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Sensorimotor Network Crucial for Inferring Amusement from Smiles

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Abstract

Understanding whether another’s smile reflects authentic amusement is a key challenge in social life, yet, the neural bases of this ability have been largely unexplored. Here, we combined transcranial magnetic stimulation (TMS) with a novel empathic accuracy (EA) task to test whether sensorimotor and mentalizing networks are critical for understanding another’s amusement. Participants were presented with dynamic displays of smiles and explicitly requested to infer whether the smiling individual was feeling authentic amusement or not. TMS over sensorimotor regions representing the face (i.e., in the inferior frontal gyrus (IFG) and ventral primary somatosensory cortex (SI)), disrupted the ability to infer amusement authenticity from observed smiles. The same stimulation did not affect performance on a nonsocial task requiring participants to track the smiling expression but not to infer amusement. Neither TMS over prefrontal and temporo-parietal areas supporting mentalizing, nor peripheral control stimulations, affected performance on either task. Thus, motor and somatosensory circuits for controlling and sensing facial movements are causally essential for inferring amusement from another’s smile. These findings highlight the functional relevance of IFG and SI to amusement understanding and suggest that EA abilities may be grounded in sensorimotor networks for moving and feeling the body.

Key words: amusement, emotion authenticity, empathic accuracy, sensorimotor system, simulation, transcranial magnetic stimulation

Introduction

Understanding whether a smiling individual is experiencing authentic amusement is a common challenge in everyday social interactions. A smile is, without any doubt, the most easily recognizable facial expression, and yet the most nuanced one. Indeed, a smile can be flexibly used to communicate a wide range of feelings (Ekman 2001; Shiota et al. 2003; Niedenthal et al. 2010). Critically, in many social contexts, it can be used deceptively by showing that amusement is felt

when it is not. People are typically accurate in classifying smiling faces as emotionally positive expressions, but commit many more errors when they are asked to evaluate the emotional feeling behind a smile (Niedenthal et al. 2010). Accurate recognition of the emotion felt by another person (a social target) is often referred to as empathic accuracy (EA), and is commonly operationalized as the correspondence between the feelings reported by the social target and the feelings that perceivers infer from the social target’s behavior (Ickes and

Stinson 1990; Levenson and Ruef 1992; Ickes 1997; Zaki et al. 2008, 2009). EA requires accurate perception of the social target's behavior and explicit inferences of the underlying feelings based on available information (e.g., facial expressions, prior knowledge or contextual information). It is believed that perceptual and cognitive processes underlying EA could provide a key mechanism for empathy, that is, the ability to share the feelings of others, which is grounded in affective brain regions engaged during first-hand emotion experiences (de Vignemont and Singer 2006; Singer and Lamm 2009; Batson 2011; Decety et al. 2012; Lamm and Majdandžić 2015; Rütgen et al. 2015a, 2015b; Zaki et al. 2016).

Inferring amusement from another person's smile requires the perceiver to visually process and integrate multiple morphological and dynamic features of the observed facial expression (Ekman 2001; Ambadar et al. 2009; Krumhuber and Manstead 2009; McLellan et al. 2010). However, for accurate recognition of the underlying emotional feeling, further nonvisual brain mechanisms are likely involved (Zaki et al. 2009, 2012). Previous studies suggest that at least 2 related but distinct sets of brain regions may be involved in EA: 1) sensorimotor "mirroring" regions that support perception and understanding of others' behavior, possibly through embodied simulation of the observed actions; and 2) "mentalizing" regions that support the ability to explicitly consider others' mental states and their sources, and to draw explicit inferences about them (Preston and de Waal 2002; Gallese et al. 2004; Amodio and Frith 2006; Frith and Frith 2006; Saxe 2006; Mitchell 2009; Gallese and Sinigaglia 2011; Decety et al. 2012; Zaki et al. 2012; Zaki 2014).

However, it is still debated whether and when these sensorimotor and cognitive networks provide routes to understanding others, or merely reflect such understanding (Gallese et al. 2011; Uithol et al. 2011; Avenanti et al. 2013b; Lamm and Majdandžić 2015). This is because knowledge of these networks is mostly based on indirect correlational imaging evidence, and the need for novel methods and causal approaches is increasingly recognized by social neuroscientists (Decety 2011; Héту et al. 2012; Avenanti et al. 2013b; Rütgen et al. 2015a, 2015b; Lamm et al. 2016; Zaki et al. 2016). In particular, to date, no studies have specifically tested the critical roles of sensorimotor and mentalizing networks in the empathic ability to infer authentic amusement from the smiles of others. Establishing these roles is the goal of this study.

Indirect correlational evidence has suggested that sensorimotor networks may support EA. For example, watching emotional motor behavior such as emotional facial expressions vicariously activates those sectors of the inferior frontal gyrus (IFG) that are involved in controlling facial movements and those sectors of the somatosensory cortex (SI) that are involved in processing sensations from the face (Carr et al. 2003; Leslie et al. 2004; Dapretto et al. 2006; Keysers et al. 2010; Tamietto et al. 2015). These observations of shared activations have motivated sensorimotor simulationist models, which suggest that perception of others' facial expressions is (at least partially) grounded in the same network that is involved in performing and sensing facial movements (Goldman and Sripada 2005; Gallese 2007; Keysers et al. 2010; Niedenthal et al. 2010; Wood et al. 2016). Yet, it should be noted that studies exploring vicarious activations during perception of emotional facial expressions have traditionally used passive viewing tasks without asking participants to make explicit inferences about the targets' emotional feelings (for a review, see Zaki et al. 2012).

However, studies focusing on the mentalizing network have commonly asked participants to make explicit judgments about

another's internal state using verbal material (i.e., scripts) or highly stylized nonverbal social cues, including vignettes, static displays of facial expressions or even more isolated cues such as target eye gaze (Amodio and Frith 2006; Frith and Frith 2006; Saxe 2006; Mitchell 2009). These studies highlighted a midline and lateral temporo-parietal network supporting mental state attribution, which includes the medial prefrontal cortex (mPFC) and the temporo-parietal junction (TPJ) (Amodio and Frith 2006; Frith and Frith 2006; Saxe 2006; Mitchell 2009). However, none of these studies presented participants with dynamic expressions of natural behaviors.

Recently, more naturalistic neuroscientific paradigms combining dynamic social cues and explicit inferential tasks (Redcay et al. 2010; Wolf et al. 2010; Spunt and Lieberman 2013) have revealed coactivation and functional coupling of sensorimotor and mentalizing networks during complex social tasks (Wheatley et al. 2007; Zaki et al. 2009; Lombardo et al. 2010; Schippers et al. 2010; Raz et al. 2014), including EA tasks. Notably, studies have shown that neural activity in both networks predicts EA performance in tasks requiring observation of others' expressive behavior and inferences of the underlying emotional feelings (Zaki et al. 2009; Harvey et al. 2013). Activity in both sensorimotor and mentalizing networks also predicts EA performance in simpler tasks, for example, when evaluating emotion authenticity from sounds of laughter (McGettigan et al. 2015). In this case, there was no contextual information about the possible source of the emotion, so the explicit inference about the emotion had to be based only on social cues.

While these studies have underscored the integrated nature of empathic processing during naturalistic social inference and the potential contributions of the sensorimotor and mentalizing networks to accurate empathic inferences, no study has thus far addressed the key question of whether these networks play causal roles in EA. Indeed, it should be noted that the above-mentioned conclusions about the involvement of sensorimotor and mentalizing networks in EA were mostly based on imaging methods. These methods can only provide indirect correlational data, and cannot establish direct causal links between brain structures and cognitive functions.

Here, we administered repetitive transcranial magnetic stimulation (rTMS) to perturb key regions within the sensorimotor network (i.e., the face representation in IFG and SI) and the mentalizing network (i.e., mPFC and TPJ), and provide direct evidence for their functional relevance to EA. To this aim, we designed a novel EA task combining dynamic displays of smiles with explicit empathic inferences of whether the social target is feeling authentic amusement or not. We used signal detection theory to test whether interference with key nodes of the 2 networks would disrupt participants' sensitivity to the authenticity of amused expressions. Our results indicate that motor and somatosensory regions are causally essential for the empathic inference of amusement from another's smile. This suggests that EA abilities may be grounded in sensorimotor networks for moving and sensing one's own body.

Materials and Methods

Participants

A total of 180 healthy subjects took part in the study. Sixty-four subjects participated in 1 of the 4 TMS experiments. In each TMS experiment, we targeted a different brain area: right IFG (16 participants, 8 females, mean age \pm SD: 23.6 \pm 1.9 years), right SI (16 participants, 8 females, 22.3 \pm 2.3 years), mPFC (16

participants, 9 females, 22.5 ± 0.5 years) or right TPJ (16 participants, 10 females, 23.6 ± 1.5 years). Additionally, 16 subjects (8 females; 25.4 ± 2.2 years) participated in a peripheral stimulation experiment and 100 subjects (50 females) were tested in 1 of 5 pilot studies, whose aim was to validate the 2 behavioral tasks (Supplementary Materials). All subjects were right-handed, had normal or corrected-to-normal visual acuity in both eyes, and were naive to the purposes of the experiment. None of the participants had neurological, psychiatric, or other medical problems or any contraindication to TMS (Rossi et al. 2009; Rossini et al. 2015). Participants provided written informed consent. The procedures were approved by the ethics committee at the Psychology Department of Bologna University and were in accordance with the ethical standards of the 1964 Declaration of Helsinki. No discomfort or adverse effects of TMS were reported by participants or noticed by the experimenter.

Stimulus Creation and Selection

Stimuli consisted of 32 dynamic movies (lasting 2 s, 60 frames) presented centrally on a 19-inch monitor (resolution: 1024×768 ; refresh rate: 60 Hz) subtending $27 \times 21^\circ$ of visual angle. Movies depicted 8 individuals (“social targets”; including 4 females and 4 males, aged 24.5 ± 2.1 years) who were filmed individually while smiling. Movies were edited using Adobe Premiere Pro C6 software in order to correct lighting, contrast and color, and remove the audio tracks.

During stimulus creation, social targets sat against a white background, and lighting equipment was used to avoid the formation of shadows. The social targets were instructed to gaze directly toward the camera and try not to move their bodies. Ten social targets (five females) were initially filmed while making smiling expressions associated with authentic positive feelings of amusement (authentically amused smiles; Supplementary Movie 1) or posed expressions associated with an emotionally neutral state (falsely amused smiles; Supplementary Movie 2). Authentic and fake expressions of amusement were recorded in 2 separate sessions that were performed under emotionally congruent contexts to provide realistic stimuli.

