

Observation of implied motion in a work of art modulates cortical connectivity and plasticity

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Following the discovery of mirror neurons, much attention has been devoted to understanding the neural responses evoked by observation of implied motion in works of art. Neuroimaging studies have demonstrated that dorsal premotor cortex (PMd) is commonly involved during observation of movements but the role of the inhibitory and excitatory connections between PMd and primary motor cortex (M1) during observation of implied motion remains uncertain. In this study, using high and low frequency repetitive transcranial magnetic stimulation (rTMS), we examined PMd–M1 connectivity and plasticity during observation of Michelangelo's frescos with and without implied motion (Sistine Chapel, 1508–1512). We found that observation of implied motion in a


painting specifically reduces the activity of inhibitory PMd–M1 connections. On the contrary PMd–M1 facilitatory connections, as examined by means of 5-Hz rTMS, were not modulated during observation of the painting. Our data suggest that observation of implied motion in a painting modulates PMd–M1 connectivity and plasticity. These results are consistent with the hypothesis that art with implied motion might be used as a plasticity-based intervention in rehabilitation.

Keywords: Implied movement, Transcranial magnetic stimulation, Art, Rehabilitation

INTRODUCTION

Several neuroimaging studies have investigated neural responses to art, aesthetic judgment and beauty (Cela-Conde et al., 2004; Kawabata and Zeki, 2004; Vartanian and Goel, 2004). On the contrary, little is known about neuronal circuits engaged during observation of implied motion (IM) in a work of art. Recent studies using transcranial magnetic stimulation (TMS) demonstrated that observation of IM in visual images and works of art, alongside with the activation of movement processing MT/V5 areas (David and Senior, 2000; Kourtzi and Kanwisher, 2000), modulates primary motor cortex (M1) excitability as well as related intracortical inhibitory and excitatory circuits (Battaglia et al., 2011). It has been proposed that similar circuits encode implied and real motion processing in the onlooker. Consequently, the activation of the

mirror neuron system has been indicated as a mechanism allowing an individual to extract dynamic information from a still image with IM (Battaglia et al., 2011; Sbriscia-Fioretti et al., 2013; Umiltà et al., 2012; Urgesi et al., 2006). Mirror neurons, first discovered in macaque monkey premotor and parietal cortices (Gallese et al., 1996), fire during both action observation and execution. Subsequently, brain stimulation and neuroimaging studies demonstrated a similar pattern of activation (mirror neuron-like activity) in the human brain (Buccino et al., 2001; Iacoboni et al., 2001). Recently, evidence has been presented supporting the facilitatory effects of action observation on congruent motor execution, motor learning (Brass et al., 2000) and cortical long-term potentiation (LTP)-like plasticity (Lepage et al., 2012; Sale and Mattingley, 2013). On the whole, these data support the hypothesis that action observation training might be used to augment traditional

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rehabilitation paradigms and speed the recovery of motor functioning (Mulder, 2007).

A recent meta-analysis suggests that the dorsal part of the premotor cortex, rather than the posterior inferior frontal gyrus and adjacent ventral premotor cortex, is consistently activated in functional magnetic resonance imaging studies of imitation (Molenberghs et al., 2009). Thus, it is conceivable that frontal regions which extend beyond the classical mirror neuron network are crucial for imitation. In healthy subjects, repetitive TMS (rTMS) studies have been used to investigate functional connectivity and plasticity between PMd and primary motor cortex (M1) (Bäumer et al., 2003; Münchau et al., 2002). To date, no studies have explored the effects of observation of IM in artistic images on the strength of PMd–M1 connections.

Since its first description in 1945 (Adrian, 1945) art therapy has been shown to improve physical, mental health and social functioning in a variety of medical conditions (Miller and Hou, 2004; Secker et al., 2007). Therefore, the effects of art as a valuable adjunct to conventional rehabilitation should be evaluated with rigorous experiments. Given that current rehabilitation treatments are capable of changing brain connectivity and inducing functional reorganization (Dimyan and Cohen, 2011), the present study aims to provide evidence that observation of IM in a works of art can modulate neuroplasticity in fundamental motor circuits. This will further our understanding of the foundation underlying the use of art in rehabilitation.

