Neuroscience Letters 653 (2017) 78–83

Contents lists available at ScienceDirect

Neuroscience Letters

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

Research article

Real-time measurement of cerebral blood flow during and after repetitive transcranial magnetic stimulation: A near-infrared spectroscopy study

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HIGHLIGHTS

- Hz rTMS influenced changes of cerebral blood flow in the unstimulated hemisphere.
- The stimulated M1 influenced the level of oxyhemoglobin in both unstimulated M1 and PM.
- It seemed to constitute a function of interhemispheric modulation of rTMS.

ARTICLE INFO

Article history:
Received 9 November 2016
Received in revised form 15 May 2017
Accepted 19 May 2017
Available online 20 May 2017

Keywords:
Near-infrared spectroscopy
Transcranial magnetic stimulation
Interhemispheric modulation
Primary motor cortex
Premotor cortex

ABSTRACT

Objectives: To confirm the interhemispheric modulation induced by low-frequency repetitive transcranial magnetic stimulation (rTMS) over the primary motor cortex, real-time regional cerebral blood flow (rCBF) was assessed using functional near-infrared spectroscopy (fNIRS) in the contralateral primary motor cortex (M1) and premotor cortex (PM).
Methods: Ten right-handed healthy subjects completed two experimental sessions that were randomly arranged for real or sham rTMS session. In the real rTMS session, fNIRS data were acquired from the right M1 and PM area, while the motor hot spot of the left M1 was stimulated with 1 Hz rTMS for 1200 pulses with two boosters. In the sham stimulation session, stimulation was delivered with a disconnected coil.
Results: During the real rTMS session, the concentration of oxyhemoglobin ([oxy-Hb]) in the right M1 increased continuously until the end of the stimulation. These changes lasted for 20 min, while the right PM did not show a change in [oxy-Hb] concentration. On the other hand, the concentration of deoxy-hemoglobin ([deoxy-Hb]) decreased continuously in the right M1 and PM during the real rTMS stimulation, and this change lasted for 20 min after the stimulation. The sham stimulation did not exhibit any significant change in both [oxy-Hb] and [deoxy-Hb] concentration during or after the stimulation.

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http://dx.doi.org/10.1016/j.neulet.2017.05.039
0304-3940/© 2017 Published by Elsevier Ireland Ltd.

Conclusions: Application of 1 Hz rTMS over M1 resulted in changes of rCBF in contralateral M1 and PM, which seemed to constitute a function of interhemispheric modulation of rTMS. The fNIRS data was able to detect this physiological change of neuromodulatory action of rTMS in real-time.

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1. Introduction

Transcranial magnetic stimulation (TMS) is a technology that is widely used in neurophysiological examinations to investigate normal brain function and various neuropsychiatric disorders [1]. It is based on electromagnetic induction of an electrical field in the brain. Repetitive transcranial magnetic stimulation (rTMS) applied to the motor cortex produces frequency-dependent changes in cortical excitability [2]. Moreover, high-frequency rTMS increases cortical excitability, as shown by the production of a persistent increase in motor evoked potentials (MEPs) amplitude, and low-frequency rTMS produces a transient reduction in cortical excitability. Repetitive TMS is also known to induce changes in the cortical excitability of the contralateral hemisphere by producing interhemispheric interaction. The effects of low-frequency stimulation on contralateral cortical excitability were investigated in some studies [3–5], and diverse results were reported. Increases in the cortical excitability of the contralateral primary motor cortex after applying 1 Hz rTMS was reported in two studies [3,5], but no change was found in another study [4]. Therefore, the interhemispheric modulation effect of low-frequency rTMS is not yet determined.

