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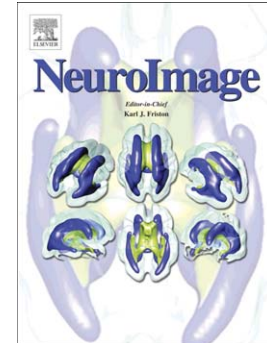
The mirror illusion induces high gamma oscillations in the absence of movement

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THE MIRROR ILLUSION INDUCES HIGH GAMMA OSCILLATIONS IN THE ABSENCE OF MOVEMENT

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Running title: Mirror illusion and high gamma oscillations

Highlights:

- We examined movement-related high gamma oscillations (HGO) in healthy humans with MEG

- Real hand movements produced sensorimotor HGO in the contralateral hemisphere

- Similar HGO response was triggered by mirror visual feedback from a moving hand

- HGO in sensorimotor cortex may reflect the neural mechanism of mirror-hand illusion

Abstract

We tested whether mirror visual feedback (MVF) from a moving hand induced high gamma oscillations (HGO) response in the hemisphere contralateral to the mirror and ipsilateral to the self-paced movement. MEG was recorded in 14 subjects under three conditions: bilateral synchronous movements of both index fingers (BILATERAL), movements of the right hand index finger while observing the immobile left index finger (NOMIRROR), and movements of the right hand index finger while observing its mirror reflection (MIRROR). The right hemispheric spatiospectral regions of interests (ROI) in the sensor space, sensitive to bilateral movements, were found by statistical comparison of the BILATERAL spectral responses to baseline. For these ROIs, the post-movement HGO responses were compared between the MIRROR and NOMIRROR conditions. We found that MVF from the moving hand, similarly to the real movements of the opposite hand, induced HGO (55-85Hz) in the sensorimotor cortex. This MVF effect was frequency-specific and did not spread to oscillations in other frequency bands. This is the first study demonstrating movement-related HGO induced by MVF from the moving hand in absence of proprioceptive feedback signaling. Our findings support the hypothesis that MVF can trigger the feedback-based control processes specifically associated with perception of one's own movements.

1. Introduction

Mirror hand phenomenon refers to the illusory percept of moving a hand while moving the opposite hand and viewing its reflection in a mirror. To induce the illusion the mirror is placed sagittally giving the impression that the stationary hand is performing the task. Clarifying the neurophysiological basis of the mirror hand illusion may have important clinical implications, given that mirror visual feedback (MVF) has proven to be an effective neurorehabilitation technique (Ramachandran and Altschuler, 2009).

First described by Ramachandran (Ramachandran et al., 1992), the mirror hand phenomenon has been considered as reflecting the vital role of visual afferent feedback for hand movement control and self-awareness of one's limb movement. Indeed, the movement of one's body part is perceived not only by proprioceptive feedback from muscles and tendons but also by visual information on the body part position which is important for motor planning and on-line control of movement (Scott, 2004). In real life, somatosensory input is congruent with motor command and visual estimate of limb position. An incongruence or conflict between motor intention and afferent feedbacks about limb position produces false-perception and/or subjective feeling that the movement is not properly performed (Tsakiris et al., 2010). Regarding MVF it has been proposed that the mismatch between visual input having perfect correspondence with the motor command for self-paced movement and a lacking proprioceptive feedback from motionless hand may lead to a dominant role of visual input over proprioceptive one in subjects' awareness of their own movement (Ramachandran and Altschuler, 2009). However, the role of interaction between MVF and motor command in hand movement awareness is far from clear.

A hypothesis originating primarily from clinical studies of MVF in patients with limb paralyses implies that MVF can accelerate recovery of limb function through increasing the excitability of primary motor cortex – M1 (Ramachandran and Altschuler, 2009).

There is a large body of evidence favoring this suggestion. Physiological studies using transcranial magnetic stimulation – TMS (Garry et al., 2005) as well as EEG and MEG recordings (Praamstra et al., 2011; Tominaga et al., 2009; Touzalin-Chretien and Dufour, 2008; Touzalin-Chretien et al., 2009, 2010) investigated brain functions during motor training with MVF and showed that mirror reflection excites the motor cortex ipsilateral to the moving hand and corresponding to its reflection. For sake of clarity, we call this hemisphere the *mirrored* hemisphere. Similarly, the hemisphere contralateral to the movement and ipsilateral to the mirror is termed the *movement* hemisphere. Most importantly, the causal link between the MVF effect on motor potentials and increased motor cortex

excitability has been proven in TMS studies demonstrating that continuous theta burst stimulation applied to the *mirrored* motor cortex disrupts the MVF effect (Nojima et al., 2012).

In addition to TMS studies lateralized readiness potentials in EEG and MEG research have been used to explore whether MVF may evoke lateralized M1 activation specifically related to the control of a moving hand (Praamstra et al., 2011; Touzalin-Chretien and Dufour, 2008; Touzalin-Chretien et al., 2009, 2010). Although the results from different research groups were contradictory, they converged on the finding of slightly increased *mirrored* motor cortical activity induced by self-produced movements observed through a mirror as compared to no-mirror condition. In line with previous findings Tominaga et al reported that MVF from the moving hand, similarly to the real opposite hand movements, enhanced the suppression of MEG oscillations in the beta band (15–30 Hz) by median nerve stimulation. The effect was expressed in the sensors overlaying *mirrored* sensorimotor cortex (Tominaga et al., 2009). Since beta band suppression was reported to indicate activation of M1 in early MEG studies (Salmelin and Hari, 1994), the authors interpreted the findings as confirming MVF effect on M1 activation. However, taking into account that the cortical source of beta suppression was recently localized to primary somatosensory (S1) cortex using more sophisticated and accurate localization technique (Gaetz and Cheyne, 2006), the results of Tominaga et al rather indicate that MVF modulates excitatory/inhibitory balance in the *mirrored* somatosensory areas. Indeed, recently (Wasaka and Kakigi, 2012) reported that MVF and real hand movements induced similar changes in the amplitudes of the short- and long-latency components of somatosensory evoked magnetic fields (SEFs) in the primary and secondary somatosensory cortex of the *mirrored* hemisphere.

A question still outstanding is how MVF triggers sensorimotor circuitry in a way specifically associated with recognition of the subject's own limb movement.

There are three main lines of explanations suggested in the current literature. One possible mechanism refers to mirror neurons in inferior frontal and inferior parietal lobes. Observation of one's own movement in the mirror may activate mirror neurons sending output to the primary sensorimotor cortex in the *mirrored* hemisphere. The mirror neuron system is thought to be the basis of perception-action coupling involved in action understanding (Rizzolatti et al., 2001). The second view implies that visual feedback from the mirror goes indirectly via *mirrored* dorsal visual stream towards *mirrored* sensorimotor cortex and further engages *mirrored* corticospinal pathways (Ramachandran and Altschuler, 2009). It has been also proposed that somatosensory-visual mismatch during MVF leads to increased attentional demands for the somatosensory information from the respective hemispace, eliciting dorsolateral frontal cortex activation and secondary modulation in *mirrored* M1 and/or S1

(Wasaka and Kakigi, 2012).

The main controversy of the suggested explanations for MVF phenomenon and its effects on neuroimaging measures relates to the finding that mere observation of another person's movement can provoke changes in somatosensory and motor cortex excitability mimicking those observed for MVF. TMS and fMRI studies showed heightened sensorimotor cortex excitability while a subject inspected another person's movements (see Fadiga et al., 2005 for a review; Gazzola and Keysers, 2009), whereas exploration of neuromagnetic evoked fields to median nerve stimulation highlighted that somatosensory responses are also modulated by viewing actions made by others (Avikainen et al., 2002). In the same line of evidence, left and right hand movements performed by an actor have been shown (van Schie et al., 2008) to generate an event-related field (ERF) over the contralateral motor cortex of an observer with a similar latency to the MVF response. These studies imply that in the visual input about biological motion and/or intended action performed by another person has rather fast access to the motor cortex in line with mirror neuron hypothesis (van Schie et al., 2008). It has been suggested (Hari, 2006) that this access is mediated by the inferior or dorsolateral frontal cortex.

