

The motor preparation of directionally incompatible movements



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ABSTRACT

This work explores, for the first time, the electro-cortical activity related to the preparation of bimanual incompatible actions. To accomplish this aim, we recorded motor-related cortical potentials (MRCPs) in 16 healthy subjects, who were asked to draw lines and/or circles during three experimental conditions: Unimanual, Bimanually Compatible (either lines or circles with both hands) and Bimanually Incompatible (a line with one hand and a circle with the other hand). We show that the electro-cortical activity recorded during the preparation of the bimanually incompatible actions included a central positivity (CP) that began approximately 2.5 s before movement onset and was localized in medial frontal areas. We then recorded a later (ca. 700 ms before movement onset) negative activity in the supplementary motor area (consistent with Bereitschaftspotential). Finally, a strong frontal lateral positivity (FLP) emerged ca. 1.8 s before the initiation of drawing that was localized in the dorsolateral prefrontal cortex. All components were bilateral. The CP component has not been described before. These data are discussed with regard to the "interference network" theory.

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Introduction

Bipedalism gave human beings the opportunity to use the upper limbs in ways other than simply walking. Many daily actions require using both arms simultaneously, and we execute many of those actions with little effort, almost automatically. In contrast, many other actions require a long period of training to coordinate the arms in orchestrated behaviors. It is surprisingly difficult to simultaneously perform two *directionally* incompatible movements (such as drawing a circle and a line) with both hands, whereas it is easy to perform compatible bimanual movements (either two circles or two lines). The difficulty of correctly accomplishing some bimanual actions suggests limitations of the executive system in motor programming and/or action execution. The distinction between these two stages (planning and motor execution) in bimanual actions has not yet been addressed in the neuroscience literature.

At behavioral level, the interference phenomena that occur in "incompatible" conditions can be observed directly; for instance, during repetitive out-of-phase movements, there is a tendency to shift towards in-phase movements (Haken et al., 1985; Swinnen, 2002), and, in case of incompatible directions, the direction of one limb's movement is systematically biased towards the direction of the other limb (Franz et al., 1991; Garbarini et al., 2012). Regarding the neural bases of the interference phenomena, neurological observation, PET, fMRI and TMS studies have provided relevant information.

The supplementary motor area (SMA) is generally thought to play a leading role in the coordination of homologous limbs; this idea was initially based on the neurological observation that SMA lesions disrupt bimanual movements in humans (Chan and Ross, 1988). PET and fMRI studies supported this view and indicated that other cortical areas work together with the SMA to coordinate bimanual movements. Debaere et al. (2001) extended the association between the SMA and bimanual (namely homologous) coordination towards forms of interlimb coordination (non-homologous limbs; i.e., the upper and lower limbs), and Sadato et al. (1997) observed that the activation of the right dorsal premotor area (PMAd) and posterior SMA was stronger during incompatible than compatible bimanual movements of the fingers. De Jong et al. (2002) identified the specific role of the right premotor and anterior parietal cortices in the case of anti-phase movements of both upper and lower limbs. Ehrsson et al. (2002) showed that the activity in the bilateral SMA/cingulate motor area (CMA), right PMAd, bilateral parietal cortex and bilateral lateral cerebellum was stronger when the thumb and fingers of one hand were moved in a non-synergistic pattern compared to a synergistic pattern. Other recent studies (Garbarini et al., 2013; Wenderoth et al., 2004, 2005a,b), which are particularly relevant because of the similarity between their task and the task used here, confirmed the crucial role of the pre-SMA, SMA (Brodmann area – BA 6) and CMA (BA 24 and 32), and they also observed specific activity in other areas, such as the dorsolateral prefrontal cortex (DLPFC, BA 9), the inferior parietal lobule (IPL, BA 40), the superior parietal lobe (SPL, BA 7), the insular cortex (BA 13), the basal ganglia (i.e., the globus pallidus and putamen) and the cerebellum. Overall, the frontal–parietal network in the right hemisphere was more strongly activated during the directionally incompatible task than during the compatible task, indicating a *right-lateralized interference network*.

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Although many studies agree with the view of Wenderoth et al. (2004, 2005a,b) and Garbarini et al. (2013), there have also been conflicting results. Diedrichsen et al. (2006) questioned the specific role of the SMA in the bimanual coordination of movements. First, these authors failed to find any effect of compatible vs. incompatible bimanual movements (for an explanation, see Diedrichsen et al., 2012). Second, they noted no difference in SMA activation during unimanual vs. bimanual tasks (for similar results, see also Ehrsson et al., 2002; Jänck et al., 2000; Sadato et al., 1997).

Regarding the interpretation of the observed cortical activity, Diedrichsen et al. (2006) focused on the cognitive stage of the selection of motor goals vs. the preparation–execution stage. They proposed that the SMA activation and CMA activation were linked to the conflict that developed during the goal assignment, rather than during the motor planning stage; in contrast, the conflict that developed during the motor planning and the execution of bimanual movements would be linked to the activation of the SPL, which is related to the spatial goal of movements. The distinction between the goal selection and motor planning phases was further considered by Garbarini et al. (2013) through the inclusion of an imagery condition in their experiment. These authors also observed different brain activities for compatible and incompatible movements during motor imagery, and they interpreted these results as a recruitment of the brain areas devoted to the intention–programming phases, rather than the execution of the movement.

A straightforward interpretation of the neuroimaging results presented above is precluded by the method itself. In fact, the temporal sequence of the previously described cortical events has never been assessed; thus, in fMRI recordings, cortical activation during the pre-movement phase (i.e., activation related to intention/goal programming and motor preparation *per se*) overlaps with activation during the execution phase, which involves activation of the primary motor area (M1) and somatosensory and visual feedback. In contrast, the motor-related cortical potentials (MRCPs), with their high temporal resolution, are a more suitable instrument for evaluating and separating the sequential brain activity related to goal fixation, motor planning and execution.

