

CURRENT STATUS OF REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION (rTMS) IN CROATIA AND IN UNIVERSITY PSYCHIATRIC HOSPITAL SVETI IVAN

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SUMMARY

This article reviews the history, evolution, and current status of repetitive transcranial magnetic stimulation (rTMS) in Croatia. University Psychiatric Hospital Sveti Ivan experts performed the first rTMS in 2015 as a first treatment and research group in Croatia. In addition to being a leading center for rTMS in clinical trials and in treating depression, University Psychiatric Clinic Sveti Ivan TMS center continues to research rTMS for depression and other neuropsychiatric disorders and conditions, exploring novel stimulation parameters and individualized treatment protocols. Since 2017 rTMS treatment for MDD in Croatia has been reimbursed by the National Insurance Fund and has been available to hospital and ambulatory patients by indication, and now is widely used in other health centers in Croatia, to treat depression and other neuropsychiatric disorders and conditions, especially when drugs are ineffective or produce harmful side effects.

Key words: transcranial magnetic stimulation - major depressive disorders - psychiatric disorders

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INTRODUCTION

The current progress of basic and clinical sciences creates a strong backing for new therapeutic appliances of brain stimulation methods in psychiatric disorders. Non-invasive brain stimulation techniques are becoming a part of psychiatrists' therapeutic arsenal, particularly in the treatment of major depressive disorder (MDD) (Baeken et al. 2019). High-Frequency (HF), Repetitive Transcranial Magnetic Stimulation Therapy (rTMS) is an established and effective treatment for treatment-resistant depression, obsessive-compulsive disorder, and several other neuropsychiatric disorders and is used worldwide (Lefaucheur et al. 2014)

REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION THERAPY IN UNIVERSITY PSYCHIATRIC HOSPITAL SVETI IVAN

University Psychiatric Hospital Sveti Ivan TMS center, one of the largest psychiatric treatment groups in Croatia, is a leader in researching and using rTMS for treatment of refractory depression and other psychiatric conditions. The history of TMS application in Croatia started in 2009, when Professor Igor Filipčić finished TMS education at the Berenson-Allen Center for Non-invasive Brain Stimulation at Beth Israel Deaconess Medical Center and Harvard Medical School, under the mentorship of Professor Alvaro Pascual-

Leone. This resulted in introducing a new treatment method in Croatia shortly after. Under his leadership, University Psychiatric Hospital Sveti Ivan experts performed the first rTMS in 2015, being the first treatment and research group of this kind in the country. The application was performed using a Magstim Rapid (Magstim Company, Spring Gardens, UK) with figure-8-coil. A figure-8-coil is advantageous in the localized stimulation of specific superficial regions of the brain and is now widely used in basic and clinical medicine. Most of the treated patients in first years suffered from treatment-resistant depression. Our center's first experiences and research confirmed that augmentative treatment with rTMS using the figure-8-coil was more effective on depression and anxiety symptoms than standard therapy alone in MDD, but with equal safety and tolerability.

Several rTMS clinical studies conducted in our Center have conclusively demonstrated how deeper brain stimulation of specific areas stimulations achieved better therapeutic effects (Filipčić et al. 2017). Realizing the importance of deeper brain stimulation, H1-coil rTMS was introduced to Clinical practice of our TMS Laboratory in 2017. Deep TMS (dTMS) delivered with the H1-coil (designed to target the prefrontal cortex bilaterally with preference for the left hemisphere), allows non-invasive stimulation of deeper brain regions. (Roth et al. 2007, Zangen et al. 2005) We performed a first and only, head to head industry-independent, randomized-controlled trial to assess differences in clinical efficacy and tolerability

between HF-rTMS modalities with the figure-8-coil and the H1-coil in the treatment of MDD. The study observed a better response rate and greater reduction of depression severity in the H1-coil group but without a significant difference in the remission rate between the two rTMS modalities. Both HF-rTMS modalities were comparably safe, with no dropouts for the adverse events. Although not specifically designed to address questions about rTMS tolerability, the high retention rate (93%) observed in our study and the absence of serious adverse events underscore the safety profile associated with both rTMS modalities (Filipčić et al. 2019). Furthermore, in our TMS laboratory, we investigated the efficacy and safety of accelerated deep TMS protocol with H1-coil. Our results do indicate comparable tolerability to the standard protocol (Filipčić et al. 2020).

