The Use of Transcranial Direct Current Stimulation (tDCS) in the Research of Cognitive Functions

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Abstract

The aim of this paper is to provide a brief overview of the use of one of the most utilized noninvasive brain stimulation technique, namely, transcranial direct current stimulation (tDCS), in studying cognitive functions. I focus on the behavioral effects of tDCS applied over central nodes of the frontoparietal network – the dorsolateral prefrontal cortex and posterior parietal cortex on associative memory, executive functions, and higher cognitive functions. The effectiveness of tDCS is discussed in the context of inconsistent findings often reported in the literature. Finally, I outline the limitations of the technique and further directions in the field of noninvasive brain stimulation.

Keywords: transcranial direct current stimulation (tDCS); dorsolateral prefrontal cortex (DLPFC); posterior parietal cortex (PPC); executive functions; cognitive abilities; associative memory

Noninvasive Brain Stimulation

Noninvasive brain stimulation (NIBS) is an innovative approach in neuroscience that allows for causal investigation of sensorimotor, cognitive, and affective brain functions and, ultimately, clinical treatment of a wide spectrum of neuropsychiatric conditions. The term refers to a set of technologies and techniques aimed at transcranial noninvasive modulation of neural excitability and activity of specific brain areas and inter-connected large-scale brain networks (Boes et al., 2018). The ability to directly affect brain activity enables causal inference about the neural underpinnings of cognitive functions. This makes NIBS a valuable tool for understanding cognitive functions on the neural level.

Transcranial Electric Stimulation

Here, I will focus on NIBS techniques that use an electric field to modulate brain activity – transcranial electric stimulation (tES). tES is an umbrella term for several brain stimulation methods that use low-intensity electrical currents (1-2 mA) to modulate brain activity. The most commonly used one is transcranial direct current stimulation (tDCS), which modulates neuronal excitability using anodal (positive) or cathodal (negative) stimulation and achieves its effects through depolarization or hyperpolarization of the resting membrane potential (Nitsche et al., 2008).

In cognitive experiments, tDCS can be applied in the so-called online or offline protocol, that is, during or after the cognitive task (see Bjekić et al., 2021 for typical tDCS setup and protocol). While the tDCS effects during stimulation are assumed to rely on increased or decreased neuronal likelihood to fire action potentials through depolarization or hyperpolarization of neuronal membranes, the after-effects are thought to be similar to long-term potentiation (LTP) and depression (LTD) and depend upon modulation of synaptic plasticity of glutamatergic and GABAergic interneurons, but acetylcholine, serotonin, and dopamine systems as well (Stagg & Nitsche, 2011).

Transcranial Direct Currents Stimulation and Cognitive Functions

tDCS showed promise for noninvasive neuromodulation of a variety of cognitive functions. When studying cognitive functions, the brain regions of interest are usually the dorsolateral prefrontal cortex (DLPFC) and posterior parietal cortex (PPC) as central stimulation-available nodes of the widely distributed frontoparietal neural network. Here I will provide a brief overview of the state-of-the-art in the field, with particular attention to the behavioral effects of tDCS applied over different brain loci within the frontoparietal network on associative memory, executive functions, and higher cognitive functions. I will focus on the effects of anodal tDCS, findings on healthy participants, and studies that used well-defined measures of cognitive functions.

Associative memory

Associative memory (AM) is an essential aspect of episodic memory, and the binding of previously unrelated pieces of information represents the core feature of AM. Since the hippocampus, as the central structure, underlying AM is not directly accessible for tES, choosing the right cortical target and showing function-specific effects can give insight into hippocampus-cortical pathways that underline AM. In contrast to the prefrontal tDCS effects, which resulted in mixed findings (Galli et al., 2019), positive function-specific effects of anodal tDCS on AM were recorded for the parietal cortex (Bjekić, Čolić, et al., 2019; Bjekić, Vulić, et al., 2019; Vulić et al., 2021). Furthermore, some findings suggest that AM enhancement induced in a single session of anodal tDCS shows a tendency to persist for up to 5 days (Bjekić, Vulić, et al., 2019). These findings highlight the role of parietal cortices in AM.

The tES also allows for exploring the functional significance of brain rhythms in cognitive functions. Namely, the role of theta oscillations (4-8 Hz) has been long implied as the “glue that binds memories” (Herweg et al., 2020). Some studies suggested that oscillatory protocols such as transcranial alternating current stimulation (tACS) could be superior to tDCS in the modulation of the AM, especially when stimulation is applied in theta-band frequency (Klink et al., 2020; Lang et al., 2019). Still, some findings (Živanović et al., 2022) point to the comparable online effects of tDCS and oscillatory protocols applied at individual theta frequency (Bjekić, Paunovic, et al., 2022; Bjekić, Živanović, et al., 2022) on overall AM accuracy. However, the observed effects are found to vary depending on the memory demand. Namely, it was shown that tDCS is more beneficial for AM when the memory demand is relatively low, while theta-oscillating stimulation predominantly facilitates AM when the memory demand is high and more efficient encoding and/ or longer retention is needed (Živanović et al., 2022). These findings suggest that the facilitation of lower-level memory processes may be achieved through increasing excitability of the neural circuits at the place of application, while binding processes can be facilitated through entrainment of theta activity in the cortico-hippocampal network (Živanović et al., 2022).