A good amount of information is available on the motor preparation involved in simple and relatively complex *unimanual* self-paced movements. Two brain waves typically characterize the motor preparation phase: the Bereitschaftspotential or BP component, which begins 1–3 s before the onset of movement and represents the slowly increasing cortical excitability and subconscious readiness for the forthcoming movement, and the negative slope or NS' component, which starts ca. 500 ms before the onset of movement and reflects conscious preparation for the intended movement. The amplitude and onset of the BP component are influenced by many factors, such as speed, force, stiffness and complexity of the movement (for a review, see Shibasaki and Hallett, 2006). The sources of the BP are the bilateral SMA and CMA, while the contralateral PMA is the main source of the NS'. Early pre-movement activity has also been found in the prefrontal cortex (PFC), which was associated with the awareness of not being able to accomplish impossible (Bozzacchi et al., 2012a) or fatiguing (Berchicci et al., 2013) actions.

The motor execution phase evokes various components: the negative motor potential (MP), which represents the activity of pyramidal tract neurons in M1, and the positive somatosensory reafferent potential (RAP) component, which is visible for brief movements such as key-press. Longer actions such as grasping and reaching are associated with prolonged negativity in motor areas, which was originally called the movement-monitoring potential (MMP) by Foit et al. (1982) and is associated with the action control phase.

It is important to note that all these MRCP studies refer to unimanual tasks. An old experiment (Shibasaki and Kato, 1975) compared unimanual and bimanual movements, and, more recently, Cui et al. (2000) compared bimanual simple and complex finger sequences. However, only compatible sequences were considered. To the best of

our knowledge, no studies have contrasted bimanually compatible and incompatible movements; filling this literature gap was the aim of the present study.

Accordingly, we used MRCPs to evaluate the sequence of cortical activation underlying: a) bimanual tasks requiring either directionally compatible or incompatible movements and b) the same task performed unimanually.

Based on the previously described fMRI literature that compared incompatible and compatible actions, we expected to find increased brain activity for incompatible actions, with the effect localized to the SMA, CMA, PMAd and parietal areas, especially in the right hemisphere. However, as already noted, previous studies failed to differentiate the brain activity related to the preparation and execution phases; furthermore, actions were triggered by external stimuli (such as auditory and visual cues), which may elicit extra activity in parietal areas (Berchicci et al., 2012, 2013; Lucci et al., 2013). Thus, the present study may allow the evaluation of the relative contribution of the preparation and execution phases of self-paced actions within the framework of the so called “interference network”.

Materials and methods

Participants

Sixteen healthy volunteers participated in the study (5 females; mean age: 24.62 years, SD = 6.02). The subjects were recruited from the local (Roman) student population. The mean education level was 16.33 (SD = 1.5) years of schooling. The participants had no history of neurological or psychiatric disorders, and all of the subjects were right-handed (Edinburgh Handedness Inventory; Oldfield, 1971). After a full explanation of the procedures, all of the subjects provided their written informed consent prior to the experiment. The study and all of the procedures were approved by the IRCCS Santa Lucia Foundation of Rome ethics committee.

Stimuli and tasks

The participants were tested individually in a sound-attenuated, dimly lit room after a 64-channel EEG cap was mounted on their scalp. Participants were seated comfortably in an armchair in front of a table equipped with a graphical tablet (dimensions: 42 × 57 cm) covered by a white paper. The height of the chair was adjusted to have the upper body within 30° of an upright position with the head aligned with the spine and the elbows at an angle between 90 and 120°. The forearm and the carpo-metacarpal joint rested on the tablet and the wrist joint angle was at around 145°. Each participant was instructed to perform blocks of unimanual (either with the right or the left hand) or bimanual pen drawings in the horizontal plane by moving their fingers only, holding the wrist still, in a relaxed attitude. The drawing action was *self-paced*, and subjects could not see their drawings while making them. In the unimanual condition, the participants held a pen in one hand, with the pen tip resting close by the tablet, while the other hand was fixed palm-down. In the Bimanual movement conditions, the participant body position was the same as for the unimanual condition, but both hands were holding a stylus having 30–60° angle between pen and paper. The movement onset was automatically detected any time the stylus applied a minimal pressure on the tablet generating the trigger for the MRCP analysis. This signal trigger was delayed of about 30 ms with respect to the real onset of the wrist movement (as it usually happens also with keyboards). Furthermore, to maintain the time between the movement onset and the trigger stable, subjects were instructed to keep constant the distance from the stylus tip to the tablet at about 1 cm and the movement speed. The small delay introduced by this trigger detection is negligible compared to the slow MRCP activity encompassing several seconds. For technical problems, we could not record the drawings on the tablet, but only the actual drawing on the paper made with

the right hand. The participants were asked to perform single unimanual and bimanual movements. For the Unimanual movement condition, the subjects drew either vertical lines or circles with the right hand (Unimanual Right) or with the left hand (Unimanual Left). For the two Bimanual movement conditions, the subjects were asked to simultaneously draw vertical lines with the right hand and circles with the left hand, or vice versa (Bimanual Incompatible), or to draw either vertical lines or circles with both hands (Bimanual Compatible). For the line drawing, the subjects were asked to perform two vertical movements (up and down), whereas for the circle drawing they were asked to perform a single rotating action; repetitive drawing was not allowed. In the preliminary trials, the subjects learned to draw with very small movements (line height/circle diameter: 2–3 cm), to limit or avoid artifacts in the EEG signal and to minimize the variability of the movement execution across individuals. The participants performed 120 trials for each condition at a slow pace (see [Results](#)). To avoid habituation, subjects were asked to alternate line and circle drawings every 30 trials.

It is known that this kind of bimanual incompatible action produce ovalization, the typical bimanual coupling effect ([Franz et al., 1991](#)); in the present task the ovalization was detectable in all subjects, but it could not be accurately measured because the present task, based on one single drawing at time, is quite different from studies in which ovalization has been measured (e.g. [Garbarini et al. 2012, 2013](#)). In these studies the incompatible actions have to be continuously repeated many times because the ovalization index is calculated as the standard deviation of the right-hand trajectories relative to a straight vertical line. In case of a single trajectory, as in present study, the standard deviation cannot be computed. We also chose to not consider the 120 trials repetition for these calculation, because subjects had to pause after each trial (pauses that often produced shifts in the drawings). The rationale of the choice to test single instead repetitive drawings is the use of the MRCP analysis to measure the brain activity concomitant to the actions independently to sensorial feedbacks that take over during repetitive movements.