However, since the observer never misinterpreted another person movements as their own, the existing neuroimaging findings on sensorimotor cortex excitation triggered by both MVF and movement observation cannot explain the illusory feeling of self-agency of mirror hand movement. Similarly, they do not clarify the specific features of M1 activation during MVF that promote limb function recovery after paralysis (see Ramachandran and Altschuler, 2009 for a review). The results rather suggest that the primary sensorimotor cortex activation on its own may not be sufficient to cause mirror hand illusion and its therapeutic effect.

From this perspective, movement-evoked high frequency gamma oscillations (HGO) observed in intracranial EEG (ECoG), MEG and even scalp EEG studies (see Crone et al., 2011 for a review) over M1 area are of clear interest. The functional response properties of high-gamma activity are distinct from movement-related synchronization and desynchronization (ERD and ERS) of mu-rhythm in lower alpha (8–13) and beta (15–30) frequencies (Pfurtscheller et al., 2003). In EEG and MEG studies bilateral mu-rhythm suppression and subsequent rebound was considered to characterize involvement of sensorimotor cortex in movement preparation and execution. In ECoG high gamma power (60–90 Hz) responses following movements of different body parts were found to occur in a more focal topographical pattern than the alpha and beta ERD phenomena. Furthermore, somatotopically defined regions on the basis of high gamma oscillations in the sensorimotor cortex were consistent with maps generated by cortical electrical stimulation (Crone et al., 1998). The same

HGO during limb movements can be detected non-invasively by MEG (Cheyne et al., 2008; Muthukumaraswamy, 2010). In their MEG study of self-paced movements Cheyne and colleagues found that these oscillations were highly time-locked to movement onset, and observed only in the contralateral motor cortex for unilateral movements. Based on narrow somatotopic localization in M1 depending on movement of the upper and lower limbs and the lack of pre-movement gamma bursts these authors suggested that HGO could be the result of reafferent proprioceptive feedback to the primary motor cortex during movement. The lack of HGO bursts during both passive movement and movement observation however (Muthukumaraswamy, 2010) suggests that movement-related HGO may relate to active motor control processes rather than just to proprioceptive inputs. Most probably, gamma oscillations following EMG onset may reflect activation of distributed networks within primary somatosensory and motor cortices involved in the processing of afferent information requiring for ongoing feedback control of discrete self-paced movements.

Based on these observations we hypothesize that the illusory percept during MVF may relate to the presence of HGO in the *mirrored* hemisphere. In other words visual feedback from the moving mirror hand during self-initiated movement may trigger the control processes specifically associated with a person's own moving hand in the *mirrored* sensorimotor cortex.

The present study addresses this question by comparing the *mirrored* spectral responses in the illusion condition to those evoked by the same kind of movements without the mirror.

2. Methods

2.1. Subjects

Fourteen healthy right-handed volunteers (8 females) aged 20–33 years (mean = 25, SD = 4) took part in the study. The study was approved by the local ethics committee of the Moscow University of Psychology and Education and was conducted following the ethical principles regarding human experimentation (Helsinki Declaration).

2.2. Experimental procedure

During the MEG recording, subjects sat in a magnetically shielded room (AK3b, Vacuumschmelze GmbH, Hanau, Germany), with their head resting securely against the helmet-shaped surface of the helium dewar.

In this study the mirror was always on the left side and therefore *mirrored* hemisphere was

always the right hemisphere and *movement* hemisphere was always the left. Prior to start of the recording, subjects placed both hands inside a box made of wood and dismountable mirrored glass. The mirror illusion was induced by a simultaneous touching of the left and the right hand index fingers performed by an experimenter hidden behind the screen (Fig. 1A). During this intervention, a subject could not see the left hand directly but saw the touching in the mirror. The appearance of illusory perception of mirror hand ownership, at least transient, was detected in all fourteen subjects judging by the subject's self-reports. The aim of these manipulations was to enhance the putative mirror-hand illusion during following recording session (Hohwy and Paton, 2010).

During the recording session, a subject remained sitting in the same position and was asked to perform one of three variants of the motor task in three separate recording blocks lasting 7–9 min with 2–5 minutes of rest between them.

In bilateral movements condition (BILATERAL) the mirror glass was removed and a subject was instructed to perform concurrent self-paced brisk extensions of both index fingers approximately every 2 s.

In right hand movements without mirror condition (NOMIRROR) similar movements were performed with right hand index finger alone.

In right hand movements with mirror condition (MIRROR) the movements were the same as in NOMIRROR with a mirror placed between the two hands so that the subjects could not see their motionless left hand but instead saw reflection of the moving right hand where the left hand should be (Fig. 1B).

In all the three conditions the subjects were asked to keep their eyes open and to gaze to the left at the left hand index finger (or at a reflection of the right hand index finger in the mirror).

The order of the condition blocks was pseudo-randomized and counterbalanced across the subjects.

After the recording session the subjects were asked about their perception of the mirror-hand illusion during the MIRROR condition. All subjects reported the presence of an illusory perception, but its degree varied from being a slight and temporary sensation to a very strong and constant awareness.

2.3. MEG recording

Movement-related neuromagnetic activities were recorded with a helmet-shaped 306-channel detector array (Vectorview, Neuromag, Helsinki, Finland), which comprised 102 identical triple sensor elements. Each sensor element consisted of two orthogonal planar gradiometers and one magnetometer

coupled to a multi-SQUID (superconducting quantum interference device) and thus provided three independent measurements of the magnetic fields. In this study, the results recorded from 204 planar gradiometers were used for analyses, because they provide an optimal signal-to-noise ratio for superficial current sources such as the pericentral mu-rhythm generator (Simoes et al., 2004).

Prior to the MEG session, the positions of HPI coils were digitized together with fiducial points using a Polhemus Fastrak 3D digitizer (Fastrak, Polhemus, Colchester, VT) and were further used to track head position inside the MEG helmet. The spatiotemporal signal space separation method (tSSS) method (Taulu et al., 2004) implemented by MaxFilter (Elekta Neuromag software) was used to suppress interference signals generated outside the brain. Head movement compensation was used as well. The data were converted to standard head position ($x = 0$ mm; $y = 0$ mm; $z = 45$ mm) across all experimental blocks.

Four electrooculogram (EOG) electrodes were used to record horizontal and vertical eye movements; EOG electrodes were placed at the outer canti of the eyes and above and below the left eye, and EOG signals were recorded with a high-pass filter of 0.1 Hz. Movements of both index fingers were constantly recorded, time-locked to MEG signal acquisition, with three-axis accelerometers (ADXL330 iMEMS Accelerometer, Analog Devices Norwood, MA) attached to the dorsal aspect of index fingers.

The MEG signals were recorded with a band-pass filter of 0.03–330 Hz, digitized at 1000 Hz, and stored for off-line analysis.

2.4. MEG data analysis

The correction of the vertical eye movements was performed for continuous data in Brainstorm (http://neuroimage.usc.edu/brainstorm, Tadel et al., 2011) using the SSP algorithm (Tesche et al., 1995; Uusitalo and Ilmoniemi, 1997).

The subsequent analyses were done using the SPM12 toolbox (http://www.fil.ion.ucl.ac.uk/spm, Litvak et al., 2011). We subjected the data to three different analysis pipelines. The first pipeline was optimized for the analysis of evoked fields, the second pipeline was for defining spatiospectral regions of interest (ROIs) and the third pipeline was used to analyze the time courses of power based on the defined ROIs.

