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Letter To Editor

Challenges and perspectives of non-invasive neurostimulation for cognitive enhancement

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This letter provides a narrative overview of the principal non-invasive neurostimulation techniques used for cognitive enhancement, including transcranial magnetic stimulation (TMS), transcranial electrical stimulation (tES), transcutaneous electrical acupoint stimulation (TEAS), and photobiomodulation (PBM). It summarizes current evidence and limitations regarding their applications in healthy populations, neurodevelopmental disorders, and age-related cognitive decline, while also discussing future directions for improving efficacy, safety, and translational potential.

Mainstream non-invasive neurostimulation techniques

TMS

TMS employs pulsed magnetic fields that penetrate the skull and act on the cerebral cortex, inducing electric currents in cortical neurons and thereby modulating neuronal excitability and synaptic connectivity. Depending on the stimulation paradigm, TMS can be classified into single-pulse TMS, paired-pulse TMS, and repetitive transcranial magnetic stimulation (rTMS). Among these modalities, rTMS has become the most widely applied approach for cognitive enhancement because of its ability to induce sustained neuroplastic changes.

tES

tES modulates cortical excitability through the application of weak electrical currents delivered via scalp electrodes. According to the type of current used, tES can be further categorized into transcranial direct current stimulation (tDCS), transcranial alternating current stimulation, transcranial random noise stimulation, and other related forms of stimulation. Compared with other neuromodulation techniques, tES offers several practical advantages, including portability, low cost, ease of operation, and suitability for prolonged intervention sessions [1].

TEAS

TEAS is based on the meridian theory of traditional Chinese medicine and modulates central nervous system activity by electrically stimulating specific acupoints on the body surface. As a non-invasive neuromodulation approach integrating principles of both traditional Chinese and Western medicine, TEAS is thought to regulate central nervous system function through neurohumoral pathways, improve cerebral blood flow, and promote the release of neurotransmitters such as dopamine and serotonin, thereby potentially enhancing cognitive function [2].

PBM

PBM is a non-invasive intervention that modulates cellular function through irradiation with red or near-infrared light at specific wavelengths. In neuroscience research, PBM influences central nervous system activity through

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transcranial scalp irradiation or intranasal light delivery [3]. Its primary mechanism involves modulation of mitochondrial activity, leading to enhanced cellular metabolism, increased adenosine triphosphate production, and reduced oxidative stress, ultimately improving cortical function and cognitive performance [4]. Prefrontal PBM has been reported to improve working memory in both healthy individuals and older adults.

In the context of cognitive maintenance in extreme environments, light-based circadian regulation has also attracted increasing attention. Naval Medical University, using China's only full-scale 1:1 submarine environment simulator, conducted the country's first large-scale human trial investigating interventions for circadian rhythm disruption among submarine crew members, namely the "Naval Submarine Environment Simulator Crew Circadian Rhythm Disruption Regulation Intervention Trial". This study addressed an important gap in China's maritime human factors engineering research concerning circadian rhythm intervention in active-duty submarine personnel during long-duration voyages. Furthermore, the research team established China's first biobank and human performance database for submarine crew members during extended sea missions. These efforts provide preliminary practical evidence supporting the use of PBM and light-based interventions for maintaining cognitive function in extreme operational environments.

Research applications and limitations of non-invasive neurostimulation for cognitive enhancement

Cognitive enhancement in healthy individuals

Anodal tDCS targeting the left dorsolateral prefrontal cortex (DLPFC) has been shown to improve executive function and decision-making accuracy during cognitively demanding tasks. However, substantial inter-individual variability in treatment response has been reported, and the long-term stability and ecological validity of these effects in real-world settings remain uncertain [5].

Cognitive intervention in patients with neurodevelopmental disorders

Anodal tDCS has demonstrated beneficial effects on inhibitory control and attentional deficits in individuals with attention-deficit/hyperactivity disorder [6]. Similarly, rTMS has shown efficacy in reducing inattentive symptoms, alleviating hyperactivity and impulsivity, and improving attention-related functioning [7, 8]. Nevertheless, current evidence is limited by relatively small sample sizes and inconsistent effect sizes. In addition, the extent to which these improvements translate into meaningful functional gains in academic and classroom settings remains unclear.

Amelioration of age-related cognitive decline

Combined interventions involving tDCS and cognitive training have been reported to significantly improve cognitive performance in older adults [9]. For instance, anodal tDCS targeting the left DLPFC, when combined with core training or strategy-based cognitive training, can produce immediate improvements in working memory, with effects superior to those achieved by cognitive training alone [10]. However, the optimal stimulation parameters, long-term efficacy, and safety of these interventions require further investigation.

Discussion and future directions

Current evidence suggests that non-invasive neurostimulation techniques possess considerable potential for cognitive enhancement across diverse populations. However, several limitations continue to hinder clinical translation, including inconsistent effect sizes, limited sample sizes, inadequate long-term follow-up data, and methodological challenges associated with sham-controlled study designs. Future research should focus on several key directions. First, individualized intervention protocols should be developed by tailoring stimulation targets, intensities, and durations according to individual characteristics such as age, baseline cognitive status, and brain functional state. Second, closed-loop neuromodulation systems integrating techniques such as electroencephalography and functional near-infrared spectroscopy should be explored to enable real-time adaptive stimulation. Third, multimodal intervention strategies combining neurostimulation with cognitive training, behavioral feedback, and pharmacological approaches may enhance overall therapeutic efficacy. Finally, greater emphasis should be placed on mechanistic studies and standardization research to clarify long-term neuroplastic changes

and establish unified safety standards and ethical guidelines.

Conclusion

Non-invasive neurostimulation technologies represent promising and generally safe approaches for cognitive enhancement, with broad potential applications in healthy individuals, neurodevelopmental disorders, and age-related cognitive decline. By addressing current methodological limitations and advancing individualized, multimodal, and mechanistically informed intervention strategies, these technologies may facilitate safer and more effective translational applications in both clinical practice and everyday settings.

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Disclosure of conflict of interest

None.

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