Electrophysiological recording

The EEGs were recorded using the BrainVision™ system (Brain Products GmbH, Munich, Germany) with 64 electrodes mounted according to the 10–10 International System that were initially referenced to the left mastoid. The EEGs were digitized at 250 Hz, amplified (band-pass of 0.01–80 Hz, including a 50 Hz notch filter) and stored for off-line averaging. Small eye movement artifacts were reduced using the Gratton and Coles algorithm ([Gratton et al., 1983](#)). Computerized artifact rejection was performed prior to averaging of the signal in order to discard epochs contaminated by large eye movements and other muscular activities. Artifact rejection procedures were applied twice: automatically, with an amplitude threshold of $\pm 100 \mu\text{V}$, and manually, by rejecting trials that were still contaminated by artifacts like ocular movements and muscular contractions. After this procedure, on average, 90 trials were retained for each MRCP. The 4 conditions (i.e., Unimanual Left, Unimanual Right, Bimanual Compatible and Bimanual Incompatible) were separately averaged into non-overlapping epochs of 4500 ms (from 3000 ms before to 1500 ms after the onset of movement). The baseline was defined by the mean voltage over the initial 500 ms of the averaged epochs (i.e., between 3000 and 2500 ms before movement onset). To further reduce high frequency noise, the averaged MRCPs were low-pass filtered (i.e., Butterworth) at 15 Hz.

MRCP analysis

The selection of the electrodes and time windows for statistical analysis was based on scalp topography, which allowed the identification of the maximal signal for each found component (see [Results](#)). The earliest activity was a bilateral central positivity called CP, and the amplitude of this component was measured as the mean amplitude between 2000

and 1000 ms before the onset of movement, pooling together the C1 and C3 and C2 and C4 electrode sites. A bilateral frontal lateral positivity (FLP) was then detected and its amplitude measured as the mean amplitude during the 900–300 ms interval before the onset of movement, pooling together the F5, F7, FC5 and FT7 and F6, F8, FC6 and FT8 electrodes. The amplitude and latency of the NS' were measured as the maximal negative activity during the 120–0 ms interval before the onset of movement on the FCz and Cz electrode sites. The amplitude and latency of the MP were measured as the maximal negative activity during the 0–300 ms interval after the onset of movement on the Cz electrode site. On the same site, the MMP was also measured as the mean amplitude between 300 and 1500 ms. Statistical analysis was not performed on the BP, because it was substantially reduced by the strong FLP in the most interesting condition (i.e., Bimanual Incompatible).

Data for the CP and FLP were analyzed with a repeated-measures ANOVA with condition (Unimanual Right, Unimanual Left, Bimanual Incompatible and Bimanual Compatible) and electrode side (Left, Right) as within-subjects factors. The C1–C3 pool and C2–C4 pool were used for the CP. The F5, F7, FC5 and FT7 pool and the F6, F8, FC6 and FT8 pool were used for the FLP. The NS', MP and MMP components that had a medial distribution were analyzed with the AVOVA with only condition as the within-subjects factor. Post-hoc analyses were performed using Tukey's HSD test. The overall alpha level was fixed at 0.05 after the Geisser–Greenhouse correction.

Topographic mapping

Voltage scalp distribution was mapped using spherical spline interpolated flat-top view 130° wide (software Analyzer 2, Brain Products GmbH, Munich, Germany) and three-dimensional realistic maps (software BESA 2000 version 5.18, MEGIS Software GmbH, Gräfenberg, Germany).

Source analysis

To produce models of the intracranial sources of the MRCP components, the Brain Electrical Source Analysis system (BESA 2000 version 5.18, MEGIS Software GmbH, Gräfenberg, Germany) was used. The electrode positions were digitized and averaged across subjects. The three-dimensional coordinates for each dipole of the BESA model were determined according to the Talairach axes and scaled to the size of the brain. In these calculations, BESA used a realistic approximation of the head (which was based on the MRI of 24 subjects), and the radius was obtained from the group average (84 mm).

A first-source model was elaborated using the spatiotemporal dipole module of BESA to estimate the position, orientation and time course of multiple equivalent dipolar sources by calculating the scalp distribution, which was obtained for any given dipole model (forward solution). This distribution was then compared with the actual MRCPs. Interactive changes in the location and orientation of dipole sources led to the minimization of the residual variance (RV) between the model and the observed spatiotemporal distribution of MRCPs. The possibility that dipoles would interact was reduced by selecting solutions with relatively low dipole moments with the aid of an “energy” constraint (which was weighted 20% in the compound cost function, as opposed to 80% for the RV). The optimal set of parameters was identified in an iterative manner by searching for a minimum in the compound cost function. Dipoles were fitted sequentially. Latency ranges for fitting were chosen (see above) to minimize overlap among successive, topographically distinct components. To minimize cross-talk and interactions between sources, the dipoles that accounted for earlier portions of the waveform were left in place as additional dipoles were added. The fit of the dipole model was evaluated by measuring its RV as a percentage of the signal variance, as described by the model, and by applying residual orthogonality tests (ROT; e.g., [Bocker et al., 1994](#)). The resulting individual time series for the dipole moments (the source waves) were subjected to an

orthogonality test, referred to as a source wave orthogonality test (SOT; Bocker et al., 1994). All t-statistics were evaluated for significance at the 5% level.

A second localization approach was based on the noise-normalized minimum-norm method and employed to estimate the current density dipoles on the cortical scalp. The minimum-norm approach is a method that is used regularly to estimate the distributed electrical current in a brain image at each time a sample is taken; it is able to resolve the inverse problem without a priori constraints and is also able to reveal the unique constellation of current elements that models the recorded electric field distribution with the smallest amount of overall current (Ilmoniemi, 1993). The algorithm employed minimizes the source vector current derived from 1426 evenly distributed dipoles located 10% and 30% below the surface of the brain using the approach adopted by Dale and Sereno (1993), where the correlation between p_i of the lead field for the regional source i and the inverse of the data covariance matrix is computed together with the largest singular value $\mu_{\max}$ of the data covariance matrix. The weighting matrix R is composed of a diagonal matrix with weights. The equation consists of the following: $1 / (1 + \mu_{\max}(1 - p_i))$. To improve the minimum norm estimate (MNE), we also included depth-weighting parameters across the entire source space because, as demonstrated by Lin et al. (2006), depth-weighted MNEs can improve spatial accuracy by allowing displacement errors within 12 mm.