Data were downsampled to 300 Hz and epoched from –0.5 to 1 s relative to the right hand index finger movement onsets. Movement onsets were marked using an automated algorithm (Zakharova et al., 2012) that detected increases in the accelerometer signal (z axis) above baseline by 3 standard

deviations, reaching peak amplitude (2.5×threshold) within a 400 ms time window, and then visually inspected for false positives. Epochs where the interval from the previous right hand movement was below 2 s were excluded from the analysis. The epochs coinciding with the occasional movement of the left hand index finger under NOMIRROR and MIRROR conditions were also excluded from an analysis by thresholding the absolute values of the left hand index finger accelerometer traces at 3 standard deviation of the values in the baseline period (–500 to –200 ms before the movement onset). The epochs with increased contamination of MEG signals with high frequency muscle activity were excluded by thresholding the mean absolute values of MEG data filtered above 60 Hz in each channel at 5 standard deviations of the mean values averaged across channels. The remaining epochs still comprising increased high-frequency signal at several MEG channels were excluded after visual inspection. Between 98 and 182 epochs for each condition were accepted for subsequent analysis (M = 123; SD = 24).

2.5. Analysis of evoked fields

For analysis of movement-related evoked fields the epoched data were averaged using a robust averaging procedure implemented in SPM (Holland and Welsch, 1977; Wager et al., 2005). The significant difference in the magnitude of movement-evoked magnetic field between MIRROR and NOMIRROR conditions was determined for the pair of sensors 1133 and 1132, representing the spatial maximum of motor evoked response at the right-hemispheric sensor array, by employing a paired t-test at each time point within 500 ms time interval starting from the hand movement onset. The average of each subject at that time point was treated as an observation. Correction for multiple comparisons with respect to the number of time points being tested was done using the FWE correction procedure implemented in the SPM.

2.6. Definition of spatiospectral ROIs

Substantial methodological problems arise when using a fixed frequency band and groups of sensors to monitor the spatial-temporal dynamics of HGO. There is a substantial variability of findings in the literature regarding the frequency boundaries and electrode sites where HGO could be observed during limb movement in MEG and ECoG studies (see Crone et al., 2011 for a review). Depending on the electrode site or even the subject, power in lower gamma frequencies (30–40 Hz) could either be increased or decreased. Furthermore, at the higher frequency part of the MEG spectrum power augmentation was reported across a wide range of frequencies, without any clear or consistent upper boundary. It is also possible that HGO spatial and frequency properties can be modulated by experimental condition.

Our analysis, therefore, proceeded in two stages: definition of spatiospectral region of interest (ROI) using exploratory SPM analysis followed by a test for our hypothesis restricted to the maximally responsive sensor in the ROI and properly corrected for multiple comparisons across time. This approach is very similar to "functional localizer" methods common in fMRI studies (e.g. Julian et al., 2012) and analogous to our approach to analysis of evoked fields with the added complication of delineating frequency bands. Our prior hypothesis was that MVF induces neural activity in the *mirrored* hemisphere in the cortical areas activated by true bilateral movement. We, therefore, used the comparison of bilateral movement of both left and right hand index fingers (BILATERAL) to baseline as the functional localizer. Subsequently we used the ROI defined in this way to test for differences of responses in the *mirrored* hemisphere between right hand index finger movements alone (NOMIRROR) and right hand index finger movements with MVF (MIRROR). This is a statistically valid and physiologically meaningful approach since the ROI was defined based on independent data to avoid any 'double-dipping' (Kriegeskorte et al., 2009) and MVF produced subject's illusory perception of moving both hands.

For efficient spectral estimation from a relatively small number of trials we used multitaper spectral analysis (Thomson, 1982) This method is based on pre-multiplying the data with a series of tapers optimized for producing uncorrelated estimates of the spectrum in a given frequency band. This sacrifices some of the frequency resolution, in a controlled manner, to increase signal to noise ratio. It does this by effectively multiplying the number of trials by the number of tapers used. We estimated the spectra in overlapping windows of 400 ms (shifted by 50 ms). The frequency resolution was set to the inverse of the time window (2.5 Hz) for up to 25 Hz, then 0.1 times the frequency for 25 to 50 Hz and then to a constant 5 Hz resolution. These settings resulted in a single taper being used for 2.5–30 Hz, 2 tapers for 32.5–42.5 Hz and 3 tapers for 45 Hz and above. The resulting time–frequency images had no discontinuities thanks to the continuous frequency resolution function.

Epoched time-frequency data were averaged using a robust averaging procedure (Holland and Welsch, 1977; Litvak et al., 2012).

To reduce inter-subject variability and to normalize power changes across different frequency bands, the averaged power was log transformed and baseline corrected using a period of 500 to 200 ms before movement onset as the baseline (LogR option in SPM). Planar channels were then combined by adding time-frequency data for pairs of channels corresponding to orthogonal sensors at the same location.

For definition of spatiospectral ROI for movement-related activity we performed statistical analysis of the movement-related spectra to detect significant differences from the baseline. Since the

SPM statistical machinery can only handle images with up to three dimensions we averaged the time-frequency data over the time window of 0 to 500 ms relative to the movement. This window is known from the literature to contain strong movement-induced spectral changes, particularly the responses of the sensorimotor areas in the high gamma band (Cheyne et al., 2008). This resulted in scalp×frequency data that were exported to Neuroimaging Informatics Technology Initiative (NIfTI) format and smoothed in space-frequency using a Gaussian smoothing kernel with Full Width Half Maximum (FWHM) of 8 mm×8 mm×3 Hz to ensure that the images conform to the assumptions of Random Field Theory (Kilner and Friston, 2010). The smoothed images were then subjected to a single-sample t-test and ROIs were defined using uncorrected threshold of $p<0.001$.

2.7. Analysis of band specific-spectral changes in selected channels

Channels and frequency bands for the analysis were determined as described above (see also in Results). Power time-courses were computed for the pre-defined bands by setting the frequency of interest to the middle of the band and the frequency resolution to half of the band width. Time windows of 400 ms shifted by 50 ms were used as in the previous analysis. For analysis of movement-related evoked fields the epoched data were averaged using a robust averaging procedure implemented in SPM (Holland and Welsch, 1977; Wager et al., 2005), log transformed and baseline-corrected with 500 to 200 ms pre-movement baseline. In robust averaging method, for each channel and time (or channel time and frequency when working with spectral data), the distribution of values over trials is considered and the outliers are down-weighted when computing the average. This makes it possible to suppress artifacts restricted to narrow time and frequency ranges without rejecting whole trials. Moreover, a clean average can be computed with no clean trials, provided that artifacts do not overlap systematically (Litvak et al., 2012).

Power time courses were then exported to one-dimensional NIfTI images, smoothed by a Gaussian kernel with FWHM of 400 ms and subjected to two-sample t-test to compare MIRROR and NOMIRROR conditions. Correction was applied to account for multiple comparisons across 2 channels in the ROI and the results were accepted as significant at $p < 0.025$ (Family Wise Error (FWE) corrected at the peak level).

3. Results

We were specifically interested in the right (*mirrored*) hemispheric response for answering the main question of the study.

Any additional activity in the right hemisphere during observation of the right finger movements in the mirror could be induced by subtle involuntary movements of the resting left hand. To

ensure that the putative difference in neurophysiological indices of right hemisphere activation is not caused by synkinesia in the MIRROR condition, we compared the magnitude of accelerometer signals for the MIRROR and NOMIRROR conditions. (Fig. 1 C, D). Although there were subtle synkinetic movements of the resting left hand (Fig. 1 C, insert), accelerometer signals under direct and mirror view conditions were practically identical (p>0.193, FWE).

Next, we aimed to characterize movement-evoked (phase-locked) responses. The well-known (Shibasaki and Hallett, 2006) movement-evoked magnetic responses from MEG sensors overlaying sensorimotor cortical areas of both hemispheres were observed under BILATERAL condition, and the right-hemispheric responses were greatly reduced under the two conditions with unilateral right hand index finger movements (Fig 2). Statistical comparisons of evoked responses to unilateral hand movements with and without MVF were performed for sensor 1133 displaying the maximal evoked field in the right hemisphere in the BILATERAL condition, and revealed that MVF did not significantly affect the response amplitude in time window from 0 ms up to 500 ms after movement onset (p>0.157, FWE).

