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# Freezing or escaping? Opposite modulations of empathic reactivity to the pain of others

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ABSTRACT

Perceiving pain in others may induce the covert simulation of both sensory and emotional components of others' pain experience. Previous transcranial magnetic stimulation (TMS) studies have investigated the motor counterpart of this resonant mapping by showing suppression of motor-evoked potentials (MEPs) during the observation of a needle entering body parts of another person. Here we explored whether MEPs recorded from an onlooker's hand (e.g., the right hand, TMS to the left motor cortex) are differentially influenced by the observation of painfully stimuli delivered to the same (right) or the opposite (left) hand in a model. Congruency between observed (model) and recorded (onlooker) hand brought about a reduction of MEPs amplitude. This resonant inhibitory response in the onlooker was specific for the muscle penetrated in the model. In contrast, observing pain on the model's hand opposite to that from which MEPs were recorded brought about a generalized increase of hand corticospinal excitability. Corticospinal inhibition and facilitation effects were comparable in the two hemispheres and specific for the corresponding and opposite hand. Results suggest that observing pain in another person's hand automatically induces the covert simulation of potentially adaptive freezing and avoidance responses in the onlooker's corticospinal system.


## 1. Introduction

Studies suggest that observing or imagining the pain of others activates neural circuits largely overlapping with those involved in the first-hand experience of pain (Avenanti and Aglioti, 2006). These circuits comprise both regions processing the affective dimension of pain (e.g., the unpleasantness of a noxious stimulus), such as the anterior insula and the anterior cingulate cortex (Singer et al., 2004), and regions processing the sensory dimension of pain (e.g., intensity, localization of a noxious stimulus) including the somatosensory cortices (Bufalari et al., 2007; Lamm et al., 2007; Cheng et al., 2008; Benuzzi et al., 2008; Valeriani et al., 2008). Using single-pulse transcranial magnetic stimulation (TMS) it has been demonstrated that the direct observation of 'flesh and bone' painful stimulations delivered to the body of a stranger human model brings about a decrease of amplitude of motor-evoked potentials (MEPs) in the onlooker (Avenanti et al., 2005; Fecteau et al., 2008). Importantly, this inhibition was specific to the muscle the subjects observed being painfully stimulated and correlated with the evaluations of the intensity (Avenanti et al., 2006, 2009) and spread (Minio-Paluello et al., 2006) of the pain ascribed to the observed model,

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suggesting that corticospinal inhibition may reflect a 'sensorimotor contagion', i.e., an automatic embodiment of sensory qualities of pain onto the observers' motor system.

What remains unclear if whether observing painful stimuli on the body of another person may induce a more complex modulation of the onlooker's motor system in addition to the resonant freezing response of the muscle vicariously involved in the painful stimulation. In principle, feeling pain on one hand may be associated to a higher reactivity of the opposite hand that can be used to try and reduce the effect of the noxious stimulus (Melzack and Casey, 1968; Williams, 2002). Therefore, it is possible that the sensorimotor contagion contingent upon the vicarious feeling of others' pain may involve not only corticospinal inhibition of the hand corresponding to that painfully stimulated in the other person (freezing) but also corticospinal facilitation of the hand opposite to the one stimulated in the model (implementation of reactions aimed at reducing pain, escaping).

We explored this issue in two groups of participants who undergone single-pulse TMS over the left or right motor cortex (M1) while they observed needles entering both the right and the left hand of a stranger model. Corticospinal reactivity to the model's pain was recorded from both the left and the right hand of the experimental subjects in order to explore the relationship between the model and the onlookers' hands and hemispheres.

## 2. Methods

### 2.1. *Participants*

Twenty-four right-handed subjects (10 men, mean age 25 y, range 21–32) free from any contraindication to TMS gave their written informed consent to take part in the study and were paid for their participation. The study was approved by Fondazione Santa Lucia ethics committee and was carried out in accordance with the ethical standards of the 1964 Declaration of Helsinki. No discomfort or adverse effects during TMS were reported or noticed.

