Transcranial stimulation lowers blood pressure in patients with resistant hypertension, study shows

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Many research groups are trying to find non-pharmacological solutions to help control resistant hypertension, and transcranial direct current

stimulation (tDCS) could be an option, according to a study recently reported in an article published in *Frontiers in Cardiovascular Medicine*.

Resistant or refractory hypertension is high blood pressure that does not respond to aggressive medical treatment, defined as daily administration of at least three classes of antihypertensive drug (including a diuretic) at maximally tolerated doses. Patients with the disease are at high risk of cardiovascular complications, including stroke and heart failure.

At the University of Campinas's School of Physical Education (FEF-UNICAMP) in São Paulo state, Brazil, the researchers evaluated the effects of a single session (acute stimulation) or ten sessions of tDCS on peripheral and central blood pressure in 13 volunteers with resistant hypertension. Six months before the start of the trial, the patients were assessed for adherence to medicational treatment, which was maintained throughout the study, as well as body weight, height and resting blood pressure, and for other clinical conditions that could influence blood pressure.

"Following acute stimulation, 24-hour systolic pressure measured by ambulatory monitoring fell in some patients by 15 mmHg [millimeters of mercury]. A reduction of this magnitude significantly mitigates cardiovascular risk," Bruno Rodrigues, principal investigator for the study told Agência FAPESP.

With a first degree in physical education, a Ph.D. in physiopathology and a postdoctoral fellowship in cardiology at the Heart Institute (InCor) of the University of São Paulo's Medical School (FM-USP), Rodrigues is currently a professor at FEF-UNICAMP.

"This was a small study, and more robust research is needed," he said. "With a larger body of evidence to corroborate our findings, it will be possible to think of tDCS as emergency-room treatment for hypertensive

crisis patients."

Tolerance

The results of the clinical trial also showed that the longer period of tDCS did not lower brachial blood pressure, measured on the brachial artery in the doctor's office and monitored for 24 hours. "One possible explanation is that stimulation for ten consecutive days led to a higher level of tolerance and only worked initially, with blood pressure rising again thereafter," Rodrigues said.

Previous research conducted by the group and also supported by FAPESP had revealed tDCS's potential as a method of modulating control of the autonomic nervous system and lowering blood pressure in patients with mild to moderate hypertension. This pointed to the possibility of its use to treat resistant hypertension.

The recently reported study was double-blind and randomized, meaning that the patients were randomly divided into groups and neither they nor the researchers knew which type of treatment they received. It was also a crossover, a type of clinical trial in which all participants receive the same two or more treatments, but in a different order, depending on the group to which they are randomly assigned.

In both the acute and longer protocols, the effects of 20-minute sessions of actual and sham tDCS were compared. Patients randomly selected for sham stimulation received electric current only during the first three minutes, remaining for 17 minutes with electrodes on their skin in sham treatment, while the others were stimulated for the full 20 minutes. After a one-week break, they were all submitted to ten consecutive sessions. After another break, those who had received sham treatment were given the full treatment and vice-versa.

The researchers also tested the effects of tDCS on the autonomic nervous system (which controls functions such as breathing, circulation, temperature and digestion, and comprises the sympathetic and parasympathetic systems), and measured biomarkers associated with blood pressure, such as cortisol, noradrenaline, acetylcholinesterase and cytokines.

Hyperactivity of the sympathetic nervous system (responsible for responses to danger or stress, including higher heart rate, blood pressure and breathing rate) is considered one of the main causes of hypertension and plays a particularly significant role in resistant hypertension. In patients with this disorder, it is associated with the risk of arrhythmia, vasoconstriction, and remodeling of the blood vessels and heart. Activation of the parasympathetic nervous system (responsible for calming the body's responses when resting or feeding) has been linked to improved cardiac functioning, lower blood pressure and less inflammation.

The study was conducted in partnership with Heitor Moreno Junior, who heads the Resistant Hypertension Clinic at UNICAMP's School of Medical Sciences.

The researchers acknowledged that some of the effects of tDCS require further study. "Both acute and more prolonged stimulation brought about a reduction in modulation by the sympathetic nervous system and boosted vagal [parasympathetic] modulation," Rodrigues said. "These findings may also be associated with increased levels of an anti-inflammatory cytokine in blood plasma, such as interleukin-10." Cytokines are proteins secreted by immune system cells.

The next step will be to find out whether tDCS can modulate the autonomic nervous system directly.

More information: Bruno Rodrigues et al, Acute and Short-Term Autonomic and Hemodynamic Responses to Transcranial Direct Current Stimulation in Patients With Resistant Hypertension, *Frontiers in Cardiovascular Medicine* (2022). DOI: 10.3389/fcvm.2022.853427