In the “authentic” session, the social targets used a laptop with loud speakers to select audio clips that elicited strong feelings of amusement and spontaneous smiles (Instruction: “Please watch the camera and smile only if you feel like doing so”). Auditory stimuli were chosen based on social targets’ preferences and were retrieved from the internet (e.g., <http://www.youtube.com>). In the “fake” session, social targets were not presented with auditory stimuli, and were instead instructed to produce a voluntary smile (Instruction: “Please watch the camera, think about something neutral and produce a smile that you think could be interpreted as an authentic expression of amusement by an observer”). They were allowed to watch the prerecorded authentic smiles in order to achieve more convincing posed facial expressions.

Notably, after each smiling expression, social targets were instructed to provide subjective evaluations of the amusement they felt while smiling using a 9-step Likert scale (0 = neutral state; 9 = maximal amusement). Moreover, they were asked to evaluate their subjective confidence in their amusement judgments using a categorical response (I am 100% sure of my judgment/I am not 100% sure of my judgment) (cf. Ickes and Stinson 1990; Levenson and Ruef 1992). These subjective reports allowed us to select only smiling expressions that were

associated with the highest subjective ratings of amusement (authentically amused smiles) or without any emotional feeling (falsely amused smiles) and with strong subjective confidence in the ratings (see Supplementary Material). This initial selection brought about a sample of 30 authentic and 30 fake expressions of amusement for each social target (600 movies).

Videos were further selected based on the results of 5 pilot studies carried out with a total of 100 subjects who did not participate in any of the subsequent rTMS or electrical stimulation experiments (Supplementary Material). These pilot studies allowed us to select a subset of 32 movies from 8 social targets, and ensured that performance on the 2 experimental tasks (see below) was similar for each stimulus used in the main experiments (~75% accuracy).

Smile Dynamics

Each movie showed a transition from a neutral/moderately positive facial expression to an apparent expression of amusement: in the initial phase (lasting 500 ms, 15 frames) the social target’s face was still, and the subsequent phase (lasting 1500 ms, 45 frames) showed the smiling expression. The last frames of each video clip contained the apex of the smile. Although smile offset can also be informative of amusement authenticity, the smile offset was excluded from the video clips in order to cover their entire duration (2 s) with a short rTMS train.

We analyzed facial markers of authentically and falsely amused smiles (Ekman 2001; Shiota et al. 2003; Ambadar et al. 2009; Krumhuber and Manstead 2009; McLellan et al. 2010; Niedenthal et al. 2010). To analyze the key muscles involved in smiling, 2 independent raters blind to the experimental conditions evaluated the activation of the orbicularis oculi (i.e., the muscle that makes crow’s feet at the outer corner of the eye; AU6 according to Ekman’s Facial Action Coding System; Ekman et al. 2002), and the zygomaticus major (i.e., the muscle that extends the mouth and pulls the lip corners upward; AU12), in the 16 authentically and 16 falsely amused smiles using a 3-point scale (scored 0, 0.5, 1). Raters’ judgments were highly correlated ($r > 0.7$) and were thus averaged. Using movement analysis software (Kinovea 0.8.15), we also tracked changes in mouth extension (distance in pixels between the 2 lip corners) over time, and checked the size of the maximal enlargement (increase in lip corner distance relative to the initial frame), when it occurred in time, and the peak velocity of the movement. Table 1 shows activation ratings, motion parameters and statistical comparisons between the 16 authentically and 16 falsely amused smile movies.

Mean AU6 and AU12 activation ratings, maximal mouth enlargement and peak velocity tended to be greater for authentically amused smiles relative to falsely amused smiles, although none of the analyses reached statistical significance. Also, maximal mouth enlargement occurred nonsignificantly earlier for authentically amused smiles than for falsely amused smiles (Table 1). In a further analysis, we z-transformed these dependent variables and submitted them to a Measure (AU6 activation, AU12 activation, maximal mouth enlargement, time of maximal mouth enlargement, mouth enlargement peak velocity) \times Expression type (authentic vs. falsely amused) ANOVA that showed a main effect of Expression type ($F_{1,30} = 5.63$, $P = 0.02$), with greater values for authentically than for falsely amused smiles. Taken together, these analyses suggest that, while none of the facial markers alone could have been used to robustly discriminate between the 2 types of facial

Table 1 Mean values \pm SD of activation ratings and motion parameters computed for authentically and falsely amused smiles

	AU6 activation rating (0–1)	AU12 activation rating (0–1)	Maximal mouth enlargement (change in pixels)	Time of maximal mouth enlargement (ms)	Mouth enlargement peak velocity (pixel/ms)
Authentic amusement	0.72 \pm .21	0.92 \pm 0.14	24.19 \pm 4.48	1510 \pm 318	0.018 \pm 0.006
False amusement	0.58 \pm .22	0.82 \pm 0.15	21.06 \pm 6.50	1515 \pm 295	0.015 \pm 0.005
Statistical comparison	$t_{30} = 1.79, P = 0.08$	$t_{30} = 1.82, P = 0.08$	$t_{30} = 1.58, P = 0.12$	$t_{30} = 0.07, P = 0.94$	$t_{30} = 1.53, P = 0.14$

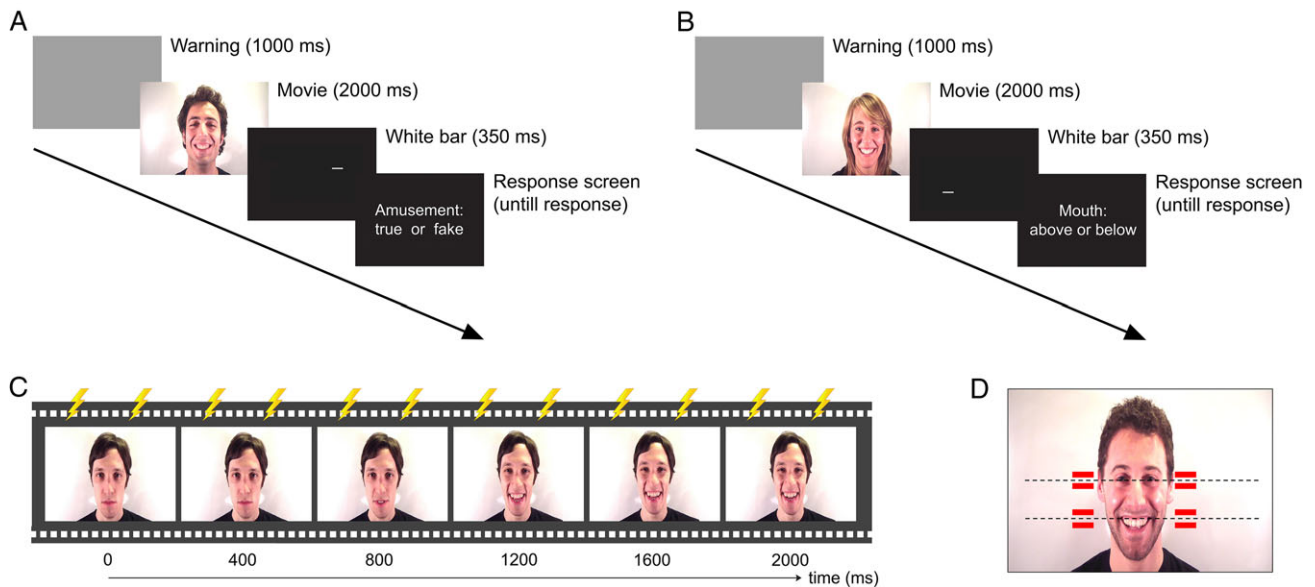


Figure 1. Schematic representation of the experimental paradigm. (A) In the EA task, participants were asked to judge whether or not the smiling social target was feeling authentic amusement. (B) In the NS task, participants had to judge whether the white bar appeared above or below the social target's mouth/eye (above the mouth in the example). (C) In both tasks, a continuous 6 Hz train of rTMS or electrical stimulation was applied at the onset of the movies. (D) Example image showing (in red) the possible locations of the white bar relative to the social target's mouth and eye.

expressions, observers could have used a combination of the different markers to infer amusement authenticity (for similar conclusions, see Abe et al. 2002; Niedenthal et al. 2010).

Experimental Tasks

In the EA task (Fig. 1A), participants were presented with authentic and falsely amused smile movies and asked to monitor the social target's expression to explicitly infer what she/he truly felt (i.e., authentic amusement, no amusement). To rule out that any change in EA task performance could have been due to nonspecific effects of rTMS, we also assessed participants' performance on a difficulty-matched nonsocial (NS) control task (Fig. 1B) using the same set of stimuli used in the EA task. Similarly to the EA task, the NS task required participants to constantly monitor the social target's face, particularly the eye and mouth regions (which are critical for discriminating between real and fake expressions of amusement; Ekman 2001; Shiota et al. 2003; Ambadar et al. 2009; Krumhuber and Manstead 2009; McLellan et al. 2010; Niedenthal et al. 2010). However, in contrast to the EA task, the NS task required participants to judge spatial features of the observed expressions (i.e., whether a white bar presented for 350 ms at the end of each clip was located below or above the social target's eye or

mouth corners), rather than empathically understanding whether these expressions were associated with authentic amusement or not (Fig. 1B,D).

Procedure

Custom software (written in C#) was used to control the video clip sequence and trigger TMS or electrical stimulation. For the rTMS experiments, participants were initially tested in electrophysiological and neuronavigation sessions in which rTMS intensity and coil position over the scalp were determined, respectively (see below). Then, participants were presented with task instructions and an example of the trial structure. Each subject performed the EA and NS tasks in 2 separate sessions presented in a counterbalanced order. For each task, 2 blocks of 16 active rTMS trials and 2 blocks of 16 sham rTMS trials were performed in an ABBA/BAAB counterbalanced order (i.e., active-sham-sham-active or sham-active-active-sham). After each block, a break of ~1 min was allowed. A break of ~5 min was allowed between the 2 sessions.

In both tasks, each trial started with a gray screen (1000 ms) followed by the video clip (2000 ms). After the clip, a white bar (24×1 pixels subtending $0.72 \times 0.03^\circ$ of visual angle) appeared on a black screen (350 ms), followed by a response screen

(presented until response). Participants provided their response by pressing one of 2 keys on the keyboard. They were asked to answer as accurately as possible, using the index and middle fingers of the right hand (ipsilateral to the target stimulation site). After the keypress, the response screen was replaced by a black screen (intertrial interval: 7000–9000 ms).