Next, we investigated induced MEG oscillations triggered by bilateral movements in the right and the left hemispheric MEG sensors (Fig. 3). This step was done to define the spatiospectral ROI for the later test of our main hypothesis. To this end, baseline-corrected time-frequency representations with subsequent averaging across time were calculated for each MEG sensor. Exploratory SPM analysis (spatial-frequency single-sample t-test at p<0.001 uncorrected) showed that bilateral movements induced significant post-movement increases in both low frequency power (2–7Hz, peaking at 2 Hz) and in gamma power (55–85 Hz, peaking at 62 Hz) with concomitant power suppression in the alpha-beta band (10–35 Hz, with peak at 22 Hz). Fig.3A shows sensor-space power maps representing the mean power of induced oscillations within each of 3 significant frequency clusters for BILATERAL condition and, for the sake of comparison, the same maps for the NOMIRROR and MIRROR conditions. Alpha-beta band and low frequency changes were wide-spread over the sensor array and were more pronounced over the central scalp region (Fig. 3A). These findings are in accord with reports from previous studies (Kaplan et al., 2012; Pfurtscheller and Lopes da Silva, 1999; Waldert et al., 2008).

Significant post-movement gamma synchronization was mainly observed at MEG sensors overlaying central scalp region (Fig. 3A). These movement-induced gamma oscillations were more narrowly localized in the sensor space than mu power modulations in accordance with Pfurtscheller et al. 2003.

The increase in gamma power was maximal at the pair of planar gradiometers 1133–1132 and

mainly characterized brain activity picked up by MEG sensor 1133 (Fig 4A,B). Both MEG sensors 1133 and 1132 were used for the subsequent analysis.

Figures 3B and 4B demonstrate that the HGO increase reached maximal intensity at latencies of about 125–175 ms after bilateral movement onset, roughly coinciding with the timing of movement-related HGO magnetic response from M1 that was reported by Cheyne et al. (Cheyne et al., 2008).

Third, we investigated the relationship between power of induced gamma oscillations at MEG sensor 1133 and 1132 and the presence of mirror visual feedback from the moving finger. The analysis was performed for the frequency band of the HGO response found for the real bilateral movement of both left and right hand index fingers. We compared the time courses of 55–85 Hz band power for the MIRROR and NOMIRROR conditions.

In the NOMIRROR condition HGO power at both MEG sensors 1133 and 1132 did not change relative to baseline, whereas it was significantly increased at MEG sensor 1133 during exactly the same movements, in the MIRROR condition (Fig. 4B, Supplementary Figure S1). This post-movement HGO increase in the MIRROR condition was significant in the time window of 0–375 ms after movement onset (p<0.025, FWE). Significant differences in HGO power between NOMIRROR and MIRROR conditions were found in post-movement time window 50–185 ms (p<0.025, FWE).

To verify that the mirror-produced HGO effect was not a result of field spread from movement hemisphere we compared the HGO power time courses in the NOMIRROR and MIRROR conditions at the left-hemispheric sensor 0433, which represented the topographical maximum of gamma frequency cluster in the movement (left) hemisphere (Fig. 3B, bottom row). No between-condition differences were found, thus ensuring that the induced HGO power increase in the *mirrored* hemisphere was the only significant effect differentiating right hand movements with and without mirror visual feedback.

Still another concern was the synkinetic left hand movements as the possible source of mirror-produced gamma oscillations. Although significant difference in intensity of subtle synkinetic left hand movements between MIRROR and NOMIRROR conditions was absent, there was still a possibility that these movements affected HGO response in right motor cortex under MIRROR condition. To verify that the mirror-produced HGO at the right-hemispheric "motor" sensor 1133 was not a result of the left hand movements we compared the mirror-produced HGO time courses between the trials sorted by the magnitude of the normalized accelerometer signal (Supplementary figure S1). No significant differences in HGO response were found between the 50% trials with strongest synkinetic movement compared to the 50% trials with weakest movement (p>0.628, FWE). This means that the HGO effect in "mirror hemisphere" could not be a consequence of subtle synkinetic left hand movements.

These findings raised the question whether the MVF-dependant post-movement induced response in the *mirrored* hemisphere was concentrated exclusively within gamma frequency band.

We tested for the effect of mirror visual feedback during unilateral finger movements on lower frequency bands (theta 2–7 Hz and beta 10–35 Hz) that were sensitive to bilateral fingers movements, looking for the differences in post-movement theta and alpha-beta power between NOMIRROR and MIRROR across the whole right hemispheric sensor array. There were significant differences between MIRROR and NOMIRROR conditions in the activities in the alpha-beta and slow frequency bands, that were observed over the temporoparietal and parietooccipital scalp regions respectively, located far from the sensorimotor cortex (Fig. 5).

4. Discussion

We hypothesized that viewing one's own moving hand through a mirror would provoke feedback control processes in the *mirrored* (ipsilateral to the moving hand) sensorimotor cortex as indexed by post-movement increase of high frequency gamma oscillations. We expected that this would result in higher amplitude of post-movement HGO in the sensorimotor cortex for both real bilateral movements and mirror viewed right hand index finger movements compared with the unilateral right hand index finger movements without mirror (control condition).

We found that bilateral movements induced a reliable post-movement HGO (55–85 Hz) increase in the right hemisphere with a topographical maximum at the MEG sensors overlaying sensorimotor cortex, whereas right finger movements without visual feedback did not change HGO in the right hemisphere. However, exactly the same unilateral movements with mirror visual feedback triggered the *mirrored* sensorimotor HGO response, whose amplitude significantly differed from that during control condition. Thus, our main finding demonstrates that mirror view observation of a person's own movement induced sensorimotor oscillations that have been considered an exclusive property of proprioceptive feedback-based control of self-paced movements.

Spectral and topographical properties of HGO response to bilateral movements will be discussed first. Previous MEG (Muthukumaraswamy, 2010) and EEG studies (Ball et al., 2008) involved the use of pre-defined frequency bands for HGO and/or different methods of spectral analysis compared to the current research. However, the 55–85 Hz range where we found movement related HGO response lies well within the frequency band where non-invasive and invasive (see Crone et al., 2011 for a review) studies previously reported movement related HGO activity, both in human and monkey motor cortex. Our movement-related increase of HGO power over the right hemispheric sensorimotor cortex during bilateral movements but not during ipsilateral right hand index finger

movements (NOMIRROR) complements previous ECoG studies looking at sensorimotor HGO power after the onset of self-initiated movements and showing increased HGO power in the sensorimotor cortex for contralateral but not ipsilateral hand movements (Pfurtscheller et al., 2003). Based on the results of intracranial studies showing exact somatotopy of HGO response (Crone et al., 2011) we expected increased movement-related HGO power in MEG sensors overlaying the hand representation area at the pre- and postcentral gyrus. Indeed, MEG sensors 1133 and 0433 showing the most pronounced movement-related HGO in the BILATERAL condition also displayed the maxima of motor-evoked response fields with presumed origin at hand areas of sensorimotor cortex (Salmelin et al., 1995). However, significant HGO increase was also observed at the central midline MEG gradiometers and sensors whose locations corresponded to more posterior parietal cortical sources (Fig. 3). These results do not support the conclusion derived from MEG studies implicating primary motor cortex as a unique source of the HGO response (Muthukumaraswamy, 2010). On the other hand, distribution of movement-related HGO beyond the region of primary motor cortex is in line with the results of ECoG (Ohara et al., 2000; Pfurtscheller et al., 2003) and EEG recordings (Ball et al., 2008) that detected movement induced HGO in primary and secondary motor and somatosensory cortical areas, as well as in parietal association cortex. Given the possible inaccuracy of localization algorithms for distributed modeling of MEG signals, further invasive cortical recordings with broader coverage are needed to delineate the cortical origin of the HGO effects that we found at the MEG sensor level.

