Transcranial direct current stimulation: effects, clinical applications, and future perspectives in neurology and physical performance

Estimulação transcraniana por corrente contínua: efeitos, aplicações clínicas e perspectivas futuras em neurologia e performance física

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ABSTRACT
Transcranial direct current stimulation (tDCS) is a noninvasive technique that allows modulation of cortical excitability and can produce changes in neuronal plasticity. The application of tDCS has recently been associated with respiratory muscles and several neurological disorders. Thus, this study is constructed in the format of an article, with the objective of discussing the effects, clinical applications and future perspectives related to Transcranial Direct Current Stimulation in the respiratory muscles, as well as discussing the applications of tDCS in other areas, such as neurological and psychological aspects. As a research methodology, a literature review will be used in this study. This study discusses the clinical applications of tDCS in several diseases, such as Alzheimer's, Parkinson's disease, depression, drug and food compulsion, as well as its application in the process of physical and respiratory performance. Recent studies suggest that a new field of applicability of tDCS may be related to a probable ergogenic effect induced by it,
especially on the production of muscle and respiratory strength, aerobic performance and perception of exertion.

**Keywords:** breathing, transcranial direct current stimulation, motor performance.

**RESUMO**
A estimulação transcraniana por corrente contínua (ETCC) é uma técnica não invasiva que permite a modulação da excitabilidade cortical e pode produzir alterações na plasticidade neuronal. A aplicação da ETCC tem sido recentemente associada à musculatura respiratória e a diversos distúrbios neurológicos. Dessa forma, constrói-se este estudo no formato de artigo, com o objetivo de discorrer sobre os efeitos, as aplicações clínicas e as perspetivas futuras relacionadas à Estimulação Transcraniana por Corrente Contínua na musculatura respiratória, bem como, discutir sobre as aplicações da ETCC em outros âmbitos, como em aspectos neurológicos e psicológicos. Como metodologia de pesquisa será utilizado neste estudo uma revisão bibliográfica da literatura. Discorreu-se neste estudo sobre as aplicações clínicas da ETCC em diversas doenças, como Alzheimer, doença de Parkinson, depressão, compulsão por drogas e alimentos, bem como, sua aplicação no processo de desempenho físico e respiratório. Estudos recentes sugerem que um novo campo de aplicabilidade da ETCC possa estar relacionado com um provável efeito ergogênico por ela induzido, especialmente sobre a produção de força muscular e respiratória, desempenho aeróbio e percepção do esforço.

**Palavras-chave:** respiração, estimulação transcraniana por corrente contínua, desempenho motor.

**1 INTRODUCTION**
Currently, various non-invasive techniques for modulating brain function have been developed, among which transcranial direct current stimulation (tDCS) stands out (Nitsche and Paulus, 2011). This approach utilizes low-cost and easily manageable equipment, employing silicone electrodes wrapped in sponges soaked in saline solution, which are positioned over the targeted cortex for stimulation. The application of a continuous electrical current, ranging from 0.4 to 2 milliamperes, is performed on the cortical region for a period of 3 to 20 minutes, allowing for modifications in cortical excitability (Nitsche and Paulus, 2000).

The chosen polarity of the electrical current can trigger different effects: anodal stimulation has been associated with increased cortical excitability, while cathodal stimulation promotes the opposite effect (Nitsche and Paulus, 2000). This technique, called tDCS, has been widely used both in clinical and therapeutic contexts as well as in experimental research, encompassing a broad field of applicability in the treatment of various neurological disorders (Boggio et al., 2007).
However, besides its clinical and therapeutic effects, tDCS has been the subject of studies related to its potential to improve physical performance, metabolism, blood pressure management, and cardiac autonomic control (Montenegro et al., 2011; Okano et al., 2013), making it a potentially ergogenic resource for sports activities (Costa et al., 2012). In pursuit of a better understanding of the mechanisms involved in the modifications induced by tDCS, several studies have been conducted. However, the literature still lacks more consistent documentation regarding the relationship between ion channels, membrane receptors, and the observed effects after tDCS, as well as its relationship with increased muscle strength and aerobic performance.

In this context, this article aims to present the effects, clinical applications, and future perspectives of Transcranial Direct Current Stimulation on the respiratory musculature. Additionally, the applications of tDCS in other areas, such as neurological and psychological aspects, will be discussed. To carry out this study, a literature review will be adopted.

2 TRANSCRANIAL DIRECT CURRENT STIMULATION - tDCS

The use of electrical current for therapeutic purposes dates back to the first century when electric discharges from electric fish were applied to patients’ heads to relieve headaches and induce numbing effects (Priori, 2003). Over time, this approach evolved in various forms, becoming a widely used therapeutic strategy for treating mental disorders.

