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Research paper

Low-frequency rTMS over the Parieto–frontal network during a sensorimotor task: The role of absolute beta power in the sensorimotor integration

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HIGHLIGHTS

- Electrophysiological rTMS-induced changes of beta power at rest and during a visuomotor task.
- Changes of absolute beta power patterns in the parietal–frontal circuit.
- To better understand the reorganization and neural plasticity mechanisms in the parieto–frontal network during the sensorimotor integration process.

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ABSTRACT

Several studies have demonstrated that Repetitive Transcranial Magnetic Stimulation (rTMS) promotes alterations in the Central Nervous System circuits and networks. The focus of the present study is to examine the absolute beta power patterns in the Parieto–frontal network. We hypothesize that rTMS alters the mechanisms of the sensorimotor integration process during a visuomotor task. Twelve young healthy volunteers performed a visuomotor task involving decision making recorded (Catch a ball in a free fall) by Electroencephalography. rTMS was applied on the Superior Parietal Cortex (SPC; Brodmann area [BA] 7) with low-frequency (1 Hz – 15 min – 80% Resting Motor Threshold). For each Frontal and Parietal region, a two-way ANOVA was used to compare the absolute beta power before and after TMS for each condition of the study (Rest 1, Task and Rest 2). The results demonstrated interactions (TMS vs. Condition) for the Frontal electrodes: Fp1, Fp2 and F7 and an effect of TMS (before and after) for F4.The results for the Parietal region showed a main effect of Condition for the P3, PZ and P4 electrodes. Thus, our paradigm was useful to better understand the reorganization and neural plasticity mechanisms in the parieto–frontal network during the sensorimotor integration process.

1. Introduction

Repetitive Transcranial Magnetic Stimulation (rTMS) is a non-invasive method consisting in inducing repeated pulses which can be used to promote a temporary functional interference at the site of its application [1,2]. Besides the focal effects, studies applying low-frequency rTMS reported modulation of neural activity [3] and task performance subtended by the stimulated region and other regions connected to the target one [4,5]. It is generally accepted that Parietal and Frontal regions are strongly interconnected comprising a neural network involved in the decision making process during visuomotor tasks [6–8]. In order to visualize the possible interferences of rTMS and their propagation resulting from the

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stimulation in areas anatomically connected to the target region, researchers have been using TMS combined with quantitative electroencephalography (qEEG) [9,10]. These integrated tools are useful to understand the reorganization and neural plasticity mechanisms during the decision making process of the sensorimotor tasks [11,12].

In the current study, we seek to investigate the alterations provoked by low-frequency rTMS on the sensorimotor integration process. We utilized a task in which individuals had to identify visual stimuli and make a decision, catch a ball in free fall or maintain the hand closed; such task was already used in other studies from our laboratory, and it allowed observing the sensorimotor integration process from a visual-motor perspective [13–15]. In this context, we investigate the changes in the absolute beta power in the stimulated region and in the Frontal areas. We hypothesize that rTMS alters the mechanisms of the sensorimotor integration process. In an attempt to test this hypothesis, we created a temporary and transient modulation, in a region classically known as a cortical area responsible for integrating different sensory information. Specifically, we tested the beta band absolute power alterations in distinct cortical regions after applying 1 Hz rTMS. We decided to choose beta, since this oscillatory activity has been investigated in studies which associate it with sensory and motor process in the Parietal and Frontal regions during decision making tasks [16] and due to few studies discuss the effects of TMS on motor tasks through beta observation, especially in decision-making situations [17,18]. With regards to the initial question, our task had required the participants to make a decision, expressed in the GO/NOGO paradigm.

2. Materials and methods

Twelve healthy, right-handed volunteers of both sexes (4 males, 8 females; mean age 24 ± 2 years), with normal or corrected-to-normal vision and no history of psychiatric or neurological disorders participated in the experiment. The Edinburgh inventory was applied to identify the hand laterality [19] and the Screening questionnaire for Transcranial Magnetic Stimulation was employed to verify if subjects had contraindications to receive TMS [20]. The study was approved by the Ethics Committee of the Federal University of Rio de Janeiro. Written informed consent was obtained before the start of the experiment, according to the Declaration of Helsinki.

