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Reviews and perspectives

Evidence that transcranial direct current stimulation (tDCS) generates little-to-no reliable neurophysiologic effect beyond MEP amplitude modulation in healthy human subjects: A systematic review

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ABSTRACT

Background: Transcranial direct current stimulation (tDCS) is a form of neuromodulation that is increasingly being utilized to examine and modify a number of cognitive and behavioral measures. The theoretical mechanisms by which tDCS generates these changes are predicated upon a rather large neurophysiological literature. However, a robust systematic review of this neurophysiological data has not yet been undertaken.

Methods: tDCS data in healthy adults (18–50) from *every* neurophysiological outcome measure reported by at least two different research groups in the literature was collected. When possible, data was pooled and quantitatively analyzed to assess significance. When pooling was not possible, data was qualitatively compared to assess reliability.

Results: Of the 30 neurophysiological outcome measures reported by at least two different research groups, tDCS was found to have a reliable effect on only one: MEP amplitude. Interestingly, the magnitude of this effect has been significantly decreasing over the last 14 years.

Conclusion: Our systematic review does not support the idea that tDCS has a reliable neurophysiological effect beyond MEP amplitude modulation – though important limitations of this review (and conclusion) are discussed. This work raises questions concerning the mechanistic foundations and general efficacy of this device – the implications of which extend to the steadily increasing tDCS psychological literature.

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1. Introduction

Nearly fifteen years ago, researchers revived a field of research that explores the effects of running a weak electric current between two electrodes placed on the scalp of healthy individuals (Konig and Ankenmuller, 1960; Hamer, 1968; Lolas 1977; Elbert et al., 1981; Nitsche and Paulus, 2000). Dubbing this technique transcranial direct current stimulation (tDCS), experiments showed a marked, time dependent, and polarity specific modulation of neuronal populations underlying the electrodes. Since this initial neurophysiologic finding, a growing number of researchers and clinicians have been exploring the effects of tDCS across a number of cognitive/behavioral domains. Today, the literature suggest tDCS can enhance a number of higher-order cognitions and behaviors ranging from working memory and motor learning to emotional regulation and focused attention (for review: Nitsche and Paulus, 2011). The claims made by cognitive and behavioral tDCS researchers largely depend upon the mechanistic framework suggested by the neurophysiologic data. However, a robust systematic review of the neurophysiologic impact of tDCS has not yet been undertaken. This is something we hope to remedy in this paper.

1.1. *tDCS: A brief overview and proposed mechanisms of action*

Modern tDCS devices typically consist of an adjustable direct current stimulator and two stimulating electrodes (an anode and a cathode). These electrodes are typically attached to two separate locations on the scalp (either directly or via larger sponge electrodes) and a weak current (0.5–2.0 mA) is run between the electrodes. As this current passes between the electrodes, it is believed a small amount of the current passes through the brain. This current flow is purported to modulate neural activity underneath the electrode and, to a lesser extent, diffuse locations in the brain (Nitsche et al., 2008; for debate: Bikson, 2013).

There are two mechanisms by which tDCS modulates brain activity that are widely accepted in the field. The first proposes tDCS modulates the resting membrane potential of neuronal populations via ionic adjustment of extracellular space. More specifically, neurons proximal to the anode are thought to become hypo-polarized whist neurons near the cathode are thought to become hyper-polarized (Stagg and Nitsche, 2011). This shift in resting membrane potential is believed to occur both *during* stimulation and for a short period of time (<5 min) following stimulation. The second proposes tDCS modulates synaptic activity in a manner akin to long term potentiation (under the anode) and long term depression (under the cathode: Stagg and Nitsche, 2011). This mechanism is believed to be active for an extended period of time (up to 120 min) following the cessation of long-duration (>7 min) stimulation. In this systematic review, we group studies into short- and long-duration stimulation to account for membrane and synaptic effects believed to be triggered by tDCS.

1.2. *Systematic review structure*

The neurophysiological effects of tDCS have largely been measured utilizing four approaches: transcranial magnetic stimulation (TMS), event related potentials (ERPs), electroencephalographic spectral analyses (EEG), and functional magnetic resonance imaging (fMRI). Accordingly, the methods and results sections (below) will be structured around these modalities. Additionally, the majority of studies exploring the neurophysiological effects of tDCS have utilized a single measure: TMS motor evoked potential (MEP) amplitude. Due to the disproportionately large number of studies exploring this measure, we have decided to dedicate an analysis