More recently, technological advances in the field of neurology have driven interest in non-invasive techniques for modulating brain polarization. Two techniques currently stand out: Transcranial Magnetic Stimulation (TMS) and Transcranial Direct Current Stimulation (tDCS). TMS, patented by Pollacek and Beer in 1902, involves applying electromagnetic fields to the scalp for the treatment of depression and neurosis, as well as for mapping studies of the motor cortex. Although it is a non-invasive and painless technique, the high cost of equipment and the need for a cooling system for the coils used make TMS expensive (Barker, Jalinous & Freeston, 1985).

On the other hand, tDCS is a simpler and more cost-effective technique for neuromodulation. By applying low-intensity direct current with electrodes on the scalp, tDCS can modulate cerebral excitability for up to an hour after stimulation (Nitsche and Paulus, 2000). The polarity of the electric current used, either anodal or cathodal,
determines the desired effects: anodal stimulation increases cortical excitability, while cathodal stimulation suppresses it (Nitsche and Paulus, 2000).

tDCS has shown efficacy in therapeutic applications, such as the treatment of depression, Parkinson's disease, stroke recovery, and chronic neuropathic pain (Murphy et al., 2009; Boggio et al., 2006; Jo et al., 2009; Fregni et al., 2007). Despite the current being applied to the scalp, studies indicate that it can penetrate the skull and reach the cerebral cortex, with cortical modulation depending on the polarity of the applied current. The simplicity, low cost, ease of administration, and non-invasiveness make tDCS an attractive approach compared to TMS (Boggio, 2006).

Transcranial direct current stimulation (tDCS) is a non-invasive technique that has shown promise in modulating brain function. Using low-cost and easily manageable equipment, tDCS utilizes silicone electrodes wrapped in sponges soaked in saline solution, which are positioned over the targeted cortex. By applying continuous electrical current, ranging from 0.4 to 2 milliamperes, for a period of 3 to 20 minutes, it is possible to induce modifications in cortical excitability (Nitsche and Paulus, 2000).

The chosen polarity of the electrical current plays a crucial role in the effects of stimulation. Anodal stimulation results in increased cortical excitability, while cathodal stimulation suppresses excitability (Nitsche and Paulus, 2000; Lang et al., 2004, 2005).

tDCS has been considered safe, although some effects such as tingling under the electrodes, mild fatigue, and itching may be observed. In rarer cases, nausea, insomnia, and headache may occur (Poreisz et al., 2007). It is important to inform individuals about these possible effects before conducting any study or clinical practice involving the technique.

To increase the safety of the technique, the use of electrodes protected by sponges soaked in saline solution with a concentration between 40 to 150nM of NaCl diluted in deionized water or Milli-Q is recommended to minimize possible unpleasant reactions resulting from direct contact of the electrode with the skin (Nitsche et al., 2008; Dundas et al., 2007).

3 MECHANISMS OF ACTION OF tDCS

Pioneering studies with tDCS investigated the effects of anodal and cathodal stimulation on the motor cortex, using the measurement of the motor evoked potential (MEP). It was found that anodal tDCS increased cortical excitability, while cathodal tDCS reduced it (Nitsche and Paulus, 2000). These effects were dependent on the
application time and current intensity, persisting for a similar period of time after the end of anodal tDCS but not after cathodal tDCS.

Liebetanz and colleagues (2002) explored possible interference of voltage-dependent sodium channel blockers (carbamazepine - CBZ) and N-methyl-D-aspartate (NMDA) receptor antagonists (dextromethorphan - DMO) in the effects of anodal and cathodal tDCS. It was observed that the administration of DMO suppressed the post-stimulation effects, both anodal and cathodal, suggesting the involvement of NMDA receptors in tDCS-induced neuronal plasticity. CBZ only suppressed the effects of anodal tDCS, indicating the participation of sodium channels in this type of stimulation.

Nitsche and colleagues (2003) continued with their hypothesis, investigating the effects of CBZ, DMO, and a calcium channel blocker (flunarizine - FLU) on the mechanisms of action of tDCS. Anodal tDCS, in conjunction with the drug, presented an initial delay in MEP amplitude, followed by an increase that extended up to 60 minutes after stimulation, indicating the involvement of gamma-aminobutyric acid (GABA) in cortical neuroplasticity. The administration of D-cycloserine, a partial agonist of the NMDA receptor, also resulted in increased neuronal excitability after anodal stimulation. Subsequent studies confirmed the involvement of other components of the glutamatergic system in the effects of tDCS.

4 tDCS APPLIED TO THE TREATMENT OF DISEASES

tDCS has demonstrated therapeutic effects in neurological and psychiatric disorders, promoting improvements in motor and behavioral areas. Long-lasting cerebral plasticity depends on changes in synaptic strength, and tDCS has been effective in promoting alterations in this strength, which may contribute to the treatment of various clinical conditions (Nitsche et al., 2008). In the next section, the main findings related to the potential therapeutic effects of tDCS in neurological and psychiatric diseases will be presented.

