Neuroscience Letters 577 (2014) 22–27

Contents lists available at ScienceDirect

Neuroscience Letters

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

The effects of 3 weeks of rTMS treatment on P200 amplitude in patients with depression

Kyung Mook Choi[a,b,c], Kyoung-Mi Jang[d], Kuk In Jang[c], Yoo Hyun Um[b], Myung-Sun Kim[d], Do-Won Kim[e], Dongkyoo Shin[f], Jeong-Ho Chae[a,b,c,*]

[a] Department of Biomedical Science, Seoul, South Korea
[b] Department of Psychiatry, Seoul St. Mary's Hospital, Seoul, South Korea
[c] Institute of Biomedical Industry, The Catholic University of Korea, College of Medicine, Seoul, South Korea
[d] Department of Psychology, Sungshin Women's University, Seoul, South Korea
[e] Department of Biomedical Engineering, Hanyang University, Seoul, South Korea
[f] Department of Computer Engineering, Sejong University, Seoul, South Korea

HIGHLIGHTS

- rTMS treatment induced changes in brain function in patients with major depression.
- ERP P200 amplitudes increased after 3 weeks of rTMS treatment.
- sLORETA showed significant activation in the left middle frontal gyrus.
- Three weeks of rTMS treatment induced changes in brain function in the patients.
- Changes in brain function induced by rTMS treatment can be identified using ERP.

ARTICLE INFO

Article history:
Received 27 February 2014
Received in revised form 12 May 2014
Accepted 3 June 2014
Available online 10 June 2014

Keywords:
rTMS
Depression
ERP
sLORETA

ABSTRACT

Previous studies have reported that repetitive transcranial magnetic stimulation (rTMS) induces neuronal plasticity in the brain. Although event-related potential (ERP) is an exploration tool, the rTMS effects on ERPs in patients with major depression have not been fully explored. We demonstrated that rTMS treatment induces changes in brain function in patients with medication-resistant major depression using the ERP. Eighteen patients with medication-resistant major depression (five males and 13 females) participated in this study. The patients received rTMS treatment for 3 weeks. All patients completed clinical scales, including the Hamilton Depression Rating Scale (HAM-D), Hamilton Anxiety Scale (HAM-A), Beck Depression Inventory (BDI), State-Trait Anxiety Inventory (SAI, TAI), Ruminative Response Scale, Emotion Regulation Questionnaire, and Cognitive Emotion Regulation Questionnaire (CERQ), as well as the ERP auditory oddball task, at their first visit (baseline) and at the 3-week visit (3-weeks). The HAM-D, HAM-A, BDI, SAI, and "blaming others" scale of the CERQ decreased significantly after rTMS treatment. In ERP auditory oddball task, when FP1, FP2, FZ, FCZ, CZ, and PZ channels were analyzed, P200 amplitudes showed a main effect for time of measurement and increased after 3 weeks of rTMS treatment. Standardized low-resolution brain electromagnetic tomography showed significant activation in the left middle frontal gyrus by 3 weeks of rTMS treatment. The results suggest that relatively longer rTMS treatment induces changes in brain function in patients with medication-resistant major depression, which can be identified using ERP.

1. Introduction

The brain has characteristic neuronal plasticity that changes with stimulation. Neuronal reorganization due to brain injury as well as learning and memory induces neuronal plasticity. This plasticity allows the brain to adapt to unexpected environmental and experiential changes [1]. Repetitive transcranial magnetic

* Corresponding author at: Department of Psychiatry, The Catholic University of Korea, College of Medicine, 222 Banpo-daero, Seocho-gu, Seoul 137-701, South Korea. Tel.: +82 02 2258 6083; fax: +82 02 594 3870.
E-mail address: alberto@catholic.ac.kr (J.-H. Chae).

http://dx.doi.org/10.1016/j.neulet.2014.06.003
0304-3940/

stimulation (rTMS) induces electrical impulses in the brain underneath an electromagnetic coil by using a rapidly changing electromagnetic field [2], and rTMS influences neuronal plasticity of the brain [3].

When rTMS is applied long term to the brain, it can induce changes. After patients with depression received 10 daily sessions of rTMS (1-Hz or 20-Hz) over the left prefrontal cortex (PFC), their brains were scanned using positron emission tomography (PET) and changes in depression-related symptoms between 1-Hz and 20-Hz rTMS were inversely correlated; 20-Hz rTMS showed better improvement in baseline hypoperfusion [4]. In a study on changes in regional cerebral blood flow (rCBF) during rTMS, 20-Hz rTMS over the left PFC (100% resting motor threshold) applied for 2 weeks increased rCBF in the bilateral frontal cortex, limbic regions, and paralimbic regions, whereas 1-Hz rTMS decreased small areas in the right PFC, left medial temporal cortex, left basal ganglia, and left amygdala [5]. Event-related potential (ERP) studies on the pharmaceutical effects of patients with depression [6,7] have been conducted, and one study demonstrated the temporal rTMS effects on healthy subjects using ERP [8]. rTMS has beneficial effects on patients with chronic depression and anxiety [9], as well as those with medication-resistant major depression [2], but the effects of longer-term rTMS on neuronal plasticity are currently incompletely understood. To our knowledge, there has been no ERP study examining the effect of 3 weeks of rTMS treatment in these patients.

