Clinical Neurophysiology 126 (2015) 1212–1220

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Observing and perceiving: A combined approach to induce plasticity in human motor cortex

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See Editorial, pages 1065–1066

ARTICLE INFO

Article history:
Accepted 30 August 2014
Available online 2 October 2014

Keywords:
Plasticity
Action observation
Peripheral nerve electrical stimulation
Motor cortex
Transcranial magnetic stimulation

HIGHLIGHTS

- Action observation combined with peripheral electrical nerve stimulation (AO–PNS) increased M1 excitability.
- AO–PNS effects on M1 excitability occurred rapidly and were long-lasting (up to 45 min).
- AO–PNS effects were specific for the stimulated muscle.

ABSTRACT

Objective: To test whether action observation combined with peripheral nerve electrical stimulation was able to evoke plasticity in the primary motor cortex (M1).
Methods: The stimulation protocol consisted in the observation of a video showing repetitive thumb-index tapping movements (AO) combined with peripheral electrical nerve stimulation (PNS) delivered on the median nerve (AO–PNS). M1 excitability, measured by means of transcranial magnetic stimulation, was compared with that assessed after AO and PNS alone.
Results: M1 excitability increased after AO–PNS, whilst no modifications occurred after AO and PNS alone. The increased M1 excitability after AO–PNS was long-lasting (45 min) and specific for the stimulated muscle.
Conclusions: This study described an innovative stimulation paradigm that exploited the mirror neuron system to induce plasticity in M1. However, this occurred only when action observation was combined with afferent signals coming from periphery.
Significance: This study supports the literature proposing the mirror neuron system as neural substrate for rehabilitation and opens a debate on the rehabilitative treatments that employ AO to improve patients' motor functions. Indeed, these results suggest that AO has to be combined with afferent inputs from periphery to evoke plasticity in the human motor system.

1. Introduction

Experimental evidence suggests that motor areas are recruited not only when actions are actually executed, but also when they are simply observed (Rizzolatti and Craighero, 2004). Indeed, neurophysiological and neuroimaging human studies based on

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http://dx.doi.org/10.1016/j.clinph.2014.08.024
1388-2457/

transcranial magnetic stimulation (TMS) (Aziz-Zadeh et al., 2002; Fadiga et al., 1995; Maeda et al., 2002; Strafella and Paus, 2000), positron emission tomography (Grafton et al., 1996; Rizzolatti et al., 1996), and functional magnetic resonance (Buccino et al., 2001; Filimon et al., 2007; Gazzola and Keysers, 2009) demonstrated an increased primary motor cortex (M1) activity while observing human movements. At the behavioral level, it has been reported that action observation (AO) combined with the reproduction of the observed actions has a positive effect in terms of retention of information (Hodges et al., 2007; Vogt and Thomaschke, 2007). Further, it has been also shown that the AO influence may vanish if motor practice is not concurrent or immediately follows it (Bove et al., 2009; Zhang et al., 2011), indicating that the temporal distance between these two events plays a crucial role in consolidating the AO effects. Therefore, one can propose that the retention effect might be a consequence of the continuous implicit comparison between the action observed and that performed. This hypothesis could be illustrated by studies showing the motor repertoire to "resonate" with that of the observed ongoing movement (Aglioti et al., 2008; Calvo-Merino et al., 2006; Rizzolatti et al., 1999). Consequently, a prompt comparison at cortical level between two sensorimotor representations of the movement – the "observed", visual and the "experienced", somatosensory – might be necessary to induce plasticity in motor areas.

Therefore, a raising question deals with the possibility to boost the AO effect on M1 by combining AO with a concomitant somatosensory stimulation in order to evoke plastic changes in the human motor system. Here, we designed a stimulation protocol in which action observation was combined with electrical stimuli delivered on a peripheral nerve. We assumed that the afferent feedback generated by the peripheral nerve electrical stimulation could potentiate and make the well-known effects of AO on motor areas cortical excitability long lasting.

To this aim, three different conditioning protocols were investigated: Action Observation associated with Peripheral Nerve electrical Stimulation of the nerve innervating the muscle involved in the observed action (AO–PNS), Action Observation (AO) and Peripheral Nerve electrical Stimulation (PNS) alone. Left M1 excitability was explored by means of TMS before and immediately after the conditioning protocols. Further, for the AO–PNS we also evaluated the topographical specificity and the possible long term effects on M1 excitability at different testing times (i.e., 15, 30 and 45 min after the stimulation) to investigate the occurrence of plasticity in M1.

