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TRANSCRANIAL MAGNETIC STIMULATION: CLINICAL APPLICATION AND SCIENTIFIC PERSPECTIVES

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Abstract:

Transcranial magnetic stimulation (TMS) is a method of neurostimulation and neuromodulation based on electrical induction of an electronic field in a given area of the brain. Since the 1990s attention to TMS has been growing steadily, because this method is considered noninvasive and potentially has broad diagnostic and therapeutic probabilities: the number of publications devoted to TMS.

Keywords: transcranial magnetic stimulation, electric field, brain,

INTRODUCTION. TMS is based on the connection between electronic and magnetic fields and the phenomenon of electrical induction, which was discovered back in 1831 by the British physicist M. Faraday. An electric coil is specified over a particular part of the brain, in which a current of some thousand amperes appears after a short discharge of a massive magnetic catalyst (capacitor). This current generates a magnetic background perpendicular to the direction of current in the coil, the intensity of which reaches 1.5-2 Tesla (T), and the duration - 100 ms. Vibrantly changing magnetic background unceremoniously penetrates inside the skull to the depth of 1.5-3 cm and induces electronic background in the brain tissue (parallel, but inversely directed with respect to the current in the electric coil). Under the influence of the induction electron field, depolarization of cortical neuronal membranes with the appearance of exposure potentials and spread of excitation in the stimulated areas of the cerebral cortex occur. The trait of the electric field in TMS depends on the shape, volume, system of the electric coil (coil) and its orientation in relation to the patient's head, on the characteristics of stimulation. More often, they use circular coils of different cross-section, coils in the form of the number 8 (in the form of a "butterfly"), in the form of a letter. With the help of an eight-shaped coil it is possible to implement local (with an accuracy of 0.5 cm) stimulation of the brain structures nearest to the scalp plane, such as the cerebral cortex of the large brain hemispheres, the cerebellum; the coil is placed tangentially to the scalp, with the possibility of stimulating the nervous structures is maximum in those areas that are aimed parallel to the central sectors of the coil. Stimulation of wider areas is performed with the support of round coils; introduction of special H-coils allows to realize stimulation of deep brain structures (hippocampus, subcortical formations, brain stem).

TMS can be performed with single stimuli (single-pulse mode), paired stimuli, or series of pulses (repetitive TMS, or pTMS). Single stimuli are used, for example, in mapping of motor cortical zones and in studying the central conduction time of motor response; paired pulses are used in studying active connections in the cerebral cortex. TMS with series of pulses is widely used for therapeutic purposes; it is possible to use the delivery of systematic repetitive single stimuli (the so-called conventional TMS or "conventional" TMS) or the delivery of patterned compositions of stimuli (pattern-based PTMS). Pattern TMC involves a brief series of high-frequency pulses broken by pauses; for example, the theta burst protocol involves brief volleys of 50 Hz pulses renewed with theta-band frequency (5 Hz) in unchanged or intermittent modes. In recent years proposed a fresh paradigm of dosing TMS, allowing influence on once and the same area of the brain by stimuli of different frequency, bilateral effects. Harmless characteristics of stimulation are reflected in detail in special manuals. The influence potential formed in a neuron under the action of TMS impulse spreads along the axon and can activate a large number of surrounding neurons of all possible modalities through synapses. As a consequence, under the action of TMS in the brain there are all chances to have the effects of both short excitation and inhibition, and any catalyst, probably, has the ability to cause both of these effects depending on its own intensity and duration. Back in the 90's it was shown that the effect of PTMS with frequency ≥ 5 Hz functions in an excitatory way, and at frequencies of 0.2-1 Hz - inhibitory way. Subsequent