Results

Behavioral data

In the unimanual condition, subject performed the self-paced drawing every 3.3–7.5 s, in the bimanual compatible condition every 3.5–6.7 s, and in the bimanual incompatible condition every 3.9–8.2 s. ANOVA between conditions showed significant differences ($F_{2,30} = 8.91$, $p = 0.020$) indicating that the mean pace of the unimanual

condition (4.48 s) was faster ($p < 0.005$) than that of the two bimanual conditions, which did not differ (5.13 s for the compatible and 5.19 s for the incompatible conditions). The draw duration was less than 1 s in all conditions, on average 800 ms for unimanual and 900 for bimanual drawings. Difference in duration was not significant ($F_{2,30} = 1.16$, ns).

MRCP waveforms: description

As it could be observed in the Fig. 1 that illustrates the grand average MRCP waveforms plotted for the four conditions, the earliest activity, beginning 2.5 s before the onset of movement, was a central long-lasting positivity (CP) recorded on bilateral electrode sites. The CP was prominent for bimanual incompatible movements and reached its peak approximately 1 s later. This component was barely detectable during the preparation of unilateral and bimanual compatible movements.

A strong positive activity was recorded at the frontal–lateral scalp sites (FLP), starting at 1.8 s and peaking approximately 500 ms before movement onset. This component was present only in the Bimanual Incompatible condition.

The BP component, typically observed in MRCP studies, was recorded on the frontal–central sites (maximal at the midline, FCz). This negative activity began earlier for unimanual and bimanually compatible movements (-1 s) compared to bimanually incompatible movements (-700 ms); the different onsets are likely due to the summation of the large CP associated with the incompatible movements at the selected electrodes.

The NS' component peaked on the vertex just before the onset of movement. The MP component showed a maximal negative peak on the medial fronto-central (FCz) electrodes 200–300 ms after the onset of movement. This activity returned to baseline 1–1.5 s after its initiation in accordance with the duration of drawing, which was shorter and smaller for the right unimanual task and longer and larger for bimanually incompatible drawings. This prolongation of the MP has been called MMP and has been associated with the action control

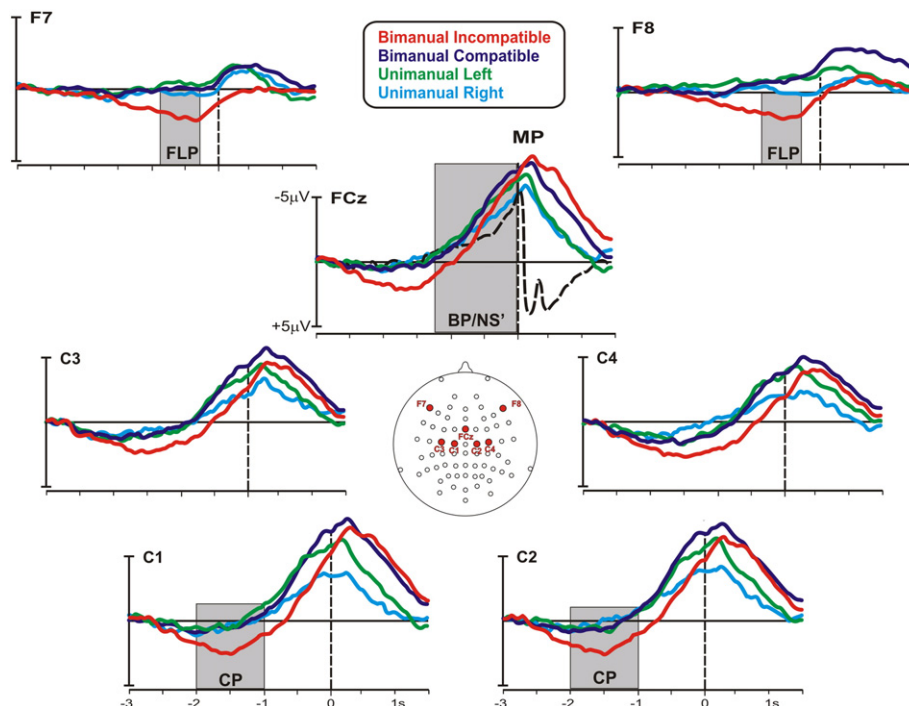


Fig. 1. Grand average of the motor-related ERPs in the four experimental conditions from electrodes over the frontal–lateral (F7 and F8; first row), frontal–central (FCz; second row) and sensorimotor (C3, C4, C1, and C2; third and fourth rows) cortices. Time zero corresponds to the onset of movement. The traces for the four conditions (Bimanual Incompatible, red trace; Bimanual Compatible, blue trace; Unimanual Left, green trace; Unimanual Right, cyan trace) are superimposed. The dashed vertical line indicates the response time (i.e., the movement onset corresponding to time zero). The gray rectangles indicate the time window for each component we analyzed: frontal–lateral positivity (FLP), Bereitschaftspotential (BP/NS') and central positivity (CP). The black dashed trace on the FCz represents the MRCP for unimanual key-press. From Bozzacchi et al. (2012b).

phase within the motor cortex (do Nascimento et al., 2006; Foit et al., 1982; Slobounov and Ray, 1988).

For comparison purposes, the MRCP from a simple unimanual key-press is reported in Fig. 1 with a black dashed line on FCz (data from Bozzacchi et al., 2012b). As is typically reported, the BP and NS' produced by the key-press were similar, but the CP and FLP were never detected following actions such as key-press; similarly, the literature (Shibasaki and Hallett, 2006) did not report either CP or FLP scalp components. In the present data, the positive post-movement RAP component was absent and a negative, more anterior, component was detected, which likely corresponds to the MMP component.