In 2019, our TMS laboratory started treatment and research with two new coils: 1. H7-coil was designed to primarily stimulate the medial prefrontal cortex (mPFC) and anterior cingulate cortex; 2. H4-coil is precisely designed to bilaterally stimulate a specific cortical target for the addiction, namely the prefrontal cortex, between the entorhinal cortex and the insula (Dinur-Klein et al. 2014).

Currently, we are conducting several trials with different coils in different psychiatric and neurological disorders with different stimulation parameters and treatment protocols. We are investigating the efficacy and safety of H7-coil HF rTMS in treating the negative symptoms of schizophrenia, applied once daily during twenty days, as augmentative therapy to the standard antipsychotic and other pharmacotherapy; LF/HF rTMS, with H7-coil applied in the treatment of idiopathic, chronic, normo-acoustic tinnitus disorder; accelerated twice daily protocols for depression. Furthermore, we are investigating the efficacy and safety of deep TMS with H4-coil and H7-coil in gambling and other addiction disorders.

The number of patients with various psychiatric disorders treated with rTMS is increasing every year with the greater availability of the devices and the increasing awareness of the public. Since the introduction of rTMS treatment in the University Psychiatric Hospital Sveti Ivan, more than 1500 patients from Croatia and 100 from the region and the EU have been treated. Until 2022 we treated 75% of patients with MDD, 10% with schizophrenia, 5% with OCD and PTSD and 5% with other disorders and conditions such as addiction, neuropathic pain, and tinnitus.

CURRENT SITUATION IN CROATIA

Since 2017, rTMS treatment for MDD in Croatia has been reimbursed by the National Insurance Fund

and has been available to all patients by indication. Croatia has a universal healthcare system, and its population is covered by a basic health insurance plan provided by statute and optional insurance administered by the Croatian Health Insurance Fund. That means that every citizen has the same accessibility to healthcare which allows the widespread use of rTMS treatment.

In Croatia, besides University Psychiatric Hospital "Sveti Ivan" TMS is being applied today by a psychiatrists at University Psychiatric Hospital Vrapče, Zagreb University Hospital Centre, Sestre milosrdnice University Hospital Centre, and Rijeka University Hospital.

In 2018, the Croatian Society for Brain Stimulation of the Croatian Medical Association was established to advance non-invasive brain stimulation in Croatia. This society works to optimize the use of rTMS while continuously developing and improving TMS therapy, educating clinicians, expanding insurance coverage, and raising public awareness.

In this respect, rTMS is now widely used in Croatia to treat depression and other neuropsychiatric disorders and conditions, especially when drugs are ineffective or produce harmful side effects.

CONCLUSIONS

The clinical field of non-invasive brain stimulation in Croatia is rapidly evolving. rTMS is widely used in Croatia to treat depression and other neuropsychiatric disorders and conditions, especially when drugs are ineffective or produce harmful side effects. Since 2015, besides being a leading center of rTMS clinical trials to treat depression, University Psychiatric Clinic Sveti Ivan TMS center has continued to research rTMS for depression and other neuropsychiatric disorders and conditions, evaluating novel stimulation parameters and individualized treatment protocols.

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Conflict of interest:

Prof. Igor Filipčić has received equipment for research from Brainsway. He has served on a scientific advisory board for Janssen and Brainsway and received personal fee from Eli Lilly and Company, Lundbeck, Pfizer, TEVA, Belupo, Gideon Richter. For the remaining authors no conflicts of interest were declared.

Contribution of individual authors:

All authors contributed to writing of this paper equally and approval of the final version.

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