

# Transcranial direct current stimulation associated with pharmacological approaches in patients infected by SARS-CoV-2

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SARS-CoV-2 was considered a worldwide health problem due to its rapid spread and lethality. Almost 3 years after the beginning of the pandemic period, people who were infected and survived are still presenting sequelae. Neurological manifestations caused by SARS-CoV-2 were identified in approximately 10% of people infected and hospitalized<sup>1</sup>. It has been suggested that SARS-CoV-2 can infect the central nervous system through olfactory and vagus nerves. Then, it releases cytokines, increasing the sympathetic nervous system activity and maintaining the inflammatory response<sup>2</sup>. Anti-inflammatory exacerbated response, pain, fatigue, cognitive issues, and physical deterioration are outcomes frequently involved in the central nervous system dysfunctions after SARS-CoV-2 infection<sup>2,3</sup>.

Noninvasive and safe strategies, such as transcranial direct current stimulation, might be an alternative to managing inflammatory response and neurological symptoms. Neuromodulation of the left dorsolateral prefrontal cortex seems to present the potentiality to decrease the recovery time of the neurological disabilities generated by SARS-CoV-2 through different mechanisms<sup>2</sup>. The sympathetic and parasympathetic autonomic nervous system response seems to be involved in inflammatory modulation<sup>4</sup>. It is important to mention that in experimental models and preliminary data in human beings, vagus nerve stimulation attenuates inflammation, modulating activity of cholinergic anti-inflammatory pathways<sup>5</sup>.

There are at least six drugs approved by the Food and Drug Administration to treat SARS-CoV-2: paxlovid, molnupiravir, fluvoxamine<sup>6</sup>, remdesivir, baricitinib<sup>7</sup>, and dexamethasone<sup>8</sup>, which have decreased the recovery time and accelerated an improvement in clinical status of patients infected by SARS-CoV-2. It has been hypothesized that their actions are related to reducing inflammatory-mediated injury and improving lymphocyte counts.

There are at least nine ongoing clinical trials registered in adults<sup>9</sup>. All the trials are designed to use transcranial direct current stimulation without pharmacological association to treat patients infected by SARS-CoV-2. We expect that future clinical trials are designed using transcranial direct current stimulation as an associated strategy with pharmacological treatment to generate a booster. In this sense, if transcranial direct current stimulation shows efficacy to recover central nervous system dysfunctions generated by SARS-CoV-2, we could start discussions to insert this tool in the public health system.

## AUTHORS' CONTRIBUTIONS

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