TRANSLATING TMS-EEG METHODS INTO CLINICAL NEUROPSYCHIATRY: ILLUSTRATIVE CASE STUDIES

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Neuropsychiatric complaints are complex and varied, and often overlap across diagnostic entities. The underlying neurophysiologic signature of specific neuropsychiatric complaints can provide insights into the proximal substrate of a given patient's disability and suggest specific therapeutic targets and strategies. TMS-EEG provides a powerful approach to identify the neurophysiologic substrate of specific neuro-psychiatric complaints and thus guide personalized therapeutics. I will show data from various clinical patients in whom TMS-EEG was used to identify bioelectrical features of their presenting and disabling complaints, and thus guide non-invasive brain stimulation treatment strategies. Single and paired pulse TMS, targeting DLPFC and M1 bilaterally, was used with concurrent EEG to map potential abnormalities in cortical excitability and inhibition balance, as well as TMS evoked response propagation patterns. These observations were used to inform and tailor noninvasive brain stimulation interventions for each patient. We report the clinical outcome of this approach and propose future directions to improve its clinical utility.

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PLACEBO AND (UN)SPECIFIC EFFECTS OF TMS

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Placebo effect is an inescapable element of nearly all treatment interventions used in health care. Nonetheless, some health conditions as well as some treatment interventions are more susceptible to its effects. In that sense, it has been repeatedly argued that a large portion of responses to various interventions used for the treatment of depressive disorder can be attributed to placebo effects. However, these portions vary significantly as expectations, formed around more or less subtle cues about care setting, change. Transcranial magnetic stimulation (hereinafter TMS) has some unique and rather distinct features when compared with other usual treatment interventions (as psychoactive medication, that is, antidepressants). The placebogenic effect TMS has been widely discussed, both in research and clinical context, however still without any kind of firm conclusions.

Here we present a series of cases in which response to TMS was unusual and unexpected. We use these outlier cases to map out and disentangle possible specific and unspecific effects that total treatment setting in general and TMS in particular yielded. Further on, practical issues and challenges related to controlling the placebo effects in care settings are discussed.

As placebo is inevitable, and we might add critical, part of treatment interventions within the realm of mental health, in care settings it should be carefully harvested, so that it serves our patients and us for better and not for the worse.

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PERSONALIZED rTMS BASED ON PREDICTION FACTORS

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Depression is a common mental disorder, globally is estimated that 5.0% of adults suffer from depression, with approximately 280 million people in the world have depression. rTMS has been approved as the treatment of depression and has been admitted in the clinical guidelines of many countries, accepted by the health insurance funds. Despite continuing advances in the development of antidepressant drugs, the condition of about 30% of patients remains refractory to drug treatment. Repetitive transcranial magnetic stimulation (rTMS) of the dorsolateral prefrontal cortex (PFC) has been established as a new effective add-on therapy for depression. European recommendations mention the effectiveness of 30 to 64% of rTMS depression treatment. A combination of predictive factors of clinical response during care, such as a short duration of the current depressive episode, higher HDRS agitation item value, lower perceived sleepiness value and a higher number of previous rTMS treatments, were identified as predictors of the efficacy of rTMS.

Yet there are many other fields than Depression whereas rTMS shows high evidence and in the future new psychiatric indication will be available.

Catatonia is one of the most common severe motor syndromes, with an estimated prevalence among psychiatric inpatients of about 15%. Benzodiazepines and electroconvulsive therapy (ECT) are the most widely studied treatment methods and are recommended as first-line-therapy. Yet, recent studies show a successful utilization of rTMS in the treatment of catatonic symptoms by an inhibitory stimulation of the supplementary motor area (SMA). Few studies show that catatonia may be successfully treated with inhibitory rTMS.

Tinnitus treatment with rTMS have been examined in a large number of studies, whereas the uniform stimulation "1 Hz for all" didn`t prove to be effective. Still, there are many important predictors that should be taken into account as depressive mood, which means that patients with severe depression and tinnitus could be better responder compared with those having тinnitus without depression. Furthermore, there is a significant interaction between BDI and the response / non-response criterion indicating a higher decrease of depression symptoms in rTMS responders.

The artificial iintelligence using мmultimodal neuroimaging methods could provide the necessary insights into individual brain characteristics and can therefore be used to personalize rTMS. Further, the individual connectivity values of the identified neuroimaging biomarkers of long-term clinical response can also be used as features in the vector machine models defining and predicting the therapeutic response of patients with depression. Predictive and personalized approach of rTMS for patients with psychiatric diagnosis is ongoing process which will should be standardised as regular procedure.

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CHALLENGES AND OPPORTUNITIES WITH TREATMENT OF MEDICATION-RESISTANT DEPRESSION IN SLOVENIA

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A review of health policies in the field of depression treatment in Slovenia has revealed certain deficiencies compared to the situation in the most developed countries. The national guidelines for the treatment of resistant depression have recently been updated. They define pathways and algorithms for the treatment of resistant depression, which include non-invasive methods of brain stimulation and drugs from new therapeutic groups. Newer forms of depression treatment are difficult to implement as publicly