are shown with the coherent electrodes marked in *grey*. The magnitude of the coherence above the significance level is *grey-scale*-coded according to the *bars* on the *right* of each figure. While the coherent areas are mostly on the side contralateral to the muscle during unilateral movements, they appeared on both sides and occasionally in a more frontal-mesial region during bilateral hand or finger movements. The coherence in the 15–30-Hz band was limited to the contralateral side during unilateral as well as bilateral isometric innervation. Note that the electrodes displaying the strongest coherence with the muscle may slightly between the areas being coherent with the right and the left muscle

calculated the partial coherences between these three hot spots. In the vast majority of these recordings (83–100 %), partial cortico-cortical coherence remained significant, no matter which signal was used as predictor and no matter whether the hot spots under study were specific to the left (2 recordings)- or right-hand (4 recordings) movement or equally represented the movements on both sides (6 recordings). Thus, none of the cortical areas seems to be dominating over the others within this network, and there is no indication in our data that two of them are only connected via the third signal.

Corticomuscular and cortico-cortical delays

Delays between the lateral central cortical area and the contralateral muscle were mostly bidirectional. They are widely scattered between 5 and 30 ms, and there is no significant difference between the corticomuscular delays in the 15–30 Hz range and at the voluntary movement frequency (Fig. 8a). However, in the 15–30-Hz band we found more unidirectional delays, especially in the efferent direction (cortex-muscle). All the distributions of corticomuscular delays were compatible with a normal distribution (Kolmogorov–Smirnov test: $p < 0.01$) with the majority of values lying between 10 and 25 ms and mean values between 13 and 17 ms (Fig. 8a). In case of the voluntary rhythm, there was also corticomuscular coherence at its first harmonic frequency. The delay calculated for this frequency did not differ from the delay at the actual movement frequency.

The vast majority of cortico-cortical delays between the different cortical hot spots were not normally distributed but rather show a bimodal distribution with one cluster of delay values in the very short range between 1 and 10 ms and another more widespread range with larger values between 15 and 30 ms. This is displayed for the cortical representations of the voluntary rhythm of the subjects' right hands during bilateral voluntary movements in Fig. 8b. These cortico-cortical delays were not significantly different for the first harmonic frequency of the movement or for the cortical representations specific to the simultaneous left-hand movements. When looking at the mode of interaction between the different cortical hot spots, we found that bidirectional cortico-cortical communication was most prevalent (Fig. 8c). In some of those recordings in which the cortical representations slightly differed between the left- and right-hand movements, we found a unidirectional flow of information at the movement frequency. Interestingly, in these cases the flow from the ipsilateral to contralateral hot spot was more common than vice versa. This is displayed for the cortical representations of the right-hand rhythm during bilateral movements in

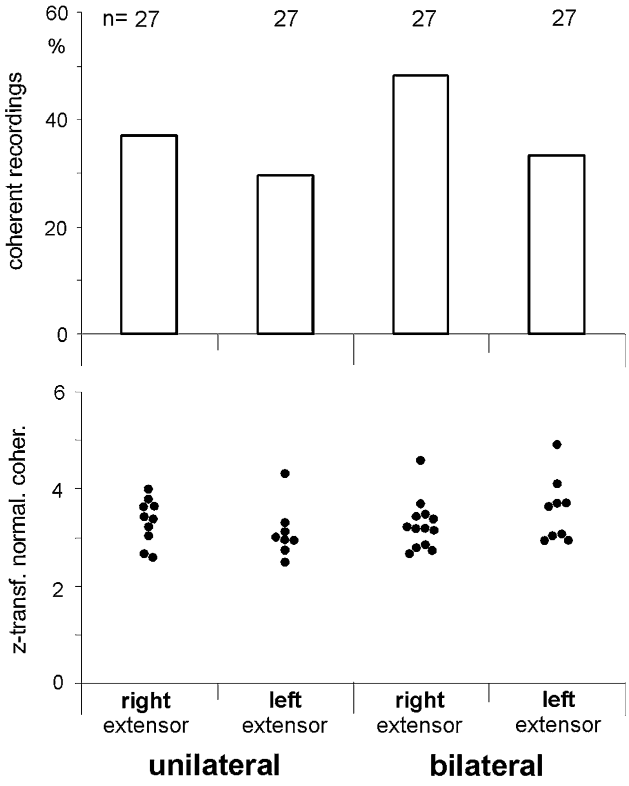

Fig. 5 Incidence and magnitude of the coherence between cortex and contralateral muscle in the 15–30-Hz band. Here again the *n* represents the number of recordings from a particular task which is followed in all the figures. Although there was a tendency towards more coherent recordings for the right than for the left muscle, there was no significant difference in the incidence of *z*-transformed normalized magnitudes of the coherence between the different recording conditions

Fig. 8c, and it looked almost identical for the left-hand representations. Although this trend did not reach the level of significance, it is well in keeping with partial coherence results (see above) indicating that the ipsilateral signal reaches the periphery mostly via the main cortical output station on the contralateral side.