The major new finding of the current study was that movement-related gamma response in the right hemisphere could be induced by ipsilateral hand movements alone if mirror view of the moving hand was available to the subject. Our study was not designed to statistically evaluate all the aspects of MVF response in detail, but concentrated on a frequency band of interest (55–85 Hz) and sensor 1133 based on the strongest responses found for (separately analyzed) bilateral movements. Importantly, MVF-triggered HGO was observed at this ROI suggesting some commonality in neural basis between MVF response and movement-related gamma oscillations in the sensorimotor cortex. The time course of HGO envelope was similar for MVF and movement-related responses, with both responses starting immediately after finger movement onset and reaching maximal strength at about 100–150 ms after it (Fig. 4). Although the MVF-triggered response (MIRROR, Fig. 4) was weaker than movement-related HGO response (BILATERAL), it contrasted sharply with plainly absent HGO increase during ipsilateral right hand movements without MVF (NOMIRROR).

We considered four possible explanations for the neural mechanism underlying HGO modulation in sensorimotor cortex due to the mirror visual feedback. One possibility is that repetitive right hand index finger movements may provoke subtle involuntary mirror movements in the opposite

hand with recurrent proprioceptive feedback to contralateral right sensorimotor cortex. Such mirrored EMG activity of the homologous muscle of the opposite hand during repetitive index finger abduction has been observed in healthy children and to much lesser degree even in adults (Mayston et al., 1999). Our accelerometer recordings did show that unilateral right finger movements were accompanied by extremely subtle displacements of index finger of opposite hand (Fig. 1 insert), and the time of onset of involuntary compared with voluntary movements was more variable but similar on average. Although this explanation cannot be ruled out completely, it seems to be rather improbable since there was no difference between MIRROR and NOMIRROR in the amplitude of accelerometer signals from the mirroring hand (Fig. 1).

We should stress that our MEG data were aligned to movement onset defined according to the accelerometer signal. Therefore, subtle gamma modulations occurring due to sub-threshold muscle tension may be missed. EMG recordings of superficial flexor digitorum and extensor digitorum muscles should be performed in the future studies to control for such sub-threshold effects.

The other possibility is that looking at the moving left hand index finger despite proprioceptive signaling of stationary left hand produced a significant enhancement of visual and tactile spatial attention to the left hemispace. Hence, observed modulation of sensorimotor cortical activity in high gamma band may stem from increased attention to the left side eliciting activation of higher-order frontal and parietal areas and secondary modulation in sensorimotor and visual cortices. While the effects of directing attention on induced movement-related HGO are not known, these effects were well described for topographically specific changes in synchronization/suppression of visual alpha and somatosensory mu rhythms induced by stimulation in the visual and somatosensory domains (Bardouille et al., 2010; Thut et al., 2006). Specifically, posterior alpha suppression and theta enhancement were shown to be influenced by deployment of visual spatial attention (Bastiaansen et al., 2002; Sauseng et al., 2005; Thut et al., 2006), leading to topographically-specific power changes in accordance with the focus of attention (Rihs et al., 2009; Sauseng et al., 2010). In our study this alternative seems probable at least regarding visual cortex excitability, given that the visual alpha oscillations were significantly suppressed and theta oscillations enhanced at the right posterior sensors during mirror condition comparatively to no-mirror condition (Fig. 5). Apart from increased attention, the repetitive visual stimulation produced by the mirror hand movements in the former case may contribute to this asymmetric posterior alpha suppression effect. The right-lateralized between-condition difference in posterior alpha and theta power changes gave indirect but insurable evidence that visual attention of our participants was directed toward their left visual hemi-field where their left hand was positioned for the most part. The above finding confirms that our participants followed the

instruction to fixate their left hand across all three experimental conditions. However, a putative MVF-related attentional modulation of the cortical excitability reflected in event-related suppression of alpha/beta band activity was confined to posterior visual sensors (Fig. 5), and did not involve alpha and beta components of sensorimotor mu rhythm power, which was also shown to be sensitive to attentional demands (Bardouille et al., 2010). Hence, increased attentional deployment in the mirror condition might potentially cause changes in oscillations power in visual cortical areas, but this factor may hardly be regarded as the main source of the frequency specific and topographically restricted HGO response in sensorimotor cortex.

The third possible account is based on the findings in the literature showing the specific functional properties of HGO that relate these oscillations to the onset of self-paced movements and putatively more generally to movement's ownerships (De Ridder et al., 2011; Muthukumaraswamy, 2010). These unique relationships between sensorimotor HGO and person's own movements make a main distinction between HGO and other measures of sensorimotor cortex excitability previously used in neuroimaging studies of mirror hand illusion and reviewed in the introduction. As Praamstra and colleagues pointed out, the numerous findings of M1 and premotor cortex activation following not only mirror hand illusion but also a mere observation of another person's intended actions and/or biological motion implies extreme flexibility of motor cortical activity, which might well be incompatible with stable function (Praamstra et al., 2011). In particular, with primary sensorimotor cortex being excitable so non-specifically, how does the brain differentiate movements of its own body from movements performed by others? We speculate that the HGO generation in response to mirror hand does reflects the same neural mechanisms on which the brain relies for perception of movement self-agency and that produce the illusory misperception of mirror hand movement as movements of person's own left hand. Firstly, observation of another person's movement did not trigger HGO (Muthukumaraswamy et al., 2006). Secondly, during unilateral movement HGO is strongly lateralized in the contralateral hemisphere and somatotopically localized (Crone et al., 2006) as would be expected of a cortical representation of a moving body part. Thirdly, it appears only after movement onset implying an essential contribution of sensory feedback (Ball et al., 2008; Cheyne et al., 2008; Pfurtscheller et al., 2003). Fourthly, it cannot be provoked by passive stretching of a person's hand, i.e. by producing proprioceptive input into motor cortex which is not accompanied by motor command for movement execution (Muthukumaraswamy, 2010). It is conceivable, therefore, that this type of oscillation may be triggered only in case of close coincidence between top-down input to the sensorimotor cortical network signaling the onset of self-motion and peripheral input conveying the feedback information on the resulting movement. Further on, HGO may be involved in a precise time synchronization of

reverberating activity across the whole network controlling arm movements in line with a general assumption on the role of gamma oscillations in the functional coordination of cortical areas in humans (Senkowski et al., 2008). In combination, functional features of HGO suggest that these movement-related oscillations in sensorimotor cortices may be a unique signature of movement agency, i.e. the feeling that moving limb of one's *body* does *belong* to one's self.

The fourth possible account could be derived from a recently developed predictive coding perspective on motor control. The theory suggests that efferent pathways descending from the cortex to the spinal cord convey command basing on expected proprioceptive input following the planned movement, which the motor plant is then bound to fulfill by executing the movement (Adams et al., 2013). This process is analogous to inferring the causes of sensory inputs in that both involve minimization of sensory prediction errors. One of the many scientific puzzles that this theory can possibly resolve is how very similar canonical cortical circuits can support both perception and action. In their recent review Bastos and Friston (Bastos et al., 2012) suggested that HGO are associated with forward connections conveying prediction errors whereas oscillations at lower frequencies are associated with backward connections conveying predictions. In the motor system some proprioceptive prediction error will necessarily arise as a consequence of movement because the ensuing afferent inputs can never be exactly predicted. This explains why HGO only appear following movement onset but not earlier. The absence of sensorimotor HGO when observing other people's movement also fits in this framework, as there is an expectation of no proprioceptive signals in this condition, which is indeed met. However, the mirror-hand illusion is different because in predictive coding terms 'illusion' basically means that the hypothesis chosen by the brain's inference machinery to account for its sensory inputs is that the hand seen in the mirror is the subject's own other (left in our case) hand. Under this hypothesis it would be expected that proprioceptive signals reach the sensorimotor cortex. The absence of these signals generates prediction error manifest as HGO. Unlike the more traditional account above, the predictive coding account views the HGO not as a cause but as a consequence of the illusion state and requires other areas generating predictions to also subserve this state. This is well in line with our findings of differences in low frequency activity not specific to the sensorimor cortex.

