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

funded health services in Slovenia, in part because it is difficult to objectively measure the success of treatment. Health authorities are aware of the importance of introducing new treatments, given the high social burden of depression. They expect us to introduce more systematic approaches to the treatment of depression in the near future, as well as more objective assessments of treatment success in individual patients and the impact of depression on their day-to-day functioning. We will present the planned approaches to these questions, which also have important consequences for the wider introduction of brain stimulation methods in the clinical practice of depression treatment in Slovenia.

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ECT IN TREATMENT-RESISTANT SCHIZOPHRENIA: CURRENT PRACTICE AND FUTURE PERSPECTIVES

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Treatment resistance continues to represent the greatest unmet need in schizophrenia care, despite the ever growing number of antipsychotics. However, about one third of patients do not show sufficient improvement with antipsychotics. About half of those patients with treatment-resistant schizophrenia (TRS) have a poor response to clozapine. The pathophysiology of TRS is highly heterogeneous and includes dopaminergic, glutamatergic, and GABAergic dysfunction. Although electroconvulsive therapy (ECT) is primarily utilized to treat patients with severe depression, it can effectively reduce the symptoms of TRS, although some patients do not respond to this treatment. ECT produces changes in different brain regions/networks, that are supposed to correlate with the pathological findings in schizophrenia. In preclinical models, ECT had both acute and chronic effects on neurogenesis, while chronic ECT reduced neuroinflammation. However, the data on peripheral markers on inflammation and growth factors in patients are often heterogeneous, and studies were carried out mostly on patients with depression, while the data in schizophrenia are scarce. The mechanism of efficacy of ECT in TRS is not known. While preclinical trials suggest it may normalize dopamine supersensitivity state, clinical data are missing. Such effects may be important for patients who were not initially resistant. Other patients may be resistant from the illness onset, which could have unaltered dopamine synthesis capacity, but show NMDA receptor dysfunction on GABA interneurons. Chronic overactivation of the immune system can also be present from the illness onset.

Establishing clinical and biological markers of TRS, as well as predictors of response to ECT, is a priority. Such markers would distinguish patients who will benefit from ECT, and provide this treatment early in the disease course, which may improve the long-term outcome.

Key words: *ECT - treatment-resistant schizophrenia - dopamine supersensitivity - neuroinflammation*

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REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION IN TREATMENT OF PSYCHIATRIC DISORDERS AND COMORBIDITY

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Repetitive transcranial magnetic stimulation (rTMS) has emerged in recent decades as a noninvasive neuromodulatory intervention for treatment-resistant depression and obsessive-compulsive disorder. However, in the last decade, there is a growing body of literature on the potential beneficial effects of