Correlation between left–right movement synchronization and its cortical representations

If the synchronous nature of bilateral voluntary rhythms really emerges from the widespread bilateral cortical representation, one would expect a correlation between the organization of this cortical network and the strength of the left–right synchronization in the periphery. These values correlated significantly with the *z*-transformed normalized coherence between the left and right muscles (Spearman-rho $= 0.46$, $p = 0.015$). This correlation remained when only the number of ipsilateral or contralateral or both of these hot spots was taken into account (Spearman-rho $=$ 0.44, $p = 0.019$; rho $= 0.46$, $p = 0.013$; rho $= 0.45$, $p = 0.015$, respectively), whereas it became insignificant when only the number frontomesial hot spots was correlated with the peripheral intermuscular coupling (Spearman-rho $= 0.13$, $p = 0.5$). Thus, the bilateral cortical representation in the central region seems to be an important factor. Given this importance of ipsilateral and contralateral cortical areas, we tested for a link between the left–right coupling strength on the cortical and the peripheral level. The maximal *z*-transformed normalized coherence between the ipsilateral and contralateral cortex indeed was significantly correlated with the *z*-transformed normalized coherence between the left and right muscles during bilateral movements (Fig. 9, Spearman-rho $= 0.58$; $p < 0.01$). This is a clear indication of the cortical network and its interconnectivity having a direct bearing on the execution of synchronized bilateral movements.

Discussion

The implications of our results are twofold. On the one hand, they show the fundamental difference to the exclusively contralateral cortical representation of bilateral motor oscillations in the 15–30-Hz band during isometric contractions; on the other hand, they provide new aspects on the composition and interconnections of the bilateral cortical network representing simple rhythmic bilateral voluntary movements. In addition to the previous studies (Pollok et al. 2004b, 2005, 2006, 2007; Gross et al. 2005) we specifically focus on that part of the EEG activity that is directly related (e.g. coherent) with the peripheral muscle activity and compare it between two differently demanding bilateral motor tasks.

Topography of the cortical representations

The bilateral voluntary rhythm is represented in both lateral hemispheres likely in the region of the primary sensorimotor cortex. The hot spots of the coherent areas clearly overlapped with the hot spots of the 15–30-Hz coherence during isometric contractions, and this 15–30-Hz activity has been shown to emerge from the primary sensorimotor cortex (Mima and Hallett 1999). In case of the unilateral hand or finger movements, the ipsilateral cortex was only rarely involved. In a number of subjects a more frontal-mesial most likely premotor area (e.g. SMA) was involved. However, while the bilateral cortical representation was present in almost all the subjects performing the bilateral movement, the frontal-mesial area was only involved in a relatively small proportion of recordings, and even in those subjects who performed the more difficult task of maintaining a reciprocal alternating rhythm between both sides, we only saw frontal-mesial involvement in less than 50 %

