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RESEARCH REPORT

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Spatial sensorimotor mismatch between the motor command and somatosensory feedback decreases motor cortical excitability. A transcranial magnetic stimulation-virtual reality study

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Abstract

Effective control of movement predominantly depends on the exchange and integration between sensory feedback received by our body and motor command. However, the precise mechanisms governing the adaptation of the motor system's response to altered somatosensory signals (i.e., discrepancies between an action performed and feedback received) following movement execution remain largely unclear. In order to address these questions, we developed a unique paradigm using virtual reality (VR) technology. This paradigm can induce spatial incongruence between the motor commands executed by a body district (i.e., moving the right hand) and the resulting somatosensory feedback received (i.e., feeling touch on the left ankle). We measured functional sensorimotor plasticity in 17 participants by assessing the effector's motor cortical excitability (right hand) before and after a 10-min VR task. The results revealed a decrease in motor cortical excitability of the movement effector following exposure to a 10-min conflict between the motor output and the somatosensory input, in comparison to the control condition where spatial congruence between the moved body part and the area of the body that received the feedback was maintained. This finding provides valuable insights into the functional plasticity resulting from spatial sensorimotor conflict arising from the discrepancy between the anticipated and received somatosensory feedback following movement execution. The cortical reorganization observed can be attributed to functional plasticity mechanisms within the sensorimotor cortex that are related to establishing a new connection between

Abbreviation: ACC, anterior cingular cortex; dPM, dorsal premotor cortex; FDI, first dorsal interosseous; M1, primary motor cortex; MEPs, motor-evoked potentials; RHI, rubber hand illusion; S1, primary somatosensory cortex; S2, secondary somatosensory cortex; SMA, supplementary motor area; TMS, transcranial magnetic stimulation; vPM, ventral premotor cortex; VR, virtual reality.

somatosensory input and motor output, guided by temporal binding and the Hebbian plasticity rule.

KEYWORDS

motor cortical excitability, sensorimotor functional plasticity, sensorimotor integration, somatosensory system, virtual reality

1 | INTRODUCTION

When interacting with the external world, most actions (especially consolidated movement patterns) are performed efficiently, with limited cognitive effort and below awareness. Effective motor control strongly relies on the continuous information exchange that occurs in the brain between the motor outputs and the sensory input feedback received (Franklin & Wolpert, 2011). Sensory integration should then be considered a crucial component of motor control. Among the sensory information involved in motor interactions, somatosensory feedback is highly relevant to motor planning and execution (Bolognini et al., 2016; Edwards et al., 2019). In mice, it has been shown that a focal lesion in the primary somatosensory cortex (S1) compromises motor control drastically, although the integrity of motor areas was preserved (Xerri et al., 1998). A similar impairment in motor control was documented in humans after somatosensory deafferentation (Rothwell et al., 1982). Not surprisingly, the motor and somatosensory cortices are anatomically and functionally interconnected to ensure an optimal exchange between perception and action, showing malleable bidirectional proprieties of neural representations (Mao et al., 2011). For instance, somatosensory perception is modulated by movement, whereby top-down cortical mechanisms induce cortical gating (a reduction of perceptual and physiological processing, known as *somatosensory gating*) during movement (Gallace et al., 2010; Palmer et al., 2016), as well as during imagery of movement (Kilteni et al., 2018). On the other side, recent investigations from non-human studies showed that the somatosensory cortex processes information from motor areas, such as the dorsal and ventral premotor cortex (dPM and vPM, respectively) and the primary motor cortex (M1) related to movement before receiving sensory feedback input (Umeda et al., 2019). This interplay between somatosensory and motor areas may reflect the neural processing of sensory anticipation based on the planning and execution of motor outputs, where S1 starts to predict and anticipate expected feedback based on information provided by motor commands. It is worth noting that motor efferences and somatosensory afferents are spatially selectively distributed with ascending and descending pathways innervating the same body part, leading to the co-activation of motor and somatosensory representations at the cortical level during sensorimotor interactions (Makin & Bensmaia, 2017). Based on the abovementioned evidence, the relationship between the sensory and motor neural representations of body districts should be considered bidirectional, for which the functionality of somatosensory areas affects the motor cortex and vice versa (Conforto et al., 2002; Edwards et al., 2019; Hummel & Cohen, 2005).

Experimental evidence suggests that somatosensory stimulation can induce functional plasticity in the relative motor area and modulate cortical excitability (measured by transcranial magnetic stimulation [TMS]-induced motor-evoked potentials [MEPs]) of the same body part. Specifically, local low-intensity vibrations on the index finger increase motor excitability in the somatotopic contralateral motor area representing that body district (Rosenkranz & Rothwell, 2003, 2006). Interestingly, motor functional plasticity mediated by somatosensory afference is not limited to the contralateral hemisphere of the stimulated hand: sensory stimulation of one hand also affects the excitability of the motor area in the non-stimulated hand. It has been shown that somatosensory vibration induces a decrease of excitability in the ipsilateral motor area of the stimulated hand, suggesting that sensory input can modulate corticospinal activity in both hemispheres simultaneously (Swayne et al., 2006). That is, somatosensory stimulation increases the excitability in the contralateral motor area and inhibits it in the ipsilateral hemisphere. This effect has been suggested to be related to transcallosal projections between the two brain hemispheres (Swayne et al., 2006; Takeuchi & Izumi, 2012). Additional evidence about the interaction between somatosensory and motor areas comes from studies that measured changes in functional motor indexes after limb deafferentation induced by an anesthetic block. Specifically, administering anesthesia to one hand results in diminished excitability in the motor cortex corresponding to the anesthetized region compared to pre-anesthetic measurements (Rossini et al., 1996; Ziemann et al., 1998). Conversely, increased excitability is observed in the motor cortex on the same side as the anesthetized hand (Brasil-Neto et al., 1992;

Werhahn et al., 2002). Comparable findings of reduced cortical excitability have been reported following prolonged arm immobilization (Facchini et al., 2002; Huber et al., 2006; Ngomo et al., 2012). Healthy participants who experienced short-term immobilization (usually 8 h) showed a reduction in motor output and sensory input from the contralateral sensorimotor cortex of the immobilized arm (together with an increase of cortical excitability to the non-immobilized arm) (Avanzino et al., 2011). These empirical findings highlight the importance of sensory flow between motor and sensory areas, suggesting rapid and transient 'functional' plasticity in the motor cortex induced by somatosensory modulation. However, previous works investigated the role of somatosensory feedback on functional sensorimotor plasticity during 'static stimulation', never involved a direct modulation of the somatosensory feedback received after performing a motor command (e.g., in anesthetization experiments, somatosensory feedback from a specific body area was removed but not altered in terms of spatial position) (Brasil-Neto et al., 1992; Facchini et al., 2002; Rossini et al., 1996; Ziemann et al., 1998).