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experiments on cats with the study of metabolic vigor in the posterior parietal cortex just after the PTMS session approved the dependence of inhibition and excitation processes in the brain on the stimulation frequency. However, the notion that rapid PTMS leads to excitatory physical effects, and unhurried PTMS leads to inhibitory ones, is considered to be very simplistic and is not always confirmed. The nature of neurophysiological shifts is significantly influenced by the mode of stimulation. For example, stimulation in an intermittent theta burst mode (2 seconds of stimulation and a 10-second pause) led to an increase in excitability, while unchanged (for 40 seconds) stimulation in the same mode led to a decrease in it. At the cellular level, the inhibitory or excitatory effect of TMS is explained by depolarization of the membrane of cortical neurons under the influence of the induction electron field, the appearance of transmembrane ion current and the effect potential with further synaptic excitation box on neuronal networks, functionally or anatomically connected with the stimulated area. From the point of view of active systems, TMS probably has the ability to influence the processes of function regulation by influencing some neurotransmitters. Thus, stimulation of the frontal lobe with a frequency of 20 Hz led to a significant elevation of dopamine in the hippocampus; stimulation of the left dorsolateral prefrontal cortex (20 Hz, 20 min a day) changed the degree of glutamate in the cortex not only on the stimulated side, but also on the reverse side. On a theoretical level, these findings have every chance to explain the device of both the therapeutic and side effects of TMS. The position of the endocrine system as a probable factor capable of attributing some of the physical effects of TMS deserves special interest. In a number of studies, it was found that the effect of TMS has the ability to lead to a short-term increase in plasma thyroid hormone (TSH) both in healthy individuals and in depressed patients. At the same time, subthreshold stimulation led to a transient decrease in plasma TSH and cortisol in volunteers, indirectly indicating a relaxing effect of subthreshold TMS in healthy individuals. It is also likely that TMS has a modulating effect on the immune system, autonomic regulation of functions, cerebral hemodynamics (reactivity of cerebral vessels). Rhythmic TMS can have not only immediate, but also delayed effects, the basis of which is probably the processes of neuroplasticity (modification of synapses under the influence of periodic cyclic influences, production of neurotrophic factors). Overall, the mechanisms of TMS effects remain largely unclear and strongly suggest further investigation. Indications for the therapeutic use of TMS are limited due to the ambiguity of the results of clinical studies of this method: to date, either there is no convincing evidence of its superiority to placebo for those or other types of pathology, or very weak benefits are demonstrated; not counting this, most studies have not adequately tested the placebo effect, which makes it doubt the actual effectiveness of the method. Currently, in the U.S., Canada and some European countries as the only approved indication for the use of TMS with a therapeutic purpose is considered resistant to drug therapy for depression, with the Office of the Food and Drug Administration USA (U.S. Food and Drug Administration, or FDA), Health Canada, the European Medical Agency gave permission to implement for medicinal purposes only specific devices specifying the manufacturers and certain titles stimulation systems.

Because neuroimaging studies of depression have shown hypometabolism in the left dorsolateral prefrontal cortex (DLPC), stimulation (high-frequency) series of pulses on the left DLPC is used more often to treat refractory depression (e.g., 10 Hz every day, 5 sessions per week, 2-6 weeks). Less frequently, inhibitory low-frequency stimulation of the right DLPC or bilateral stimulation is used. The characteristics, localization, and duration of stimulation have not yet been standardized. Efficacy of TMS in therapy of depression is proved by randomized research works. A meta-analysis of data from 34 placebo-controlled studies and 6 studies comparing TMS to electroconvulsive therapy for depression found that TMS was actually more effective in treating depression than placebo, with TMS monotherapy being more effective than a combination of TMS and antidepressants, but less effective than electroconvulsive therapy for depression. According to some reports, the best effect with the support of TMS has the possibility to be achieved in persons of more young age. Not all studies and not all reviews recognize the therapeutic effect of TMS in depression. Negative outcomes have all chances to be justified by the lack of basic knowledge about those parameters of TMS applied in therapy of depression.