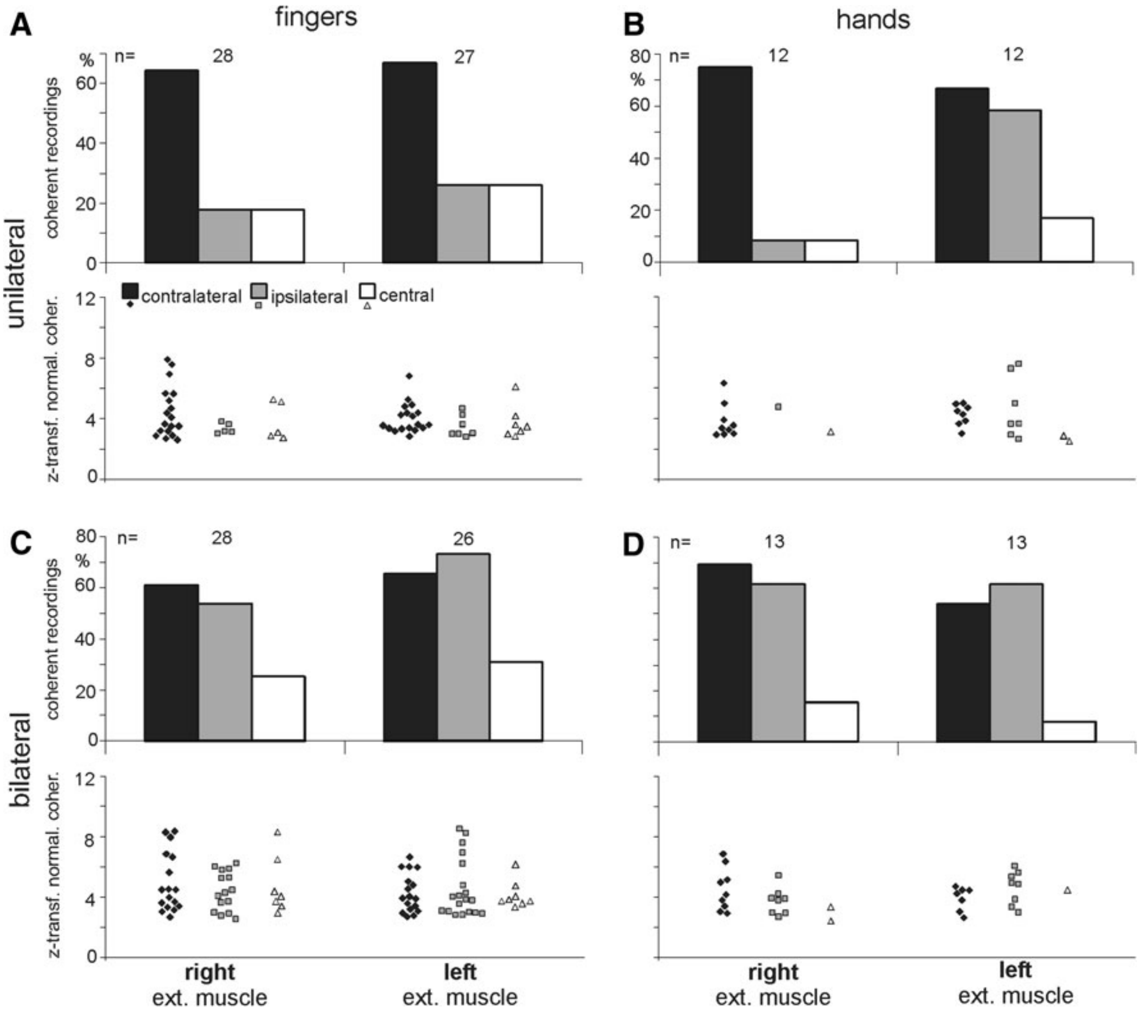

Fig. 6 Incidence and magnitude of the corticomuscular coherence in the contralateral, ipsilateral and frontal-mesial hot spots. **a** In unilateral finger movements the ipsilateral and frontal-mesial coherence was much rarer than the contralateral coherence ($p < 0.01$). **b** In the unilateral hand movements the situation was similar for right-sided movements ($p < 0.01$), whereas the ipsilateral coherence was as frequent as the contralateral coherence in left-hand movements and significantly more frequent than in the right-hand movements ($p < 0.05$). **c/d** In the bilateral movements there were no significant differences between the incidence of the contralateral and ipsilateral coherence for all conditions, only the frontal-mesial coherence remained significantly rarer than the lateral coherences ($p < 0.05$). The z-transformed normalized magnitude of the corticomuscular coherence was not different between any of the cortical areas or conditions