These considerations raise an interesting question about how the motor system responds to a prolonged sensorimotor mismatch (and thus not only a lack of feedback) while actively performing a motor command. According to the *feed-forward* model of sensorimotor control, the sensorimotor system works as a 'comparator machine' between sensory expectations (based on a 'prior' representation of somatosensory-motor interaction) and the feedback received from the environment (Franklin & Wolpert, 2011). Whenever we execute a movement, a copy of the motor command (efference copy) is used to predict the sensory consequences of our movement and to compare it with the actual feedback (Blakemore et al., 1998; Kilteni et al., 2020). A mismatch between expectation and feedback generates a 'prediction error', the warning signal adopted by the brain to notify unfilled expected outcomes and to correct goal-directed movements (Shadmehr et al., 2010; Welniarz et al., 2021). On the contrary, respected sensory expectation attenuated self-generated sensations (known as *somatosensory attenuation*) compared to external stimuli (Job & Kilteni, 2023; Kilteni, 2023). This feed-forward loop guarantees a distinction between expected and self-generated versus external and uncontrolled events. Spatiotemporal factors are essential for preserving attenuation in self-generated sensations (Bays & Wolpert, 2008). A delay in time between the motor signal and somatosensory response (approximately 150 ms or greater) disrupts the attenuation of self-generated tactile sensations, leading to greater somatosensory and cerebellum responses with increased connectivity with motor areas (Kilteni et al., 2023). Similarly, a spatial mismatch between the motor action and sensory feedback (ranging from 10 to 30 cm) or employing a slider-device to generate external force diminishes the level of attenuation (Bays et al., 2006). However, attenuation in somatosensory perception remains for distantly self-produced touches using a tool (Kilteni & Ehrsson, 2017b), a result compatible with previous evidence supporting the embodiment of tools in the body schema (Maravita & Iriki, 2004). Nevertheless, recent studies demonstrated that the sensorimotor system can readapt its spatiotemporal constraints after being exposed to new statistical regularities in sensorimotor interactions. For instance, repeated exposure to a 100 ms delay between movement and somatosensory feedback led to the shift of the temporal windows for somatosensory attenuation (Kilteni et al., 2019). This sensorimotor learning process (e.g., being able to attenuate somatosensation for delayed trials after the training) involved modulation at the level of secondary somatosensory cortex (S2, involved in high-level somatosensory processing), cerebellum (internal forward model) and anterior cingular cortex (ACC, involved in the monitoring of cognitive conflicts) (Kilteni & Ehrsson, 2024). Furthermore, it has been demonstrated that illusory self-touch is attenuated after experiencing a rubber hand illusion (RHI), although the real hand was placed in the farthest position (25 cm) from the trunk, making contact unplausible (Kilteni & Ehrsson, 2017a). This result suggests that the anticipation of sensory outcomes following the RHI was constructed based on the position of the artificial hand rather than the actual hand. Interestingly, somatosensory attenuation decreased when participants experienced the illusion of a rubber hand placed 25 cm away from the real hand, indicative of disownership of the real hand. Thus, the brain seems to readapt its predictions in accordance with the spatiotemporal regularities governing previous sensorimotor experiences. However, neurophysiological markers associated with the adaptations of the sensorimotor system following prolonged exposure to a mismatch between motor commands and somatosensory feedback, particularly in the spatial domain, are not yet well investigated. For example, functional or morphological changes of the motor and somatosensory cortices to novel associations between action and feedback involving unrelated body parts are mainly unknown. This area remains underexplored, partly because we lack practical methods—aside from animal models (Jain et al., 2000) to re-wire the sensory input from motor output in neurologically healthy participants. Whenever we execute an action with a body part, the sensory input of that action is always congruently generated by the same body part that is moved. However, this practical limitation can now be overcome through the integration of virtual reality (VR) and haptic stimulation, allowing sensorimotor experiences where the interaction with objects may generate sensory stimulation in different body parts, which could be related or unrelated to the effector of the movement. Previous studies reported interesting results concerning the readaptation of the sensorimotor system guided by presenting new temporal regularities in sensorimotor interaction (Kilteni et al., 2019), an embodiment of fake hands (Kilteni & Ehrsson, 2017a), or tool use (Kilteni & Ehrsson, 2017b). However, they were mainly focused on somatosensory attenuation mechanisms. On the contrary, changes at the cortical level of the motor area due to temporal or spatial mismatch in the action-feedback sensorimotor loop remain unexplored. Considering previous results highlighting the relevance of somatosensory feedback in modulating brain motor activity, investigation in this domain is certainly relevant for advancing our understanding of the sensorimotor system and its plastic organization.

