Managing neuropsychiatric disease with transcranial magnetic stimulation

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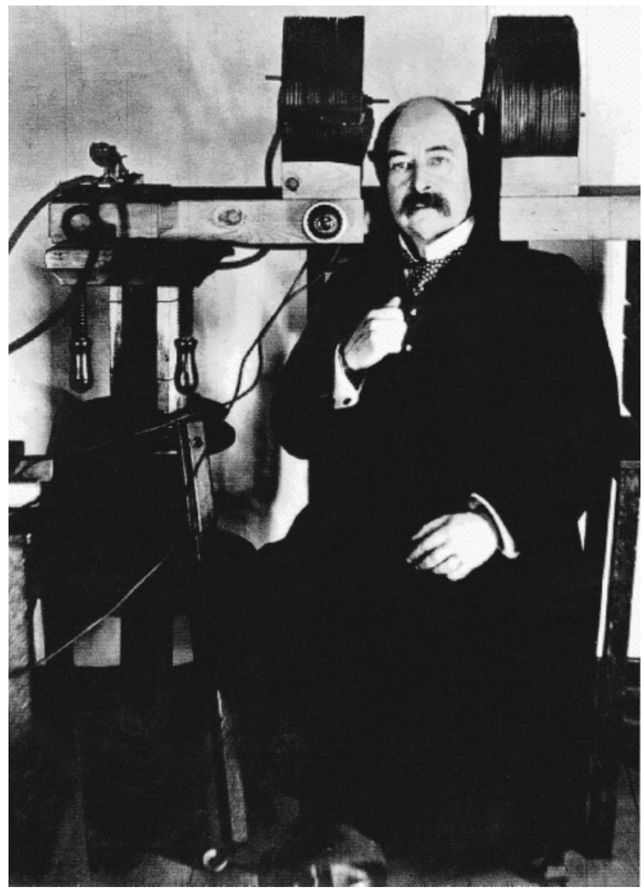
Technology: Transcranial magnetic stimulation (TMS)
Use: A substantial proportion of patients with depression fail to respond to conventional treatment. Transcranial magnetic stimulation (TMS) is a powerful new technology that holds promise both as an antidepressant treatment and as an investigative tool in understanding the pathophysiology of depression. The magnetic stimulator consists of a power supply, a capacitor and the controlling electronics. The capacitor discharges 3000 to 8000 amps through a handheld wire coil, momentarily creating a 2- to 3-Tesla magnetic field around the coil. When the coil is held against the skull, a secondary electrical current is painlessly induced in underlying cortical neurons and action potentials may be triggered. It is also possible to induce changes in the neurons' electrochemical excitability, which last long after the stimulation has been terminated. This process appears to be directional and frequency-dependent, with high-frequency pulses increasing and low-frequency pulses decreasing cortical excitability.
History: Since the days of Mesmer, magnetic forces have been thought to hold special power over human behaviour. The earliest scientific attempts to use magnetic energy to alter brain activity were conducted by D'Arsonval in 1898 and Thompson in 1910 (figure[1]). They built magnetic stimulators powerful enough to activate retinal cells, causing subjects to perceive light flashes, but the fields generated were too weak to stimulate brain tissue. It was not until 1985 that Anthony Barker designed an instrument with sufficient power to activate cortical neurons. Barker's device was quickly adopted by neurologists, who now routinely use single-stimulus TMS instruments to measure nerve-conduction time. The therapeutic potential of TMS was not realized until the repetitive stimulator (rTMS), which can generate up to 30 pulses per second, became available in the 1990s. Using rTMS, 2 groups of investigators[2,3] independently demonstrated that mood could be altered in healthy subjects. These same groups went on to show that rTMS could also improve mood even in patients with medication-resistant depression.[4,5] Although the magnitude of the antidepressant effect was reported to be either statistically[6] or clinically[7] nonsignificant in some studies, in others with higher levels of stimulation energy or larger numbers of subjects, or both, major improvement was reported in 48%[8] to 65%[4] of patients. Use of the rTMS machine for treatment is currently considered experimental and requires regulatory agency approval in Canada and the United States.
Promise: Although further work is required, several blind, controlled studies have demonstrated antidepressant efficacy for TMS,[4,7,8] suggesting that this technology may soon occupy an important place in the psychiatric armamentarium. An open trial[9] has reported comparable antidepressant efficacy for TMS and electroconvulsive therapy (ECT). If replicated, this will represent a tremendous therapeutic advance, because ECT is widely considered the most powerful of all antidepressant treatments. However, unlike ECT, TMS does not require anesthesia or cause cognitive impairment and can be administered by a single operator in an outpatient setting.
Problems: The side effects of rTMS include mild headache, which responds to mild analgesics, and potential hearing dam-



Sylvanus P. Thompson eliciting retinal light flashes with a primitive magnetic stimulator, 1910. Reproduced, with permission, from Barker.[1]

age, which can be prevented with ear plugs. In early studies seizures were induced by high-intensity rTMS. However, when subjects with a history of seizures are excluded, drugs that lower the seizure threshold are discontinued and stimulus safety guidelines are followed, seizures are very rare. The long-term effect of exposure to high-power magnetic fields is unknown, but the experience with MRI equipment suggests that serious adverse effects are unlikely.

Prospects: The theoretical possibilities offered by TMS are enormous. With the capacity to increase or decrease cortical activity, rTMS could potentially "tune" the cortex, to correct for pathological neuronal over- or under-activity. Besides the treatment of selected psychiatric conditions characterized by regional brain dysfunction, other applications are possible. Epilepsy might be improved by reducing cortical excitability, and Parkinson's disease might be treated by increasing the responsivity of the motor cortex. Theoretically, the speed with which the cortex "learns" or acquires new function, for example in post-stroke rehabilitation, could be increased when the activation threshold of cortical neurons is reduced with high-frequency rTMS.

Competing interests: None declared.

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