of the recordings. And we could show that strength of the peripheral left–right coupling was unrelated to the presence or absence of a separate frontal-mesial hot spot. This is somewhat different from other studies suggesting a more consistent role of the frontal medial wall (e.g. SMA) in the control of bimanual movements (Tanji et al. 1987; Kazennikov et al. 1999; Immisch et al. 2001; Donchin et al. 2002; Debaere et al. 2004). Several reasons may account for these differences. We specifically look at the representation of the peripheral voluntary rhythm while previous studies rather looked at the preferred frequency of intracortical interaction or simply ‘activation’ of cortical areas. Thus, our analysis seems to be closer to the executional level of the bimanual movements, and we may miss some of the higher-order motor integration the coding of which may be independent from the actual peripheral rhythm (Andres et al. 1999; Gross et al. 2005; Pollok et al. 2009). As we were explicitly interested in the cortical representation and origin of the bimanual rhythm, we limited our analysis to the frequencies or first harmonics of the oscillations under study. The spatial resolution of the EEG is limited, making it difficult to safely distinguish a separate frontal coherent hot spot which may often perish in the spread of lateral central coherent activity to more frontal electrodes. The advantage of MEG over EEG in source identification results mainly from the transparency of the skull and other extracerebral tissues to the magnetic field, in contrast to the substantial distortion and smearing of the