4.1 tDCS IN PARKINSON'S AND ALZHEIMER'S DISEASES:

Parkinson's disease (PD) is a neurological condition characterized by the degeneration of dopaminergic neurons in the substantia nigra of the brain. This results in a deficiency in dopamine production, affecting multiple neuroanatomical pathways and leading to motor and non-motor disturbances. Some studies have explored the use of tDCS as a therapeutic approach for PD.
One study analyzed the effects of anodal tDCS applied to the left dorsolateral prefrontal cortex (DLPFC) and the primary motor cortex (M1) in medication-naive PD patients. They found that anodal tDCS applied to M1 resulted in a significant improvement in motor function compared to placebo tDCS. In another study, a significant improvement in working memory in PD patients was demonstrated after the application of anodal tDCS to the left DLPFC with 2 mA. These results suggest the possibility of specific therapeutic effects of tDCS for PD patients (Fregnie et al., 2006; Boggio et al., 2006).

Regarding Alzheimer's disease (AD), which is one of the leading causes of dementia, some studies have been conducted with tDCS to improve recognition memory in patients with mild AD. In one of these studies, anodal tDCS was applied over the temporo-parietal region and resulted in a significant improvement in recognition memory. However, cathodal tDCS applied to the same region significantly decreased accuracy in the word recognition task (Ferrucci et al., 2008).

Another study investigated the effects of anodal tDCS applied to the temporal cortex and the left DLPFC in patients with mild to moderately severe AD. Anodal tDCS resulted in a significant improvement in visual recognition memory but had no effect on working memory (Boggio et al., 2009).

These initial studies suggest that tDCS may have positive effects on cognitive function and memory in patients with PD and AD. However, more research is needed to fully understand the therapeutic potential of tDCS in these neurodegenerative diseases.

4.2 tDCS IN DEPRESSION AND DRUG AND FOOD CRAVING

Major depression is a mood disorder that can affect affective, behavioral, and cognitive functions. Some studies have investigated the use of tDCS as an approach for the treatment of depression, mainly targeting stimulation to the left prefrontal cortex. Results have shown improvement in working memory and cognitive performance associated with positive emotional stimuli after the application of anodal tDCS in this area (Fregnie et al., 2006; Boggio et al., 2006).

Additionally, tDCS has been explored as a possible intervention to reduce cravings or compulsions for alcohol, drugs, and food. Studies have demonstrated that tDCS can decrease cravings for cigarettes, cocaine, alcohol, and food in individuals with compulsive behaviors (Boggio et al., 2008; Eichhammer et al., 2003).
Recently, tDCS has been investigated in relation to appetite control and food intake. Anodal stimulation applied to the left dorsolateral prefrontal cortex suppressed appetite, and the anorexic effect was amplified when combined with moderate-intensity aerobic exercise (Montenegro et al., 2012).

These findings suggest that tDCS may be a promising approach for the treatment of depression and compulsive behaviors related to drugs and food. However, further research is needed to better understand the effectiveness and underlying mechanisms of these effects.

tDCS in rehabilitation and physical performance of the respiratory musculature: Neural plasticity is the brain's ability to adapt to different stimuli, and it is this property that makes tDCS a promising technique in motor rehabilitation. Some studies have explored the effects of tDCS in the rehabilitation of neurological patients, such as those who have had a stroke, and found improvements in movement execution after tDCS application (Madhavan & Weber, 2011).

However, most studies on the effects of tDCS on physical performance have been conducted on small groups, and more research is needed to fully understand how tDCS can be used to improve rehabilitation and physical performance in various populations. Future studies should investigate the long-term effects of tDCS and its combination with physical training in healthy individuals and those with neurological conditions.

5 FINAL CONSIDERATIONS

Transcranial Direct Current Stimulation (tDCS) is a non-invasive technique that modulates brain function, with its main mechanisms of action related to N-methyl-D-aspartate (NMDA) receptors and the influence of neurotransmitters such as serotonin, dopamine, adrenaline, GABA, and acetylcholine.

There is growing evidence of the clinical efficacy of tDCS in the treatment of neurological disorders, including Alzheimer's, Parkinson's, chronic depression, and compulsions related to drugs, alcohol, and food.
Recent studies point to a potential use of tDCS as an ergogenic technique, with possible benefits in muscle and respiratory strength, aerobic performance, and perceived effort. Furthermore, it is suggested that tDCS may have positive effects on post-exercise energy expenditure and blood pressure control.

To better understand and confirm the clinical potential of tDCS in various areas, more research is needed to investigate its effects in different dimensions and clarify the mechanisms involved. Ongoing research in this area may lead to significant advances in the treatment of various neurological conditions and in enhancing physical performance.
REFERENCES


