Non-Invasive Brain Stimulation

Transcranial magnetic stimulation for Alzheimer's disease

Transcranial magnetic stimulation (TMS) modulates cortical activity non-invasively (4). Repetitive transcranial magnetic stimulation (rTMS) creates magnetic pulses to the scalp delivered through a coil at a rhythmic repetition rate. The magnetic pulse causes cortical neurons to depolarize (8). TMS is an important cortical stimulation method for the adjunctive treatment of neurodegenerative disorders such as Parkinson's disease (9). Furthermore, TMS can improve cognitive function in neuropsychiatric disorders (10). RTMS studies revealed the pivotal role of the prefrontal cortex (PFC) during information encoding and retrieval (11–15). Furthermore, as neuroimaging studies revealed, heightened activity in the dorsolateral PFC (DLPFC) is one of the brain abnormalities associated with AD (16, 17). These changes in brain activity in the DLPFC underpin the recruitment of compensatory networks (18, 19). It would thus make sense to modulate the PFC's neural activity to modify memory function, the most prominent feature of disturbed cognition in AD. There is solid evidence that high-frequency rTMS over the DLPFC is superior to low-frequency rTMS in treating cognitive dysfunction in AD patients as measured by the mini mental state examination (MMSE) (20). The first studies using TMS in AD showed that high-frequency rTMS of the DLPFC improves naming accuracy. Demented patients often display impaired naming ability (21). RTMS improved both action and object naming in a group of advanced AD patients (22, 23). Auditory verbal comprehension of continuous daily DLPFC–rTMS over 4 months was increased for up to 2 months after stimulation (24). As the inferior PFC plays a role in controlling memory (25), stimulating that part of the PFC in AD patients is a reasonable approach. Indeed, stimulation of the left inferior PFC resulted in enhanced episodic memory function (26). Alongside the PFC, the parietal cortices are important for information retrieval (27). RTMS of the parietal cortex advances the associative memory capacity in patients with mild cognitive impairment (MCI) (15). The combination of cognitive training with rTMS seems to benefit cognitive functions as much as treatment with cholinesterase inhibitors (28, 29). Moreover, TMS is useful for identifying early AD patients with cholinergic degeneration (30), and for monitoring the drug response (7). The biomarker of central cholinergic activity such as short-latency afferent inhibition (SAI) assessed by TMS is relevant to the drug response (31). Other TMS measures such as long-interval intracortical inhibition (LICI) are also worth considering for measuring drugs. Patients undergoing monotherapy or combination therapy with acetylcholinesterase inhibitors demonstrated impaired LICI when compared to healthy controls (7). Remarkably, the LICI values correlated with Alzheimer's Disease Assessment Scale–Cognitive Subscale (ADAS–Cog) scores. These findings indicate that these neurophysiologic TMS parameters help us measure the response to anti-dementia drugs (7).

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