

# Repetitive transcranial magnetic stimulation in management of medically unexplained symptoms: challenges and scopes

## Letter to the Editor

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### To the editor:

People with medically unexplained symptoms (MUSs), also known as functional neurological disorders, are one of the biggest challenges in medical settings as well as psychiatric settings. Often people with MUSs consult in the medical setups due to the typical nature of their symptoms, which delays the diagnosis, increases the unnecessary treatment cost, and prolongs the suffering. Notwithstanding the treatment efforts, such patients struggle to resume their work by gaining functionality.<sup>1</sup> Psychological interventions have been the mainstay of treatment for MUSs. Antidepressants are used to treat co-occurring features of anxiety and depression. Over the past few decades, the newer neuromodulation techniques like repetitive transcranial magnetic stimulation (rTMS), transcranial direct current stimulation, vagus nerve stimulation, and deep brain stimulation have gained popularity in the management of psychiatric disorders like depression, schizophrenia, obsessive compulsive disorder, dementia, addictive disorders, and movement disorders.<sup>2</sup>

There is a limited but growing body of evidence that suggests the possible role of neuromodulation techniques like rTMS in the management of MUSs.<sup>3–5</sup> Evidence support that high-frequency rTMS over the primary motor cortex (M1), contralateral to the side of pain, is effective in reducing the pain symptoms in neuropathic pain.<sup>2</sup> The high-frequency protocols used frequencies like 5 Hz, 10 Hz, and 20 Hz were found to be effective in pain control, whereas no analgesic effect was observed with low-frequency protocols.<sup>2</sup> The analgesia was proposed to be mediated through modulation of neurotransmitters like endogenous opioids, GABA, glutamate, and dopamine, which in turn facilitates the development of long-term neuroplastic changes (synaptic plasticity) in the pain pathway.<sup>2</sup> Researches also targeted various other brain areas like vertex, parietal opercular region, insula, cingulum, premotor cortex, and dorsolateral prefrontal cortex (DLPFC) for pain management.<sup>2</sup>

Attempts were taken to evaluate the efficacy of rTMS in the pain of psychogenic origin and fibromyalgia. It was found that high-frequency rTMS over the left primary motor cortex and left DLPFC were effective in reducing the pain.<sup>2</sup> An Indian study used high-frequency rTMS over left DLPFC in persistent somatoform pain disorder (n = 5) and found that all the patients had significant improvement in pain symptoms.<sup>5</sup> The effectiveness of rTMS has been studied in psychogenic nonepileptic seizures (PNESs). The right temporoparietal junction was stimulated by using high-frequency rTMS and intermittent theta-burst stimulation successfully in the management of PNESs.<sup>4</sup>

As the MUSs are of various types resembling symptoms of the nervous system, gastrointestinal, cardiorespiratory, genitourinary system, and so on, the cortical targets may vary as per the symptom category, a potential challenge in determining the protocol of rTMS. Similarly, an index individual may have MUSs involving multiple systems, which makes it difficult to choose a protocol based on the symptoms. Patients with MUSs often have significant psychological distress and distorted attributions or explanations to their physical symptoms. The misattributions may be explained based on the cognitive errors (linked to DLPFC), irrespective of the nature of symptom and physical system involved. Furthermore, DLPFC is a key region involved in the top-down regulation of information from the somatic sensory system. Hence, the DLPFC (left) may be a more feasible and universal target in MUSs. There is a need of more research to evaluate the effectiveness of various rTMS treatment protocols in patients with various categories of MUSs, and the practice guidelines need to consider these treatment modalities with existing level of evidences.

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