ISSUE TOPIC
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WHAT IS A TRANSCRANIAL MAGNETIC STIMULATION?

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Abstract

Transcranial magnetic stimulation (TMS) is a noninvasive method of stimulating the brain through the intact scalp by induction of electric field. We can distinguish different stimulating parameters, like single pulse TMS which can cause twitching of the specific muscle or group of muscles depending which part of the primary motor cortex is being stimulated, or repetitive TMS consisting of repeated pulses that can have more prolonged effects on the brain. Additionally, single pulse TMS is used to record motor evoked muscle responses in target muscles while mapping primary motor cortex. This TMS technique is also applied clinically in therapy of depression and in the research of therapeutical effects in pain, stroke recovery, epilepsy, and movement disorders. In recent years, navigated TMS is used in the operating room to guide surgery and has taken a prominent place in the field of presurgical functional mapping techniques. Although TMS has clearly made a clinical contribution in therapy and preoperative neurosurgical mappings, further work is needed to prove its value in treating pain, stroke recovery and mapping specific cognitive functions like speech and language.

KEYWORDS: depression, neuronavigation, preoperative mapping, TMS, transcranial magnetic stimulation

INTRODUCTION

Transcranial magnetic stimulation (TMS) is a method of stimulating the brain through the intact scalp without causing pain. The stimulator produces a magnetic field that lasts for only about a millisecond. The magnetic field easily penetrates the scalp and skull, and because it changes rapidly (from zero to a very high value, then back to zero again), it induces electrical currents.[1] The induced electrical stimulus activates a mixture of neurons (the axons of neurons in the cortex and subcortical white matter) in the area of the brain beneath the coil. The final outcome of such stimulation might be complex because some synapses are excitatory, others inhibitory and the projection of some neurons goes far from the site of stimulation. Most of the knowledge about TMS on the human cortex comes from studies of the primary motor cortex. Mapping of primary motor cortices with single TMS pulse evokes activity in muscles on the opposite side of the body which can be recorded with electromyography (EMG) as the motor evoked responses. A single stimulus evokes a burst of activity in the corticospinal tract that also causes twitching of the specific muscle or group of muscles depending which part of the primary cortex is being stimulated. The size of the response depends on, first, the level of activity in the cortex at the time the stimulus is given and, second, the orientation of the TMS coil on the head. The muscle response is larger if the stimulus is applied when subjects are actively contracting the target muscle than if they are relaxed. The standard procedure for mapping the precentral gyrus of the primary motor cortex is perpendicular orientation (position) of the TMS coil to the central sulcus. Compared to single TMS pulses, repetitive magnetic pulses (rTMS) can have more prolonged effects on the brain. The duration of the after-effects is often 30 to 60 min, but depends on the number of pulses applied, the rate of application and the stimulation intensity. For example, application of the stimulation over the motor cortex at 1 Hz for about 25 min (1,500 total stimuli) reduces motor cortical excitability.[1] Stimulation at frequencies higher than 1 Hz tends to increase cortical excitability.[1] This showed that rTMS could interfere with processes that contribute to natural behaviours, a necessary step when considering possible therapeutic applications.