MATERIALS AND METHODS

Subjects

We studied 12 healthy volunteers (mean age \pm standard deviation, 32 ± 8 years; 5 females). All participants were right-handed according to the Edinburgh inventory 25–50 (Oldfield, 1971) and gave written informed consent to participate in the experiment according to the declaration of Helsinki. The study was approved by the local ethics committees (New York College of Podiatric Medicine).

Experimental procedure

During the experiment subjects were seated comfortably in an armchair with both arms relaxed and were instructed to keep their eyes open in front of a computer monitor. The electrophysiological experiments were performed either during the observation of a painting with IM or during observation of a “static” (without IM, no-IM) painting. Stimuli were presented on a computer monitor

using the Presentation software (Neurobehavioral Systems Inc., Berkeley, CA, USA). First the participants were instructed to focus their attention on the computer monitor (appearance of a plus sign in the center of the monitor). The videos of the paintings started after 5 sec and the images were presented continuously throughout the TMS paradigms. For the IM condition we selected Michelangelo's *Expulsion from Paradise* (Sistine Chapel, 1508–1512), with its depiction of the gesture which Adam makes with his extended right hand to keep the sword-bearing angel at bay. For the no-IM condition we selected Michelangelo's *Creation of Adam* in which Adam leans on his right forearm in a clearly static posture (Sistine Chapel, 1508–1512) (Fig. 1). The experiments were block randomized and there was an interval of 5 days between the blocks.

Electromyography and TMS

Surface electromyography (EMG) was recorded from the right extensor carpi radialis (ECR) muscle with disposable adhesive disk electrodes placed in a tendon-belly arrangement on the skin overlying the ECR muscle. The signal was amplified, filtered (band-pass 2 Hz to 5 kHz), digitized (Micro 1401, Cambridge Electronics Design, Cambridge, UK) and stored in a laboratory computer for off-line analysis. TMS was performed with a standard figure-of-eight coil and Magstim 200 stimulators (Magstim Co., Whitland, UK). The coil was placed at the optimal position for eliciting MEPs from the right ECR muscle (“hot spot”). The coil was held tangentially to the skull with the handle pointing backwards and laterally at an angle of 45° to the sagittal plane. Thus, the electrical current induced in the brain was approximately perpendicular to the central sulcus. This orientation of the induced electrical field is thought to produce a predominantly transsynaptic activation of the cortico-spinal neurons (Rothwell et al., 1999). During the experiments EMG activity was continuously monitored by visual (oscilloscope) and auditory (speakers) feedback to ensure complete relaxation. Resting motor threshold (RMT) was determined as the minimum stimulator intensity (to the nearest 1%) to produce an MEP of 50 μ V in five of 10 trials. Mean peak-to-peak MEP amplitudes were determined with 20 monophasic magnetic stimuli delivered to the motor hot spot of the ECR muscle at rate of 0.1 Hz at a stimulation intensity of 120% RMT. TMS parameters were tested according to published guidelines for the use of TMS in clinical neurophysiology (Rothwell et al., 1999). Ipsilateral PMd–M1 connectivity and plasticity were tested by means of PMd conditioning with rTMS. High and low frequency PMd were performed according to a previous described methodology (Rizzo et al., 2004). In brief, rTMS was delivered