On each trial, a time-locked single train of subthreshold 6 Hz rTMS (12 pulses) was administered using a figure-of-eight coil (diameter: 70 mm) connected to a Magstim Rapid2 stimulator (Magstim). The coil was placed over a target brain region that differed by participant group (IFG, SI, mPFC or TPJ). The rTMS train lasted 2 s. It was administered at the onset of the movie and thus covered its entire duration (Fig. 1C). The stimulation intensity corresponded to 90% of the resting motor threshold (rMT) (see below). During active rTMS blocks, the intersection of the coil was placed tangentially to the scalp and directly above the scalp location of the target region. Sham rTMS blocks were performed by tilting the coil at 90° over the same target region, to provide some scalp sensations and TMS sounds similar to active stimulation but without inducing a current in the brain.

Since online rTMS may cause slight activations of facial muscles, and altering facial mimicry can impair visual recognition of positive expressions (Oberman et al. 2007; Wood et al. 2016), we performed a peripheral site (PS) control experiment. In the PS experiment, we directly stimulated participants' face using electric pulses. Specifically, we stimulated the right masseter muscle by applying a time-locked single train of 6 Hz electrical square wave pulses (pulse duration: 0.2 ms), thus mimicking the stimulation frequency used in the rTMS experiments. Ag-AgCl surface electrodes connected to a DS7A Digitimer Constant Current Stimulator (Digitimer) were placed between the condyle and the coronoid process of the mandible, immediately below the zygomatic process. Electrode position and stimulation intensity were individually adjusted to evoke facial contractions that were visually similar to those evoked by active rTMS (mean intensity = 0.41 mA, SD = 0.06). For each task, 2 blocks of 16 active stimulation trials and 2 blocks of non-stimulation (control) trials were performed in an ABBA/BAAB counterbalanced order.

At the end of the experimental session, participants in the TMS or PS experiments were asked to provide subjective unpleasantness ratings of the sensations caused by the magnetic or electrical stimulation, using a 5-point Likert scale ranging from 1 ("not unpleasant at all") to 5 ("extremely unpleasant").

Electrophysiological and Neuronavigation Sessions

To set rTMS intensity, the rMT was estimated for all participants in a preliminary phase of the experiment using standard procedures (Rossi et al. 2009). Motor-evoked potentials (MEPs) induced by stimulation of the right motor cortex were recorded from the left first dorsal interosseous (FDI) by means of a Biopac MP-35. Electromyography (EMG) signals were band-pass filtered (30–500 Hz) and digitized (sampling rate: 5 kHz). Pairs of Ag-AgCl surface electrodes were placed in a belly-tendon montage with a ground electrode on the wrist. The intersection of the coil was placed tangentially to the scalp with the handle pointing backward and laterally at a 45° angle away from the midline. The rMT was defined as the minimal intensity of stimulator output that produces MEPs with an amplitude of at least 50 μ V in the FDI with 50% probability (Rossini et al. 2015).

Each brain area was individually targeted using image-guided neuronavigation. The coil position was identified on

each participant's scalp using the SofTactic Navigator System (Electro Medical Systems). Skull landmarks (nasion,inion and 2 preauricular points) and -80 points providing a uniform representation of the scalp were digitized by means of a Polaris Vicra digitizer (Northern Digital), as in our previous research (Avenanti et al. 2007, 2012, 2013a; Tidoni et al. 2013; Jacquet and Avenanti 2015). An individual estimated magnetic resonance image (MRI) was obtained for each subject through a 3D warping procedure that fits a high-resolution MRI template with the participant's scalp model and craniometric points. This procedure has been proven to ensure a global localization accuracy of roughly 5 mm, a level of precision closer to that obtained using individual MRIs than can be achieved using other localization methods (Carducci and Brusco 2012).

Stimulation sites were identified on the basis of previous fMRI studies, using the SofTactic Navigator (IFG, SI and TPJ) or established anatomical methods (mPFC). For IFG, SI and TPJ, Talairach coordinates of target regions and corresponding scalp projections were automatically estimated by the SofTactic Navigator from the MRI-constructed stereotaxic template. When necessary, coordinates in Talairach space were obtained by converting MNI coordinates reported in previous studies using GingerALE 2.3.1. To target sensorimotor regions, we selected Talairach coordinates corresponding to the cortical face representations in premotor and somatosensory sites. The IFG scalp site was localized based on the following coordinates: $x = 47$, $y = 8$, $z = 28$, which were identified on the basis of previous fMRI meta-analyses exploring activations associated with the execution and/or observation of facial movements and emotional expressions (Molenberghs et al. 2009; Caspers et al. 2010; Grosbras et al. 2012). The S1 site was identified based on the following coordinates: $x = 56$, $y = -16$, $z = 40$, corresponding to the face representation in the post-central gyrus (Huang and Sereno 2007; Dresel et al. 2008; Kopietz et al. 2009; Holle et al. 2013).

Key nodes of the mentalizing network were identified as follows: the mPFC site was identified at one-third of the distance between the nasion and the inion on the midline between the left and the right preauricular points, as in previous TMS studies (Harmer et al. 2001; Mattavelli et al. 2011, 2013). The right TPJ site was localized based on the following coordinates: $x = 51$, $y = -54$, $z = 21$, which were identified on the basis of neuroimaging studies exploring areas related to theory of mind and mentalizing (van Overwalle and Baetens 2009; Mar 2011; Bzdok et al. 2012).

Locations of scalp regions identified by neuronavigation (IFG, SI, TPJ) or anatomical methods (mPFC) were marked with a pen on each participant's head and used to place the rTMS coil. Then, individual Talairach coordinates corresponding to the projection of the targeted scalp sites on the surface of the MRI-constructed stereotaxic template were automatically estimated through the neuronavigation system. These estimated coordinates indicate the most superficial cortical site where rTMS effects are expected to be maximal. Brain surface coordinates were converted to MNI space (using GingerALE 2.3.1) for visualization with the MRICron software (MRICron/NPM/dcm2nii). Figure 2 illustrates the estimated group mean MNI surface coordinates.

Data Analysis

Behavioral data were processed offline. Accuracy on each task (EA, NS) was converted into measures of sensitivity (d') and

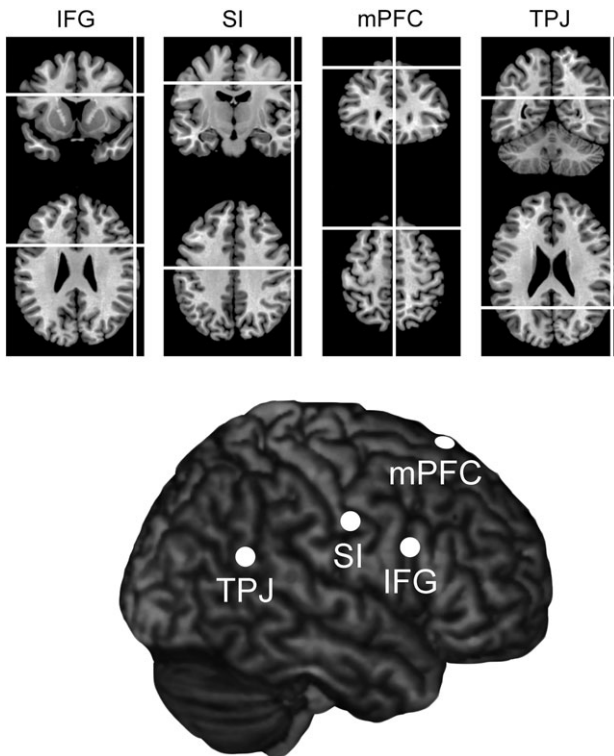


Figure 2. Schematic representation of the brain stimulation sites reconstructed on a standard template using MRICron. Talairach coordinates corresponding to the projection of the IFG, SI, mPFC and TPJ scalp sites on the brain surface were individually estimated through the neuronavigation system and then converted to MNI space. Group mean MNI brain surface coordinates \pm SD for the IFG site were $x = 62.2 \pm 1.3$; $y = 12.7 \pm 1.3$; $z = 26.3 \pm 2.5$. Coordinates for the SI were $x = 64.1 \pm 1.0$; $y = -12.4 \pm 0.9$; $z = 39.6 \pm 1.2$. Coordinates for the mPFC were $x = 1.5 \pm 0.7$; $y = 28.2 \pm 5.2$; $z = 32.4 \pm 15.6$. Coordinates for the TPJ were $x = 64.3 \pm 1.0$; $y = -54.3 \pm 1.9$; $z = 24.7 \pm 1.7$.

response bias (β) in accordance with signal detection theory (Macmillan and Creelman 1991) for each stimulation type (active, control) and stimulation site (SI, IFG, TPJ, mPFC, PS). For the EA task, 2 types of responses were scored as correct: a “fake” response to a false expression of amusement (hit) and a “true” response to an authentic expression of amusement (correct rejection). Two types of responses were scored as incorrect: a “fake” response to an authentic expression (false alarm) and a “true” response to a fake expression (miss). For the NS task, responses were coded as follows: “above” to a white bar above the mouth or the eye (hit), “below” to a white bar below the mouth or the eye (correct rejection), “above” to a white bar below the mouth or eye (false alarm) and “below” to a white bar above the mouth or eye (miss). Mixed-factor ANOVAs were performed on d' and β with stimulation type (active, sham) as a within-subjects factor and stimulation site (IFG, SI, mPFC, TPJ, PS) as a between-subjects factor. Post hoc analysis was performed using the Newman-Keuls test to correct for multiple comparisons. $Partial \eta^2$ was computed as a measure of effect size for the main effects and interactions, whereas repeated measures Cohen’s d was computed for post hoc comparisons. To test the robustness of the ANOVA results, we additionally performed Wilcoxon matched-pairs tests to confirm the significance of critical comparisons (i.e., sham vs. active stimulation) across stimulation sites.

Results

rTMS Over IFG and SI Interferes with EA Task Sensitivity, not Response Bias

The stimulation type \times stimulation site ANOVA conducted on measures of EA task sensitivity (d') revealed significant main effects of stimulation site ($F_{4,75} = 3.02$, $P = 0.02$, $Partial \eta^2 = 0.14$) and stimulation type ($F_{1,75} = 11.79$, $P = 0.001$, $Partial \eta^2 = 0.14$; Fig. 3A). Importantly, these 2 main effects were qualified by a significant two-way stimulation site \times stimulation type interaction ($F_{4,75} = 4.82$, $P = 0.001$, $Partial \eta^2 = 0.20$). Post hoc analysis showed that the interaction was accounted for by the strong reduction in task sensitivity found in the IFG and SI groups during active rTMS (mean d' value \pm SD: IFG = 1.20 ± 0.10 ; SI = 1.07 ± 0.09) compared with sham rTMS (IFG = 1.81 ± 0.13 ; SI = 1.58 ± 0.14 ; all Cohen’s $d > 0.94$, all $P < 0.002$). No change in sensitivity due to active stimulation was found when stimulating mPFC (sham rTMS: 1.87 ± 0.81 ; active rTMS: 1.80 ± 0.65 ; $P = 0.96$), TPJ (sham rTMS: 1.66 ± 0.18 ; active rTMS: 1.65 ± 0.11 ; $P = 0.96$), or the peripheral site (no stimulation: 1.84 ± 0.18 ; active stimulation: 1.94 ± 0.14 ; $P = 0.80$).