TMS IN THERAPY OF DEPRESSION AND OTHER CONDITIONS

The initial clinical trials of rTMS began more than 15 years ago and now there are over 15 meta-analyses and numerous systematic reviews with investigations in patients with drug-resistant depression. It is known that patients with depression have reduced activity in the left prefrontal cortex. Therefore, rTMS studies were designed to excite this area with high-frequency stimulation, and to achieve a long-lasting effect by applying rTMS during several daily sessions. More recently, investigators have focused on the idea that there is an imbalance in the activity of the frontal lobes, with hypo-function in the left frontal lobe being caused by excess inhibition from the right frontal lobe. This led to the idea that an alternative treatment would be application of low-frequency (suppressive) rTMS of the right prefrontal cortex. It seems that the investigators were not necessarily relying on rTMS alone to produce a lasting correction in brain activation. An assumption was that rTMS might interact with some natural process and lead to restoration of normality in malfunctioning neural circuits. Although most studies suggest that rTMS does improve depression (and there are no reports that it makes depression worse), a number of authors suggest that it offers little, if any, advantage over placebo rTMS. Evidence of satisfactory clinical benefit should have been verified with standardized, validated clinical depression rating scales. Examples of such scales include the Patient Health Questionnaire, 9-Item Scale or the Quick Inventory of Depressive Symptoms.[2] It is considered that this technique might help some patients slightly more than placebo, but currently we do not know the most effective dose nor the best group of patients to target. Diagnostically simpler conditions that have been studied more recently, such as auditory hallucinations in schizophrenia and tinnitus may prove more tractable. TMS is also applied clinically for multiple neurological disorders including chronic pain, stroke recovery, epilepsy, and movement disorders. Parkinson's disease research followed a similar logic to depression, namely because motor cortex excitability is low, increasing it with rapid rTMS might improve movement, but so far, benefits have been too mild for clinical approval.[3] Because tinnitus involves overactivity of the auditory cortex, slow rTMS is used to suppress it, but clinical benefit is uncertain. Epilepsy is also treated with suppressive TMS.[4] Improving recovery from stroke is complex and may require increasing and decreasing different types of cortical excitability. Besides depression, for rTMS treatment, best results are considered to be in treating chronic pain.[4] Research has established that a coil delivering biphasic pulses should be placed over the precentral gyrus (primary motor cortex) contralateral to the painful side with a posteroanterior orientation. High frequency (10 or 20 Hz) should be used to activate projecting axons and local interneurons. Repeated TMS sessions can provide pain reductions for at least several weeks after 10 consecutive weekday sessions, but the optimal timing for long-term efficacy and safety are undefined. It is also largely unexplored whether rTMS should also be considered for acute pain, such as postoperative, acute or nociceptive/inflammatory pain, and whether it should be combined with medications or physical therapy. Most research studies provide proof-of-concept that rTMS can improve some chronic pain syndromes. Neuropathic pain syndromes are reported to benefit most, but they have been insufficient to confirm specific indications and best methods.[5]

TMS IN PREOPERATIVE FUNCTIONAL CORTICAL MAPPING

The surgical removal of brain tumours is frequently associated with a high risk of causing disabling postoperative deficits. Among the preoperative techniques proposed to help neurosurgical planning and procedure, navigated transcranial magnetic stimulation (nTMS) is increasingly performed. Intraoperative stimulation mapping provides reliable functional anatomical information on the cortical and subcortical location of motor control and represents the ''gold standard'' technique in this context. In recent years, nTMS has taken a prominent place in the field of presurgical functional mapping techniques, as a noninvasive approach to mimic intraoperative stimulation mapping by probing the cortex with transcranially produced intracortical electrical stimulation. Not long after the introduction of TMS, the use of it to perform functional mapping of the motor cortex was proposed, including in preoperative testing. The nTMS technique of cortical mapping is performed by stimulating multiple points on the scalp of the patient corresponding to the possible cortical motor regions and by concomitantly recording motor evoked potentials for each stimulation point. The stimulated area must cover the precentral gyrus and the adjacent anterior and posterior gyri, since functionally relevant motor function can be located outside of the precentral gyrus. The motor response to each stimulation spot is usually visualized with a colour code, corresponding to the value of motor evoked potentials amplitude. The resulting nTMS maps generally have the appearance of coloured markers corresponding to all the stimulation spots and placed on the individual patient's magnetic resonance imaging. These data can be transferred to the neuronavigation system used in the operating room to guide surgery. We should also consider indications for nTMS motor cortical mapping other than brain tumour surgery. For example, it was proposed to guide radiosurgical planning or the surgical treatment of intracranial arteriovenous malformations. The mapping data produced by nTMS can sometimes be very different from the expected cortical somatotopy, demonstrating that the neural representation of motor function can undergo great changes related to plasticity processes induced by the presence of the tumour. In correlation with intraoperative intraoperative stimulation mapping, preoperative nTMS improves surgical outcomes by increasing the extent of resection, without compromising patient safety and motor function, which is associated with a better postoperative quality of life.[6] Future improvements of the nTMS technique are expected, for example by integrating fibre-tracking data provided by diffusion tensor imaging in addition to structural MRI. The use of diffusion tensor imaging tractography may help to reduce the remaining inaccuracy of the nTMS approach and help to overcome its restriction to the cortical level. Furthermore, many studies so far used rTMS in cortical mappings of speech and language functions by producing different errors in speech and language (i.e. speech arrest, phonological paraphasia). However, further studies need to develop optimal methodologies for mapping cognitive functions like speech and language, memory, and calculation that could be used in preoperative mappings of patients undergoing surgical procedure.