Executive functions

Executive functions (EF) are thought to mainly rely on the prefrontal cortex – dorsolateral prefrontal cortex (DLPFC) in particular. Thus, previous studies aiming to modulate updating of information in working memory (WM) primarily focused on DLPFC. They showed WM enhancement following single-session of anodal tDCS over both left (e.g., Fregni et al., 2005; Zaehle et al., 2011) and right DLPFC (e.g., Stanković et al., 2021; Živanović et al., 2021). However, a number of studies using DLPFC areas as stimulation loci did not find tDCS effects on WM (e.g., Hill et al., 2017, 2018). A meta-analysis (Hill et al., 2016) found evidence for the effects of anodal tDCS over DLPFC for offline but not online protocols. In another meta-analysis, it was shown that anodal unilateral tDCS produced significant effects on updating tasks (Imburgio & Orr, 2018).

Neuroimaging studies show that the neural underpinnings of WM extend beyond the anterior brain areas and include PPC as one of the main neural nodes underlying WM (Owen et al., 2005). In line with that, we showed that PPC could be an effective cortical target for the tDCS-induced modulation of WM (Živanović et al., 2021).

Several brain areas critically involved in inhibitory control emerged as promising stimulation targets for this EF, namely, DLPFC, pre-supplementary motor area (pre-SMA), inferior frontal gyrus (IFG), anterior cingulate cortex (ACC), and orbitofrontal cortex (OFC). Some findings show that tDCS over left DLPFC effectively enhances inhibitory control (e.g., Jeon & Han, 2012); still, some studies did not find such effects (Baumert et al., 2020; Živanović, 2019). Meta-analytic evidence suggests that the stimulation of the right DLPFC does not affect inhibition; however, it shows the significant effects of tDCS over right IFG on response inhibition (Schroeder et al., 2020). Similarly, studies found evidence of the beneficial effects of tDCS over pre-SMA on response inhibition (e.g., Hsu et al., 2011; Yu et al., 2015). Moreover, some studies found that tDCS over ACC (To et al., 2018), as well as OFC (Ouellet et al., 2015), are efficient in modulating inhibitory control.

Similarly, as for WM, parietal brain areas were far less examined as potential cortical targets for modulating inhibition, despite converging evidence on their involvement in inhibitory control (Alvarez & Emory, 2006). For example, one of our studies found that stimulation over the right PPC has a facilitatory effect on inhibition of spatial information, while the same stimulation applied over the left PPC has no effect on inhibitory control (Živanović, 2019).

Only a few studies focused on the effects of tDCS on cognitive performance measured by typical shifting tasks, and the results are inconclusive. For example, one study showed that cross-hemisphere stimulation of left/right DLPFC can modulate switching performance (e.g., Leite et al., 2013); however, some studies did not find that unilateral tDCS over left or right DLPFC modulates task switching (Živanović, 2019). In addition, we did not find that tDCS over both left and right PPC is effective in modulating shifting performance (Živanović, 2019).

Higher cognition

Both EF and complex cognition largely rely on the same frontoparietal neural network (Jung & Haier, 2007). Although EF can be modulated by tDCS, studies rarely examine whether these effects translate to the more complex functions mimicking the psychometric relationship between EF and cognitive abilities.

In a study that simultaneously tested tDCS effects on both EF and performance on cognitive ability measures (Živanović, 2019), we found that tDCS significantly modulated cognitive performance on *Gf*, *Gv*, and *Gs* measures but not *Gc* measures. Furthermore, these findings were in line with the higher reliance of *Gf*, *Gv*, and *Gs* on EF, as evidenced by their relationships obtained on a psychometric level. Moreover, we found that tDCS effects on *Gv* and *Gs* measures are likely mediated by the facilitation of updating of representations in WM, suggesting a causal role of WM in these abilities. These findings show that tDCS can be a useful tool for studying not only EF but higher cognition too.

Limitations and Further Directions

Despite the immense potential of tDCS in studying neural underpinnings of cognition, the current state-of-the-art is far from conclusive. Additional evidence on the tDCS effects across different cortical areas is needed for memory, EF, and especially more complex cognitive functions. One of the main challenges in aggregating the existing evidence lies in the significant variability of stimulation parameters/ protocols, tasks, and experimental designs. Further limitations stem from the technique itself, as its focality, the duration of effects, and exact mechanisms in large neuronal populations are still not fully understood. To realize the full potential of NIBS as a tool in experimental cognitive neuroscience, systematic variation of stimulation parameters combined with a careful selection of outcome measures is needed.

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