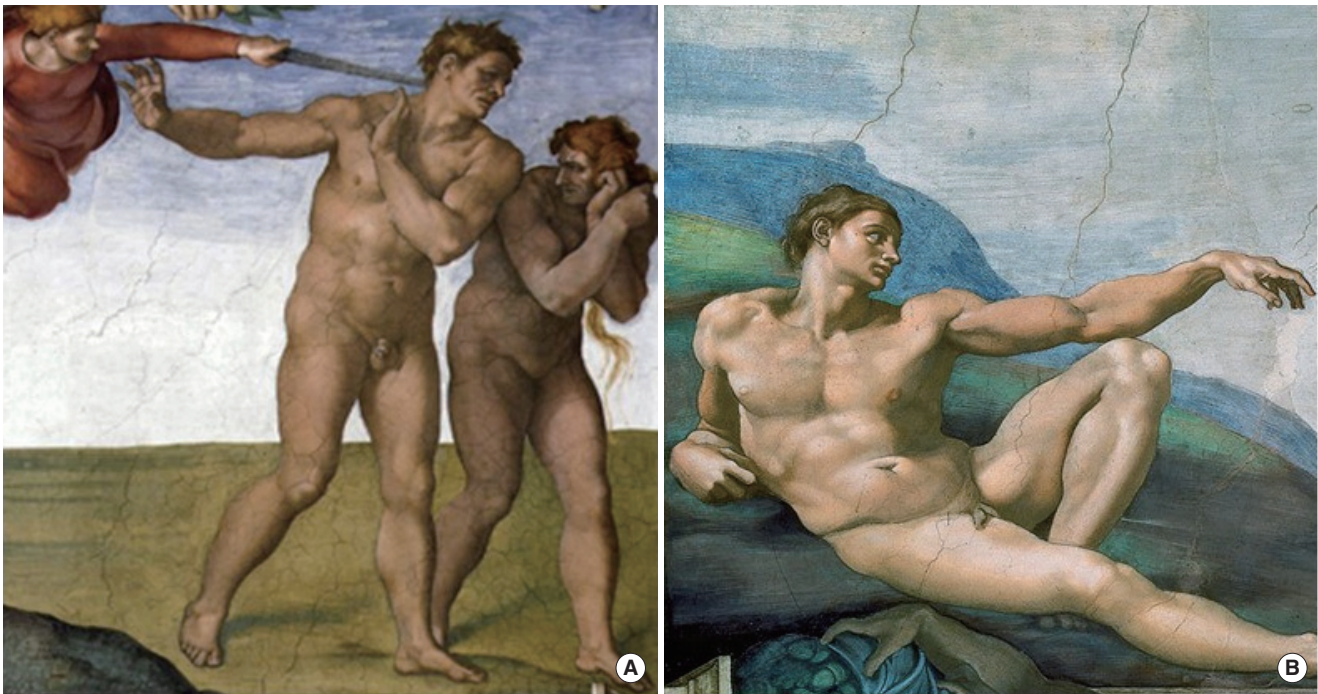


Fig. 1. Experimental paradigm used to assess cortical excitability and dorsal Premotor-Primary motor cortex connectivity and plasticity during observation of a painting with and without implied motion. Two digitized video sequences were presented. In one sequence (implied motion, IM) subjects were instructed to observe Adam's gesture in Michelangelo's *Expulsion from Paradise*. In a second video (no-IM) subjects were instructed to observe Michelangelo's *Creation of Adam*. Before each video the participants were instructed to focus their attention on the computer monitor (appearance of a plus sign in the center of the monitor). The videos started after 5 sec and the images were presented continuously throughout the transcranial magnetic stimulation paradigms. The experiments were block randomized.

using a standard figure-of-eight coil connected to a Magstim Rapid stimulator (Magstim Co.). The coil was held tangentially to the skull with the handle pointing 45° posterolaterally. First, we searched for the optimum site for stimulating the ECR motor hot spot and determined individual active motor threshold (AMT). AMT was defined as the minimum stimulus intensity that produced a liminal motor evoked response (about $100 \mu\text{V}$ in 50% of 10 trials). For PMd stimulation we placed the coil 2.5 cm anterior to M1 ECR hot spot. The 5-Hz rTMS session consisted of five trains of 300 stimuli separated by an intertrain interval of 1 min (10 min in total). The 1-Hz rTMS session consisted of five trains over the left PMd, 300 stimuli each, with a pause of 1 min between train. The intensity of premotor rTMS was set at 90% of AMT because this is the optimum intensity to modulate cortical excitability in ipsilateral M1 (Gerschlagler et al., 2001). rTMS conditioning was performed during observation of the two paintings. The stimulation intensity was matched during the two experimental conditions in order to obtain an MEP of 0.4–0.5 mV. We recorded ten MEPs at baseline, 15, and 30 min after conditioning (T15 and T30).