The stimulation type \times stimulation site ANOVA performed on the β index (Table 2) showed no significant main effects or interactions (all $F < 2.14$, $P > 0.1$), indicating that neither magnetic stimulation of the cortex nor electrical stimulation of the face muscles affected response bias in the EA task.

The stimulation type \times stimulation site ANOVA performed on d' for the NS task (Fig. 3B) showed no significant main effects or interactions (all $F < 0.61$, $P > 0.66$). A further ANOVA performed on the β index (Table 2) showed no main effects or interactions (all $F < 1.51$, $P > 0.22$).

Thus, performance on the NS task was not affected by interference with sensorimotor regions, the mentalizing network, or peripheral facial muscles. This suggests that rTMS over sensorimotor regions did not simply impair visual processing of facial stimuli but specifically worsened the ability to accurately infer mental states based on such processing.

Changes in Task Sensitivity are Selective

In a further analysis, we directly compared performance on the 2 tasks. A task (EA, NS) \times stimulation type \times stimulation site mixed-factor ANOVA on d' showed significant main effects of stimulation type ($F_{1,75} = 5.69$, $P = 0.02$, $Partial \eta^2 = 0.07$) and stimulation site ($F_{4,75} = 2.65$, $P = 0.04$, $Partial \eta^2 = 0.12$), a significant two-way task \times stimulation type interaction ($F_{1,75} = 4.83$, $P = 0.03$, $Partial \eta^2 = 0.06$) and, critically, a significant three-way task \times stimulation type \times stimulation site interaction ($F_{3,75} = 2.69$, $P = 0.04$, $Partial \eta^2 = 0.13$). This interaction was driven by greater active rTMS interference with EA task performance, relative to NS task performance, in the IFG and SI groups, compared with the mPFC, TPJ and PS groups $\{[(\text{sham-active})EA - (\text{sham-active})NS]_{\text{IFG,SI}} > [(\text{sham-active})EA - (\text{sham-active})NS]_{\text{mPFC,TPJ,PS}}; 2 \text{ sample } t\text{-test}, P = 0.002\}$. The significance of the triple interaction provided the statistical grounds for carrying out separate stimulation type \times stimulation site ANOVAs for the 2 tasks (see previous paragraph).

To directly test the interferential effect of rTMS over different brain regions, a stimulation site \times task mixed-factor ANOVA was conducted on the difference in sensitivity (d') between the sham and active rTMS conditions for each group of participants (Fig. 4). The ANOVA showed no significant main effect of stimulation site ($F_{4,75} = 2.01$, $P = 0.10$), a significant

main effect of task ($F_{1,75} = 4.83, P = 0.03, \text{Partial } \eta^2 = 0.06$) and, most importantly, a significant stimulation site \times task interaction ($F_{4,75} = 2.69, P = 0.04, \text{Partial } \eta^2 = 0.13$). Greater interference with EA task performance was obtained with IFG (0.61 ± 0.45) and SI stimulation (0.51 ± 0.57) than with mPFC (0.07 ± 0.69), TPJ (0.01 ± 0.51), and PS (-0.09 ± 0.63) stimulation (all Cohen's $d > 0.69$, all $P < 0.042$) which in turn did not differ from one another (all $P > 0.63$). Statistically comparable interferential effects were found for EA task performance when stimulating IFG and SI ($P = 0.64$). These interferential effects were greater for the EA task than for the NS task when stimulating the same regions (all Cohen's $d > 0.74, P < 0.013$). No significant effects were found for the NS task (all $P > 0.49$).

To ensure that any interferential effects of rTMS were not due to speed-accuracy trade-offs, we also analyzed response times (RTs) in the 2 tasks (Table 3). The task \times stimulation type \times stimulation site ANOVA performed on RTs revealed no main effects or interactions (all $F < 1.42, P > 0.23$), ruling out any speed-accuracy trade-offs.

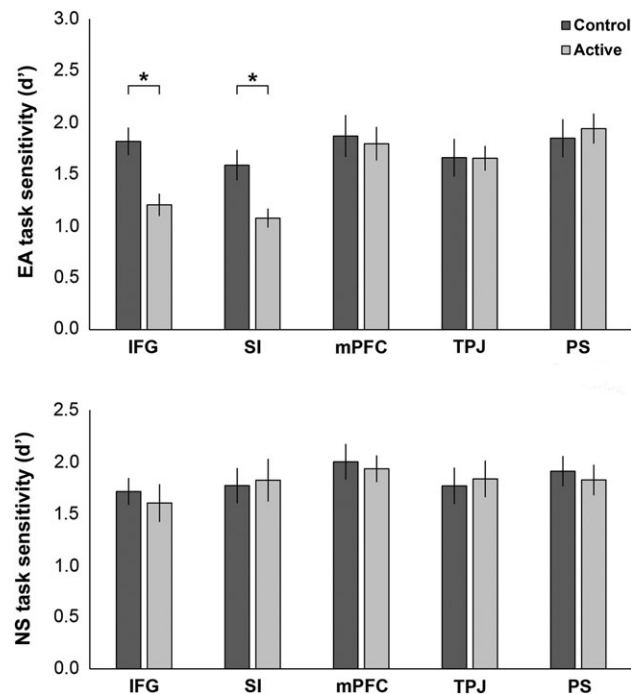


Figure 3. (A) Mean sensitivity (d') in the EA task. Dark-gray and light-gray columns represent control and active stimulation, respectively. Active stimulation of IFG and SI, but not of mPFC, TPJ or PS, reduced sensitivity in the EA task. (B) Mean sensitivity (d') in the NS task. Dark-gray and light-gray columns represent control and active stimulation, respectively. No change in sensitivity due to active stimulation was observed. Asterisks indicate significant post hoc comparisons ($P < 0.05$). Error bars denote s.e.m.

Ruling Out Nonspecific Effects

Finally, we performed a series of control analyses to test the influence of nonspecific effects. We checked whether the unpleasantness of the stimulation could explain our results. A one-way ANOVA on unpleasantness ratings showed no significant effect of stimulation site ($F_{4,75} = 2.06, P = 0.1$; see Table 4). Adding these ratings as covariates in the preceding analyses (d', β, RTs) did not change the pattern of statistical results reported above and revealed no main effects of or interactions with the covariate.

In a series of analyses restricted to the four rTMS groups (IFG, SI, mPFC, and TPJ), we checked the influence of rTMS intensity. Values of rMT (mean \pm SD) were not statistically different across the four rTMS groups, although there was a non-significant trend (IFG group: $55 \pm 4\%$; SI group: $59 \pm 6\%$; mPFC group: $48 \pm 4\%$; TPJ group: $57 \pm 8\%$; $F_{3,60} = 2.53, P = 0.07$). To rule out that rTMS intensity affected our results, we first repeated all the previously reported mixed factors ANOVAs on d', β , and RTs, focusing only on the 4 rTMS groups, and fully replicated the pattern of statistical results reported above for the rTMS groups. Then, we entered stimulation intensity as a covariate (alone or in combination with unpleasantness ratings) in the same analyses and found no influence of such covariate(s).

Nonparametric Control Analyses of Task Performance

The main analyses indicated that EA task sensitivity (d') was strongly affected by rTMS over IFG and SI, as shown by the large effect sizes of the critical comparisons (active vs. control stimulation). Although d' values were normally distributed (Shapiro Wilk tests: all $P > 0.18$), to further show the robustness of our findings, we additionally performed nonparametric analyses on the critical comparisons.

Wilcoxon matched-pairs tests performed on d' values in the EA task confirmed the significance of the critical comparisons for the IFG and SI groups (all $P < 0.0097$), whereas the same comparisons were not significant for the mPFC, TPJ, or PS groups (all $P > 0.53$). No significant comparisons were found for the NS task across groups (all $P > 0.36$).

Additionally, confirming the results of the parametric analyses, Wilcoxon matched-pairs tests performed on the β index (Table 2) and RTs (Table 3) showed no significant differences between active and control stimulations across tasks and groups (all $P > 0.36$).

Discussion

Sensorimotor and mentalizing networks have often been conceptualized as supporting mutually exclusive mechanisms for social perception and empathy. However, recent theoretical (Keysers and Gazzola 2007; Uddin et al. 2007; Zaki et al. 2012; Lamm and Majdandžić 2015) and empirical (Wheatley et al. 2007; Zaki et al. 2009; Lombardo et al. 2010; Redcay et al. 2010; Schippers et al. 2010; Wolf et al. 2010; Lamm et al. 2011; Spunt and Lieberman 2013; Raz et al. 2014) work suggests that both

Table 2 Mean β index \pm SD computed for the EA task and the NS task in the control (sham rTMS or no electrical stimulation) and active interference conditions (active rTMS or active electrical stimulation)

	IFG		SI		mPFC		TPJ		PS	
	Control	Active	Control	Active	Control	Active	Control	Active	Control	Active
EA task	2.2 \pm 3.1	1.5 \pm 0.5	1.2 \pm 1.2	0.9 \pm 0.3	1.3 \pm 0.6	1.2 \pm 0.7	1.2 \pm 0.6	1.1 \pm 0.6	1.5 \pm 1.0	1.3 \pm 0.9
NS task	1.7 \pm 1.8	1.6 \pm 1.4	1.7 \pm 1.4	1.9 \pm 1.4	1.9 \pm 1.6	1.8 \pm 1.8	1.6 \pm 1.3	1.4 \pm 1.1	2.5 \pm 1.8	1.6 \pm 1.2

networks are recruited during complex social tasks and could provide routes to understanding others. Therefore, a central aim of neuroscience is to clarify the circumstances in which these networks are critical for social cognition (Mitchell 2009; Zaki et al. 2012; Avenanti et al. 2013b).