In the present study, we used immersive VR and real-time haptic feedback to study the neural effects of generating a conflict between sensory input and motor output during an 'active' interaction with objects (i.e., spatial input–output incongruence). Specifically, we used a VR-sensorimotor paradigm in which the spatial location of the somatosensory input, received after a motor command, did not correspond to the expectation generated by the movement effector. Participants performed a visuomotor task in which they were required to move a virtual cube in space using a stick controlled by the right hand. Experimental manipulation concerned the location of somatosensory feedback (vibration buzz through vibrotactile actuator) received during the interaction between right-hand movement and the virtual object (time-locked with cube collision). The feedback was provided to the right hand (congruent condition) or the left ankle (incongruent condition). Changes in TMS-MEP were used as an index of modifications in the sensorimotor system (della Gatta et al., 2016; Kilteni et al., 2016). In line with somatosensory deprivation studies (Avanzino et al., 2011; Murphy et al., 2003; Rossini et al., 1996), we hypothesize a decrease in motor cortical excitability after exposure to a prolonged mismatch between motor and somatosensory signals as an after-effect of sensorimotor conflict. Continuously providing somatosensory input to a body part contralateral to movement's effector might potentially reduce the excitability of the motor cortex associated with that body part. Such a result would be suggestive of direct modulation of motor cortex activity, not only by suppression of input (such as in anesthetization) but also by rewiring of sensory-motor interactions and/or the update of feed-forward prediction models. This exploration could shed light on the significance of the spatial dynamics between the motor and somatosensory systems in establishing and sustaining a stable sensorimotor representation of the body and how this might be altered by novel sensory-motor stimulation patterns.

2 | METHODS

2.1 | Participants

The sample size for this study was calculated using G*Power 3.1 (Faul et al., 2007) and based on repeated measurement ANOVA as statistical test (four measurements and two within factors). G*Power indicated that, with $\alpha = 0.05$ power $(1-\beta) = 0.80$, and a small effect size (0.3), the estimated sample size for this study was at least 17 participants. Twenty-one participants were enrolled in the experiment. Two participants were excluded before starting the experiment (one was left-handed, and another one was due to past traumatic brain injury). Two participants were excluded because of technical problems during data collection. A final sample of 17 participants (female = 13; mean age = 23.7 years; SD = 2.7) was used for the study. All participants were right-handed and performed the two sessions of TMS with at least 3 days between the first and the second ones (order of presentation counterbalanced across participants). Before the first TMS session, each participant completed a questionnaire to evaluate compatibility with TMS. None of the volunteers reported neurological problems and had familiarity with seizures, nor was taking any medication that could interfere with neuronal excitability. Written informed consent was obtained from all participants before the experiment. The local ethical committee (University of Milano-Bicocca) approved the protocol (number of protocol RM-691). Participants' treatment was conducted in accordance with the Declaration of Helsinki.

2.2 | Experimental design

The experimental design involved participants performing two different VR visual-motor-haptic tasks (congruent vs. incongruent) on different days. During each session, the motor cortical excitability was measured before and after the VR task, by TMS-induced MEPs on the right first dorsal interosseous (FDI). The FDI muscle was chosen as the most proximal muscle used for grasping the VR controller. The VR task had the same length and characteristics for both sessions, except for the spatial location of haptic feedback received during the task. Participants

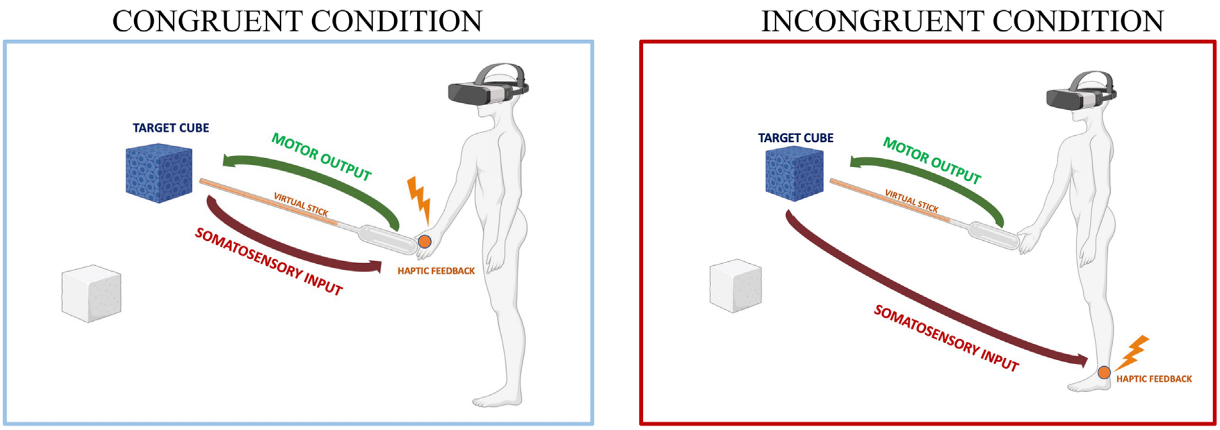

FIGURE 1 Experimental paradigm for congruent versus incongruent condition.

had to move a virtual cube toward a destination point using a virtual stick controlled by the right hand. Whenever the virtual stick touched the cube, haptic feedback was provided in two possible body parts (congruent vs. incongruent with the effector). In the case of the congruent condition, haptic feedback was provided to the right hand (which controlled the virtual stick, Figure 1, left panel). In the incongruent condition, the collision between the cube and the virtual stick caused an haptic feedback in the participant's contralateral (left) ankle, generating a sensorimotor conflict (Figure 1, right panel).

2.3 | Hardware and software

The VR equipment used for the experiment included a Meta Quest 2 head mounted display (HMD), with a resolution of 1920 × 1832 pixel per eye. The HMD was connected via Oculus Link to an Asus ROG Strix notebook, featuring an AMD Ryzen 95900HX CPU, 32 GB of RAM, a GeForce RTX 3080 GPU and a 17.3″ screen with a resolution of 1920 × 1080 pixel. The VR environment was developed with the Unity graphical Engine. In the case of right-hand haptic feedback, the controller vibration system was used and synchronized with the virtual environment. In the case of left ankle haptic feedback, a coin-shaped vibrotactile actuator (3v) was used to provide the vibration and tapped into the body part. The vibrotactile actuator was powered using an Arduino Uno board connected to the VR notebook and synchronized with the virtual environment using the Uduino library.