Statistical analysis of MRCP components

The analysis of the amplitude of the CP revealed a significant effect of condition [$F_{3,45} = 6.17$; $p = 0.001$], but the effect of side and the condition-side interaction was not significant. Post-hoc comparisons showed that the amplitude was larger in the Bimanual Incompatible condition (2.06 μV) than in the other conditions (Bimanual Compatible $p = 0.039$, 0.5 μV ; Unimanual Right $p = 0.009$, 0.06 μV ; and Unimanual Left $p = 0.018$, 0.26 μV), which did not differ from one another or from zero. The analysis of the latency of the CP component did not reveal any significant effects.

The analysis of the amplitude of the FLP revealed a significant effect of condition [$F_{3,45} = 7.07$; $p = 0.00054$], but the effect of side and the condition-side interaction was not significant. Post-hoc comparisons showed that the FLP amplitude was larger in the Bimanual Incompatible condition (1.53 μV) than in the other conditions (Compatible $p = 0.012$, $-0.17 \mu V$; Unimanual Right $p = 0.037$, 0.14 μV ; and Unimanual Left $p = 0.005$, $-0.14 \mu V$), which did not differ from one another or from zero. The analysis of the latency of the FLP component did not reveal any significant effect.

The analysis of both the amplitude and latency of the NS' component did not reveal any significant effect.

The analysis of the amplitude of the MP revealed a significant effect of condition [$F_{3,45} = 4.24$; $p = 0.01$]. Post-hoc comparisons showed that the MP amplitude was smaller in the Unimanual Right condition ($-4.11 \mu V$) than in the Unimanual Left condition ($-6.09 \mu V$) (although the difference failed to reach the pre-defined significant level; $p = 0.087$), which was smaller than in the Bimanual Compatible ($p = 0.002$; $-7.82 \mu V$) and Incompatible ($p = 0.007$; $-7.33 \mu V$) conditions. The MP amplitudes in the latter three conditions did not differ from one another. The analysis of the latency of the MP component did not reveal any significant effects.

The analysis of the amplitude of the MMP yielded results similar to the results for the MP for both amplitude and latency.

Topographical mapping and source analysis of the MRCP components

A topographical voltage distribution of the MRCP components is shown in Fig. 2 using flat-top views chronologically ordered from left to right. The CP component (first column) was especially evident in the Bimanual Incompatible condition (last row) and was barely detectable in the other three conditions. The CP was focused bilaterally in medial frontal areas. The FLP component (second column) was present only in the Bimanual Incompatible condition, with a positive bilateral prefrontal dorsal distribution. The BP component (second column) showed the typical negative medial frontal distribution, which became slightly more posterior for the NS' component (third column) and somewhat more anterior for the MP component (last column), without topographical differences across conditions. The MMP showed a similar distribution. The topographical patterns are also shown on 3D maps (Fig. 3a).

The spatiotemporal source analysis of the MRCPs in the Bimanual Incompatible condition localized the source of the CP component to the lateral PMAd (BA 6) of both hemispheres (Talairach x, y, z

coordinates ± 32 , -15 , 40), the FLP was localized to the bilateral DLPFC (within BA 46; ± 46 , 10, 21), the BP was localized to the medial premotor cortex (Talairach x, y, z coordinates 2, -2 , 60), an area compatible with the SMA, and the NS' was bilaterally localized to the precentral gyrus (medial PMA) very close to the source of the MP and the MMP, which were both clearly localized to M1 (Fig. 3b). Source time courses for all the components and conditions are shown in Fig. 3c and indicate that the main difference between the Bimanual Incompatible condition and the other types of actions was the presence of large activity in the DLPFC and an increase in activity in the lateral PMAd. Due to their proximity, the medial PMAd and the M1 sources were represented with the same time course. The RV model was lower than 4.7% in the time windows from -2 to 1 s.

Minimum-norm estimation (Fig. 4) yielded similar results as the spatiotemporal source analysis, confirming that the MRCP components in the four conditions originated in similar cortical areas, except for the source of the FLP in the Bimanual Incompatible condition, which extended over the DLPFC to include the inferior frontal gyrus (i.e., BA 44 and BA 45).

Incompatible minus compatible difference wave

Previous fMRI studies on bimanual incompatible movements revealed lateralization effects applying subtraction logic. Therefore, to better compare present results to previous data, we also computed a subtraction between the two bimanual conditions (Incompatible minus Compatible) obtaining a difference wave enhancing the extra activity found for the incompatible condition.

Fig. 5a shows the subtractive waveform on frontal central and parieto-occipital areas, confirming that the main differences involve the FLP and the CP components, while the other MRCP components were completely erased by subtraction. Subtraction also showed that the FLP component lasted for the whole movement duration, while the CP component terminated concomitantly to the movement onset. Starting about 1 s before the movement and peaking at -150 ms, a parietal activity on the right hemisphere was also present. This activity terminated about 300 ms after the movement. The scalp topography showed that the distribution of the CP and the FLP was quite similar to the un-subtracted waves, but the right-lateralized parietal activity (Fig. 5b) was undetectable before subtraction. Source analysis of this parietal activity localized it in the SPL (BA 7; Talairach coordinate: 29, -65 , 30) as indicated by the yellow circle in Fig. 5c.

Discussion

The main result of the present study is the description of the sequence of cortical activity associated with bimanual, directionally incompatible actions, with a particular focus on the preparation phase. The Incompatible condition (i.e., drawing a line with one hand and a circle with the other) involved strong motor control. Consistently with many PET and fMRI studies (De Jong et al., 2002; Ehrsson et al., 2002; Garbarini et al., 2013; Sadato et al., 1997; Wenderoth et al., 2004, 2005a,b), we observed a larger electrical brain activity for incompatible actions compared to that for compatible actions. Many features of the "interference network" were also similar to those described by previous studies. However, the present data add novel information to the literature.

First, the earliest preparatory activity (the CP component, localized in the lateral PMAd or BA 6) was mostly evident for the bimanually incompatible drawings; in contrast, the later preparatory phase (the BP component, localized in the pre-SMA and SMA) did not show important differences across conditions. Second, in the early preparatory phase, we found additional activity (the FLP component) within the DLPFC.