### 2.2. *Visual stimuli*

Different types of video-clips were presented on a 19-inch screen located 80 cm away from the participants. Video-clips showed the following: (i) fixation cross; the static view of the dorsal surface of (ii) a right or (iii) a left hand of a stranger male model depicted from a first-person view point; needle deeply penetrating the first dorsal interosseus (FDI) muscle of the same (iv) right or (iv) left hand. To minimize habituation, three different versions of the stimuli were presented. All the videos had been already used in our previous studies (Avenanti et al., 2005; Minio-Paluello et al., 2006).

### 2.3. *TMS and electromyographic (EMG) recording*

MEPs were recorded simultaneously from the FDI muscle (in the dorsal region of the hand between the index finger and the thumb) and the thenar eminence (TE, on the palm region just beneath the thumb) by means of a Viking IV (Nicolet biomedical, U.S.A.) electromyograph. EMG signals were band-pass filtered (20–2.5 kHz, sampling rate fixed at 10 kHz), digitized and stored on a computer for off-line analysis. Twelve subjects (6 men, mean age 25 y) received TMS over their left M1 and twelve subjects (4 men, mean age 25 y) over their right M1 while MEPs were recorded from the contralateral FDI and TE muscles. Thus, in subjects who received TMS over the left M1, MEPs were recorded from the right hand during presentation of right (congruent) and left (opposite) hand stimuli. By the same token, in the subjects who received TMS over the right M1 MEPs were recorded from the left hand during presentation of left (congruent) and right (opposite) hand stimuli.

Pairs of Ag–AgCl surface electrodes were placed in a belly-tendon montage on each muscle, with further ground electrodes on the wrist. A figure-of-8 coil connected to a Magstim Super Rapid Transcranial Magnetic Stimulator (Magstim, Whitland, U.K.) was placed over the motor cortex (with the handle pointing backward at 45° from the midline) contralateral to the recorded muscles. The optimum scalp position (OSP) was chosen so as to produce maximum amplitude MEPs in the FDI muscle. Pulse intensity was set at 120% of the resting motor threshold (rMT), defined as the lowest level of stimulation able to induce MEPs of at least 50 μV in both muscles with 50% probability. Thus, in each subject, the rMT was based on the higher threshold muscle. This way a stable signal could be recorded from both muscles. Importantly, previous studies suggest that modulations due to pain observation are independent from the chosen OSP (Avenanti et al., 2005, 2006), at least when the two recording muscles have a contiguous motor representation in the cortex. The absence of voluntary contraction before the TMS pulse was continuously verified visually and, prior to the recording session, by auditory monitoring of the EMG signal.

### 2.4. *Procedure*

The experiment was programmed using Matlab software to control video-clips, and to trigger EMG and TMS. Each type of video-clip was presented in separate blocks. This block-design paradigm has been proved to be adept to explore the corticospinal response to others' pain in previous research (e.g., Avenanti et al., 2005; Fecteau et al., 2008). The first and the last block served as baseline and consisted of video-clips showing the fixation cross. The order of the other four blocks (congruent static hand, pain on congruent hand, opposite static hand, pain on opposite hand) was counterbalanced. The fixations blocks consisted of 15 trials each, the static hand and pain blocks consisted of 18 trials each.

In each block, a central cross (1000 msec duration) indicated the beginning of a trial and initiated EMG recording. The duration of each video was 1800 msec. In each trial, a magnetic pulse was randomly delivered between 200 and 600 msec before the end of the movie to avoid any priming effects that could affect MEP size. A black screen was shown for 7.2 sec in the intertrial intervals.

In all observation conditions, participants were asked to pay attention to the events shown in the video-clips and to focus on what the stimulated individual may have felt. After each TMS session, subjects were presented with all pain videos and asked to rate the intensity of the pain ascribed to