2.4 | VR environment and task

The paradigm was a customized version of a VR-sensorimotor task already used in other studies (Girondini et al., 2024a; Girondini et al., 2024b). An empty room was used as the virtual space. When the participant wore the HMD and took the right controller, a virtual stick appeared as the tool to interact with the virtual environment, controlled by his/her right hand. Once the participant was familiarized with the virtual environment and the virtual stick, the experiment began with the first trial after pressing the controller button. At the beginning of each trial, a blue virtual cube (the target cube) appeared in the center of the virtual environment, while a semi-transparent cube appeared randomly in one of four locations in the virtual room (bottom-left, bottom-right, upper-left, upper-right). In both sessions, each participant received the same instruction: touch-and-move the target cube using the virtual stick to match its position with that of the semi-transparent cube. Every time the virtual stick collided with the target cube, the participant received haptic feedback (to the right hand or the left ankle, according to the experimental condition). Once the target cube reached the semi-transparent cube, the trial ended, and a new target cube appeared in the center of the virtual room. The task had a fixed duration of 10 min, and the experimental manipulation (i.e., the body part that the haptic feedback will stimulate) was masked until the beginning of the task.

2.5 | TMS and electromyography

TMS pulses were delivered by using a figure-of-eight coil (70 mm) connected to a Magstim Super Rapid2 stimulator (Magstim, Whitland, UK). Single TMS pulses were applied at an intensity of 120% of the resting motor threshold (rMT) over the FDI muscle to assess motor cortical excitability. The right-hand FDI muscle's motor hotspot was first determined by calculating 5 cm lateral and 1 cm frontal from Cz. To find the best hotspot, we moved the coil in 0.5 cm steps around the presumed motor hand area using a slightly supra-threshold stimulus. TMS was applied with the handle pointing 45° postero-laterally away from the midline. The stable TMS coil placement and position during the whole experimental sessions were constantly monitored with a neuronavigation system (SofTaxic 2.0, E.M.S., Bologna, Italy, www.softaxic.com). The rMT was determined using the software-based 'adaptive method' developed by Awiszus (2003) (Motor Threshold Assessment Tool, version 2.0: https://www.clinicalresearcher.org). A MEP ≥ 50 μV peak-to-peak amplitude was fed back to the software as a valid response. MEPs were recorded by using 10-mm Ag/AgCl surface cup electrodes. The active electrode was placed over the FDI muscle of the right hand and the reference electrode over the metacarpophalangeal joint of the index finger. The electromyographic (EMG) signal was sampled and amplified by using a Digitimer D360 amplifier (Digitimer Ltd, Welwyn Garden City, UK) through filters set at 20 Hz and 2 kHz with a sampling rate of 5 kHz, digitized by an analog-digital converter (Power 1401, Cambridge Electronic Design Cambridge, UK) and then stored using the Signal software (Cambridge Electronic Design, Cambridge, UK).

2.6 | Procedure

Participants arrived at the laboratory and signed the informed consent form. Before starting the experiment, each participant was informed about how TMS works and its use in the study. After this preliminary information, the participant filled out a questionnaire to evaluate compatibility with TMS procedures (Rossi et al., 2021) and the handedness questionnaire (Oldfield, 1971). In case of no adverse condition, the experiment procedure began. This experiment consisted of a within-measurement design. The following experimental procedure was carried out similarly for both sessions that were performed on different days. The baseline measurement for motor cortical excitability was recorded after the TMS-MEP setup preparation (see above). During this phase, the participant was seated in a comfortable chair, with the right hand resting on the desk. When the participant was ready, 30 MEPs to the right FDI, induced by TMS output at 120% of each subject rMT intensity on left M1, were recorded. The experimenter checked the absence of voluntary contractions of the muscle using a 2D monitor. When the baseline measurement was concluded, the participant wore the HMD and the right controller. The vibrotactile actuator was placed in one of the two target positions (right hand or left ankle). The VR task started for a total duration of 10 min (software time-controlled). Meanwhile, the experimenter was in the same room to check the correct functioning of the VR setup and the vibrotactile actuator. When the task ended, the participant wore off the HMD and the post-task TMS-MEP recording began. In this phase, the previous hotspot for left M1 was found through a neuronavigation system to evoke MEP in the same cortical area of the baseline measurement. Thus, 30 MEPs to the right FDI, with the same intensity of the baseline measurement, were recorded (Figure 2). After the post-task MEP recording, the EMG electrodes were detached, and the experiment was concluded. After the second session, a debrief regarding the meaning of the study was provided to each participant.

2.7 | Statistical analysis

Preprocessing data and statistical analysis were performed using Signal, R software, and Jamovi. The analysis focused on MEPs (amplitude) and performance during the VR task (number of trials completed in 10 min). MEP amplitude of the right FDI muscle was measured as the peak-to-peak distance (in mV), and MEPs of amplitude lower than 50 μV were discarded from the analysis. After this filtering, the MEP amplitude was averaged for each time point (*pre* vs. *post*) in both conditions (*congruent* vs. *incongruent*) for each subject. Raw data (MEP amplitude) violated the normality assumption, as indicated by a Shapiro *t*-test with a *p*-value <0.05. To address this point, we employed a log transformation to bring the data compliant with the normal distribution assumption (Kilteni et al., 2016; Spaccasassi et al., 2022). A two-way repeated measure ANOVA was performed with the dependent variable as the log-transformed MEP amplitude and two within factors as time (pre vs. post) and condition (congruent vs. incongruent). Bonferroni correction for multiple comparisons was used for post-hoc analysis. We additionally investigated changes in motor cortical excitability by employing the delta difference as an index to assess changes in cortical excitability (based on raw values). This procedure involved utilizing baseline-corrected values extracted for each participant and calculated as a percentage using the formula ((MEPpost − MEPpre) / MEPpre * 100). The delta difference quantifies, in numerical terms, the extent of MEP changes relative to the baseline. Delta values violated the assumption of normal distribution, and the analysis was performed using the paired-sample Wilcoxon signed-rank test. Nevertheless, we opted against the log transformation of these values to maintain a quantitative measurement of MEP amplitude changes following both congruent and incongruent. A similar approach (one-