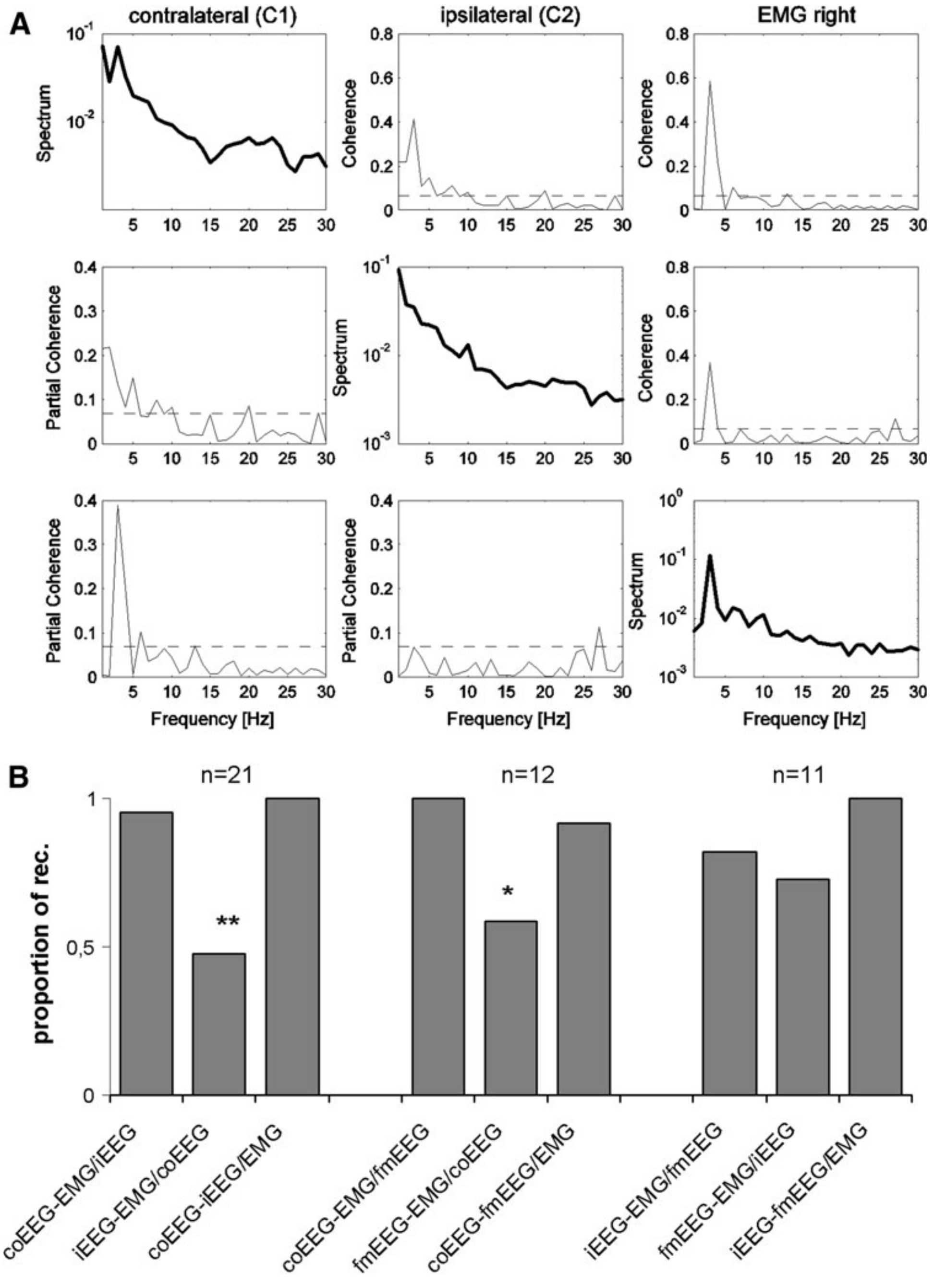

Fig. 7 Partial corticomuscular coherence. **a** Example of contralateral and ipsilateral corticomuscular and intracortical coherence and partial coherence. The power spectra of the cortical of the two cortical and the EMG signal are given in *bold* in the *diagonal*. The ordinary coherence for the three signal combinations is given in the *upper right part of the figure*. The partial coherences between two of the signals using the third as a predictor are given in the *lower left part of the figure*. While the partial coherence between the two cortical signals and between the contralateral cortex and muscle remains significant, the partial coherence between ipsilateral cortex and muscle becomes insignificant when the contralateral cortex is used as a predictor. **b** Proportion of significant partial coherences for all cortical areas coherent with the right muscle during bilateral movements. The partial corticomuscular coherence for the ipsilateral and frontomesial areas regularly became insignificant when the contralateral cortical signal was used as a predictor, whereas the other corticomuscular coherences remained significant in almost all of the recordings (first two histograms $p < 0.01/0.05$). Using the ipsilateral signal as predictor for the frontomesial coherence or vice versa leads to a similar, smaller reduction in partially coherent recordings (very right histogram). All the cortico-cortical coherences remained significant in virtually all the recordings after partialization for the muscle signal