TMS SAFETY ISSUES

Treatment with TMS causes few side effects and is generally well tolerated by participants. However, it cannot be applied to an individual with metal parts in his or her brain, because these may have electrical currents induced and move in the magnetic field. Implanted brain stimulators and cochlear implants may be damaged by the magnetic fields. The greatest cause for concern is the potential risk of inducing a seizure in subjects with history of epilepsy. Single pulse TMS is usually regarded as safe in this respect, but repeated stimulation, particularly at certain frequencies, is potentially epileptogenic. Because risk is higher in people with previous seizures or brain lesions, or with use of medications that reduce the seizure, we consider these parameters as a relative contraindication to medical use of TMS. The most common complaint is headache, usually after TMS treatment. These may be caused by pressing the coil against subjects' heads for extended periods or by the muscle contractions induced. Other reports include pain at the stimulation site, neck pain, muscle aches, dizziness, nausea, tiredness, and tinnitus. The outcomes above lead to the development of guidelines for the safe administration of TMS.[7]

CONCLUSION

TMS has clearly made a contribution for treatment of depression and is a valid technique to optimize preoperative surgical planning. Further progress, is expected in research of therapy effects in other conditions like pain, recovery after stroke, as well as in development of optimal methodologies for preoperative mappings of specific cognitive functions like speech and language, memory and calculation.

Acknowledgments:
I am especially thankful to Maja Rogić Vidaković, PhD (Department of Neuroscience, Laboratory for Human and Experimental Neurophysiology (LAHEN), School of Medicine, University of Split) for her generous help in reading the manuscript and for providing insightful comments.

References:

1. Ridding MC, Rothwell JC. Is there a future for therapeutic use of transcranial magnetic stimulation? Nature Reviews Neuroscience. 2007; 8: 559-567.
2. Perera T, George MS, Grammer G, Janicak PG, Pascual-Leone A, Wirecki TS. The Clinical Tms Society Consensus Review and Treatment Recommendations for Tms Therapy for Major Depressive Disorder. Brain Stimul. 2016; 9(3): 336-46.
3. Strafella AP, Paus T, Fraraccio M, Dagher A. Striatal dopamine release induced by repetitive transcranial magnetic stimulation of the human motor cortex. Brain 2003; 126: 2609–15.
4. Klein MM, Treister R, Raij T, et al. Transcranial magnetic stimulation of the brain: guidelines for pain treatment research. Pain. 2015; 156(9): 1601-14.
5. O'Connell NE, Wand BM, Marston L, Spencer S, DeSouza LH. Noninvasive brain stimulation techniques for chronic pain. Cochrane Database Syst Rev 2014; 4: CD008208.
6. Lefaucheur JP, Picht T. The value of preoperative functional cortical mapping using navigated TMS. Neurophysiol Clin. 2016; 46(2): 125-33.
7. Rossini PM, Burke D, Chen R, et al. Non-invasive electrical and magnetic stimulation of the brain, spinal cord, roots and peripheral nerves: Basic principles and procedures for routine clinical and research application. An updated report from an I.F.C.N. Committee. Clin Neurophysiol. 2015; 126: 1071-107.

ŠTO JE TRANSKRANIJSKA MAGNETSKA STIMULACIJA (TMS)?

Sažetak

Transkranijska magnetska stimulacija (TMS) je neinvazivna metoda kojom se može pobuditi mozak kroz lubanju induciranjem električnog polja. Postoje različiti parametri stimulacije, kao što je stimulacija s jednim pulsom i stimulacija serijom repetitivnih pulseva. Metoda pojedinačnih stimulusa koristi se za snimanje motoričkih evociranih potencijala i izazivanje kontrakcija specifičnog mišića ili mišićnih skupina tijekom mapiranja primarne motoričke kore mozga. Repetitivna stimulacija može imati dugotrajnije učinke na podražljivost mozga, stoga se koristi u terapiji depresije i istraživanjima terapijskih učinaka kod boli, moždanog udara, epilepsije, i motoričkih poremećaja. Od nedavno, navigacijska TMS se koristi u preoperativnom neurokirurškom planiranju operacije mozga i trenutno zauzima vodeće mjesto među preoperativnim funkcionalim metodama. Iako TMS metoda ima značajan doprinos u preoperativnom funkcionalnom mapiranju mozga i terapiji depresije, potrebna su daljna istraživanja za dokazivanje učinkovitosti u liječenju boli, oporavka od moždanog udara, te razvoj optimalnih metodologija u mapiranju govorno-jezičnih područja.

KLJUČNE RIJEČI: depresija, neuronavigacija, preoperativno mapiranje, TMS, transkranijska magnetska stimulacija

Received December 1, 2016.
Accepted April 11, 2017..