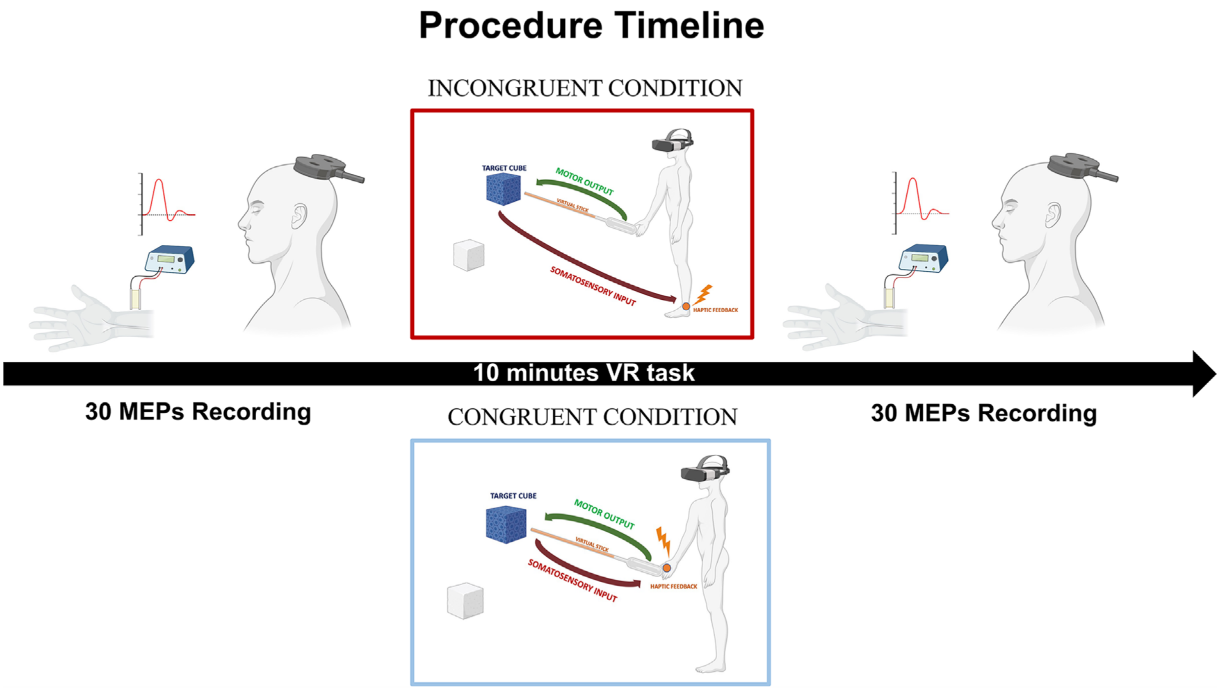

FIGURE 2 Procedure timeline. Note that the two sessions were performed on different days. MEPs, motor-evoked potentials; VR, virtual reality.

sample Wilcoxon signed-rank test against zero) was used to assess whether the delta difference between the congruent and incongruent conditions differed significantly from zero. Task performance was quantified by the number of trials completed within a 10-min duration for each condition, representing the cubes successfully reaching the target position. Analysis was conducted using a two-tail paired-sample *t*-test.

3 | RESULTS

3.1 | VR task

A paired-sample *t*-test showed no significant difference in the number of trials completed between the congruent and the incongruent condition during the VR task ($t = -0.442$, df $= 16$, $p = 0.665$). Participants completed, on average, 213 trials (SD $= 48.4$) in the incongruent condition and 218 trials (SD $= 41.4$) in the congruent condition, suggesting similar performance across both conditions.

3.2 | MEPs

Averaged MEPs are represented in Figure 3, and descriptive values are reported in Table 1. A two-way repeated measurement ANOVA revealed a significant main effect of time ($F_{(1,\ 16)} = 09.23$, $p = 0.008$, $\eta_p{}^2 = 0.366$), and significant interaction time * condition ($F_{(1,\ 16)} = 6.16$, $p = 0.024$, $\eta_p{}^2 = 0.278$). No significant effect of condition ($F_{(1,\ 18)} = 0.02$, $p = 0.610$, $\eta_p{}^2 = 0.017$) was found. Post-hoc analysis (Bonferroni correction for multiple comparisons) showed a significant decrease in motor cortical excitability only when comparing pre- and post-recording of MEP amplitude in the incongruent condition ($p = 0.010$). No significant change was observed comparing pre versus post in the congruent condition ($p = 0.565$). None of the other comparisons resulted significant (all $p > 0.05$, reported in Table 2).

3.3 | Decrease of motor cortical excitability

We computed the percentage of delta values in the two experimental conditions to determine the magnitude of reduced motor cortical excitability. Wilcoxon signed-rank test on the percentage confirmed a difference in the delta percentage between congruent and incongruent. The main effect of condition was significant (W $= 123$, df $= 16$, $p = 0.028$, *Rank biserial correlation* $= 0.608$, mean difference $= 12.0$, SE difference $= 8.94$). On average, the decrease in MEP amplitude was approximately -28.06% (SE $= 08.24$) in

