Transcranial Alternating Current Stimulation – A Novel Way Forward in Mild Cognitive Impairment and Dementia Therapeutics

Dear Editor,

With improvements in healthcare, there is an increase in the longevity of humans and, consequently, an increase in the prevalence of neurodegenerative disorders. Hence, it is imperative to focus on the early diagnosis and effective management of these neurodegenerative disorders to improve the quality of life among the aging population. Since these disorders have no definitive cure, therapeutic modalities aim at delaying their progression. A recent development in this regard has been the use of transcranial alternating current stimulation (tACS) as a therapeutic modality for mild cognitive impairment (MCI) and dementia.

In this letter, we seek to highlight the utility of tACS in MCI and dementia, along with updates on latest developments.

MCI is an acquired deterioration in cognitive abilities, more than what is expected to occur due to aging. Dementia, on the other hand, refers to significant cognitive deterioration that affects the performance of activities of daily living. Presently, there is no definitive cure for dementia caused by neurodegenerative disorders. However, noninvasive brain stimulation (NIBS) techniques have been found to be effective in slowing the progression of neurocognitive disorders, one such technique being tACS.

tACS is a form of NIBS, which delivers sinusoidal alternating current via scalp electrodes for neuromodulation, thereby making it a potential therapeutic modality. In addition, its relative lack of both short- and long-term adverse effects makes it an attractive tool to implement in treatment of patients with cognitive disorders.

tACS acts by initiating alternate depolarization and hyperpolarization in cell bodies of neurons in specific areas of the brain.[1] These "oscillations" of current cause a subthreshold stimulation of neurons, which modifies the likelihood of their firing in a frequency- and location-specific manner. As a result, there are "online effects" (lasting for the duration of stimulation) and "offline effects" (lasting even after the stimulation ceases), which have been proposed to occur due to the phenomena of entrainment and spike-timing-dependent-plasticity (neuroplasticity), respectively.[2] In addition to the amplitude and frequency of the applied tACS, the temporal dynamics of voltage application and the relative orientation of neurons and current also influence its effects on the brain.[3]

As part of the process, tACS electrodes of appropriate sizes are placed over different target areas of the scalp, which are often predetermined. The applied current can be varied based on the parameters of frequency (Hz), amplitude (mA), phase shape, phase timing, and duration of application.[4] Pre- and post-test scores of cognitive assessment tests, magnetic resonance imaging (MRI), electroencephalogram (EEG), and cerebrospinal fluid (CSF) levels of beta-amyloid/tau protein are often used as test parameters.[5]

This technique has several advantages over other methods of NIBS. For instance, it can be used to manipulate specific endogenous brain oscillations by the process of entrainment. Due to its alternating voltage, endogenous oscillations may be promoted or suppressed by depolarization and hyperpolarization, respectively. Unlike transcranial direct current stimulation (tDCS), even imperceptible current strengths can produce physiological entrainment. In addition, the ability to manipulate endogenous brain oscillations enables researchers to determine behavioral causality from neurophysiology. tACS can also be combined with EEG and other NIBS techniques to increase experimental interface.[6]

Furthermore, the side effects produced by tACS are transient, which include phosphene perception, dizziness, and pressure sensation. Mild headache, back pain, and neck stiffness have also been reported. In addition, tACS produces fewer instances of muscle twitching, discomfort, and nausea than other NIBS techniques.[6]

Presently, research is ongoing to determine therapeutic potential of tACS in improving cognitive function in patients as well as in healthy adults.[7] Based on the applied frequency, gamma-tACS has been found to improve cognition, working memory, selective attention, motor performance, and learning and reduce tau protein burden, but not improve executive functions.[8-10] Theta-tACS has been found to be beneficial in working memory, declarative memory, and executive functions. Alpha-tACS has been seen to increase sustained attention but decrease selective visual and auditory attention. Anti-phase beta-tACS reduces attentional blink.[10]

Studies have also examined the effect of the technique on individual neurocognitive disorders. tACS has produced demonstrable improvement in episodic memory, associative memory, and cholinergic transmission in patients with Alzheimer's disease (AD).[5] Though it produces tremor suppression in Parkinson's disease (PD), its effect on improving cognitive symptoms has yet to be studied.[11] There are preliminary reports of alpha-tACS being used to modulate brain activity associated with apathy in Huntington's disease (HD).[12] Clinical trials for use of tACS in dementia with Lewy bodies (DLB) are currently ongoing.

In conclusion, although there are pharmacological interventions that can delay the progression of neurodegenerative diseases, no interventions have been developed to improve cognition and memory after disease progression. The therapeutic potential of tACS, therefore, can be considered a promising area for psychiatric research. If applied with appropriate parameters, tACS can effectively alter the disturbed neural oscillations, thereby resulting in a better cognitive outcome without any serious side effects.

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Conflicts of interest
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