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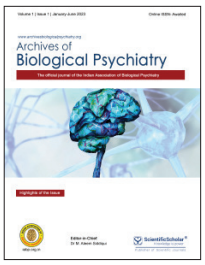

Editorial *Psychiatry*

Repetitive transcranial magnetic stimulation an ideal avenue for biological psychiatry?

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For many patients suffering from mental illness, pharmacological and/or psychological interventions are helpful, although they are not always beneficial. There is an obvious need for innovative therapies because they may have unfavorable consequences or be disliked by patients. Clinical neuromodulation is defined as "the alteration of nerve activity through targeted delivery of a stimulus, such as electrical stimulation or chemical agents," to effect brain changes and improvements in mental state. Transcranial magnetic stimulation (TMS) is one of the novel non-invasive versions of neuromodulation. It acts through changing the magnetic field (up to 1.5 tesla) and modulating a 1–3 cm cortical strip. It is a glad tiding that the recent advent of deep TMS has enabled the neuromodulation of deeper edifices within the brain. The Food and Drug Administration has approved 24 TMS devices across an array of disorders such as major depressive disorder (MDD), obsessive-compulsive disorder, migraine with aura, smoking cessation, anxiety comorbid with MDD, and cortical mapping.[1] Apart from being a therapeutic tool, there is great scope for TMS being used to create *in vivo* temporary lesions (cortical hotspots) and study the psychophysiological constructs both in normal individuals ("online paradigms") and in psychiatric disorders *per se*. Although there is a lack of consensus on optimal treatment parameters, safety parameters need to be followed.

With the release of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, in 2013, the National Institute of Mental Health Research Domain Criteria project sparked a greater focus on biomarker research. The whole purpose of the advent of biomarker research is to promote personalized medicine, called "precision psychiatry" in our context. The ongoing sprouting search for biomarkers of clinical response to TMS shall be beneficial in reducing the heterogeneity. For e.g., as per a recent review evaluating the robustness of TMS magnetic resonance imaging (MRI) and EEG biomarkers for depression has found functional MRI-based functional connectivity MRI (fcMRI) between the dorsolateral prefrontal cortex and subgenual anterior cingulate cortex and task-induced EEG frontal-midline theta as among the few. The recent surge of studies exploring E-field models to approximate the directionality and amplitude of the induced electrical current in the brain based on the orientation and location of the coil may open new avenues to reduce interindividual variability.[2] TMS-functional near-infrared spectroscopy (TMS-fNIRS) also offers an all-inclusive approach to study the effects of TMS (both online and offline) due to its immunity to electromagnetic interference. This method provides the stimulation of specific brain regions (using TMS) while simultaneously monitoring cerebral blood flow (with fNIRS) and could be vital in unfolding the exact mechanisms behind neuroplasticity. Another incursion to study neuroplasticity is TMS-positron emission tomography, which would

simultaneously measure brain stimulation and changes in cerebral blood flow or glucose metabolism. Rhythmic TMS patterns coupled with neural oscillations of specific frequencies and closed-loop TMS and TMS genetics are other attempted aspects of precision medicine.

Pragmatism is an important measure in the evolution of novel treatment paradigms and a critical measure in defining the feasibility. Not so long ago, there was discovery of theta burst stimulation (TBS), which was interestingly found to mimic endogenous hippocampal theta neural activity and provide short bursts of stimulation at very high frequencies in a matter of a few minutes, is a healthy promotion for pragmatism. Recent VALIANT trials such as Stanford Accelerated Intelligent Neuromodulation Therapy, an accelerated, high-dose resting-state fcMRI-guided intermittent TBS protocol, employing 50 sessions over five days and an enormous 18000 pulses/day benefiting resistant depression might invite a paradigm shift. Similar replicable templates and novel protocols would generate immense interest in neuromodulation's role in the therapeutic context.[3]

Psychotherapy-TMS: TMS efficacy may vary with the context determining the internal states, specifically in disorders like OCD. Varying brain states may confound heterogeneity in treatment response. Basic behavioristic psychological approaches like cue exposure have been shown to change the context and augment TMS. Combining psychotherapeutic techniques (e.g., exposure and response prevention in OCD) with TMS is an enthusing option, but how to pool, type, and time of psychotherapy remains an important question. These approaches need formal comparison in control conditions to emanate recommendations.[2]

Moreover, inherent clinical benefits in psychiatric disorders have a large share of placebo effects and are explained by varied structural models. Importantly, TMS, along with its coliseum effects, has significant potential to squeeze placebo advantage. Though, there is a scope for argument regarding the sustainability of these effects.

All in all, we have stimulating times ahead with repetitive TMS (rTMS) as an avenue for biological psychiatry, and we are not so far away from having the first biomarker in psychiatry to which rTMS should be an important contributor!!

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