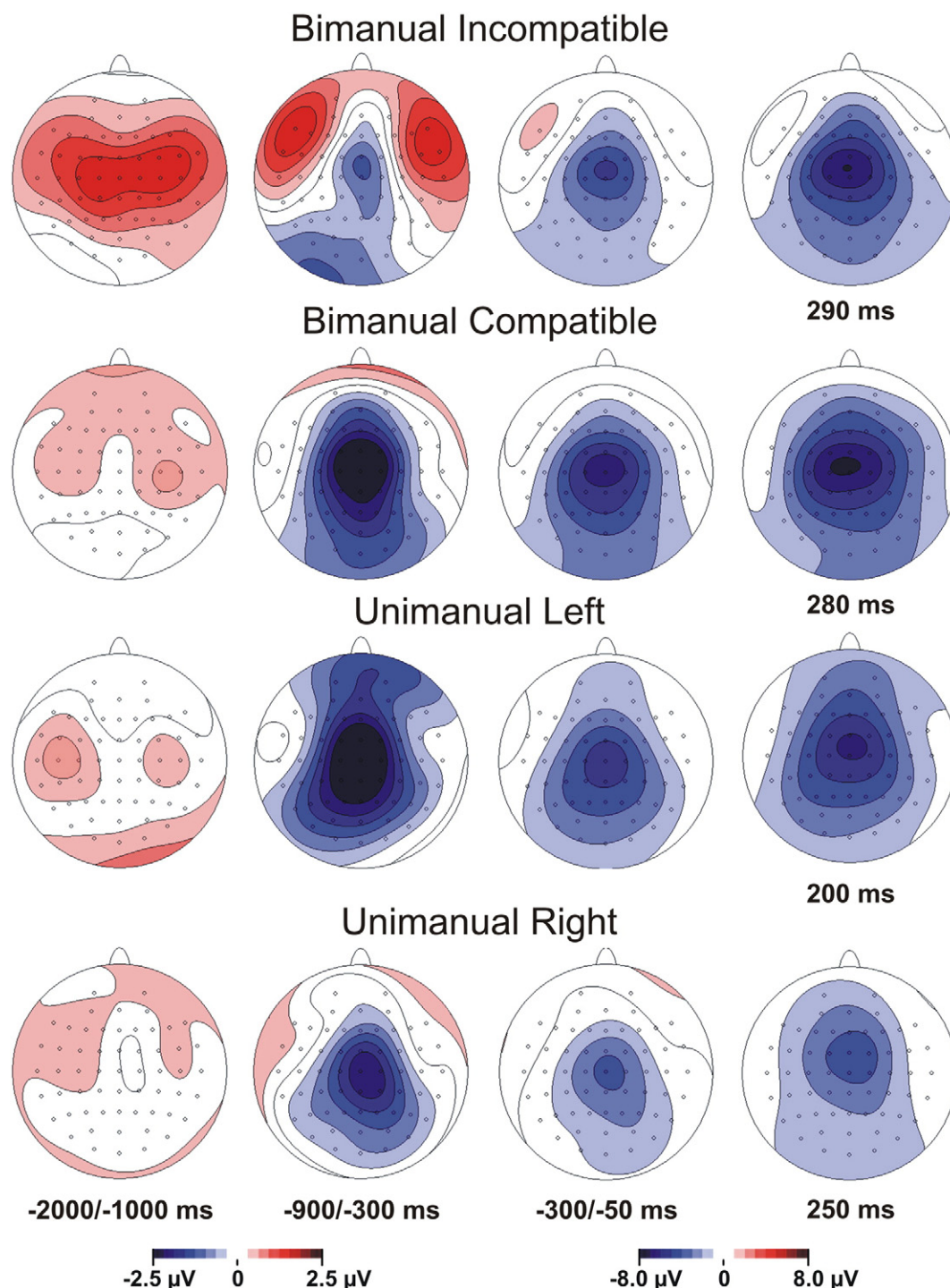


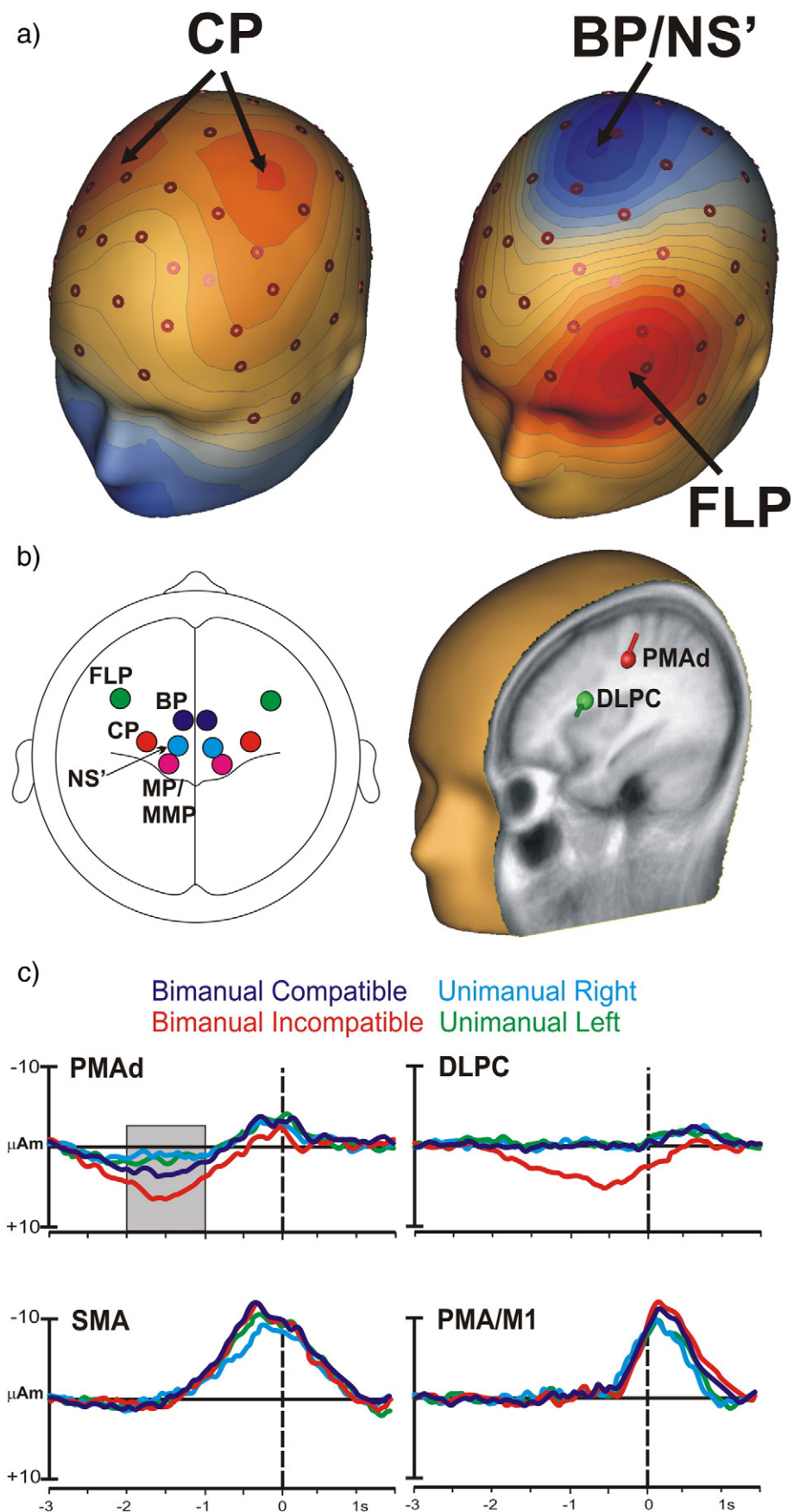
Fig. 2. The scalp topographies of the grand average MRCPs in the four experimental conditions (Bimanual Incompatible, Bimanual Compatible, Unimanual Left and Unimanual Right). The maps are presented for four relevant and consecutive time windows, aligned from left to right and are represented with a top-flat view having 130° field of view.