Functional near-infrared spectroscopy (fNIRS) is a tool to assess changes in regional cerebral blood flow (rCBF) by comparing the concentration of oxygenated hemoglobin ([oxy-Hb]) and deoxygenated hemoglobin ([deoxy-Hb]). The most beneficial aspect of fNIRS is the ability to record immediate hemodynamic responses in part or whole cortical regions on a real-time basis [6]. Subjects can perform some activities, or even walk, during the recording of rCBF, which constitutes another benefit of fNIRS in terms of examining rCBF changes related to movement or rehabilitative treatment [7]. Hada et al. examined the effect of low-frequency rTMS on the rCBF of the stimulated cortex [3]. They stimulated the left primary motor cortex (M1) at a frequency of 0.5 and 2 Hz and an intensity of 80% and 120% of the resting motor threshold (RMT). At stimulating 2 Hz and 120% of RMT in the stimulated M1 area, the maximum decrement of oxy- and total-Hb concentrations were approximately −0.02 mM cm (millimole centimeter) and the maximum increment of deoxy-Hb concentration was approximately +0.003 mM cm [3]. Few studies have been conducted using fNIRS to evaluate the interhemispheric modulation effect of rTMS at brain regions contralateral to the stimulated hemisphere. Chiang et al. examined the change of [oxy-Hb] and [deoxy-Hb] in the left motor cortex after applying 1 Hz rTMS over the right motor cortex for 20 min [8]. They reported that [oxy-Hb] in the contralateral motor cortex increased after 1 Hz rTMS. However, in that report, the result might have reflected the effect of hand movement to increase blood flow, because the participants performed finger tapping while regional blood flow was measured. The hemodynamic changes in M1 and premotor cortex (PM) without hand movement while contralateral M1 was stimulated by low-frequency TMS were still unclear.

The aim of this study was to elucidate the interhemispheric interactions between bilateral motor cortices during and after low-frequency rTMS over the left primary motor cortex by assessing regional cerebral blood flow using fNIRS.

2. Methods

2.1. Participants

Eleven healthy volunteers without any neurophysiological disorder (11 females; 42.9 ± 9.3 years) were recruited. All subjects were right-handed, as assessed by the Edinburgh Handedness Inventory. The experimental procedures used in this study were approved by the Ethics Committee of the Samsung Medical Center and were performed in accordance with the Declaration of Helsinki.

2.2. Functional near-infrared spectroscopy

A time-domain fNIRS system (OMM-3000; Shimadzu, Kyoto, Japan) was utilized to measure the change of [oxy-Hb] and [deoxy-Hb] at a 5 Hz sampling rate. Near-infrared laser diodes with two wavelengths, 790 and 830 nm, were used as the light source, and transmittance data of the light beams were obtained every 200 ms. To reduce jitter and laser intensity fluctuation, the fNIRS system was warmed up during 20 min before measurement. The fNIRS data were detected by time-correlated single photon counting technique and acquired 1 min prior to stimulation, during the 19 min of stimulation, and 20 min after stimulation. [oxy-Hb] and [deoxy-Hb] were calculated from transmittance data.

The fNIRS probes were positioned over the region of the M1 and PM. Measurement points (mid-points between 8 emitters and 8 detectors which were apart from about 30 mm on the surface of the head) were placed on the right M1 and PM. Optodes were attached against the scalp with their tips directly touching the skin for maximum efficiency of light coupling to the tissue. The hair strands under optodes were manually moved away using combs to facilitate optimal optode-scalp contact. This helped avoid contamination by light absorption in hair (Fig. 1). To place the probes in a fixed position on the scalp, a plastic cap was utilized. The equipment appeared like a mesh weaved of plastic straps with holes on the intersections of the straps. The subjects wore the caps on their heads and then the probes were placed at the holes. However, the maximal thickness was 1 cm, the thickness need to be taken into consideration when identifying the M1 location and conducting the stimulations. All of the processes were performed with a plastic cap worn on the scalp.

2.3. Repetitive transcranial magnetic stimulation

All subjects were asked the standard screening questions suggested in the guidelines of rTMS for exclusion of contraindications or precautions. All subjects took wash-out periods between real rTMS and sham stimulation sessions at least 48 h.

The process of identification of optimal coil location was conducted while subjects wore the plastic cap on their head. Each patient received single-pulse TMS to determine the optimal location for M1 and to evaluate the cortical excitability. They were seated in a reclining armchair with both hands pronated. Electromyography (EMG) data were recorded from the contralateral first dorsal interosseous muscle via surface electrodes. EMG activity was amplified using the Medelec Synergy EMG/EP system (Medelec, Oxford, UK), and the data were band-pass filtered at

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