Transcranial Magnetic Stimulation as a Promising Tailored Medicine for Neurological Disorders: Beyond Chemical Drugs

Opinion

Despite an ever-growing knowledge of brain function, the cellular and molecular mechanisms that ultimately lead to distinctively human processes such as memory and cognition remain an enigma. Thus, the study of brain is an exciting area of research. Alterations in these pathways seem to play a crucial role in the onset and development of neurodegenerative diseases, both those linked to ageing like Alzheimer and Parkinson diseases, and others such as multiple sclerosis, which presents in young people, limiting quality of life and productive capacity. The management of patients with these conditions impacts negatively on health care systems, especially those public ones in which resources are more limited. Understanding the mechanisms and pathways underlying CNS disorders is critical for the design of therapeutic strategies which not only prevent their evolution but also revert and cure them.

Transcranial magnetic stimulation (TMS) is a novel tool that is helping to reveal how different brain areas and neuronal structures are connected to execute a single coordinating function or process. In addition to its utility for the study of brain networks, TMS is becoming a potent non-invasive instrument, with minimal side effects, for the treatment of neuropsychiatric disorders. The magnetic field generated by TMS is translated into electrical current in the brain when this energy passes through the skull, leading finally to diverse biochemical effects, such as: attenuation of inflammation and oxidative/nitrosative stress, improving cell density by reducing necrotic/apoptotic processes, and promoting neurotrophic/neuro genetic phenomena [1].

Especially interesting is the effect on brain plasticity induced by some paradigms of TMS [1]. These studies have revealed that TMS modifies the expression of genes and proteins that mediate these phenomena, such as cFos (10 Hz repetitive TMS) and zif268 (10 Hz intermittent theta-burst stimulation) [2]. Moreover, repetitive TMS appears to induce the activity of the cyclic AMP-cyclic AMP response element binding protein pathway in cell cultures [3]. A protein crucial for brain plasticity is brain-derived neurotrophic factor (BDNF), which can also be induced by TMS. In 2012, our group demonstrated that application of 60-Hz extremely low frequency magnetic field generated by TMS is translated into electrical current in the brain when this energy passes through the skull, leading finally to diverse biochemical effects, such as: attenuation of inflammation and oxidative/nitrosative stress, improving cell density by reducing necrotic/apoptotic processes, and promoting neurotrophic/neuro genetic phenomena [1].

There is little doubt that TMS can be an extremely versatile tool. When preparing a session of TMS, it is essential from the beginning to define which effects one desires to achieve. Different stimulation settings concerning frequency and intensity of the pulse, number of trains, pulses/train, and area/angle of stimulation may lead to equivalent or antagonist effects. Besides, the same paradigm of transcranial brain stimulation applied with different settings may result in excitatory or inhibitory stimulations (Table 1), extending the therapeutic potential of TMS. Such is the case for depression in which stimulation with repetitive low-frequency TMS (1Hz) over the right dorsolateral prefrontal cortex (an inhibitory protocol) has been reported to present a quite similar antidepressant effect than repetitive high-frequency TMS (5-20 Hz) over the left dorsolateral prefrontal cortex (an excitatory protocol) - emphasizing the complexity of brain networks and TMS therapy [11]. Pre-treatment studies using functional brain tests such as functional magnetic resonance imaging, positron emission
Conclusion

To conclude we would like to stress that:

i. TMS is a novel, versatile therapeutic strategy with great possibilities to combat neurodegenerative diseases.

ii. Well-controlled clinical trials as well as experimental studies are still necessary to confirm TMS therapeutic potential and elucidate the mechanisms and pathways involved in its beneficial effects.

iii. The effectiveness of TMS therapy will be linked to how its application is tailored. Genetic studies and functional brain imaging open new paths to optimize the treatment with TMS.

References


Table 1: Excitatory or inhibitory effect of several paradigms of transcranial brain stimulation.

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<th>Conventional rTMS</th>
<th>PPS</th>
<th>QPS</th>
<th>PAS</th>
<th>TBS</th>
<th>tDCS</th>
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<tbody>
<tr>
<td>Excitatory effect</td>
<td>&gt; 5 Hz</td>
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<td>Short intervals</td>
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<tr>
<td>Inhibitory effect</td>
<td>≤ 1 Hz</td>
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PPS: Paired-Pulse Stimulation; PPS: Paired-Pulse Stimulation; QPS: Quadri Pulse Stimulation; RTMS: Repetitive Transcranial Magnetic Stimulation; TBS: Theta Burst Stimulation; tDCS: Transcranial Direct Current Stimulation