The central positivity (CP) component

The CP component, which was the earliest activity (2.5 s before the movement), was particularly enhanced during the preparation of

bimanually incompatible movements and its source was focused in the bilateral PMA. Thus, the present findings confirm the specific involvement of the PMA within the “interference network” previously described using brain imaging techniques (both PET and fMRI: [De Jong et al.](#),

Fig. 3. (a) Tri-dimensional mapping of the brain activity that precedes the bimanually incompatible drawings and shows the positive CP, the FLP and the negative BP and NS'. (b) Source model of the MRCP components projected on a schematic and a realistic model of the brain. Cortical sources were found in the lateral premotor cortex (PMA; BA 6) of both hemispheres for the CP component, the bilateral dorsolateral prefrontal cortex (DLPFC; BA 46) for the FLP component, the supplementary motor area (SMA) for the BP component, the bilateral precentral gyrus (medial PMA) for the NS' component and slightly more posteriorly in the bilateral primary motor areas (MI) for the MP and the MMP components. (c) Time course of the cortical sources reported in Fig. 3b. The traces from the experimental conditions are superimposed for each cortical source (because of their vicinity, the NS', the MP and the MMP were well represented by a single trace).



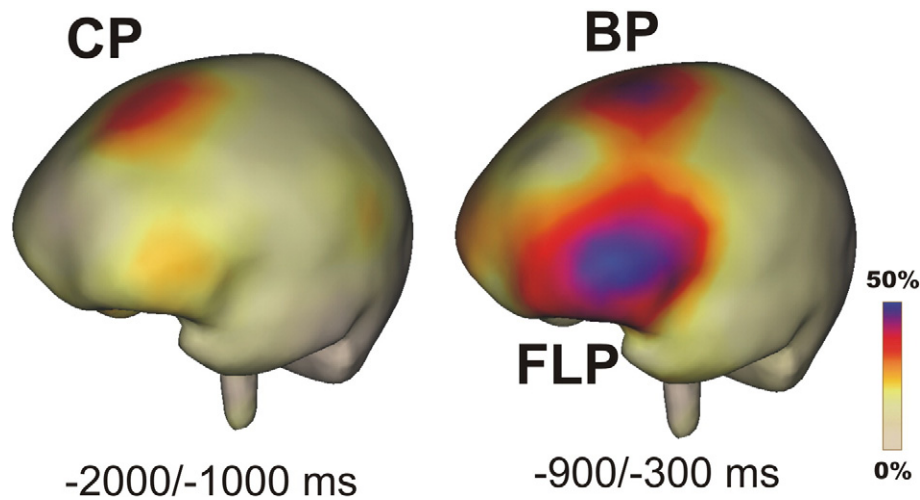


Fig. 4. Noise-normalized minimum-norm source estimations of the brain activity preceding the bimanually incompatible actions within the time window of the CP and FLP components.

2002; Diedrichsen et al., 2012; Ehrsson et al., 2002; Garbarini et al., 2013; Sadato et al., 1997; Wenderoth et al., 2004, 2005a,b).

This bilateral positive activity has never been reported in previous MRCP studies that considered unimanual actions, such as finger movements, reaching and grasping. It is possible that the bilateral PMA activity reflects some specific characteristics of the drawing task, such as the complexity of the preparation for drawing a specific object (a line or a circle) with respect to the preparation of simple actions such as finger flexion, limb extension and even reaching towards external objects, as generally studied. In any case, the amplitude of the PMA activity was related to the complexity of the task, which was lower in both the Unimanual and Bimanual Compatible conditions and higher in the Bimanual Incompatible condition.

The frontal–lateral positivity (FLP)

Only in the Incompatible condition, a strong positive activity that started at approximately 1.8 s and peaked approximately 500 ms before the movement was recorded. The source of this activity was consistent with the DLPFC, which is widely involved in executive functions, especially in specifying a set of responses suitable for a given task and in biasing these responses for output selection (“sculpting the response space”, Nathaniel-James and Frith, 2002). This pre-motor function is reminiscent of the top-down biasing of competition between stimuli proposed in the model of Desimone and Duncan (1995) and is analogous to the component of the Supervisory Attentional System that modulates the Contention Scheduling System (Norman and Shallice, 1986).

