Choosing to improve or to impair

What for a long time appeared as a dream, has now become routine: the targeted and specific modulation of brain activity from outside, effortless without training or attention. Transcranial magnetic stimulation (TMS) alters human behavior and perception through magnetic pulses that induce currents in the brain. When single magnetic pulses are applied from outside the skull over a selected brain region, neurons within this area become transiently suppressed, resulting in what has been called a "virtual lesion" (Pascual-Leone et al., 1999), and this allows studying in an intact brain the contribution of a particular brain region to a particular behavior. In contrast, when magnetic pulses are repetitively applied, modulations of brain activity result that outlast the period of stimulation (Schieber and Rothwell, 2003), and resemble learning processes (Tegenthoff et al., 2005). In fact, many lines of evidence suggest that repetitive transcranial magnetic stimulation (rTMS) causes forms of synaptic plasticity, and many groups now use rTMS as a tool to study learning processes in human individuals.

Cellular studies have focused on long-term potentiation (LTP) and long-term depression (LTD) of synapses in the hippocampus and cortical areas to understand the requirements for persistent changes in the connection strength between neurons (Bliss and Lomo 1973; Malenka and Bear, 2004). LTP at groups of synapses can be induced reliably through intermittent high-frequency theta- namic stimulation, while application of lower frequencies induces LTD (Lomo 1973; Malenka and Bear, 2004). LTP at groups of synapses causes forms of synaptic plasticity, and many groups now use rTMS as a tool to study learning processes in human individuals.

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Clinically, straightforward prerequisites for possible applications for clinical populations are protocols that have the potential to improve function. Therefore, approaches such as high-frequency TMS or repetitive sensory stimulation are widely used as intervention. However, there are conditions of hypersensitivity or hyperactivity, where individuals would benefit from protocols that diminish performance. As mentioned by Rai and colleagues, cerebral palsy is associated with hyper-responsiveness to tactile stimuli, and this is also true for autism, while patients with prefrontal damage have difficulty inhibiting task-irrelevant information (Rai et al., 2012). Also, forms of chronic pain such as typically seen in patients with complex regional pain syndrome might benefit from protocols that provide suppressive action, and which therefore allow a targeted improvement or impairment of human behavior. This poses a novel, yet difficult problem, namely to choose the most appropriate protocol for intervention. In many cases such as in dystonia patients it is not a priori clear whether to further enhance or suppress cortical excitability in order to mediate beneficial behavioral effects, and this holds true for many other examples.

Data from the motor and the sensory domains provide converging evidence that rTMS modulates perception, behaviour and cognition. However, to be efficient, stimulation must conform to requirements described for protocols specifically altering synaptic transmission and synaptic efficacy. The persistence of changes, the ease of application and the wide range of effects make such approaches ideal tools for targeted brain intervention. Given that the use of TMS is a rather recent development, we may be only at the beginning of an era, in which targeted brain manipulation will offer completely new scenarios of learning and intervention, with implications that cannot yet be foreseen.

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References


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