This is particularly relevant for the development of mechanistic models of EA (i.e., the ability to accurately recognize and understand what another individual is experiencing; Ickes and Stinson 1990; Levenson and Ruef 1992; Ickes 1997; Zaki et al. 2008, 2009), but also for empathy in general, as sensorimotor and cognitive processes underlying EA are supposed to provide a key mechanism for evoking affective sharing processes underlying empathic responses (Preston and de Waal 2002; Singer and Lamm 2009; Batson 2011; Decety et al. 2012; Bird and Viding 2014; Zaki 2014). Previous empathy research has established a close link between vicarious experiences of the emotions felt by others and neural activity in affective brain regions like the anterior insula and the anterior midcingulate cortex (Wicker et al. 2003; Singer et al. 2004; Jabbi and Keysers 2008; Fan et al. 2011; Lamm et al. 2011; see in particular Corradi-Dell'Acqua et al. 2011; Rütgen et al. 2015a, 2015b; Zaki et al. 2016 for recent advancements supporting a simulative account of affective sharing).

Yet, multiple mechanisms are likely involved in EA, possibly depending on task demands and the information available to make inferences about what other people are feeling.

In the present study, we provide causal evidence that sensorimotor networks, more so than mentalizing networks, play a crucial role in evaluating the authenticity of observed smiles. We designed a new EA task adapted from previous psychological and neuroscientific research (Ickes and Stinson 1990; Levenson and Ruef 1992; Ekman 2001; Shiota et al. 2003; Zaki et al. 2008; Ambadar et al. 2009; Krumhuber and Manstead 2009; McLellan et al. 2010; Tidoni et al. 2013) and used rTMS to

test whether sensorimotor (IFG and SI) and mentalizing areas (mPFC and TPJ) are necessary for drawing explicit inferences about the amusement supposedly felt by smiling social targets.

We observed that active rTMS administered over the observer's face representation in the IFG and SI, but not over the mPFC or TPJ, disrupted EA. Thus, the reduction in EA performance was not due to nonspecific effects of rTMS, but to interference with fronto-parietal regions involved in controlling and sensing facial movements. A further control experiment also ensured that the reduction in EA was not due to the peripheral interference with facial muscles indirectly caused by rTMS. Indeed, direct electrical stimulation of facial muscles (PS stimulation) did not affect EA. Thus, the reduction in EA performance was due to cortical sensorimotor interference. Our signal detection approach demonstrated that the EA disruption consisted of a pure reduction in participants' sensitivity to the authenticity of amused expressions, rather than a change in participants' response bias. Further analyses ruled out that the decrease in sensitivity was caused by a trade-off in which participants achieved faster RTs by sacrificing accuracy. Moreover, differences in stimulation unpleasantness or rTMS intensity could not explain the results.

Remarkably, no change in performance due to sensorimotor (or mentalizing network) interference was found in a difficulty-matched NS task requiring participants to monitor the social target's expression but not to explicitly infer amusement authenticity. Thus, the reduction in EA performance did not simply reflect impaired low-level processing of the social target's facial movements (i.e., the emotion expression), but, rather, a disruption of explicit inferences about the covert mental state underlying those movements (i.e., the social target's emotional feeling). These findings highlight, for the first time, the functional relevance of IFG and SI to accurate recognition of the authenticity of amused expressions, and thus suggest a grounding of EA in sensorimotor networks.

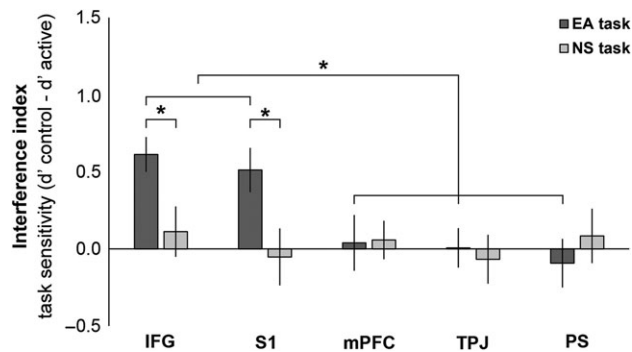


Figure 4. Interferential effect of active relative to control stimulation on sensitivity (d') in the EA (dark-gray) and NS (light-gray) tasks. Positive values indicate greater interference with task performance. Greater EA interference was obtained with IFG and SI stimulation relative to mPFC, TPJ, and PS stimulation. No similar effects were found for the NS task. Asterisks indicate significant post hoc comparisons ($P < 0.05$). Error bars denote s.e.m.

From Neural Correlates to Neural Bases of EA

Mounting evidence suggests that both sensorimotor and mentalizing networks are engaged during EA tasks (Zaki et al. 2009; Harvey et al. 2013), although none of these studies have used causal methods to establish the neural bases for discrimination between authentic and false emotional expressions. Zaki et al. (2009; see also Harvey et al. 2013) recently found that both sensorimotor and mentalizing networks show increased activity

Table 4 Mean subjective ratings \pm SD of the unpleasantness felt during active brain stimulation (active rTMS over IFG, S1, mPFC and TPJ) or peripheral stimulation (electrical stimulation of the PS)

IFG	SI	mPFC	TPJ	PS
3.0 ± 1.3	2.3 ± 0.9	2.1 ± 0.5	2.4 ± 1.2	2.6 ± 0.8

Table 3 Mean RTs \pm SD computed for the EA task and the NS task in the control (sham rTMS or no electrical stimulation) and active interference conditions (active rTMS or active electrical stimulation)

	IFG		SI		mPFC		TPJ		PS	
	Control	Active	Control	Active	Control	Active	Control	Active	Control	Active
EA task	665 ± 281	689 ± 240	659 ± 200	633 ± 191	730 ± 243	712 ± 227	756 ± 349	721 ± 295	689 ± 213	689 ± 246
NS task	727 ± 322	675 ± 256	670 ± 230	651 ± 233	699 ± 247	735 ± 255	712 ± 348	705 ± 356	668 ± 235	682 ± 179

during accurate relative to inaccurate explicit inferences about social targets' emotional states. In their EA task, participants watched individuals discussing emotional autobiographical events and had to infer the underlying emotional feelings (Zaki et al. 2009; Harvey et al. 2013). In the auditory domain, McGettigan et al. (2015) investigated brain activity associated with the ability to discriminate between authentic and fake laughter. As already mentioned in the Introduction, in that study, inferences about laughter authenticity had to be based on social cues only, as participants had no prior knowledge or contextual information about the laughter. Under these conditions, McGettigan et al. (2015) found that neural activity in both networks predicted accurate emotion recognition. However, those correlational data could not answer the key question of whether sensorimotor and mentalizing networks are also essential for EA.

Here, by using a novel EA task and active stimulation of cortical sites, compared with control stimulations, we were able to provide the first direct causal evidence that the motor and somatosensory face representations in the IFG and SI are functionally relevant to empathic inference of amusement authenticity from smiles, whereas frontal and parieto-temporal regions involved in mental state reasoning, that is, the rTPJ and mPFC, do not appear to play similarly critical roles. These findings indicate that EA performance is (at least partially) grounded in the self: inferring amusement authenticity from smiling facial expressions requires one's own sensorimotor networks for making and sensing facial movements.

Sensorimotor Grounding of EA

A growing body of evidence suggests that sensorimotor regions play key roles in emotion processing and social cognition (Pobric and Hamilton 2006; Avenanti et al. 2007; D'Agata et al. 2011; de Gelder et al. 2012; Tidoni et al. 2013; Bolognini et al. 2014; Costa et al. 2014; Urgesi et al. 2014; Jacquet and Avenanti 2015; Tamietto et al. 2015; Valchev et al. 2016). It is well established that the IFG and SI show overlapping activations when participants make emotional expressions and when they see the same expressions or hear associated nonverbal vocalizations (Carr et al. 2003; Winston et al. 2003; Leslie et al. 2004; Dapretto et al. 2006; Warren et al. 2006; Keysers et al. 2010). The IFG and SI are also active both during the execution and the observation of actions, and are considered to be part of a mirroring network involved in simulating observed actions within one's own sensorimotor system (Caspers et al. 2010; Keysers et al. 2010; Gallese and Sinigaglia 2011; Avenanti et al. 2013b; Valchev et al. 2016). Also, previous studies have shown that more empathic people show stronger activation in the IFG and SI (and interconnected sensorimotor regions) than less empathic people when they are watching the actions or the emotions of others (Gazzola et al. 2006; Schulte-Rüther et al. 2007; Pfeifer et al. 2008; Avenanti et al. 2009). However, a major issue hampering the development of a neuroscientific model of EA has been the lack of established connections between these neuroimaging findings and key behavioral indices of EA (but see Zaki et al. 2009; Harvey et al. 2013; McGettigan et al. 2015). Our study significantly expands upon previous evidence by demonstrating that those sectors of the IFG and SI showing vicarious activations are not only correlated with stable empathic dispositions for sharing emotions, but also critical for EA performance. These findings establish a strong and direct causal link between sensorimotor brain networks and emotion

understanding that was only suggested in the past (e.g., Carr et al. 2003; Avenanti et al. 2005).

What is the specific role of sensorimotor networks in understanding others' emotions? Theoretical models propose that one mechanism for inferring the unobservable emotional feelings of others is to simulate their observed facial movements within one's own sensorimotor system (Adolphs et al. 2000; Adolphs 2002; Gallese et al. 2004; Goldman and Sripada 2005; Gallese 2007; Keysers et al. 2010; Niedenthal et al. 2010; Gallese and Sinigaglia 2011; Avenanti et al. 2013b; Wood et al. 2016). According to these models, sensory representations of observed facial expressions in high-order visual regions (e.g., the superior temporal sulcus, STS) would be coupled with sensorimotor representations of the same expressions in the IFG and SI. This sensorimotor embodiment would help observers to intuitively grasp what the other person is experiencing. Some theorists also maintain that sensorimotor simulation would support access to stored knowledge, grounded in the distributed emotion system (including the anterior insula and cingulate cortex), about the emotional states associated with the facial expressions (Goldman and Sripada 2005; Niedenthal et al. 2010; Wood et al. 2016). Thus, when observing facial expressions in others, activity in sensorimotor networks may partially or fully reactivate related concepts and affective states and thus contribute not only to accurate cognitive inferences about the underlying emotional feeling (i.e., EA) but also its sharing—as theorized by current neuroscientific models of empathy.

Remarkably, these theoretical models imply that sensorimotor regions are essential not only for perceptual processing of overt movements (i.e., the social target's facial expression), but also for accurate inference of the covert mental state underlying those movements (i.e., the social target's emotional feeling).

