

● LETTER TO THE EDITOR

Is transcranial magnetic stimulation useful in posttraumatic disorders?

Dear editor,

We have read with great interest the recent paper by Herrold et al. (2014) published in *Neural Regeneration Research*. There is evidence that approximately 20–90% of patients with mild traumatic brain injury develop posttraumatic symptoms, and 40% of these patients have persistent symptoms after trauma (Bazarian et al., 1999; Koski et al., 2015). Therefore, mild traumatic brain injury becomes an important cause of temporary disability. Indeed, posttraumatic disorders have a significant epidemiological relevance, even though it is still undervalued in most of the trauma centers (Bazarian et al., 1999) and there is no specific treatment method (Koski et al., 2015). Recently, many neurological and posttraumatic stress disorders had been treated with noninvasive brain stimulation (Boggio et al., 2010; Fox et al., 2012). Since repetitive transcranial magnetic stimulation (rTMS) was approved by the United States Food and Drug Administration for use in the treatment of resistant major depressive disorder (Herrold et al., 2014), it provided a strong basis to apply rTMS in the treatment of posttraumatic stress disorder. Herrold et al. (2014) described interventions for alcohol use disorder, mild traumatic brain injury, and posttraumatic stress disorder using rTMS. TMS seems to be a well-suited intervention for the treatment of co-occurring neurological and psychiatric disorders (Bazarian et al., 1999).

A strong point of the paper from Herrold et al. (2014) is the detailed description of pathways (neural regions and networks) involved in neuromodulation mechanism in patients with alcohol use disorder, mild traumatic brain injury and posttraumatic stress disorder. Herrold et al. (2014) described that there existed substantial gaps in the understanding of the precise neurophysiological mechanisms of rTMS from the perspective of behavior, but they presented interesting explanations about the neurophysiological response to rTMS applied to the dorsolateral prefrontal cortex. The rationale in choosing the dorsolateral prefrontal cortex is usually based on previous results (Boggio et al., 2010; Van Dijk et al., 2010) regarding the treatment of depression by stimulating the same target with rTMS. Our group has a particular interest in the role of rTMS in patients with mild traumatic brain injury. Chen et al. (2007) reported that mild traumatic brain injury is a specific pattern of deficient activation of the dorsolateral prefrontal cortex in work memory task, which is correlated to the severity of patient's symptoms.

However, we cannot conclude whether this is the target that should be chosen in future studies because in most recently studies (Koski et al., 2015), headache was the most responsive symptom as compared to mood symptoms. Indeed, stimulation of other targets, such as the primary motor cortex given its connectivity with thalamic areas (Van Dijk et al., 2010; Fox et al., 2012), may show better results in posttraumatic stress disorders.

In another interesting paper cited by Herrold et al. (2014), Koski et al. (2015) studied 15 adult patients with mild traumatic brain injury who present with persistent post concussion syndrome. They explored the safety, tolerability, and efficacy of high-frequency rTMS placed over the left dorsolateral prefrontal cortex. The important point that needs to be highlighted is the contribution of this study to the development of rTMS as a potential therapeutic tool in posttraumatic syndrome, the ultimate goal of this initial pilot study. Authors chose to conduct an open-label study. Although uncontrolled studies have significant limitations, they are useful at the initial stage of clinical development. They applied a protocol involving 20 sessions. Number of sessions is an important point to be discussed using rTMS as a therapeutic tool for posttraumatic disorders.

Based on prior successful experience on the treatment of psychiatric and neurological disorders, a high-frequency rTMS (10 Hz) protocol can be a good option (Pallanti et al., 2010).

Practical decision about the number of sessions is a hard decision. Twenty sessions of stimulation is a common option for neurological

diseases (Koski et al., 2015), however, it may be unfeasible in most of traumatic brain injury subjects. So, ten sessions of stimulation is more feasible and would provide good results.

A double-blind, randomized clinical trial should be performed to investigate whether rTMS is a good treatment method for patients with alcohol use disorder, mild traumatic brain injury, and posttraumatic stress disorder. It is important to find the optimal, or at least the most effective, stimulation parameters for the treatment of alcohol use disorder, traumatic brain injury, and posttraumatic stress disorder.

Furthermore, the reported results may be because of a placebo effect or spontaneous recovery, since most of the patients with these disorders improve spontaneously (Alves et al., 1993; McClincy et al., 2006; Covassin et al., 2007). Nevertheless, it is fundamental to eliminate at least the chance that future randomized clinical trials addressing this question are negative because of poor choice of stimulation parameters.

Nowadays, we have no treatment methods for persistent posttraumatic symptoms. What can we expect in the future? So, the idea of rTMS protocol seems an interest tool to treat these disorders.

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References

- Alves W, Macciocchi SN, Barth JT (1993) Postconcussive symptoms after uncomplicated mild head injury. *J Head Trauma Rehabil* 8:48-59.
- Bazarian JJ, Wong T, Harris M, Leahey N, Mookerjee S, Dombrov M (1999) Epidemiology and predictors of post-concussive syndrome after minor head injury in an emergency population. *Brain Inj* 13:173-189.
- Boggio PS, Rocha M, Oliveira MO, Fecteau S, Cohen RB, Campanhã C, Ferreira-Santos E, Meleiro A, Corchs F, Zaghi S, Pascual-Leone A, Fregni F (2010) Noninvasive brain stimulation with high-frequency and low-intensity repetitive transcranial magnetic stimulation treatment for posttraumatic stress disorder. *J Clin Psychiatry* 71:992-999.
- Chen JK, Johnston KM, Collie A, McCrory P, Prito A (2007) A validation of the post concussion symptom scale in the assessment of complex concussion using cognitive testing and functional MRI. *J Neurol Neurosurg Psychiatry* 78:1231-1238.
- Covassin T, Schatz P, Swanik CB (2007) Sex differences in neuropsychological function and post-concussion symptoms of concussed college athletes. *Neurosurgery* 61:345-351.
- Fox MD, Buckner RL, White MP, Greicius MD, Pascual-Leone A (2012) Efficacy of transcranial magnetic stimulation targets for depression is related to intrinsic functional connectivity with the subgenual cingulate. *Biol Psychiatry* 72:595-603.
- Herrold AA, Kletzel SL, Harton BC, Chambers RA, Jordan N, Pape TL (2014) Transcranial magnetic stimulation: potential treatment for co-occurring alcohol, traumatic brain injury and posttraumatic stress disorders. *Neural Regen Res* 9:1712-1730.
- Koski L, Kolivakis T, Yu C, Chen JK, Delaney S, Prito A (2015) Noninvasive brain stimulation for persistent postconcussion symptoms in mild traumatic brain injury. *J Neurotrauma* 32:38-44.
- McClincy MP, Lovell MR, Pardini JP, Collins MW, Spore MK (2006) Recovery from sports concussion in high school and collegiate athletes. *Brain Inj* 20:33-39.
- Pallanti S, Bernardi S, Di Rollo A, Antonini S, Quercioli L (2010) Unilateral low frequency versus sequential bilateral repetitive transcranial magnetic stimulation: is simpler better for treatment of resistant depression? *Neuroscience* 167:323-328.
- Van Dijk KR, Hedden T, Venkataraman A, Evans KC, Lazar SW, Buckner RL (2010) Intrinsic functional connectivity as a tool for human connectomics: theory, properties, and optimization. *J Neurophysiol* 103:297-321.