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RTMS OVER THE DORSOLATERAL PREFRONTAL CORTEX INCREASES THE SERUM PROBDNF/BDNF RATIO: A SHAM-CONTROLLED STUDY IN SUBJECTS WITH COCAINE USE DISORDER

Mauro Pettorruso^{1,2}, Andrea Miuli², *Francesco Di Carlo¹, Gianluca Mancusi¹, Katia Clemente³, Stefania Chiappini⁴, Giacomo D'andrea¹, Giovanni Martinotti^{1,5}

¹Department of Neuroscience, Imaging and Clinical Sciences, "G. d'Annunzio" University, Chieti, Italy, ²Department of Mental Health, ASL 2 Abruzzo Lanciano-Vasto-Chieti, Italy, ³Clinical Pathology Unit, ASL 2 Abruzzo Lanciano-Vasto-Chieti, Italy, ⁴Psychopharmacology, Drug Misuse and Novel Psychoactive Substances Research Unit, School of Life and Medical Sciences, University of Hertfordshire, Hatfield, UK, ⁵Department of Pharmacy, Pharmacology, Clinical Science, University of Hertfordshire, Herts, UK

Background: Repetitive transcranial magnetic stimulation (rTMS) is a promising neuromodulation technique for treating cocaine use disorders (CUDs) [1]. The brain-derived neurotrophic factor (BDNF) and its precursor proBDNF are critical neurotrophins altered in this disorder [2]. proBDNF is increased in patients in withdrawal and is positively related to relapse rates [3]. According to evidence from depressive disorders, these neurotrophins may be positively modulated by rTMS, a technique with great therapeutic potential for CUD [4].

Aims and Objectives: Given the critical role of serum BDNF levels in cocaine addiction and the promising reports on modulating effects of rTMS on the neurotrophin, this study aimed to explore the impact of rTMS on serum levels of BDNF, proBDNF, and the proBDNF/BDNF ratio in a cohort of CUD patients.

Methods: In a sham-controlled pilot study, we assessed changes in BDNF and proBDNF blood levels after rTMS treatment on the left dorsolateral prefrontal cortex (DLPFC) of CUD patients. Thirty-seven treatment-seeking CUD patients were enrolled, randomized in a 1:1 design, and treated with 20 rTMS or sham sessions. Each rTMS session was delivered at 15 Hz frequency and 100% resting motor threshold (RMT) intensity and applied to the left dorsolateral prefrontal cortex (DLPFC). Blood samples for neurotrophin evaluation were collected before and after treatment.

Results: Serum BDNF and proBDNF levels did not show significant changes in both groups. However, the proBDNF/BDNF ratio significantly increased in favor of higher levels of proBDNF after treatment in the active group ($p = 0.038$).

Discussion and Conclusions: This is the first trial to assess the effects of rTMS on peripheral serum neurotrophins in subjects with CUD. The negative findings related to changes in BDNF and proBDNF levels are concordant with most of the results in depressed patients. However, the imbalance in the ratio toward proBDNF may represent a peripheral effect of neuromodulation. Although only preliminary, these findings could help shed light on the neurobiological activities of rTMS and the complex connections between neuromodulation and the production of biobehavioral effects.

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