In an additional experiment subjects were required to observe the movement for 20 min; we then tested the effect of 5-Hz PMd conditioning protocol on MEP amplitude. In this way, the participants had a longer exposure to the paintings. The stimulation protocols were in accordance with published safety guidelines for rTMS (Wassermann, 1998).

Statistical analysis

RMT, AMT, and MEP amplitude recorded during observation of IM and no-IM were analyzed with analysis of variance (ANOVA) (main effects "Condition"). The effects of 5- and 1-Hz rTMS conditioning on PMd–M1 connectivity and plasticity were assessed using a mixed model repeated-measure design with main effect "time" as within subject (three levels T0, T15, T30); main effect "stimulation" (two levels, 5- and 1-Hz rTMS) and "condition" (two levels, IM and no-IM) as between subjects factors. A Greenhouse–Geisser correction was used when appropriate. When an F value was significant, *post hoc* paired-sample t -tests were performed. All values in figures are expressed as mean \pm standard error. Data were analyzed using IBM SPSS Statistics ver. 20.0 (IBM

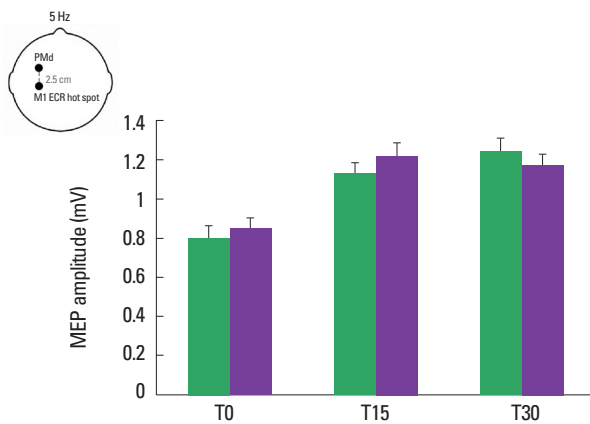


Fig. 2. Motor-evoked potential (MEP) facilitation before and after dorsal pre-motor cortex (PMd) conditioning with 5-Hz repetitive transcranial magnetic stimulation (rTMS) during observation of a painting with implied motion (IM) and without IM. Each point corresponds to the mean amplitude of MEPs recorded at baseline (T0), 15 min (T15), and 30 min (T30) after conditioning. 5-Hz rTMS PMd conditioning increased MEP amplitude during observation of both paintings. Error bars indicate standard errors. M1, primary motor cortex; ECR, extensor carpi radialis.

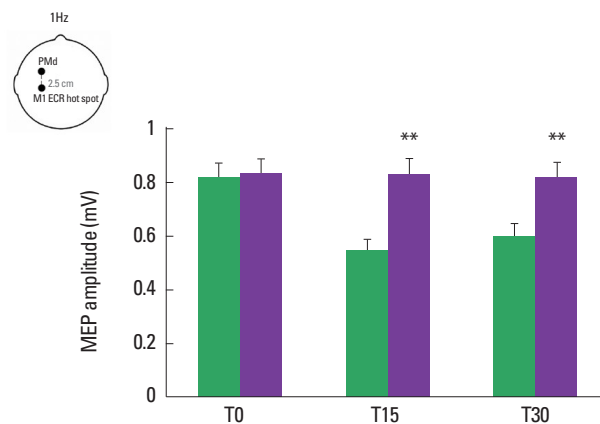


Fig. 3. Motor-evoked potential (MEP) facilitation before and after dorsal pre-motor cortex (PMd) conditioning with 1-Hz repetitive transcranial magnetic stimulation (rTMS) during observation of a painting with implied motion (IM) and without IM. Each point corresponds to the mean amplitude of MEPs recorded at baseline (T0), 15 min (T15), and 30 min (T30) after conditioning. 1-Hz rTMS PMd conditioning decreased MEP amplitude only during observation of a painting without implied motion. Error bars indicate standard errors. M1, primary motor cortex; ECR, extensor carpi radialis. ** $P < 0.01$.