The cerebral network, through which visual feedback from moving mirror hand reaches sensorimotor cortex in perfect synchrony with motor execution command, remains debatable. Such cross-modal integration might be achieved through the transmission of visual information about moving hand via dorsal visual stream to the *mirrored* posterior parietal cortex. In monkeys posterior parietal areas contain neural populations involved in visual and somatosensory on-line control of arm

movements (see Fogassi and Luppino, 2005 for a review), and both visual and kinesthetic information converge on these regions. Efference copies of motor commands, probably generated in the frontal lobes, are also relayed to the posterior parietal cortex and provide information about initial motion plan (Andersen et al., 1997). On the other side, these neurons display a 'feedforward' pattern of projections towards primary and secondary somatosensory and premotor cortex (Rozzi et al., 2006) and could be a source of visual information on mirror hand movements to the primary sensorimotor hand-related areas.

5. Conclusions

In conclusion, using non-invasive MEG recordings we show evidence that high-frequency gamma activity in the sensorimotor cortex may be triggered not only by proprioceptive feedback due to onset of conralateral finger movements but also by visual feedback from mirror image of moving finger. The functional role of these sensorimotor cortex oscillations remains unsettled. If the view that HGO reflect the proprioceptive feedback control of discrete movements is correct, our current results suggest that visual information about movement execution being synchronized with motor command may change the processing mode in the sensorimotor cortex in a way, which is highly specific for person's own movement. We speculate, that fast frequency response to mirror hand in sensorimotor cortex may, at least partly, reflect the neural mechanism that underlies the mirror-hand illusion.

6. Acknowledgements

7. **References**

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Figure captions

Fig. 1. Experimental setup for the mirror condition.

Upper panel A – before recording session the subject faced the mirror to obtain mirror visual feedback of tactile stimulation overtly applied to right hand index finger, while left hand index finger hidden behind the mirror was stimulated synchronously. B – during recording session while the subject moved her right hand, the mirror provided a view of the moving left hand, which was resting behind the mirror. Lower panels depict grand average of accelerometer traces (combined across x, y and z axis) from left (C) and right (D) index fingers under 3 conditions: bilateral movements (BILATERAL) – solid line, right hand movements (NOMIRROR) – dotted line and right hand movements with mirror (MIRROR) – dashed line. Time 0 is where the accelerometer signal crossed the defined amplitude threshold. Scale bar for C and D is 0.5 V. Upper right corner's insert of panel C represents the same signals as in C, but with the scale changed to condition-specific standardized values (z-scores comparatively to baseline values). Note, that synkinetic movements of resting left hand index finger are very small relative to right hand index finger movements (only visible with normalization) and do not differ between MIRROR and NOMIRROR conditions.

Fig. 2. Movement-evoked fields for all sensors.

Inserts show responses from MEG sensors 0433 and 1133 which had the strongest response magnitude over the left and right hemisphere respectively. Bilateral movements evoked a clear response with topographical maximum over the central areas of both left and right hemispheres. Both types of right hand finger movements produced evoked response which was strongly lateralized to the left hemisphere, with no significant differences between the two conditions.

Fig. 3. SPM analysis of movement-induced oscillations.

A – spatial-frequency clusters for the three conditions. The left column shows three spatial-frequency clusters (2–7 Hz, 10–35 Hz, 55–85 Hz) thresholded at $p < 0.001$ (uncorrected) showing where the effects were significantly different from the baseline for bilateral movements. Subsequent columns depict sensor-space power maps representing the mean power of induced oscillations within each of 3 significant frequency clusters for BILATERAL, NOMIRROR and MIRROR conditions. In 2–7 Hz and 55–85 Hz clusters power increased and in 10–35 Hz cluster power decreased comparatively to baseline.

Despite the between-condition difference in the response magnitude, gamma power distribution over the right-hemispheric central scalp area is similar for BILATERAL and MIRROR conditions, suggesting that mirror visual feedback alone is capable of triggering sensorimotor HGO in the mirror hemisphere. MIRORR/NOMIRROR differences are evident not only at central scalp regions but also at posterior ones, where they are, most probably, related to variations in the intensity of visual input resulted in broadband modulation of activity of visual cortex.

B − time courses of post-movement changes in oscillatory power for the clusters shown in A for bilateral and right hand index finger movements. Time courses of mean baseline-normalized power are shown for the sensors MEG1133 and MEG 0433 corresponding to the right (top row) and left (bottom row) hemispheric topographical maxima of three spatial-frequency clusters: left − theta band (2–7 Hz), middle − alpha-beta band (10–35 Hz) and right − high gamma band (55–85 Hz). Red solid line − bilateral movements, green dotted line − right hand movements without mirror, blue dashed line − right hand movements with mirror. Horizontal axis − time in milliseconds relatively to movement's onset, vertical axis − log normalized power changes comparatively to baseline. The power increase within high gamma band at right-hemispheric sensor MEG1133 is the only significant effect differentiating right hand finger movement with and without mirror visual feedback.

Fig. 4. Comparison of movement-induced high gamma oscillatory (HGO) response at the right (*mirrored*) hemisphere between experimental conditions.

A and B − time courses of post-movement changes in HGO power for BILATERAL (red solid line), NOMIRROR (green dotted line) and MIRROR (blue dashed line) for two sensors MEG1132 and MEG1133 positioned at right hemispheric topographical maximum of the gamma frequency cluster. Shaded areas represent standard error of the mean. Bars beneath each figure indicate the time windows for which the movement-induced HGO power was significantly above baseline ($p<0.025$, FWE) for BILATERAL (upper strip) and MIRROR (middle strip). No significant HGO power increase was found for NOMIRROR. Note that although individual time points for MIRROR and NOMIRROR in A were significantly above baseline at the uncorrected level as evident from the error bars, this effect did not survive FWE correction. Lower strip indicates time window, in which the difference in HGO power between MIRROR and NOMIRROR was significant ($p<0.025$, FWE). C − time-frequency plots of spectral power changes across BILATERAL, MIRROR and NOMIRROR conditions at sensor MEG 1133. Vertical dashed line denotes the movement onset, horizontal dashed lines marks the lower and upper boundaries of gamma frequency cluster (55–85Hz) according to SPM results. Please, note that

the frequency range (55–85 Hz) and time course of gamma oscillations power increase under MIRROR condition, mimics, although in a subtler form, the features of gamma response triggered by left hand movement in BILATERAL condition. This response is virtually absent during right hand movement without mirror (NOMIRROR).

Fig. 5. Comparison of movement-induced theta and alpha-beta response at right (*mirrored*) hemisphere between MIRROR and NOMIRROR conditions.

Spatial clusters thresholded at $p < 0.05$ (FWE correction for the whole search volume) showing significant between-condition differences for theta (2–7 Hz) and alpha-beta (10–35 Hz) frequency clusters. The gray-scale depicts the absolute t-value. In 2–7 Hz frequency band power was higher under MIRROR condition compared to NOMIRROR one and in 10–35 Hz frequency band *vice versa*.