The experimental procedure was performed in a sound-protected and light-attenuated room, to minimize sensory interference. Subjects were seated on a comfortable chair and, during the execution of the task; the right arm was resting on a pedestal, to minimize muscular artifacts. The study consisted of seven stages. In the first, third, fifth and seventh stages, qEEG signal were acquired at rest for 3 min. In these stages the subjects were instructed to keep still and keep their eyes open. In the second and sixth stages, the visuomotor task was executed with simultaneous qEEG collection in 4 blocks of 20 trials each (10 'GO' and 10 'NOGO'). In the fourth stage, TMS was applied for 15 min without qEEG recording. Timeline of Experimental design: Rest 1 before rTMS (3 min); time lag between Rest 1 and task (2 min); task (4×4.67 –18.68 min); time lag between task and Rest 2 (∼2 min); Rest 2 before rTMS (3 min); TMS procedures (∼10 min); rTMS application (15 min); time lag between rTMS application and Rest 1 after rTMS (∼2 min); Rest 1 after rTMS (3 min); time lag between Rest 1 and task (∼2 min); task (4×4.67 –18.68 min); time lag between task and Rest 2 (∼2 min); Rest 2 after rTMS (3 min).

Catching a ball in a free fall is a visuomotor task designed by our laboratory, consisting of an electromagnetic system composed by two tennis-ball releasing solenoids placed in front of the subjects, so that the balls were released at 80 cm above the floor, straight onto the subject's right hand. Light-emitting diodes (LED) coupled to the system issued three kinds of visual stimuli at eye level. The first LED (blue color) blinked for 400 ms as a cue (S1), an attention signal. After an inter-stimuli break of 2-sec, the next LED was lit up 3 sec in one of two colors, representing the stimuli 'GO' or 'NOGO' (S2–green and red, respectively). If 'GO' appeared on the screen, a ball was instantaneously released, and subjects were instructed to open their right hand and catch the falling ball. If 'NOGO' appeared, the ball was not released and the subjects were instructed to maintain the hand closed. The exhibition of 'GO' and 'NOGO' stimuli was randomized; each of them accounted for 50% of all trials within each block of the study.

TMS pulses were delivered through a figure-eight air cooled coil with a 70-mm diameter connected to a Neuro-MS Stimulator (made by Neurosoft medical equipment, Brazil). Prior to the rTMS session, we determined the Resting Motor Threshold (RMT) for each subject. TMS single-pulses around 40% of the stimulator intensity were initially applied on the motor cortex [21]. We moved the coil around this reference point, corresponding to approximately 5 cm on the left of the vertex, in order to find the stimulation that would elicit Motor Evoked Potentials (MEPs) in the right Abductor Pollicis Brevis muscle (APB) recorded by electromyography (EMG). The TMS stimulator intensity was gradually increased by 5% steps until we recorded at least 5 of 10 consecutive MEPs with a peak-to-peak amplitude of at least 50 μV [21]. We chose to apply 80% of each subjectís RMT ($\bar{X} = 47.4$; SD = 9.41), since this intensity has been used in several studies as a safety measure to avoid seizures [21].

The Superior Parietal Cortex (SPC) was the brain area selected to receive the rTMS. The SPC has been associated with the initial stage of the sensorimotor integration process, which encodes exteroceptive information and sends them to Frontal regions that will create the motor plans [22,23]. The SPC was localized using the correspondence of the Pz electrode (10–20 EEG system). The coil was stabilized and immobilized by a mechanical support, a 3D articulated arm. The orientation of the coil was along the rostro-caudal axis, with the handle pointing caudally [23]. During 15 min, wearing earplugs for their hearing protection, subjects received TMS stimulation with low-frequency (1 Hz).

Data was acquired at rest and during the visuomotor task through the International 10/20 system for electrodes [24], using a 20-channel Braintech-3000 EEG system (EMSA-Medical Instruments, Brazil). The 20 electrodes were arranged on a nylon cap (ElectroCap Inc., Fairfax, VA, USA), yielding mono-pole derivations to linked earlobes, set as reference points. In addition, two 9-mm diameter electrodes were attached above and on the external corner of the right eye, in a bipolar electrode montage, in order to monitor artifacts on eye-movements (EOG). Impedance of EEG and EOG electrodes was kept below 5 K Ω. The data acquired had total amplitude of less than 100 μV. The EEG signal was amplified, with a gain of 22,000, analogically filtered between 0.01 Hz (high-pass) and 100 Hz (low-pass), and sampled at 240 Hz. The software Data Acquisition (Delphi 5.0), developed at the Brain Mapping and Sensorimotor Integration Laboratory, was employed to filter the raw data: notch (60 Hz), high-pass of 0.3 Hz and low-pass of 100 Hz.

In order to quantify artifact-free data, a visual inspection and Independent Component Analysis (ICA) were applied to identify and remove possible sources of artifacts produced by the task, i.e., eye blinks and ocular movements [25]. Using this technique, the signal was decomposed into statistically independent components, and the most artifact-resembling components were removed. Data from individual electrodes exhibiting loss of contact with the scalp or high impedances (>10 k Ω) were not considered. The ICA-filtered data were re-inspected for residual artifacts. The mean and SD of the eliminated components were: mean: 3.2813; SD: 0.829. A classic estimator was applied to the Power Spectral Density (PSD),