






# Transcranial direct current stimulation as a strategy to manage COVID-19 pain and fatigue

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## SUMMARY

The novel coronavirus disease (COVID-19) has infected millions of people worldwide and generated many sequels in the survivors, such as muscular pain and fatigue. These symptoms have been treated through pharmacological approaches; however, infected people keep presenting physical limitations. Besides, the COVID-19 damage to the central nervous system has also been related to the presence of some physical impairment, so strategies that focus on diverse brain areas should be encouraged. Transcranial Direct Current Stimulation (tDCS) is a non-pharmacological tool that could be associated with pharmacological treatments to improve the central nervous system function and decrease the exacerbation of the immune system response. tDCS targeting pain and fatigue-related areas could provide an increase in neuroplasticity and enhancements in physical functions. Moreover, it can be used in infirmaries and clinical centers to treat COVID-19 patients.

**KEYWORDS:** Coronavirus infections. Betacoronavirus. Transcranial direct current stimulation.

## INTRODUCTION

Muscular pain and fatigue have been presented in about 36% of the patients infected by the novel coronavirus disease (COVID-19)<sup>1</sup>. The cause of these symptoms is still poorly understood, however, treatment strategies aiming to reduce pain and fatigue symptomatology must be discussed, in order to quickly offer the best treatment approach to decrease the suffering of the infected people. Several pharmacological methods have been proposed to reduce pain, such as opioids, which can lead to endocrine alterations and suppress the immune system<sup>2</sup>, besides steroids that have been related to bone mineral density and muscular dysfunctions as side effects<sup>3</sup>. Nonpharmacological methods to decrease pain and fatigue have been studied and showed some

efficacy without side effects. Noninvasive brain stimulation might help some people infected by COVID-19 through the application of current on the scalp for some minutes<sup>4,5</sup>.

Transcranial direct current stimulation (tDCS) emerges as a noninvasive and nonpharmacological alternative to treat pain through the neuromodulation of pain-related areas. Due to the central nervous system affected by COVID-19, the use of electric current to modulate some brain areas would be important to reduce the symptoms and bring more comfort to the patients<sup>6</sup>. Cortical areas, such as the primary motor cortex, which is part of the region of neuromatrix of pain, have been widely investigated as a site that controls the pain threshold and perception. It is emphasized that tDCS over the primary motor cortex has

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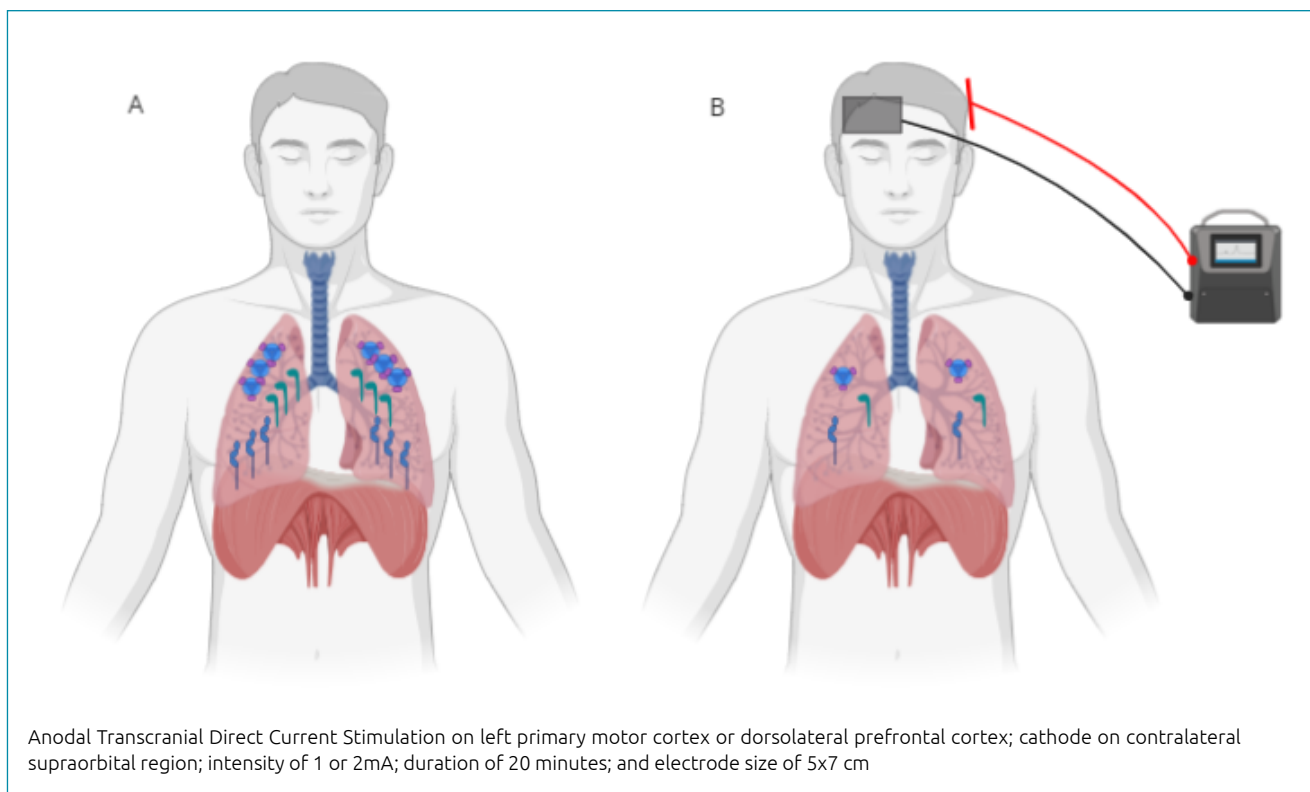
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**Figure 1.** (A) Lung COVID-19 infection with the presence of inflammatory cells. (B) An expected reduction in the inflammatory response after transcranial direct current stimulation. In the box there is a suggestion of Transcranial Direct Current Stimulation parameters for COVID-19 based on the studies related to chronic pain and fatigue. Created with BioRender.