Supplementary Figure S1. Comparison of mirror-induced high gamma oscillatory (HGO) response at the right (*mirrored*) hemisphere between the trials sorted by the magnitude of the normalized accelerometer signal for the left hand during MIRROR condition. Mirror-induced HGO power changes at sensor 1133 did not differ significantly between the 50% trials with strongest synkinetic movements (blue line) compared to the 50% trials with weakest movements (red line). Shaded areas represent standard error of the mean. Thus, the HGO effect in "mirror hemisphere" was not a consequence of subtle synkinetic left hand movements.
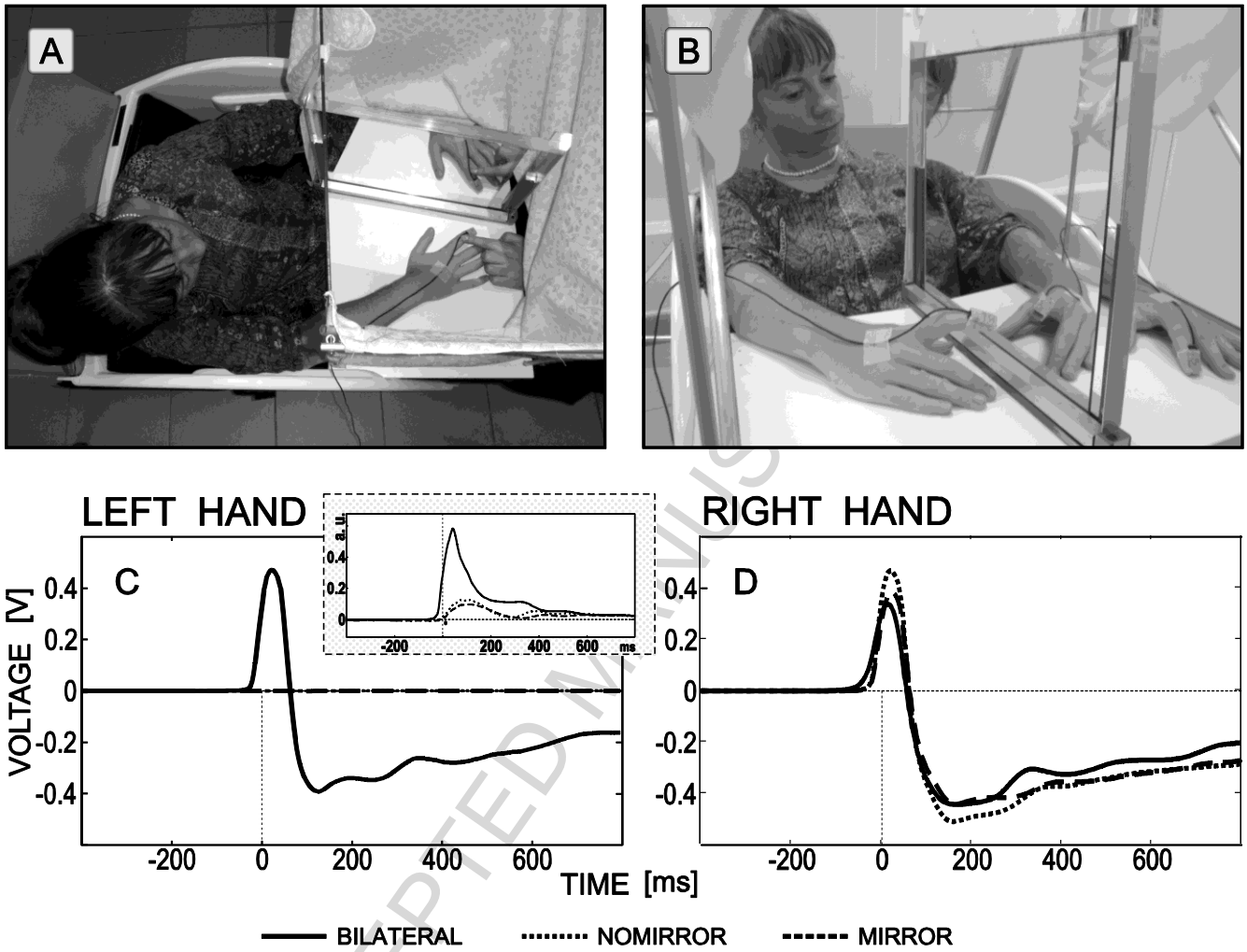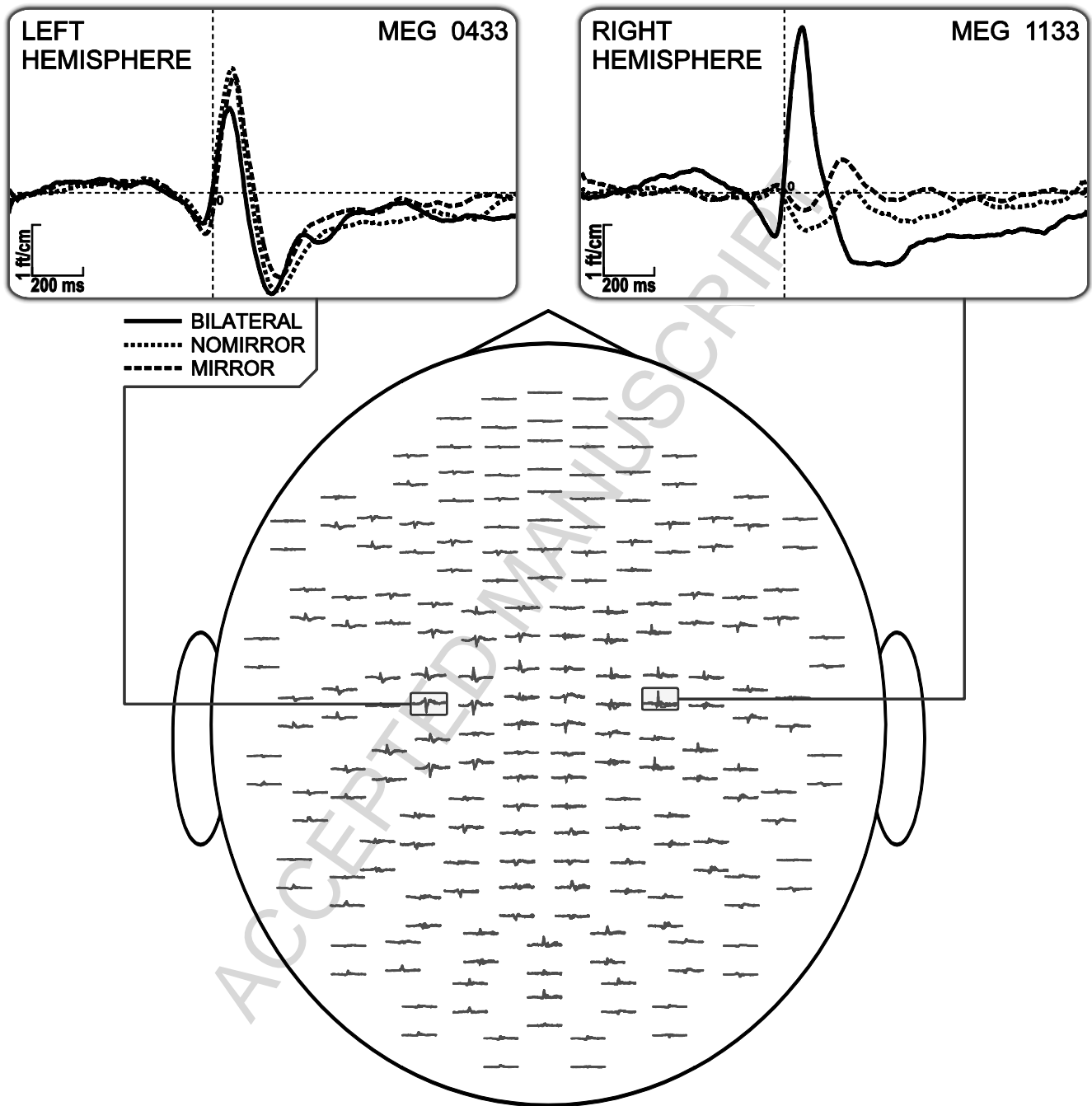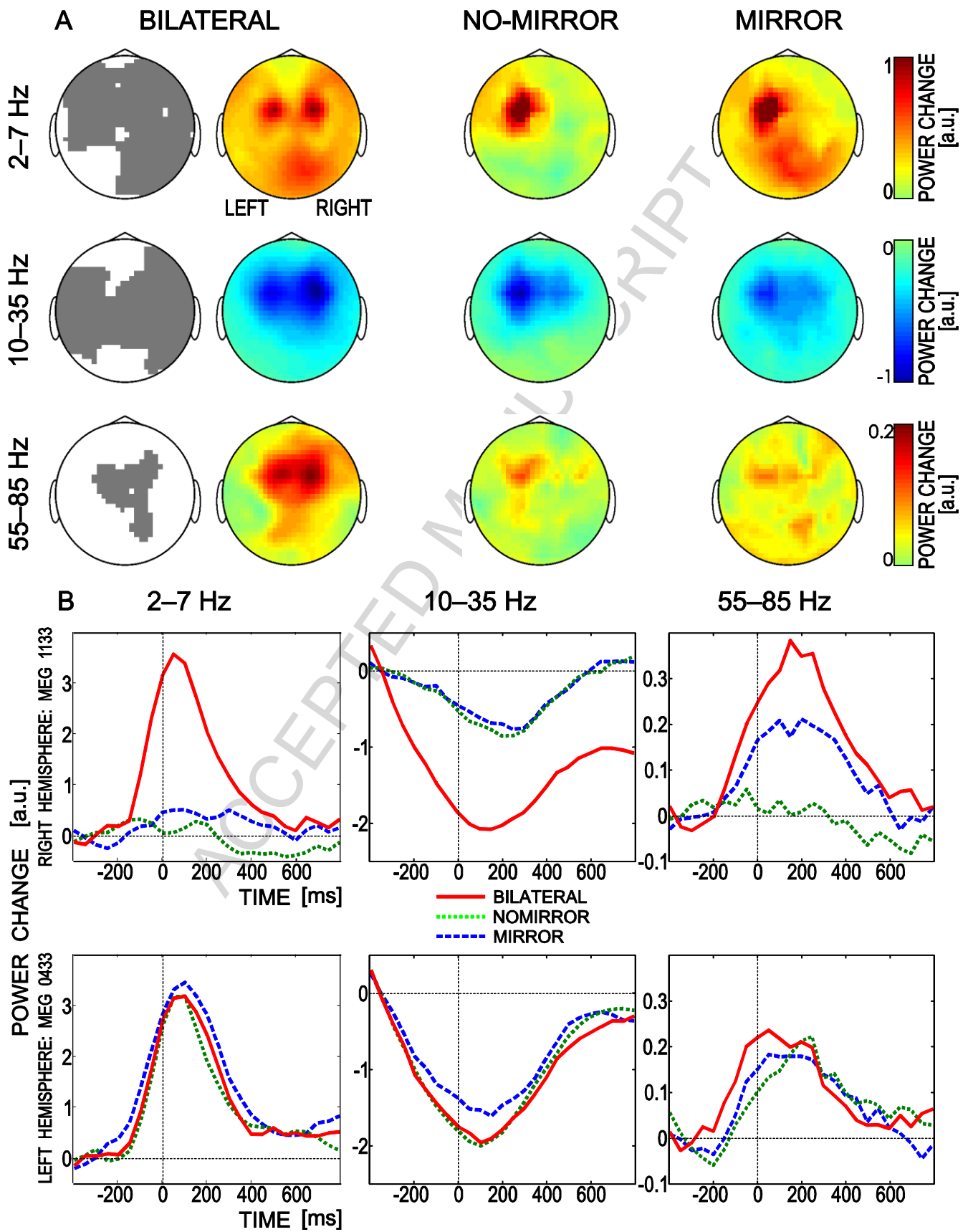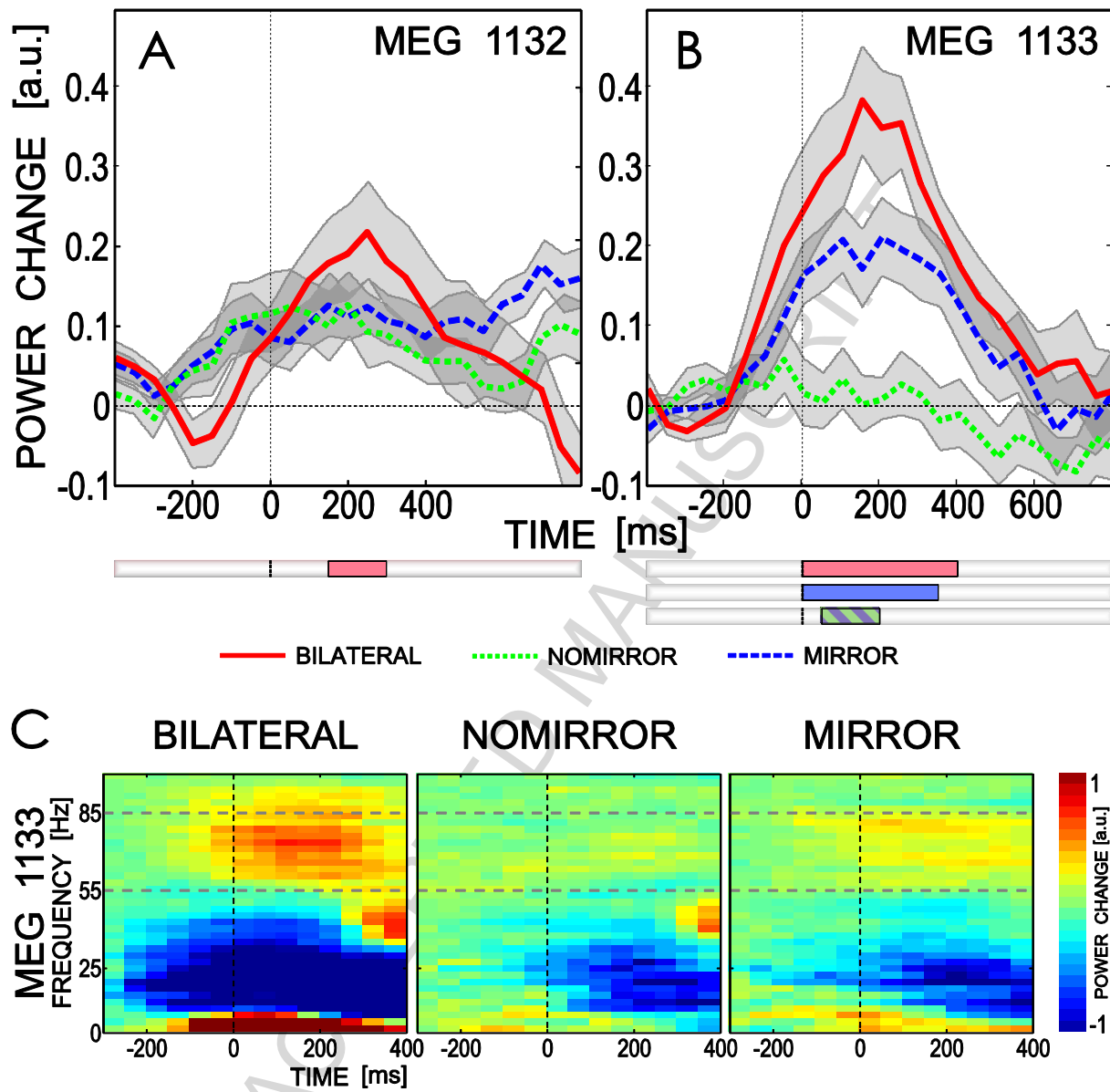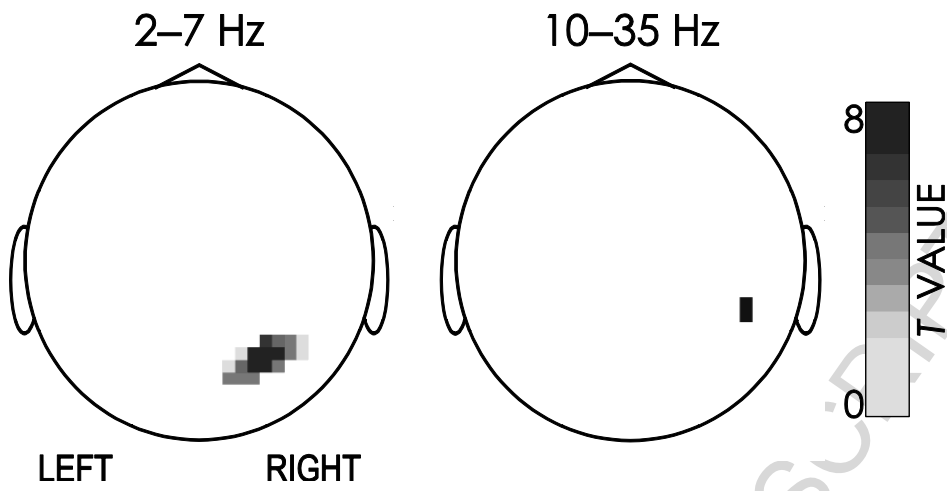
Figure 1

Figure 2

Figure 3

Figure 4

Figure 5