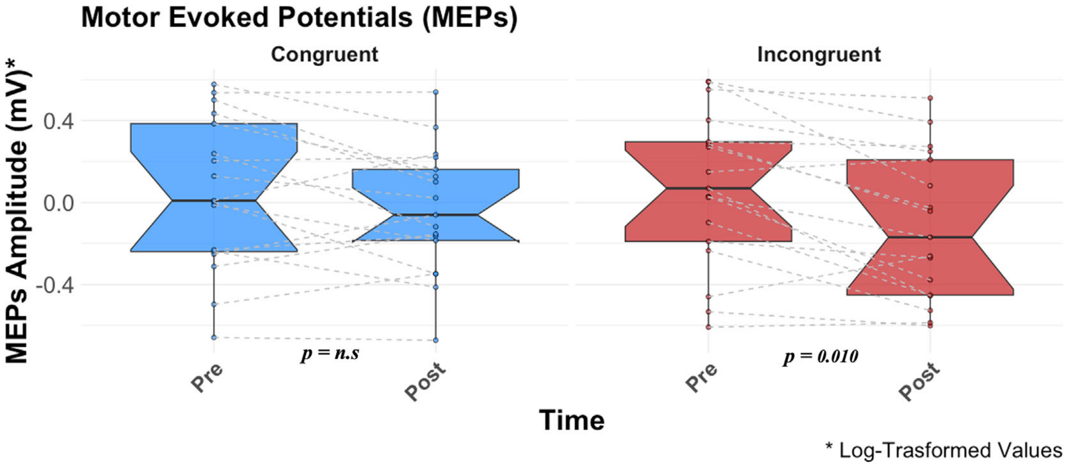

FIGURE 3 Boxplot of log-transformed values of motor-evoked potential (MEP) amplitude before and after the virtual reality (VR) task, for congruent versus incongruent condition (dots represent individual data).

TABLE 1 Descriptive values of raw motor-evoked potential (MEP) amplitude.

Descriptives (mV)	Incongruent_Pre	Incongruent_Post	Congruent_Pre	Congruent_Post
Mean	1.6	1.04	1.53	1.14
Std. error mean	0.297	0.212	0.281	0.199
Median	1.17	0.677	1.02	0.87
Standard deviation	1.23	0.874	1.16	0.821
Minimum	0.247	0.25	0.22	0.213
Maximum	3.89	3.23	3.78	3.46

TABLE 2 Post-hoc table of two-way ANOVA time * condition.

Post-hoc comparisons—time * condition								
Time	**Condition**	**Time**	**Condition**	**Mean difference**	**SE**	**df**	***t***	***p* Bonferroni**
Pre	Incongruent	Pre	Congruent	0.019	0.066	16	0.29	1
Pre	Incongruent	Post	Incongruent	0.1874	0.0494	16	3.79	0.01
Pre	Incongruent	Post	Congruent	0.1075	0.0594	16	1.81	0.536
Pre	Congruent	Post	Incongruent	0.1685	0.0865	16	1.95	0.414
Pre	Congruent	Post	Congruent	0.0885	0.0497	16	1.78	0.565
Post	Incongruent	Post	Congruent	−0.08	0.0576	16	−1.4	1

the incongruent condition and −09.56% (SD = 10.18) in the congruent condition (Figure 4). Finally, a one-sample *t*-test was used to investigate whether the MEP delta significantly differed from zero in the two conditions. The analysis revealed a non-significant effect for the congruent condition (W = 59.0, df = 16, $p = 0.431$, *Rank biserial correlation* = −0.229) Conversely, the one-sample *t*-test against zero yielded a significant result for the incongruent condition (W = 21, df = 16, $p = 0.007$, *Rank biserial correlation* = −0.725).

4 | DISCUSSION

The present study investigated the effect of a prolonged (10 min) condition of spatial sensorimotor incongruency between a motor command and the consequent somatosensory feedback on motor cortical excitability of the movement effector. This condition was compared, within the same participants, to a control condition in which the somatosensory feedback was spatially congruent with the body part that performed the movement. By combining VR and classic neuroscientific methods (TMS-MEPs),