However, to date, these hypotheses have received only partial empirical support from studies using causal methods. Those studies have established that both stable brain lesions and transient rTMS interference with inferior frontal and somatosensory regions reduce performance on tasks requiring participants to process mouth actions (Pazzaglia et al. 2008; Michael et al. 2014) and emotional facial expressions (Adolphs et al. 2000; Pitcher et al. 2008; see also Keysers et al. 2010; Avenanti et al. 2013b). However, they used static pictures of actions or facial expressions and did not clarify to what extent the IFG and SI: 1) are necessary for perceptual processing of the dynamic facial movements that constitute the observed emotional expressions; or 2) play a role in higher level explicit inferences about the emotional feelings underlying those facial movements (possibly via access to stored knowledge in affective brain regions). Our study provides evidence supporting the latter hypothesis. Indeed, one important feature of our findings is that rTMS over the IFG and SI selectively disrupted performance on the EA task but not on the NS task. Similarly to the EA task, the NS task required participants to monitor and track facial movements. Thus, we suggest that rTMS over sensorimotor regions did not simply interfere with visual processing of facial movements. Rather, rTMS disrupted sensorimotor processing necessary for making sense of those movements and inferring the underlying emotional feelings.

Altering Facial Feedback Does Not Affect EA

Our study appears to support an “as-if” loop hypothesis (Damasio 1994; Adolphs et al. 2000; Atkinson 2007; Wood et al. 2016) more than the classical facial feedback hypothesis (for

excellent reviews, see [Goldman and Sripada 2005](#); [Niedenthal et al. 2010](#)), as we obtained behavioral impairments while interfering with cortical sensorimotor networks for moving and sensing the face (rTMS over the IFG and SI), but not while interfering with peripheral facial muscles (PS stimulation). However, our findings do not necessarily speak against the facial feedback hypothesis or conflict with the evidence that altering facial feedback impairs recognition of emotional expressions. Effective manipulations of facial feedback typically require participants to constantly bite a pen ([Oberman et al. 2007](#)), to wear mouthguards ([Rychlowska et al. 2014](#)), or to prevent mimicry over time, either intentionally ([Davis et al. 2009](#)) or as a consequence of botulinum toxin-induced denervation of target muscles ([Neal and Chartrand 2011](#)). On the other hand, manipulations like chewing gum that only transiently alter facial mimicry (and somatosensory facial feedback) are not effective at altering emotion recognition ([Oberman et al. 2007](#)). It should be noted that our PS stimulation was not designed to constantly alter facial feedback during observation of smiles, but rather to mimic the potential peripheral consequences of rTMS, that is, the transient contractions of facial muscles. Thus, while our data do not conflict with the facial feedback hypothesis, they can firmly rule out that rTMS-induced facial contractions per se are the key factor driving our EA impairments.

It should further be considered that effective facial feedback manipulations reported in the literature are sensorimotor rather than purely somatosensory in nature, as they also entail altered facial motor commands. However, many of these manipulations also plausibly alter several brain processes (e.g., they may reduce attention or increase cognitive load) in addition to affecting sensorimotor brain regions controlling and sensing facial movements. Therefore, our study extends prior behavioral research by showing that selective targeting of cortical face representations in the IFG and SI disrupts EA performance. Indeed, based on our findings, it could be suggested that sensorimotor regions like the IFG and SI may mediate the behavioral effects that are known to be induced by altering facial feedback.

Mentalizing Network and EA

Our study provides insights into the neural bases of EA under conditions in which explicit inferences about another's emotional feelings can be drawn only on the basis of social cues. Indeed, similarly to [McGettigan and colleagues \(2015\)](#), our dynamic social cues were not embedded in a context that could provide information about "why" the actors were smiling. Thus, in these experimental conditions the mentalizing network would have little information to work with. The lack of any causal effect with mPFC and TPJ stimulation is nonetheless informative for interpreting apparent discrepancies in the literature. Indeed, previous imaging studies have shown that watching deceptive actions ([Grèzes et al. 2004](#)) and discriminating between authentic and false emotional vocal expressions ([Drolet et al. 2012](#)) activate a mentalizing network encompassing the mPFC and TPJ regions, and this network was found to predict accurate emotion recognition, as in the study of [McGettigan et al. \(2015\)](#). It could thus be suggested that an attempt to infer another's mental state—even if based on social cues only—might be sufficient to trigger neural activity in the mentalizing network, even when the social cues are not contextually embedded. Our study suggests that, under these conditions, activity in mentalizing areas is epiphenomenal to mental state inference from observed social cues (e.g., the

amusement behind a smile), which critically relies on sensorimotor networks.

A possible limitation of our study is that we provided only a simple dissociation and, in principle, associative regions like the mPFC and TPJ may require higher stimulation intensities to show sensitivity to rTMS interference. However, targeting these regions at intensities comparable to those used here successfully affected performance in tasks requiring participants to draw inferences and consider another's mental state based on prior knowledge or contextual information ([Costa et al. 2008](#); [Young et al. 2010](#); [Ferrari et al. 2016](#)), making it unlikely that rTMS intensity could explain site-specific effects in our study (for a review of brain stimulation studies addressing the mentalizing network, see [Héту et al. 2012](#)). Rather, as we have argued above, this specificity stems from the features of our EA task. Thus, future studies could manipulate task features to provide double dissociations within the same set of experiments, and/or use contextually-embedded social cues to test the generalizability of the present findings to "real-life" scenarios involving multiple sources of information.

Final Remarks

Two final issues require attention for drawing appropriate conclusions from our findings. First, although we show site-specific effects of rTMS, it is unlikely these effects are site-limited. The effect of IFG or SI stimulation might be at least partially due to the spread of TMS-induced excitation along interconnected regions ([Siebner et al. 2009](#); [Avenanti et al. 2013b](#); [Valchev et al. 2015, 2016](#)) that may have contributed to the observed impairment in EA. The IFG and SI are strongly interconnected with other parietal regions of the sensorimotor mirroring network, but also anterior insular and frontal opercular regions involved in affective sharing mechanisms of empathy ([Wicker et al. 2003](#); [Gallese et al. 2004](#); [Jabbi and Keysers 2008](#); [Lamm et al. 2011](#)). Therefore, in keeping with simulationist models ([Goldman and Sripada 2005](#); [Niedenthal et al. 2010](#); [Wood et al. 2016](#)), it is possible that interconnected affective regions—possibly involved in emotional rather than sensorimotor simulation—may contribute to explicit inferences about the authenticity of amused expressions.

Second, while it is widely assumed that seeing emotional facial expressions triggers sensorimotor simulation in the observer's IFG and SI face representation—and, indeed, we may have interfered with simulation processes necessary for EA—caution is needed when using such reverse inference logic because IFG and SI functioning may include additional processes ([Avenanti et al. 2013b](#); [Borgomaneri et al. 2015](#); [Press and Cook 2015](#); [Zaki et al. 2016](#)). For example, studies have suggested that cortical motor areas (near to or interconnected with the sector of the IFG we have stimulated) may be involved in interval timing or orienting processes ([Eimer et al. 2005](#); [Schubotz 2007](#); [Coull et al. 2008](#); [Borgomaneri et al. 2015](#); [Press and Cook 2015](#)), which in turn could contribute to processing the temporal dynamics of facial expressions, and thus to EA task performance. Although these domain-general motor system processes themselves have been interpreted within the simulation framework ([Schubotz, 2007](#)), the possibility that our rTMS effects were partially due to interference with nonsimulative processes should not be excluded. This does not undervalue our findings that the IFG and SI are crucial for EA, as it is theoretically plausible that domain-general processes could contribute to domain-specific social cognitive functions ([Michael and D'Ausilio 2015](#)). Yet, our study allows us to

conclude that, under our experimental conditions, EA performance is grounded in sensorimotor networks that are primarily involved in controlling face movements and sensing feelings from the face.

Supplementary Material

Supplemental material can be found at www.cercor.oxfordjournals.org/.