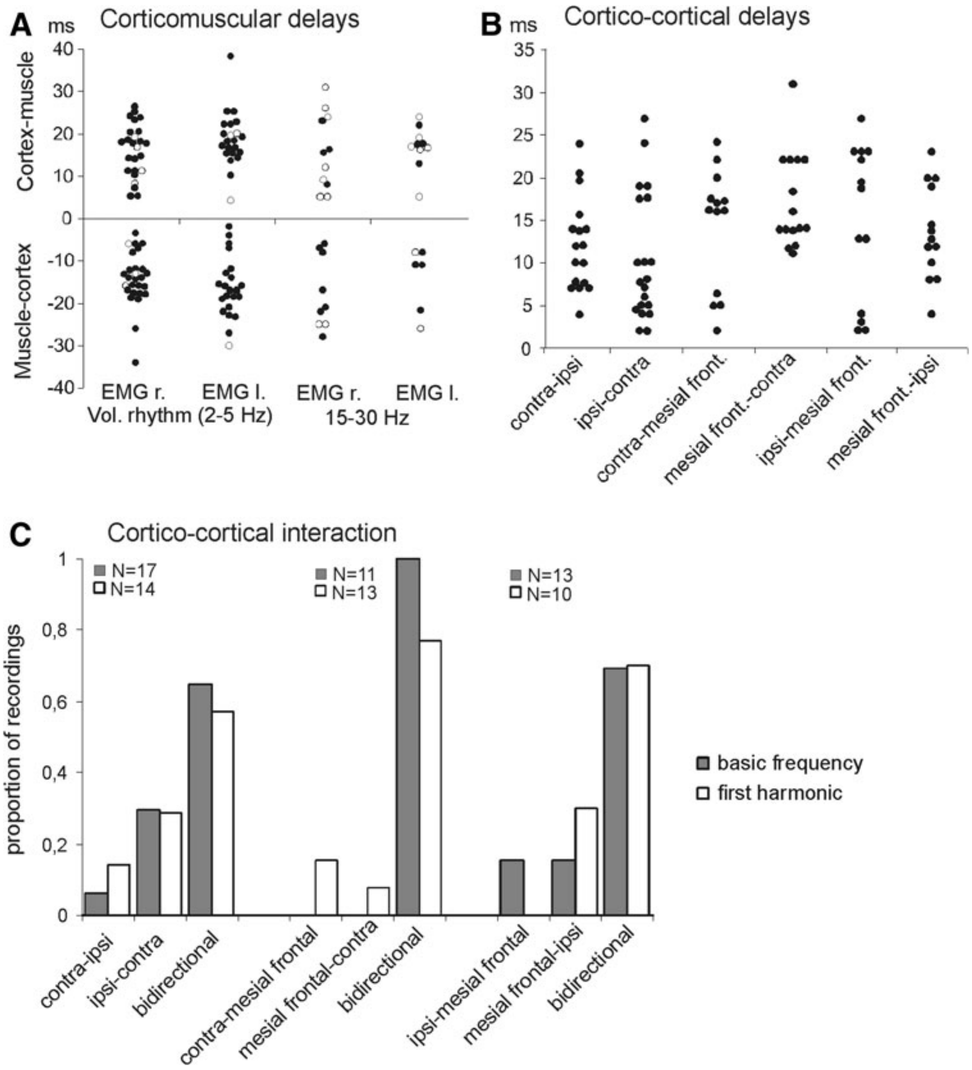

Fig. 8 Corticomuscular and cortico-cortical delays. **a** Corticomuscular delays between contralateral cortex and muscle were mostly bidirectional (*filled circles*), and only occasionally we found unidirectional delays in either direction (*open circles*). Unidirectional interactions in the corticomuscular direction were found slightly more often in the 15–30-Hz band. The delays themselves were widely scattered with the main part of the distribution in the 12–25 ms range in both directions. There was no significant difference between the corticomuscular and musculocortical delays at the voluntary movement frequency and in the 15–30-Hz band. **b** Cortico-cortical delays between the different cortical representations of the movement frequency in the right-hand muscle in bilateral movements were widely scattered with a more bimodal distribution becoming most evident in the ipsilateral–contralateral, contralateral–mesial frontal and ipsilateral–mesial frontal directions. The short latencies (2–10 ms) are compatible with a direct cortical interaction, while the longer delays (15–30 ms) may rather indicate a subcortico-cortical route. Very similar delays were obtained for the rarer interactions at the first harmonic of the movement frequency and for the left-hand muscle representations. **c** In the majority of the recordings there was a bidirectional interaction between the three cortical representations of the right muscle at the basic bilateral movement frequency and its first harmonic. In case of a unidirectional interaction between ipsilateral and contralateral cortex, the ipsi–contra direction was more common than vice versa. Almost identical results were found for the interaction between the (occasionally slightly different) representations of the left muscles

electric potentials. The isocontour lines of a dipole source are tighter in the case of MEG; this is because the concentric electric inhomogeneities smear only the electric potentials (Hari 2005). Nevertheless, our data clearly show that bilateral voluntary rhythmic hand movements are represented in a distributed bilateral cortical network likely consisting of both sensorimotor cortices, and premotor areas are likely involved.

Routes of interaction and output pathways in the central network

The broad distribution of the cortico-cortical delays may be a methodological effect but may also be an indication of not only direct cortico-cortical routes of transmission but possibly a common subcortical rhythm generator [e.g. the thalamus (Llinas et al. 2005)] controlling both cortical

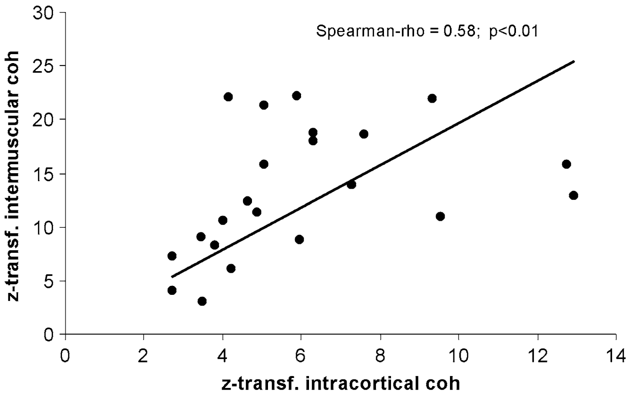

Fig. 9 Correlation of the maximal z-transformed normalized coherence between left and right cortical representations at the movement frequency or its first harmonic with the peripheral left–right coherence between muscles at the same frequency during bilateral rhythmic movements

coherent areas or connecting them indirectly. One may speculate that the short delays below 12 ms are in keeping with direct (e.g. transcallosal) cortico-cortical interactions (Civardi et al. 2001; De Gennaro et al. 2003, 2004; Fling et al. 2011), and the longer delays between 15 and 30 ms possibly reflect communication via subcortical centres. This could be the cerebellum the left and right hemispheres of which have been shown to be linked (Rosina and Provini 1984) likely playing an important role in bimanual coordination (Brown and Jahanshahi 1998; Pollok et al. 2008). The thalami which also seem to have left–right connections (Raos and Bentivoglio 1993) or the basal ganglia both of which have been shown to be linked also to contralateral cortical motor centres (Smith and Alloway 2010) could also be involved (Carson 2005). Whereas the vast majority of these connections within the cortical network were bidirectional in nature, it was mainly the ipsilateral cortex that projected to the contralateral cortical area in case of unidirectional interactions.