Co., Armonk, NY, USA). Statistical significance was set at 0.05.

RESULTS

RMT and AMT recorded in the right ECR muscle did not differ between conditions (RMT: IM, $41\% \pm 3.6\%$; no-IM, $40.1\% \pm 2.8\%$, $F [1, 22] = 0.9$, $P = 0.8$; AMT: IM, $32.2\% \pm 2.7\%$; no-IM, $33.7\% \pm 3.2\%$; $F [1, 22] = 1.1$; $P = 0.9$). We next tested the effect of IM on MEP size. Observation of the picture with IM induced an increase in MEP size (IM, 0.82 ± 0.04 mV; no-IM, 0.61 ± 0.038 mV; $F [1, 22] = 7.2$; $P = 0.006$) (data not showed).

Regarding the PMd–M1 connectivity and plasticity paradigm, three-way repeated measure ANOVA yielded a significant main effect of “stimulation” ($F [1, 44] = 81.5$, $P < 0.0001$); “condition” ($F [1, 44] = 7.4$, $P < 0.009$) and “time” ($F [1, 44] = 7.5$, $P < 0.001$) without a “stimulation” X “condition” X “time” interaction ($F [2, 88] = 2.5$, $P < 0.08$). The assumption of sphericity was not violated. *Post hoc* analysis indicated that MEPs recorded 15 and 30 min after PMd conditioning were significantly different from baseline ($P = 0.005$ and $P = 0.0004$, respectively). We then performed paired samples *t*-tests follow-up analysis to ascertain the effect of 5- and 1-Hz rTMS PMd on MEPs recorded during observation of IM and no-IM. The 5-Hz rTMS paradigm increased MEPs amplitude during both IM and no-IM condition compared to T0 (IM: T15 [$P = 0.0002$], T30 [$P = 0.001$]; no-IM: T15 [$P = 0.001$], T30 [$P = 0.004$]). Furthermore, there was no difference in baseline MEP amplitude

between the two condition ($F [1, 22] = 1.1$, $P = 0.3$) (Fig. 2). Similar results were obtained in a control experiment using a longer exposure to the conditions (total duration 25 min) (IM: T0, 0.78 ± 0.03 mV; T15, 1.36 ± 0.05 mV; T30, 1.12 ± 0.05 mV; no-IM: T0, 0.82 ± 0.04 mV; T15, 1.29 ± 0.05 mV; T30, 1.36 ± 0.04 mV (main effect “condition” $F [1, 22] = 0.33$, $P = 0.6$; main effect “time” $F [2, 28] = 28.2$, $P < 0.0001$; “condition” X “time” interaction: $F [2, 44] = 2.01$, $P = 0.31$) (data not showed).

On the contrary, the 1-Hz rTMS conditioning decreased MEPs amplitude only during the IM condition compared to T0 (IM; T15 [$P = 0.01$], T30 [$P = 0.008$]; no-IM: T15 [$P = 0.8$], T30 [$P = 0.4$]) (Fig. 3). On the whole, the data indicate that observation of IM in a work of art modulated connectivity and plasticity of PMd–M1 inhibitory circuits.

DISCUSSION

In this study we investigated whether IM information from a static image of a painting affects cortical excitability, connectivity and plasticity. Our results demonstrated that observation of an image with IM increases MEP size. Furthermore, using rTMS, we showed that IM in a work of art modulates PMd–M1 plasticity and connectivity.