2. Methods

This work was composed of five experiments (Fig. 1). The study was conducted in accordance with the Declaration of Helsinki. Sixty-seven participants were recruited for this study. All the participants who took part in the study were naive to the purpose of the experiment. They reported no previous history of neurological disorders or orthopedic problems for the right-dominant hand – as determined by the Edinburgh Handedness Inventory (Oldfield, 1971). Subjects had no contraindication to TMS, and they participated in this study after giving an informed consent. The study has been approved by the local ethics committee.

In all the experiments, TMS was used to evaluate changes in the left M1 excitability induced by different conditioning protocols. Intensities were expressed as a percentage of the maximum output of the stimulator. TMS was performed with a single Magstim 200 magnetic stimulator (Magstim Company) connected with a figure-of-eight coil with wing diameters of 70 mm. The coil was placed tangentially to the scalp with the handle pointing backward and laterally at a 45° angle to the sagittal plane inducing a postero-anterior current in the brain. This orientation was chosen based on the findings that the lowest motor threshold is achieved when the induced electrical current flows approximately perpendicular to the line of the central sulcus (Werhahn et al., 1994). The optimal position for activation of the right abductor pollicis brevis (APB) muscle was determined by moving the coil in 0.5 cm steps around the presumed motor hand area. Prior to the experimental procedure, the intensity of stimulation was individually defined to reliably elicit peak-to-peak MEPs amplitude of approximately 1 mV in the APB muscle at rest.

Motor evoked potentials (MEPs) were recorded from the right APB muscle and the right abductor digiti minimi (ADM) muscle (ADM activity was recorded only in the Experiment 2 and 5), using silver disc surface electrodes taped to the belly and tendon of the muscles. The ground electrode was placed at the elbow. Electromyographic signals (EMG) were digitalized, amplified and filtered (20 Hz to 1 kHz) with a Biopac system, and stored on a personal computer for display and later offline data analysis. Each recording epoch lasted 400 ms, of which 100 ms preceded the TMS. Participants were constantly reminded to always keep their hand relaxed during the whole experiment. EMG signal was monitored visually by the experimenter and trials with background EMG activity were excluded from analysis.

2.1. Experiment 1: to test the phase-specific modulation of M1 excitability during action observation

Experiment 1 aimed at evaluating whether during the observation of thumb-index tapping movements left M1 excitability in the APB muscle area was modulated by the phase of this motor action, i.e., thumb-index aperture and closure.

2.1.1. Experimental protocol

Seven participants (5 females and 2 males, mean age ± std = 25.8 ± 6) took part in this experiment. Participants were requested to relax and to look at a computer screen where a video (total duration 4 s) showing a right hand performing 8 repetitive thumb-index-tapping movements at natural frequency (2 Hz) (Bove et al., 2007; McAuley et al., 2006) was displayed. This movie clip was obtained by filming on a black background the right hand of a human demonstrator who performed 8 repetitive thumb-index tapping movements paced with a metronome at 2 Hz. While observing the visual stimulus, participants' left M1 was stimulated with TMS in correspondence of APB muscle area at a predetermined intensity able to evoke a 1 mV MEPs at rest (S1 mV). No audio accompanied the video presentation. Custom-made MatLab software managed the synchronization between the presentation of the visual stimulus and the delivery of the magnetic stimulation. The magnetic stimulus was delivered while the hand was opening (2.24 s after the beginning of the video presentation) or closing (2.51 s after the beginning of the video presentation). The stimuli were presented randomly and ten MEP were recorded in each experimental condition from APB muscle.

2.1.2. Statistical analysis

The average MEPs amplitude for each condition was taken as representative MEP size. All measures were normally distributed according to the Shapiro–Wilk W test. A paired t-test was applied to compare MEPs recorded in the two experimental conditions.

2.2. Experiment 2: to test the muscle specificity of M1 excitability during thumb-index tapping movement observation

The aim of Experiment 2 was to evaluate whether during the observation of thumb-index tapping movements there was a spe-