The indications for diagnostic application of TMS in medical practice in the real time are limited by mapping of motor and speech cortical areas in the preoperative period of neurosurgical intervention on the brain. There are 2 leading strategies of obtaining information about cortical localization of functions: (1) registration of brain vigor during performance of tasks (passive) and (2) supervision of the effects of evoked/inhibited neuronal vigor in specific cortical areas. The first strategy is implemented with the support of electroencephalography (EEG), positron emission

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tomography (PET), and active magnetic resonance imaging (fMRI); the second strategy is supported by TMS; the superiority of the latter is the least servility of the results to the cooperative efforts of the subject; the possibility of studying intracortical interactions and identifying specific cortical areas that are critical in performing that or another function. For the purpose of mapping of cerebral functions, a uninomial TMC is used. To study cortical muscle consulteration, the inducer is placed over the scalp according to this projection of the primary motor cortex with the coordinate system referenced to the vertex. In response to a single presented catalyst, a volley of descending waves of excitation is seen in the motor cortex, which are directed to the alpha-motoneurons of the spinal cord, and from there through the peripheral nerves to the target muscle on the contralateral side of the body. EMG recording of target muscle reduction (motor evoked potential) allows studying these characteristics, such as motor threshold (minimum magnetic field strength important to reach the motor evoked potential in the target muscle); latent stage of the evoked motor response; central motor conduction time (difference of latent periods in responses evoked by cortical and cervico-spinal TMC); amplitude and configuration of the evoked motor response. Stimulation of various areas of the scalp highlights the possibility to quite literally qualify facets of the cortical consulate of skeletal muscles, because the targeted delivery of a magnetic pulse has the ability to cause isolated movement, including only the 1st finger. Preoperative TMS mapping in patients with brain tumors allows timely detection of motor area configurations due to tumor-induced anatomical and physical restructuring of functions.

Speech zone mapping has been developed to a lesser extent, however, this purpose is actively developing. Back in the 90's, it was found that local influence of the magnetic field on the speech zones can lead to a speech function disorder. In order to map the speech functions using the TMS method, a patient is presented with all kinds of speech tests and the dynamics of their performance results under the influence of TMS is considered. Thus, T. Picht et al. studied 20 neurosurgical patients with left hemisphere loss, presenting them with the analysis of naming objects; the highest level of coincidence between the results obtained during preoperative TMS-mapping and intraoperative mapping (when the patient wakes up) was demonstrated. Thus, with the support of TMS is possible to qualify those areas of the cortex, which can be safely, without risk of becoming a postoperative neurological deficit, send during resection of a tumor or epileptogenic focus. The accuracy of monitoring corresponds to that obtained with the support of invasive mapping of cerebral functions during specific intracranial electrostimulation. The leading problem is made by impossibility of clear proportion of a point of stimulation with anatomic formations of a brain in view of significant personal variants. For example, the reference zone in cortical mapping is the initial motor area of the thumb, which, however, contains important personal variants, and the localization of the brain area relevant to this space varies even more due to all kinds of head volumes and differences in cortical morphology. Fresh generation apparatuses using navigation systems and combining TMS with fMRI allow to increase mapping accuracy to a significant degree, to make structural and functional maps of the brain.

Epilepsy Some modes of PTMS (e.g., low-frequency ≤ 1 Hz PTMS or unchanged TMC in theta burst mode) have all chances to destroy excitation in the cortex, quite possibly as a result of modulation of gamma-aminobutyric acid (inhibitory mediator) energy and increase in the threshold of convulsive readiness. In connection with this, the ability of TMS to promptly terminate a seizure was considered, for example, in focal status epilepticus and in unchanged partial epilepsy. In locally determined epilepsy with the support of TMS it is likely to affect the cortical focus-focus of epileptic energy or in subcortical focus - on the adjacent cortical area; in this medial temporal lobe, for example, is not available to stimulation. Quite all, but not all studies have shown a reduction in the frequency of epileptic seizures when exposed to TMS, not counting such, not all of them were randomized placebo-controlled. In some cases, the poor efficacy of TMS has been attributed to the inappropriateness of the epileptogenic focus; it is likely that modern navigation systems will allow for better therapy outcomes.

CONCLUSIONS: Thus, TMS is considered to be a noninvasive method of neurostimulation with great diagnostic and therapeutic potential. Further study of devices for the effect of an alternating magnetic field on the brain, clarification of good magnetic coil localization and stimulation characteristics for all possible forms of pathology, investigation of the magnitude and persistence of the achieved effects, and evaluation of healing risks will be required. Conclusion of these questions will allow to expand indications for clinical use of TMS, to make progress in our understanding of pathophysiology of psychoneurological disorders.

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