The corticomuscular interaction delays are in keeping with transmission via fast corticospinal pathways and feedback. However, previous studies in the time domain looking at movement-related cortical potentials (MRCPs) related to repetitive hand/finger movements have shown longer latencies (Gerloff et al. 1997, 1998). MRCPs most likely do not only reflect the muscle activation itself but also other central, more time-consuming processing steps related to each single movement whereas we looked at the representation of the muscle activity only in the present approach. The partial coherence analysis revealed that the main output station for both muscles is the contralateral hemisphere. The ipsilateral cortices only connect to the muscle via this output station. In combination with the cortico-cortical delay analysis showing mainly bidirectional interactions between ipsilateral and contralateral cortex and between contralateral cortex and muscle, we can conclude that there are two main pathways for the output information from the bilateral cortical network. One is from right cortex to left cortex to right muscle, and the other is from left cortex to right cortex projecting to left muscle. This is in good keeping with the basic anatomy and physiology of the cortical motor systems. Nevertheless, the question arises as to how such an opposite flow of output information for the two muscles emerges simultaneously within the bilateral cortical network representing bilaterally synchronous hand movements. The fact that the bilateral hot spots of maximal coherence in the isocoherence maps slightly differed for the corticomuscular coherence with the right- compared to left-hand muscles seems to indicate anatomically somewhat distinct bilateral networks for both hands. Further, we saw an involvement of the ipsilateral cortex in more than 60 % of the unilateral movements of the left hand. Thus, the cortices on both sides can be involved simultaneously in the production of strictly unilateral movements. We therefore suggest that the bilateral cortical representations of bimanual rhythmic movements are distinct for the left and right hand, which is separate but coupled cortical networks for the left and right muscles during bilateral rhythmic movements. It has been hypothesized before that the control of both unilateral and bilateral movements on both sides by default involves bilateral cortical motor areas (Oda and Moritani 1996; Farmer et al. 2004), the only difference being, however, that the ipsilateral cortical representation is largely inhibited during unilateral movements, most likely via transcallosal routes (Ferbert et al. 1992; Chiarello and Maxfield 1996).

Different representations of isometric and voluntary rhythmic movements

Our data clearly show that the 15–30-Hz coherence during bimanual isometric contractions and the coherence at the frequency of voluntary motor rhythms show fundamentally different cortical representations. The bilateral distribution of the cortical areas being coherent with voluntary bimanual rhythms is obviously involved in bimanual coordination. The interaction within this cortical network and the corticomuscular delays showing a transmission of the voluntary frequency from cortex to muscle confirms its role in maintaining the voluntary rhythm; the correlation between the cortico-cortical and intermuscular left–right coupling demonstrates a direct influence of the cortical representations and their interactions on the synchronization between the two hands during bimanual movements.

Conversely, the 15–30-Hz rhythm during isometric contractions is represented strictly contralateral to the moving hand and mainly in the region of the primary sensorimotor cortex. Thus, this is more localized and does not activate a widespread cortical network. This does not seem to be necessary in bilateral isometric movements; they do not require as much coordination between both hands as active isotonic movements (e.g. repetitive rhythmic hand movements studied here). It has been hypothesized that the 15–30-Hz coherence in isometric movements may fulfil more basic functions, for example, as a calibratory signal of the corticospinal system (Kilner et al. 2000; Riddle and Baker 2006). The clear difference to the representation of a voluntarily produced motor rhythm supports this notion.

Conclusion

Our data show that EEG–EMG and EEG–EEG coherence in connection with partial coherence and delay analysis can dissect the nature of cortical motor networks representing repetitive movements. Using this approach on bimanual motor control, we show that each hand's repetitive rhythmic movement is represented in a bilateral cortical network showing strong interactions with each other. The strength of these interactions between both hands' networks is strongly correlated with the coupling between both hands in the periphery. Conversely, the 15–30-Hz coherence during bimanual isometric contractions in the same subjects is only unilaterally and independently represented in the contralateral cortex of each hand. Our results show that the cortical representation of different movements adapts to their demands. They are in keeping with different functions of the different coherent frequencies which may act in parallel in slower repetitive movements.

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