First we replicated earlier findings indicating that MEP amplitude increases upon observation of pictures with IM (Battaglia et al., 2011; Urgesi et al., 2006). This suggests that motor resonance

to IM in paintings might be due to the activation of mirror neuron/action observation-execution and motor imagery networks (Battaglia et al., 2011). Furthermore, using a well-characterized paradigm to explore functional connectivity and plasticity (Münchau et al., 2002; Passingham, 1985; Rizzo et al., 2004), our results revealed that long-term decrease in MEP amplitude induced by 1-Hz rTMS PMd conditioning are prevented during observation of a painting with IM. Thus, IM observation facilitates PMd–M1 functional connectivity through a specific effects on inhibitory connections. PMd is not considered part of the mirror system in humans and primates (Rizzolatti and Craighero, 2004). Furthermore, PMd neurons play a pivotal role in externally cued arm movements (Wise, 1985) and exhibits similar activity patterns during both action observation, motor imagery and performance (Cisek and Kalaska, 2004; Szameitat et al., 2007). In addition, single-unit activity within both M1 and PMd is similar during observation and execution of a familiar task (Tkach et al., 2007). It is noteworthy that our findings do not imply the presence of classical mirror neurons in PMd but rather illustrate a modulation of the PMd–M1 connections that, supposedly, leads to the activation of motor pathways. However, some words of caution are required when interpreting the proposed sequence of effective connectivity networks during processing of IM in a painting. PMd is part of a rather large frontoparietal network that transforms sensory information into actions (Chouinard et al., 2003; Geyer et al., 2000; Rizzolatti and Fadiga, 1998). It has been reported that 1-Hz rTMS of the left PMd induces compensatory excitatory activity in both contralateral and ipsilateral hemisphere (O’Shea et al., 2007). It is thus conceivable that plastic changes induced by observation of a painting with IM might take place in a more extensive connectivity network still to be investigated.

Our results are in accordance with previous findings reporting modulation of premotor-motor connectivity during movement observation. Observation of whole hand grasp and precision grip modulate ventral-premotor–M1 connectivity probed with a paired-pulse paradigm (Davare et al., 2008; Koch et al., 2010). By using a different paradigm we showed that observation of IM in a work of art induces a similar modulation in a different subregion of premotor cortex. The mechanism by which rTMS modulates cortical activity is not fully understood. It has been suggested that it may be related either to long-term depression/LTP (Chen et al., 1997) and/or changes of cortical excitability (Touge and Takeuchi, 2001). It is likely that the after-effects induced by PMd rTMS conditioning are linked to long-lasting changes in synaptic efficacy rather than changes in membrane resting potential (Rizzo

et al., 2004). PMd–M1 connectivity is particularly relevant for motor recovery and residual motor output after stroke (Fridman et al., 2004; Johansen-Berg et al., 2002) and successful rehabilitative treatments are associated with strengthening of these connections (Rehme et al., 2012). Hence, our results further point toward the use of art with IM as plasticity-based intervention in rehabilitation. Future studies are needed to investigate whether observation of paintings with IM movements induces a similar modulation in intrinsic M1 inhibitory circuits recruited with M1 1-Hz rTMS conditioning.

We would be the first to acknowledge that factors such as expertise in art, prior exposure, individual temperament and particular psychological traits can influence the aesthetic and emotional responses to the artwork. Moreover, it is clear that the extraction of dynamic information from still images entails visual perception, association of the represented form with an action and mental imagery. Thus, individual mental imagery abilities and personal memories of the execution of an action might have affected neural responses to IM (Mizokami et al., 2014). Limitations like these will need to be addressed in future studies in order to ascertain the degree to which our finding might be generalized to other forms of dynamic art (abstract vs. figurative art, different artists and periods, stylistic and structural properties, emotional content).

The fact that our results highlight a complex modulation of premotor-motor networks during observation of a painting with IM support the hypothesis that observation of art might be used to augment traditional rehabilitation paradigms and speed the recovery of motor functioning. Future clinical studies are required to confirm this hypothesis.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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