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Notes

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References

- Abe J, Beetham M, Izard C. 2002. What do smiles mean? An analysis in terms of differential emotions theory. In: Abe M, editor. *An empirical reflection on the smile*. Lewiston (NY): Edwin Mellen Press. p. 83–110.
- Adolphs R. 2002. Recognizing emotion from facial expressions: psychological and neurological mechanisms. *Behav Cogn Neurosci Rev*. 1:21–62.
- Adolphs R, Damasio H, Tranel D, Cooper G, Damasio AR. 2000. A role for somatosensory cortices in the visual recognition of emotion as revealed by three-dimensional lesion mapping. *J Neurosci*. 20:2683–2690.
- Ambadar Z, Cohn J, Reed L. 2009. All smiles are not created equal: morphology and timing of smiles perceived as amused, polite, and embarrassed/nervous. *J Nonverbal Behav*. 33:17–34.
- Amodio DM, Frith CD. 2006. Meeting of minds: the medial frontal cortex and social cognition. *Nat Rev Neurosci*. 7: 268–277.
- Atkinson A. 2007. Face processing and empathy. In: Farrow T, Woodruff P, editors. *Empathy in mental illness*. Cambridge (UK): Cambridge University Press. p. 360–386.
- Avenanti A, Annella L, Candidi M, Urgesi C, Aglioti SM. 2013a. Compensatory plasticity in the action observation network: virtual lesions of STS enhance anticipatory simulation of seen actions. *Cereb Cortex*. 23:570–580.
- Avenanti A, Annella L, Serino A. 2012. Suppression of premotor cortex disrupts motor coding of peripersonal space. *Neuroimage*. 63:281–288.
- Avenanti A, Bolognini N, Maravita A, Aglioti SM. 2007. Somatic and motor components of action simulation. *Curr Biol*. 17: 2129–2135.
- Avenanti A, Buetti D, Galati G, Aglioti SM. 2005. Transcranial magnetic stimulation highlights the sensorimotor side of empathy for pain. *Nat Neurosci*. 8:955–960.
- Avenanti A, Candidi M, Urgesi C. 2013b. Vicarious motor activation during action perception: beyond correlational evidence. *Front Hum Neurosci*. 7:185.
- Avenanti A, Minio-Paluello I, Bufalari I, Aglioti SM. 2009. The pain of a model in the personality of an onlooker: influence of state-reactivity and personality traits on embodied empathy for pain. *Neuroimage*. 44:275–283.
- Batson CD. 2011. These things called empathy. In: Decety J, Ickes W, editors. *The Social Neuroscience of Empathy*. Cambridge (MA): The MIT Press. p. 3–16.
- Bird G, Viding E. 2014. The self to other model of empathy: providing a new framework for understanding empathy impairments in psychopathy, autism, and alexithymia. *Neurosci Biobehav Rev*. 47:520–532.
- Bolognini N, Rossetti A, Fusaro M, Vallar G, Miniussi C. 2014. Sharing social touch in the primary somatosensory cortex. *Curr Biol*. 24:1513–1517.
- Borgomaneri S, Gazzola V, Avenanti A. 2015. Transcranial magnetic stimulation reveals two functionally distinct stages of motor cortex involvement during perception of emotional body language. *Brain Struct Funct*. 220:2765–2781.
- Bzdok D, Schilbach L, Vogeley K, Schneider K, Laird AR, Langner R, Eickhoff SB. 2012. Parsing the neural correlates of moral cognition: ALE meta-analysis on morality, theory of mind, and empathy. *Brain Struct Funct*. 217:783–796.
- Carducci F, Brusco R. 2012. Accuracy of an individualized MR-based head model for navigated brain stimulation. *Psychiatry Res*. 203:105–108.
- Carr L, Iacoboni M, Dubeau M-C, Mazziotta JC, Lenzi GL. 2003. Neural mechanisms of empathy in humans: a relay from neural systems for imitation to limbic areas. *Proc Natl Acad Sci USA*. 100:5497–5502.
- Caspers S, Zilles K, Laird AR, Eickhoff SB. 2010. ALE meta-analysis of action observation and imitation in the human brain. *Neuroimage*. 50:1148–1167.
- Corradi-Dell'Acqua C, Hofstetter C, Vuilleumier P. 2011. Felt and seen pain evoke the same local patterns of cortical activity in insular and cingulate cortex. *J Neurosci*. 31:17996–18006.
- Costa A, Torriero S, Oliveri M, Caltagirone C. 2008. Prefrontal and temporo-parietal involvement in taking others' perspective: TMS evidence. *Behav Neurol*. 19:71–74.
- Costa T, Cauda F, Crini M, Tatu M-K, Celeghin A, de Gelder B, Tamietto M. 2014. Temporal and spatial neural dynamics in the perception of basic emotions from complex scenes. *Soc Cogn Affect Neurosci*. 9:1690–1703.
- Coull JT, Nazarian B, Vidal F. 2008. Timing, storage, and comparison of stimulus duration engage discrete anatomical components of a perceptual timing network. *J Cogn Neurosci*. 20:2185–2197.
- D'Agata F, Caroppo P, Baudino B, Caglio M, Croce M, Bergui M, Tamietto M, Mortara P, Orsi L. 2011. The recognition of facial emotions in spinocerebellar ataxia patients. *Cerebellum*. 10: 600–610.
- Damasio AR. 1994. *Descartes' error: emotion, reason and the human brain*. New York City: Grosset/Putnam.
- Dapretto M, Davies M, Pfeifer J. 2006. Understanding emotions in others: mirror neuron dysfunction in children with autism spectrum disorders. *Nat Neurosci*. 9:28–30.
- Davis JI, Senghas A, Ochsner KN. 2009. How does facial feedback modulate emotional experience? *J Res Pers*. 43:822–829.
- de Gelder B, Hortensius R, Tamietto M. 2012. Attention and awareness each influence amygdala activity for dynamic bodily expressions—a short review. *Front Integr Neurosci*. 6:54.
- de Vignemont F, Singer T. 2006. The empathic brain: how, when and why? *Trends Cogn Sci*. 10:435–441.
- Decety J. 2011. The neuroevolution of empathy. *Ann NY Acad Sci*. 1231:35–45.

- Decety J, Norman GJ, Berntson GG, Cacioppo JT. 2012. A neuro-behavioral evolutionary perspective on the mechanisms underlying empathy. *Prog Neurobiol*. 98:38–48.
- Dresel C, Parzinger A, Rimpau C, Zimmer C, Ceballos-Baumann AO, Haslinger B. 2008. A new device for tactile stimulation during fMRI. *Neuroimage*. 39:1094–1103.
- Drolet M, Schubotz R, Fischer J. 2012. Authenticity affects the recognition of emotions in speech: behavioral and fMRI evidence. *Cogn Affect Behav Neurosci*. 12:140–150.
- Eimer M, Forster B, Van Velzen J, Prabhu G. 2005. Covert manual response preparation triggers attentional shifts: ERP evidence for the premotor theory of attention. *Neuropsychologia*. 43:957–966.
- Ekman P. 2001. *Telling lies: clues to deceit in the marketplace, politics, and marriage*. New York (NY): Norton.
- Ekman P, Friesen WV, Hager JC. 2002. *Facial action coding system*. Salt Lake City: A Human Face.
- Fan J, Gu X, Liu X, Guise KG, Park Y, Martin L, de Marchena A, Tang CY, Minzenberg MJ, Hof PR. 2011. Involvement of the anterior cingulate and frontoinsula cortices in rapid processing of salient facial emotional information. *Neuroimage*. 54:2539–2546.
- Ferrari C, Lega C, Vernice M, Tamietto M, Mende-Siedlecki P, Vecchi T, Todorov A, Cattaneo Z. 2016. The dorsomedial prefrontal cortex plays a causal role in integrating social impressions from faces and verbal descriptions. *Cereb Cortex*. 26:156–165.
- Frith CD, Frith U. 2006. The neural basis of mentalizing. *Neuron*. 50:531–534.
- Gallese V. 2007. Before and below “theory of mind”: embodied simulation and the neural correlates of social cognition. *Philos Trans R Soc Lond B Biol Sci*. 362:659–669.
- Gallese V, Gernsbacher MA, Heyes C, Hickok G, Iacoboni M. 2011. Mirror neuron forum. *Perspect Psychol Sci*. 6:369–407.
- Gallese V, Keysers C, Rizzolatti G. 2004. A unifying view of the basis of social cognition. *Trends Cogn Sci*. 8:396–403.
- Gallese V, Sinigaglia C. 2011. What is so special about embodied simulation? *Trends Cogn Sci*. 15:512–519.
- Gazzola V, Aziz-Zadeh L, Keysers C. 2006. Empathy and the somatotopic auditory mirror system in humans. *Curr Biol*. 16:1824–1829.
- Goldman AI, Sripada CS. 2005. Simulationist models of face-based emotion recognition. *Cognition*. 94:193–213.
- Grèzes J, Frith C, Passingham RE. 2004. Brain mechanisms for inferring deceit in the actions of others. *J Neurosci*. 24:5500–5505.
- Grosbras MH, Beaton S, Eickhoff SB. 2012. Brain regions involved in human movement perception: a quantitative voxel-based meta-analysis. *Hum Brain Mapp*. 33:431–454.
- Harmer CJ, Thilo KV, Rothwell JC, Goodwin GM. 2001. Transcranial magnetic stimulation of medial-frontal cortex impairs the processing of angry facial expressions. *Nat Neurosci*. 4:17–18.
- Harvey PO, Zaki J, Lee J, Ochsner K, Green MF. 2013. Neural substrates of empathic accuracy in people with schizophrenia. *Schizophr Bull*. 39:617–628.
- Héту S, Taschereau-Dumouchel V, Jackson PL. 2012. Stimulating the brain to study social interactions and empathy. *Brain Stimul*. 5:95–102.
- Holle H, Banissy MJ, Ward J. 2013. Functional and structural brain differences associated with mirror-touch synaesthesia. *Neuroimage*. 83:1041–1050.
- Huang RS, Sereno MI. 2007. Dodecapus: an MR-compatible system for somatosensory stimulation. *Neuroimage*. 34:1060–1073.
- Ickes W. 1997. *Empathic accuracy*. New York (NY): The Guilford Press.
- Ickes W, Stinson L. 1990. Naturalistic social cognition: empathic accuracy in mixed-sex dyads. *J Pers Soc Psychol*. 59:730–742.
- Jabbi M, Keysers C. 2008. Inferior frontal gyrus activity triggers anterior insula response to emotional facial expressions. *Emotion*. 8:775–780.
- Jacquet PO, Avenanti A. 2015. Perturbing the action observation network during perception and categorization of actions’ goals and grips: state-dependency and virtual lesion TMS effects. *Cereb Cortex*. 25:598–608.
- Keysers C, Gazzola V. 2007. Integrating simulation and theory of mind: from self to social cognition. *Trends Cogn Sci*. 11:194–196.
- Keysers C, Kaas JH, Gazzola V. 2010. Somatosensation in social perception. *Nat Rev Neurosci*. 11:417–428.
- Kopietz R, Sakar V, Albrecht J, Kleemann AM, Schöpf V, Yousry I, Linn J, Fesl G, Wiesmann M. 2009. Activation of primary and secondary somatosensory regions following tactile stimulation of the face. *Klin Neuroradiol*. 19:135–144.
- Krumhuber E, Manstead ASR. 2009. Can Duchenne smiles be feigned? New evidence on felt and false smiles. *Emotion*. 9:807–820.
- Lamm C, Bukowski H, Silani G. 2016. From shared to distinct self-other representations in empathy: evidence from neurotypical function and socio-cognitive disorders. *Philos Trans R Soc Lond B Biol Sci*. 371:20150083.
- Lamm C, Decety J, Singer T. 2011. Meta-analytic evidence for common and distinct neural networks associated with directly experienced pain and empathy for pain. *Neuroimage*. 54:2492–2502.
- Lamm C, Majdandžić J. 2015. The role of shared neural activations, mirror neurons, and morality in empathy—a critical comment. *Neurosci Res*. 90:15–24.
- Leslie KR, Johnson-Frey SH, Grafton ST. 2004. Functional imaging of face and hand imitation: towards a motor theory of empathy. *Neuroimage*. 21:601–607.
- Levenson RW, Ruef AM. 1992. Empathy: a physiological substrate. *J Pers Soc Psychol*. 63:234–246.
- Lombardo MV, Chakrabarti B, Bullmore ET, Wheelwright SJ, Sadek SA, Suckling J, Baron-Cohen S. 2010. Shared neural circuits for mentalizing about the self and others. *J Cogn Neurosci*. 22:1623–1635.
- Macmillan NA, Creelman CD. 1991. *Detection theory: a user’s guide*. New York: Psychology Press.
- Mar RA. 2011. The neural bases of social cognition and story comprehension. *Annu Rev Psychol*. 62:103–134.
- Mattavelli G, Cattaneo Z, Papagno C. 2011. Transcranial magnetic stimulation of medial prefrontal cortex modulates face expressions processing in a priming task. *Neuropsychologia*. 49:992–998.
- Mattavelli G, Rosanova M, Casali AG, Papagno C, Romero Lauro LJ. 2013. Top-down interference and cortical responsiveness in face processing: a TMS-EEG study. *Neuroimage*. 76:24–32.
- McGettigan C, Walsh E, Jessop R, Agnew ZK, Sauter DA, Warren JE, Scott SK. 2015. Individual differences in laughter perception reveal roles for mentalizing and sensorimotor systems in the evaluation of emotional authenticity. *Cereb Cortex*. 25:246–257.