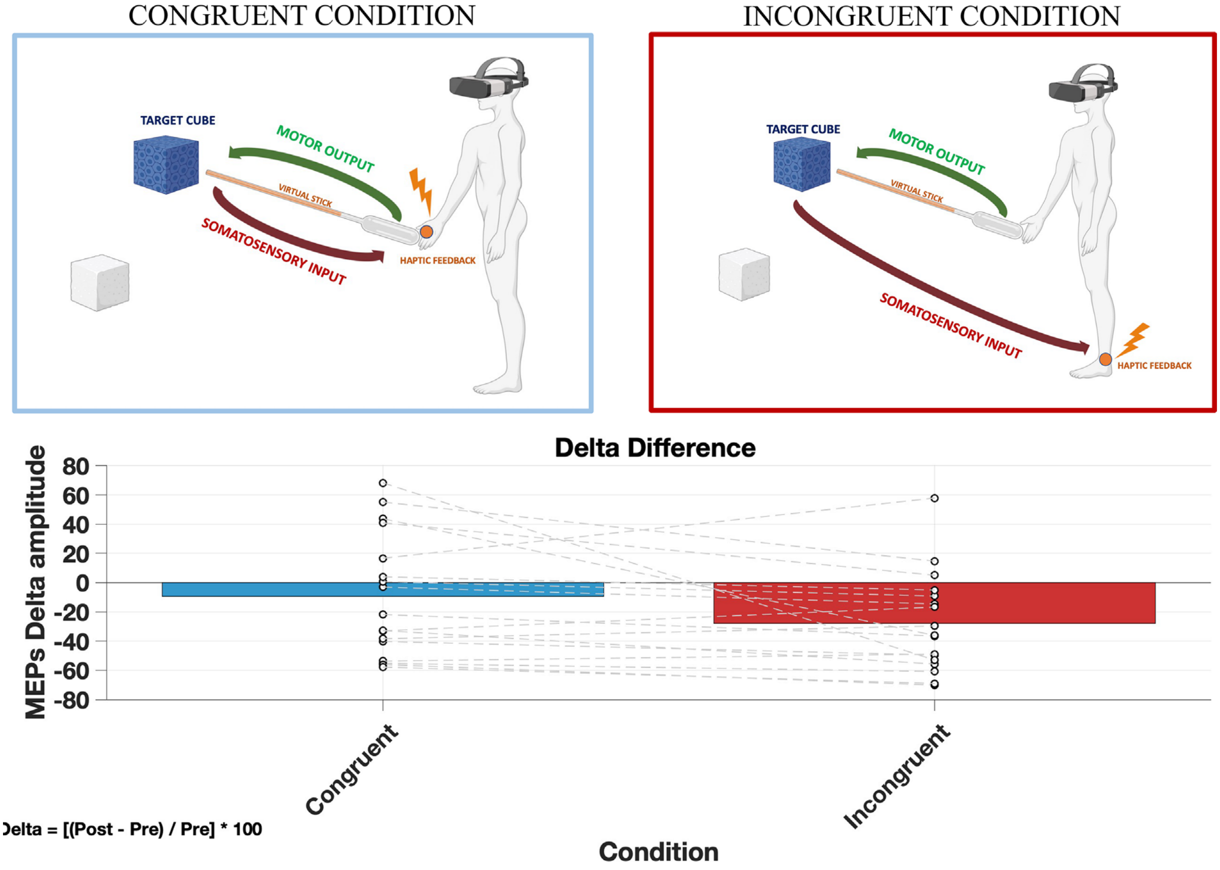

FIGURE 4 Delta difference in percentage of motor cortical excitability for congruent versus incongruent condition (dots represent individual data). MEPs, motor-evoked potential.

it was possible to induce a sensorimotor conflict between the somatosensory and motor system, observing its neural consequences. The prolonged discrepancy between the visually induced expectation of somatosensory feedback (driven by the motor command performed by the right hand) and the received somatosensory feedback (provided on the left ankle) caused a decrease in the motor cortical excitability of the body part that performed the movement. This effect was not found in the congruent condition, where the movement-related expectations and their somatosensory consequences matched (further confirmed by analyzing the delta difference against zero). The task duration and number of completed trials were comparable between conditions, thereby eliminating potential confounding effects attributed to these factors. To the best of our knowledge, no studies have investigated how the motor system reacts to spatial somatosensory conflict during active interactions, and the result of our study can be considered a first step toward addressing this critical question.

The observed reduction in cortical excitability in our results could be attributed to the new spatial configuration between motor commands (output) and somatosensory afferents (received as feedback input) presented for a relatively prolonged period (10 min) during the incongruent condition (right hand-left ankle). A substantial piece of literature has already documented the relationship between motor and somatosensory systems utilizing MEPs to measure functional cortical plasticity in the motor cortex. Specifically, previous studies demonstrated that the presence (vibration) or absence (deafferentation) of somatosensory input in a specific body part can either heighten or diminish the excitability of the motor cortex. Short-term somatosensory deafferentation induced by ischemic nerve block leads to a reduction in MEP amplitude in the contralateral motor cortex, but it also increases excitability in the ipsilateral hemisphere due to an imbalance between the afferent and deafferented body sides (Murphy et al., 2003; Rossini et al., 1996; Ziemann et al., 1998). Similar findings were observed following short-term arm immobilization (Avanzino et al., 2011). Conversely, low-intensity vibration also modulates the motor cortex response, enhancing MEP amplitude for the stimulated body part while exerting an inhibitory effect in the ipsilateral motor area of the stimulated side (Rosenkranz & Rothwell, 2006;

Swayne et al., 2006). In our incongruent sensorimotor condition, the left motor cortex, responsible for task-related movement, and the right somatosensory cortex, continuously receiving afferent feedback from right-hand movement, were concurrently activated. Considering that (*a*) the lack of afferent information decreased excitability in the contralateral cortex (Brasil-Neto et al., 1992; Facchini et al., 2002; Murphy et al., 2003) and (*b*) somatosensory stimulation decreased excitability in the ipsilateral hemisphere (Swayne et al., 2006), the reduced excitability after incongruent condition can be attributed to the functioning of both mechanisms presented at the same time. Indeed, the right hand not only did not receive somatosensory information for the interaction (lack of afferent information), but instead, somatosensory inputs reached the opposite hemisphere (afferent information on the opposite hemisphere). It is thus possible that the prolonged simultaneous activation of the ipsilateral somatosensory area during the motor task, temporally bound with the movement due to the virtual interaction, might have led to functional (plasticity) changes between the somatosensory and the motor area of the two hemispheres via the subcortical connections (Takeuchi et al., 2012). Indeed, a repeated sensorimotor binding between efference and afferent information of two non-related body districts should reinforce masked neural pathways within the sensorimotor cortexes. This, in turn, might have caused a decrease in the efficiency of the intra-hemispheric crosstalk between motor and somatosensory cortices while reinforcing latent inter-hemispheric connections as a form of experience-driven brain functional plasticity. Another conceivable explanation for the observed decrease in motor cortical excitability in this study could be associated with a ‘blurred’ representation of the motor hand (e.g., reduced strength of cortical connections representing such body part or increased weight of competing connections) driven by prolonged exposure to a sensorimotor spatial incongruency (Dempsey-Jones et al., 2019; Wesselink et al., 2022). In this regard, the discrepancy between motor output and somatosensory input may have diminished the strength of cortical motor representation of the right hand in M1. This might explain why the TMS pulse induced a lower MEP at the same intensity and in the same cortical hotspot (e.g., FDI).