The ERP oddball task reflects various cognitive functions relevant to brain activities through the N100, P200, N200, and P300 components. N100 and P200 are considered exogenous sensory components related to attention and sensory processing [10]. N100 reflects aspects of attentional processes [11]. P200 is related to evaluating the task relevance of stimulus items, such as suppressing irrelevant features or enhancing relevant features [12]. N200 represents pattern recognition, stimulus classification [13], and response selection [14]. P300 represents attention allocation, decision-making [15], context updating [16], and context closure [17]. We hypothesized that a 3-week rTMS treatment would induce changes in brain function of patients with medication-resistant major depression. Thus, we observed physiological changes after 3 weeks of rTMS treatment through various components induced by the ERP oddball task.

2. Materials and methods

2.1. Participants

Twenty-six patients who were diagnosed with major depression according to Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision criteria [18] were enrolled at Department of Psychiatry, The Catholic University of Korea. They had medication-resistant major depression; that is, they were refractory to at least two different classes of antidepressants. All were tested using rating scales and ERP at baseline (pre-treatment). However, eight of the patients dropped out due to pain from the rTMS stimuli (six patients), a personal situation (one patient), and hospitalization (one patient). Therefore, 18 patients (five males and 13 females) participated at baseline and at 3 weeks (post-treatment). All patients were outpatients during the trial. Their mean age was 35.3 years old (standard deviation, 15.2 years; range, 19–67 years). All patients were under pharmacotherapy for depression before the start of rTMS treatment but changes in drugs or dosages were not permitted during the 3-week rTMS treatment. Patients were excluded if they had a history of neurological illness, substance abuse, major head trauma, or seizure. Patients with pacemakers or hearing aids were also excluded.

All subjects signed a written informed consent form that was approved by the Institutional Review Board of The Catholic University of Korea prior to their participation in the study.

2.2. TMS procedure

rTMS was performed using a TAMAS stimulator with a figure-of-8 coil (CR Tech, Daejon, Korea). In all patients, rTMS treatment was applied to the left dorsolateral PFC, which was determined by moving the TMS coil 5 cm anterior to the thumb area of the motor cortex along a left superior oblique plane with a rotation point about the tip of the patient's nose [19]. Intensity was 110% of the resting motor threshold of the right abductor pollicis brevis muscle at 10 Hz for 5 s, with an intertrain interval of 25 s. Treatment sessions lasted for 30 min (60 trains) and included 3000 pulses. Patients visited the outpatient clinic 5 days every week for 3 weeks and received 15 treatment sessions (a total of 45,000 pulses).

2.3. Rating scales

Patients were tested for rating scales before and 3 weeks after the start of rTMS treatment, including the Hamilton Depression Rating Scale (HAM-D) (17-items) [20], Hamilton Anxiety Scale (HAM-A) [21], Beck Depression Inventory (BDI) [22], State-Trait Anxiety Inventory (SAI and TAI) [23], Ruminative Response Scale (RRS), Emotion Regulation Questionnaire (ERQ), and Cognitive Emotion Regulation Questionnaire (CERQ). The RRS has 22 items assessing brooding, reflective pondering, and depressive rumination [24]. The ERQ consists of 10 items (cognitive reappraisal factor [six items] and expressive suppression factor [four items]) [25]. The CERQ assesses a broad set of specific cognitive emotion regulation strategies as follows: self-blame, acceptance, focus on thought/rumination, positive refocusing, refocus on planning, positive reappraisal, putting into perspective, catastrophizing, and blaming others [26].

2.4. EEG recording and analysis

Electrophysiological assessments were performed before and 3 weeks after the start of rTMS treatment. The patients were seated in a comfortable chair in a sound-attenuated room. Stimulus and data synchronization with an EEG were provided using E-Prime (Psychology Software Tools, Pittsburgh, PA, USA). The auditory oddball consisted of infrequent target tones of 1500 Hz and frequent standard tones of 1000 Hz, which were presented randomly at a proportion of 85% and 15%, respectively. The tone duration was 100 ms, with rise and fall times of 10 ms, and the interstimulus interval was 1500 ms. In total, 400 auditory stimuli were presented. After a practice block of 20 stimuli, the patients performed an experimental block consisting of 400 stimuli. The auditory oddball stimuli were delivered via MDR-XB500 headphones (Sony, Tokyo, Japan) at 85 dB SPL. The patients were asked to press a button promptly with the index finger of right hand in response to target tones of 1500 Hz.

EEG activity was recorded and amplified using a NeuroScan NuAmps amplifier (Compumedics USA, Ltd., El Paso, TX, USA), and 34 Ag–AgCl electrodes were mounted in a Quik Cap using a modified 10–20 placement scheme to record the EEG from 34 positions (FP1, FP2, F7, F3, Fz, F4, F8, FT7, FC3, FCz, FC4, FT8, T3, C3, Cz, C4, T4, TP7, CP3, CPz, CP4, TP8, T5, P3, Pz, P4, T6, O1, Oz, O2, FT9, FT10, PO1, and PO2). A vertical electrooculogram (EOG) was recorded using two electrodes, one located above and one below the right eye. The horizontal EOG was recorded at the outer canthus of each eye. EEG data were recorded with a 0.1–100-Hz band-pass filter at