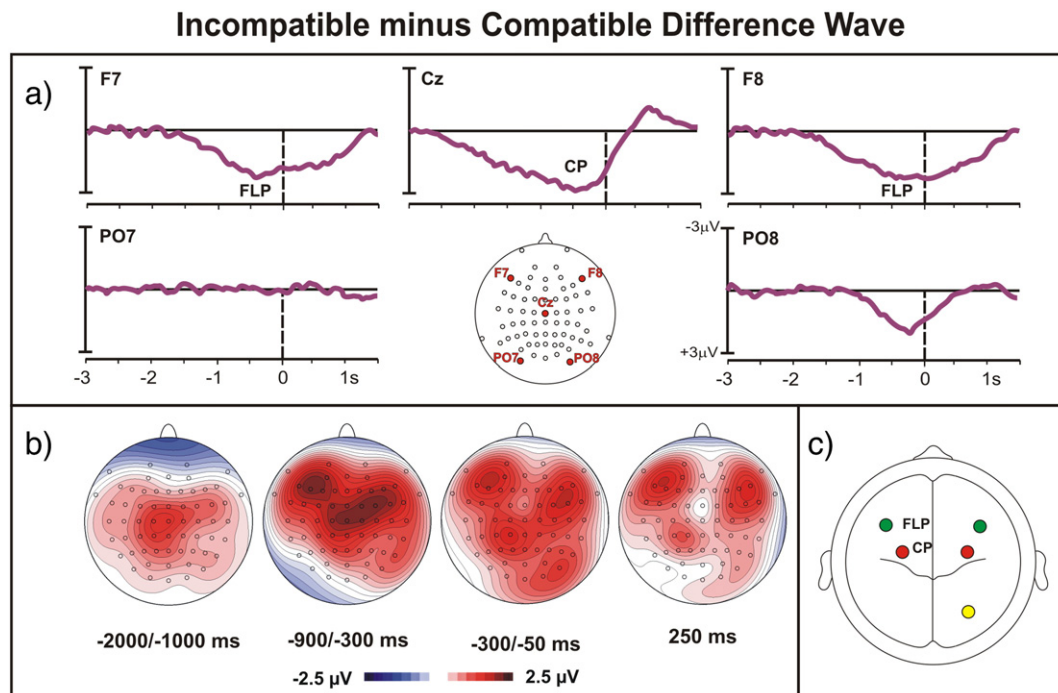


Fig. 5. (a) Difference waves for bimanual conditions (Incompatible minus Compatible) in frontal (F7, F8), central (Cz) and parieto-occipital (PO7, PO8) sites. (b) Scalp topographies of the differential activity. The maps are presented for the same time windows shown in Fig. 2. Additionally to the anterior CP and FLP topographies, a posterior distribution over right parieto-occipital areas was present. (c) Source model of the differential activity projected on a schematic model of the brain (130° top-flat view). Cortical sources were localized again in the lateral premotor cortex (PMA; BA 6) of both hemispheres for the differential CP component, and in the bilateral dorsolateral prefrontal cortex (DLPFC; BA 46) for the differential FLP component. Additionally, the subtraction showed a source in the right superior parietal lobe (SPL; BA 7), as indicated by the yellow circle.

Furthermore the DLPFC is involved in mediating cross-temporal contingencies in action planning (Fuster, 2013).

We propose that the positive prefrontal activity recorded during the preparation of bimanually incompatible drawings could represent an additional preparatory control that also involves the inhibition of bimanually compatible motor engrams, which are not totally inhibited, as shown by the “ovalization” of circles during incompatible drawings (Franz et al., 1991). The DLPFC activity might be related to a partially successful attempt to inhibit compatible actions when difficult (or impossible) incompatible actions are required. This area tries to resolve competition and to establish the mappings needed to perform the task; indeed, the overlap between the set defining different spatial constraints within a tight temporal coupling could be a ripe source of interference, requiring high control at the central hierarchical level. In support of this hypothesis, similar activity in the DLPFC was also present during the preparation of unimanual impossible grasping (Bozzacchi et al., 2012a,b).

Our data are also consistent with the Omni-BP MRCP component found by Kunieda et al. (2004) using epicortical recording, which is a positive Bereitschaftspotential recorded during different body movements from BA 45. This activity was supposed to regulate higher motor praxis and execution.

Parietal activation and right-lateralization

Previous fMRI studies (De Jong et al., 2002; Ehrsson et al., 2002), and particularly Wenderoth et al. (2004, 2005a,b) and Garbarini et al. (2013) using tasks quite similar to the one used in the present study, reported parietal activation, especially in the case of incompatible movements and strong right-lateralized activity during bimanually incompatible tasks (De Jong et al., 2002; Garbarini et al., 2013; Sadato et al., 1997; Wenderoth et al., 2004, 2005a,b). Following the subtraction logic typical of the fMRI studies, and employing the subtraction waves to the MRCPs we observed a right-lateralized parietal activity, which was surprisingly not detectable without subtraction. Right parietal activity was present both during the preparatory phase, peaking 150 ms before movement, and during the execution phase.

Limit and perspectives

One limit of the present study is the lack of detailed kinematic and kinetic measures of the drawing actions. In particular we were not able to correlate the MRCP data to behavioral data as the ovalization index. This limit (explained in the *Method* section) rose from the choice to study single instead repetitive drawings. This is the first MRCP study on directional incompatible actions; future studies may compare the MRCP of these two types of actions, focusing on the relation between electrocortical (MRCP effects) and kinematics (ovalization index) variables.

Future research may also describe how the timing of the activity of the “interference network” is characterized in special populations such as musicians (experts in the execution of bimanually incompatible movements), or, at the opposite end of the spectrum in terms of competence, right-brain-damaged patients with anosognosia for hemiplegia (who deny their motor deficit and act as though they can still move their paretic limb).

Conclusion

In summary, the present results confirm the activation of the “interference network” in motor tasks requiring the execution of different actions by two hands, and add a novel description of the time course of the recruitment of different areas in this network to the literature. When performing bimanual movements with different spatial trajectories in both upper limbs simultaneously, pattern of “interference network” emerges well before the execution of the action, i.e., 2.5 s before the initiation of the movement, characterized by the CP component in

the bilateral PMA. After the PMA, the DLPFC is the most activated area in the incompatible condition, as revealed by the FLP component; this activation may be related to the effort to resolve competition between the well-established and actually incompatible bimanual motor engrams. Finally, a right parietal activity was detected during both preparation and execution phases of incompatible task.

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Conflict of interest

None of authors have conflicts of interest.

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