Although the current design makes it difficult to distinguish the exact contribution of the absence of versus novel anticipated feedback from the stimulation of an incongruent body part, it is noteworthy that cutaneous afferent information from the right hand remained intact during the task, especially proprioceptive signals driven by effector movement. Thus, it is more plausible that the effect observed here is primarily driven by spatial mismatch rather than by the absence of anticipated feedback, exacerbated by the double mismatch between the body part (hand vs. ankle) and the body side (contralateral vs. ipsilateral). Future studies are certainly relevant for elucidating the neurophysiological mechanisms underlying the observed effect, ranging from the absence of feedback to varying degrees of spatial mismatch between the involved body parts. These levels of mismatch might include differences between ipsilateral and contralateral body sides, homologous body segments (e.g., hand-hand) versus different body segments (e.g., hand-ankle) and disparities between body parts closely represented in S1 compared to those represented further apart. Furthermore, it is relevant to note that, even though we cannot entirely rule out the hypothesis that our observed effect may be influenced by attentional capture toward another body part, it seems implausible that the decrease in motor cortical excitability is solely attributable to an attentional orientation toward a non-moving, invisible body part (conveying only tactile signals) compared to a visible, moving body part that also involves synchronous visual and proprioceptive signals. Instead, the somatosensory feedback provided to the participant (in the two different spatial locations, e.g., left ankle or right hand) was time-locked every time the virtual tool touched the virtual cube, reinforcing the sensorimotor binding between the motor command and somatosensory feedback (it is worth considering that multisensory integration needs a temporal window in order to process different sensory modalities into a unitary perception) (Chen & Spence, 2017; Holmes & Spence, 2005; Spence & Squire, 2003). Lastly, the equal duration of both sessions and the similar number of trials performed under congruent and incongruent conditions unequivocally rule out the possibility that any observed effects result from disparities in task exposure. Likewise, the same association pattern (right hand-left ankle) repeated for 10 min should prevent the interpretation of results coming from a ‘surprise effect’.

Finally, we pose the question of whether the change in motor excitability that we observed following sensory-motor incongruence might represent the first neural step toward the adaptation of the sensory-motor systems to a new association between input and output signals, likely driven by multisensory temporal congruency. In fact, during the incongruent condition, the somatosensory input received as feedback from motor command contrasted the ‘prior’ prediction provided by the efference copy. However, it is plausible to suppose that, after the first trials, participants begin to anticipate and expect somatosensory feedback on the left ankle as a result of learning the new statistical regularities in sensorimotor interaction. One might then question how these changes affect the prior model in our sensorimotor system, how long this process takes (and lasts for), and whether or not it is possible to develop entirely new predictions about the sensory consequences of our actions (or if some constraints limit our adaptation to bind input and output signals) (Steptoe et al., 2013). How are these changes reflected in the morphological and functional readaptation of the brain? In the context of somatosensory attenuation, brief temporal perturbation between motor command and somatosensory feedback induced increased responses in the somatosensory areas (S1 and S2) and the cerebellum compared to non-delayed trials. Moreover, connectivity studies showed that temporal delay decreased connectivity between the cerebellum and the somatosensory cortex, while increased connectivity appeared between the cerebellum and contralateral supplementary motor cortex (SMA) of the moved hand (Kilteni et al., 2023). These results suggest that, under temporal output–input mismatch, increased communication between SMA (deputed to motor preparation) and cerebellum (which received the efference copy to monitoring the expected feedback) might reflect computation processing related to establishing prediction errors. Remarkably, prolonged exposure with new temporal regularities between motor command and somatosensory consequences (constantly introduced with a delay) was able to produce attenuation for delayed trials in the following phase, meaning a learning effect for predicting feedback presented with temporal delay (Kilteni et al., 2019). This result has been interpreted as a prediction-error learning process, for which the brain can readapt the temporal boundaries of self-generated sensory consequences. Such recalibration involves functional modifications occurring at both sensorimotor and cognitive brain regions (Kilteni & Ehrsson, 2024). However, up to date, neurophysiological correlates of sensorimotor learning through statistical regularities in efference-afferent dynamics during environmental interaction are far from being completely understood, for instance, by investigating the possibility of predicting sensory consequences after dedicated training on a different body part of the one performing a movement. We are confident that new paradigms involving virtual simulation and haptic technologies will offer insights to address these questions in the near future.

5 | LIMITS OF THE STUDY AND FUTURE DIRECTION

It is important to consider some limitations present in this study. First, our incongruent condition involved only one body part, and further investigation is required to disentangle the relationship between the body effector (hand vs. ankle) and body side (ipsilateral vs. contralateral) inducing changes in motor cortical excitability. Further experiments are currently planned to better characterize the neurophysiological readaptation of the sensorimotor system to spatial sensorimotor mismatch. Regarding the VR task used here, one limit concerned the motor interaction that did not directly involve the participant's hand but a virtual tool (held by the participant). Despite the amount of evidence that reports the integration of tool use within the body schema after prolonged interaction (Cardinali et al., 2009; Maravita & Iriki, 2004), as well the similarity in somatosensory information processing localized on the hand and the tool (Miller et al., 2019) and the presence of somatosensory attenuation using a tool (Kilteni & Ehrsson, 2017b), future studies will need to test the same sensorimotor conflict during direct hand interaction (e.g., by using virtual gloves that reproduce and track the entire hand). Another limitation is related to the somatosensory feedback provided during the interaction (a buzz) that does not correctly mimic ecological somatosensory feedback, given that in real scenarios, both tactile and proprioceptive (force feedback) information are typically present. By employing our paradigm, it would be intriguing to explore alternative somatosensory cues, such as force-feedback devices capable of inducing different levels of pressure on the skin.

6 | CONCLUSION

The current study revealed that prolonged exposure to spatial mismatch between motor output and somatosensory input resulted in decreased motor cortical excitability. Specifically, associating right-hand motor commands with left ankle somatosensory feedback led to a decrease of MEP amplitude recorded on the right hand. Conversely, no significant difference was observed in the congruent condition, where motor output and somatosensory input aligned within the same body part. Results demonstrated the presence of functional plasticity at the level of the motor cortex due to spatial mismatch in the action-feedback motor-somatosensory loop. Future research employing this paradigm is essential to delve into the neurophysiological mechanisms responsible for the motor cortex reorganization induced by spatial sensorimotor mismatch.

AUTHOR CONTRIBUTIONS

Matteo Girondini: Conceptualization; investigation; data curation; formal analysis; methodology; writing — original draft; writing — review and editing. **Massimo**

Montanaro: Software. **Carlotta Lega**: Methodology; writing — review and editing. **Alberto Gallace**: Conceptualization; methodology; writing — original draft; project administration; writing — review and editing.

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CONFLICT OF INTEREST STATEMENT

The author(s) declare no conflict of interest.

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DATA AVAILABILITY STATEMENT

Experimental data and analysis performed are available for open access: https://osf.io/87435/.

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