shown the potential to decrease pain caused by several diseases<sup>7</sup>. Moreover, fatigue has been associated with changes in neural excitability of cortical areas, such as the primary motor cortex<sup>8</sup>. In this sense, as tDCS has been implicated in improving neural function, the modulation of the primary motor cortex in people infected by COVID-19 could provide an improvement in both pain and fatigue.

Beyond the cortical region chosen to be neuromodulated, the parameters used to promote changes in brain function through direct current must be contemplated. Most of the studies have shown similar protocols, and the intensity of 1 or 2mA, anodal polarity as the active electrode, electrode size of 5x7 cm, and the frequency of 5 times a week are frequently found in the literature<sup>7</sup>. The definition of a parameter model pattern could facilitate the use of the tDCS in hospitals and clinics by the medical team.

Furthermore, the alterations generated by COVID-19 in the immune system through cytokine release and storm and the activity of interleukins have mainly affected and damaged the respiratory tract<sup>9</sup>. tDCS over the dorsolateral

prefrontal cortex also could interfere with the function of these inflammatory cells, improving their response or avoiding exacerbations<sup>10</sup>. Thus, the use of tDCS as a cheap and nonpharmacological tool in people infected by COVID-19 could neuromodulate the function of the immune system and decrease the damage of the central nervous system and peripheral organs. Figure 1 represents the human lungs and the exacerbation of the inflammatory cells (cytokines, interleukins, and the tumor necrosis factor) from the immune system generated by COVID-19, and what would be expected after the use of tDCS.

## CONCLUSIONS

Nonpharmacological approaches must be encouraged to improve the muscular pain and fatigue caused by COVID-19. At this moment, there is no gold standard medication against the virus nor a vaccine to prevent the infection. So, a simple, easy-to-use and cheap tool such as tDCS could emerge as an alternative to be used in the infirmaries and COVID-19 treatment centers. It

is important to consider the use of tDCS after recovery because the presence of after-effects in people who presented moderate and severe symptoms has been frequently reported. Thus, tDCS could act by reducing the time of recovery and physical limitations. We expect that future clinical trials be developed to test its efficacy in people with different symptomatology intensities generated by COVID-19.

## AUTHORS' CONTRIBUTIONS

ESF: Conceptualization, Writing – Original Draft, Writing – Review & Editing. JAA: Conceptualization, Writing – Original Draft, Writing – Review & Editing. SM: Writing – Original Draft, Writing – Review & Editing. ACS: Writing – Original Draft, Writing – Review & Editing. MSBS: Writing – Original Draft, Writing – Review & Editing.

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