

Mini Review





Transcranial direct current stimulation in dementia: a possible breakthrough?

Introduction

Dementia is associated with substantial economic and societal costs, as its worldwide cost in 2015 was estimated to be (US) \$818 billion, an increase of 35% since 2010. While there are a number of drugs to manage some of its behaviorial symptoms, pharmacological treatment only has a limited degree of efficacy, including undesirable side effects; in this sense, it is crucial to develop additional treatments. As such, there is a growing interest in non-pharmacological approaches for frontotemporal dementia (FTD), which does not have any specific pharmacological intervention. One area that has recently garnered considerable clinical and research interest in this field is the use of non-invasive brain stimulation.

Transcranial direct current stimulation (tDCS) is a non-invasive neuromodulation technique that delivers a low electrical current, through two scalp electrodes, which induces bi-directional polaritydependent changes in the cerebral cortex. It attempts to facilitate focal, prolonged shifts in cortical excitability at or around the time stimulation is provided. Typically, an anodal and cathodal electrode is placed on the scalp in accordance with the International 10-20 system.3 This intervention is considered safe and noninvasive, as it does not involve implantation, injection, or any skin penetration.⁴ Different electrode configurations are believed to affect the focality of stimulation and the path of current flow. The electrical currents of tDCS are believed to modulate neuronal resting membrane potentials, which occur in a bidirectional radial manner between electrodes.5 Cathodal tDCS is correlated with decreased cortical excitability due to subthreshold incremental hyperpolarization of membrane potentials. Anodal tDCS (a-tDCS), in which the positively-charged electrode is placed over the targeted cortical region, is thought to lead to increased cortical excitability (upregulation), similar to long-term potentiation (LTP); this is due to incremental depolarization of membrane potentials. Combining tDCS with behavioral-based approaches has been found to enhance the learning process and increase the likelihood of retention. Specifically, tDCS has been shown to have a positive effect on cognitive functions in several studies in healthy humans,6 and in neuropsychiatric symptoms such as depression.7 Neuromodulation studies targeting cognition in non-Alzheimer dementias and mild cognitive impairment were almost nonexistent,8 although recent studies started to address other types, including Lewi Body Dementia (LBD)9 and FTD.10 The conceptual framework is that by improving plasticity, tDCS becomes a promising approach to reduce cognitive decline. As such, a recent study using 30 minutes of anodal (2 mA) tDCS stimulation applied to the parietal lobe (P3) showed some improvement in anomia, AD, and FTD patients, which demonstrates significant relevance for two-months post stimulation.¹¹ Another investigation aimed to assess memory changes after five consecutive sessions of bilateral temporal anodal tDCS in patients with AD; this shows significant improvement in visual recognition memory for at least four weeks after stimulation.12 A bilateral frontotemporal anodal stimulation (2 mA, 20 min, five consecutive days) showed improvement of behavioral scores in FTD patients.¹³ A second cross-over double-blind study with AD and FTD patients

Volume 9 Issue I - 2019

Inês Tello RM Rodrigues

Institute of Health Sciences, Universidade Católica Portuguesa, Portugal

Correspondence: Inês Tello RM Rodrigues, Center of Interdisciplinary Investigation in Health, Institute of Health Sciences, Universidade Católica Portuguesa - Lisbon, Portugal, Email inestellorodrigues@gmail.com

Received: June 23, 2018 | Published: January 29, 2019

revealed improvements in picture naming.¹⁴ A specific study with a variant of FTD (primary progressive aphasia) used anodal tDCS applied to the left dorsolateral prefrontal cortex during individualized computerized anomia training, along with a positive effect in object naming.¹⁵ Another study with FTD patients aimed at a similar outcome (verbal fluency), but failed to convey any beneficial effect.¹⁶

Conclusion

The general outlines are promising, but the number of studies investigating the outcomes of tDCS on dementia is limited, especially with regard to clinically meaningful long-term effects. Additionally, most clinical trials are comprised of inadequate control arms and small samples, with few to no data reported in several dementia groups (e.g., VaD, LBD, and PDD). Several challenges exist in terms of stimulation parameters, a specific montage, and sample selection to establish clinical significance. Nevertheless, the continuous progress and optimization of stimulation protocols might soon provide a different and alternative therapeutic paradigm for symptom management in dementia patients.

Acknowledgments

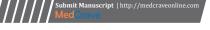
None.

Conflicts of interest

The authors declare no conflicts of interest.

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