- McLellan T, Johnston L, Dalrymple-Alford J, Porter R. 2010. Sensitivity to genuine versus posed emotion specified in facial displays. *Cogn Emot.* 24:1277–1292.
- Michael J, D'Ausilio A. 2015. Domain-specific and domain-general processes in social perception—A complementary approach. *Conscious Cogn.* 36:434–437.
- Michael J, Sandberg K, Skewes J, Wolf T, Blicher J, Overgaard M, Frith CD. 2014. Continuous theta-burst stimulation demonstrates a causal role of premotor homunculus in action understanding. *Psychol Sci.* 25:963–972.
- Mitchell JP. 2009. Inferences about mental states. *Philos Trans R Soc Lond B Biol Sci.* 364:1309–1316.
- Molenberghs P, Cunnington R, Mattingley JB. 2009. Is the mirror neuron system involved in imitation? A short review and meta-analysis. *Neurosci Biobehav Rev.* 33:975–980.
- Neal DT, Chartrand TL. 2011. Embodied emotion perception: amplifying and dampening facial feedback modulates emotion perception accuracy. *Soc Psychol Personal Sci.* 2: 673–678.
- Niedenthal PM, Mermillod M, Maringer M, Hess U. 2010. The Simulation of smiles (SIMS) model: embodied simulation and the meaning of facial expression. *Behav Brain Sci.* 33: 417–433; discussion 433–480.
- Oberman LM, Winkielman P, Ramachandran VS. 2007. Face to face: blocking facial mimicry can selectively impair recognition of emotional expressions. *Soc Neurosci.* 2:167–178.
- Pazzaglia M, Pizzamiglio L, Pes E, Aglioti SM. 2008. The sound of actions in apraxia. *Curr Biol.* 18:1766–1772.
- Pfeifer JH, Iacoboni M, Mazziotta JC, Dapretto M. 2008. Mirroring others' emotions relates to empathy and interpersonal competence in children. *Neuroimage.* 39:2076–2085.
- Pitcher D, Garrido L, Walsh V, Duchaine BC. 2008. Transcranial magnetic stimulation disrupts the perception and embodiment of facial expressions. *J Neurosci.* 28:8929–8933.
- Pobric G, Hamilton AF. 2006. Action understanding requires the left inferior frontal cortex. *Curr Biol.* 16:524–529.
- Press C, Cook R. 2015. Beyond action-specific simulation: domain-general motor contributions to perception. *Trends Cogn Sci.* 19:176–178.
- Preston SD, de Waal FBM. 2002. Empathy: its ultimate and proximate bases. *Behav Brain Sci.* 25:1–20; discussion 20–71.
- Raz G, Jacob Y, Gonen T, Winetraub Y, Flash T, Soreq E, Hendler T. 2014. Cry for her or cry with her: Context-dependent dissociation of two modes of cinematic empathy reflected in network cohesion dynamics. *Soc Cogn Affect Neurosci.* 9: 30–38.
- Redcay E, Dodell-Feder D, Pearrow MJ, Mavros PL, Kleiner M, Gabrieli JDE, Saxe R. 2010. Live face-to-face interaction during fMRI: a new tool for social cognitive neuroscience. *Neuroimage.* 50:1639–1647.
- Rychlowska M, Cañadas E, Wood A, Krumhuber EG, Fischer A, Niedenthal PM. 2014. Blocking mimicry makes true and false smiles look the same. *PLoS One.* 9 (3):e90876.
- Rossi S, Hallett M, Rossini PM, Pascual-Leone A. 2009. Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. *Clin Neurophysiol.* 120:2008–2039.
- Rossini PM, Burke D, Chen R, Cohen LG, Daskalakis Z, Di Iorio R, Di Lazzaro V, Ferreri F, Fitzgerald PB, George MS, et al. 2015. Non-invasive electrical and magnetic stimulation of the brain, spinal cord, roots and peripheral nerves: basic principles and procedures for routine clinical and research application. An updated report from an I.F.C.N. Committee. *Clin Neurophysiol.* 126:1071–1107.
- Rütgen M, Seidel E-M, Riečanský I, Lamm C. 2015a. Reduction of empathy for pain by placebo analgesia suggests functional equivalence of empathy and first-hand emotion experience. *J Neurosci.* 35:8938–8947.
- Rütgen M, Seidel EM, Silani G, Riečanský I, Hummer A, Windischberger C, Petrovic P, Lamm C. 2015b. Placebo analgesia and its opioidergic regulation suggest that empathy for pain is grounded in self pain. *Proc Natl Acad Sci USA.* 112:E5638–E5646.
- Saxe R. 2006. Uniquely human social cognition. *Curr Opin Neurobiol.* 16:235–239.
- Schippers MB, Roebroeck A, Renken R, Nanetti L, Keysers C. 2010. Mapping the information flow from one brain to another during gestural communication. *Proc Natl Acad Sci USA.* 107:9388–9393.
- Schubotz RI. 2007. Prediction of external events with our motor system: towards a new framework. *Trends Cogn Sci.* 11: 211–218.
- Schulte-Rüther M, Markowitsch HJ, Fink GR, Piefke M. 2007. Mirror neuron and theory of mind mechanisms involved in face-to-face interactions: a functional magnetic resonance imaging approach to empathy. *J Cogn Neurosci.* 19:1354–1372.
- Shiota MN, Campos B, Keltner D. 2003. The faces of positive emotion: prototype displays of awe, amusement, and pride. *Ann NY Acad Sci.* 1000:296–299.
- Siebnner HR, Hartwigsen G, Kassuba T, Rothwell JC. 2009. How does transcranial magnetic stimulation modify neuronal activity in the brain? Implications for studies of cognition. *Cortex.* 45:1035–1042.
- Singer T, Lamm C. 2009. The social neuroscience of empathy. *Ann NY Acad Sci.* 1156:81–96.
- Singer T, Seymour B, O'Doherty J, Kaube H, Dolan RJ, Frith CD. 2004. Empathy for pain involves the affective but not sensory components of pain. *Science.* 303:1157–1162.
- Spunt R, Lieberman M. 2013. The busy social brain evidence for automaticity and control in the neural systems supporting social cognition and action understanding. *Psychol Sci.* 24: 80–86.
- Tamietto M, Cauda F, Celegghin A, Diano M, Costa T, Cossa FM, Sacco K, Duca S, Geminiani GC, de Gelder B. 2015. Once you feel it, you see it: insula and sensory-motor contribution to visual awareness for fearful bodies in parietal neglect. *Cortex.* 62:56–72.
- Tidoni E, Borgomaneri S, di Pellegrino G, Avenanti A. 2013. Action simulation plays a critical role in deceptive action recognition. *J Neurosci.* 33:611–623.
- Uddin LQ, Iacoboni M, Lange C, Keenan JP. 2007. The self and social cognition: the role of cortical midline structures and mirror neurons. *Trends Cogn Sci.* 11:153–157.
- Uithol S, Van Rooij I, Bekkering H, Haselager P. 2011. What do mirror neurons mirror? *Philos Psychol.* 24:607–623.
- Urgesi C, Candidi M, Avenanti A. 2014. Neuroanatomical substrates of action perception and understanding: an anatomic likelihood estimation meta-analysis of lesion-symptom mapping studies in brain injured patients. *Front Hum Neurosci.* 8:344.
- Valchev N, Čurčić-Blake B, Renken RJ, Avenanti A, Keysers C, Gazzola V, Maurits NM. 2015. cTBS delivered to the left somatosensory cortex changes its functional connectivity during rest. *Neuroimage.* 114:386–397.
- Valchev N, Gazzola V, Avenanti A, Keysers C. 2016. Primary somatosensory contribution to action observation brain activity—combining fMRI and cTBS. *Soc Cogn Affect Neurosci.* 11:1205–1217.

- van Overwalle F, Baetens K. 2009. Understanding others' actions and goals by mirror and mentalizing systems: a meta-analysis. *Neuroimage*. 48:564–584.
- Warren JE, Sauter D a, Eisner F, Wiland J, Dresner MA, Wise RJS, Rosen S, Scott SK. 2006. Positive emotions preferentially engage an auditory-motor “mirror” system. *J Neurosci*. 26: 13067–13075.
- Wheatley T, Milleville SC, Martin A. 2007. Understanding animate agents: distinct roles for the social network and mirror system. *Psychol Sci*. 18:469–474.
- Wicker B, Keysers C, Plailly J, Royet JP, Gallese V, Rizzolatti G. 2003. Both of us disgusted in my insula: the common neural basis of seeing and feeling disgust. *Neuron*. 40:655–664.
- Winston J, O'Doherty J, Dolan R. 2003. Common and distinct neural responses during direct and incidental processing of multiple facial emotions. *Neuroimage*. 20:84–97.
- Wolf I, Dziobek I, Heekeren HR. 2010. Neural correlates of social cognition in naturalistic settings: a model-free analysis approach. *Neuroimage*. 49:894–904.
- Wood A, Rychlowska M, Korb S, Niedenthal P. 2016. Fashioning the face: sensorimotor simulation contributes to facial expression recognition. *Trends Cogn Sci*. 20:1–14.
- Young L, Camprodon JA, Hauser M, Pascual-Leone A, Saxe R. 2010. Disruption of the right temporoparietal junction with transcranial magnetic stimulation reduces the role of beliefs in moral judgments. *Proc Natl Acad Sci U S A*. 107:6753–6758.
- Zaki J. 2014. Empathy: a motivated account. *Psychol Bull*. 140: 1608–1647.
- Zaki J, Bolger N, Ochsner K. 2008. It takes two: the interpersonal nature of empathic accuracy. *Psychol Sci*. 19:399–404.
- Zaki J, Ochsner KN, Ochsner K. 2012. The neuroscience of empathy: progress, pitfalls and promise. *Nat Neurosci*. 15:675–680.
- Zaki J, Wager TD, Singer T, Keysers C, Gazzola V. 2016. The anatomy of suffering: understanding the relationship between nociceptive and empathic pain. *Trends Cogn Sci*. 20:249–259.
- Zaki J, Weber J, Bolger N, Ochsner K. 2009. The neural bases of empathic accuracy. *Proc Natl Acad Sci USA*. 106:11382–11387.