

Transcranial direct current brain stimulation for chronic pain

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Related to, doi:[10.1136/bmj.h1640](https://doi.org/10.1136/bmj.h1640)

Not recommended; early promise is fading fast as trial methods improve

Transcranial direct current stimulation (tDCS) is a form of non-invasive brain stimulation that delivers low intensity direct current stimulation to the brain through electrodes applied to the skin over the target area. It has been found to modulate cortical excitability at the target site leading some researchers to investigate it as a possible treatment for chronic pain and a host of other conditions. tDCS has clear appeal; it is cheap, relatively easy to use, and seems to be safe. In a linked article, Luedtke and colleagues (doi:[10.1136/bmj.h1640](https://doi.org/10.1136/bmj.h1640)) report the results of a randomised controlled trial of transcranial direct current stimulation for chronic low back pain.[1]

The motor cortex is the most common target of brain stimulation for chronic pain. Based largely on studies of invasive epidural stimulation of the motor cortex, researchers hypothesised that tDCS might reduce pain by modulating activity in cortical and subcortical areas of the brain involved in pain processing and by facilitating descending inhibitory mechanisms.[2-4] As the experience of pain is ultimately generated by the brain, artificially modulating brain activity might alter the experience of pain.

Early clinical trials reported beneficial effects in both patients with fibromyalgia and those with pain associated with spinal cord injury.[5] [6] In our own 2010 Cochrane review we found limited evidence that tDCS to the motor cortex might have short term effects on chronic pain, though the scarcity of high quality studies precluded firm conclusions.[7] Last year we published an update of that review and, on the basis of additional studies,

concluded that the available evidence did not suggest that tDCS was effective, with the caveat that future evidence could alter this conclusion.[8]

The trial reported by Luedtke and colleagues makes an important and substantial contribution to the available evidence.[1] With adequate power, rigorous design, and full reporting of outcomes, their trial stands out among its peers in the existing evidence base. Because this trial delivered tDCS before a multimodal rehabilitation programme with a cognitive behavioural focus, it not only tests the basic question “does tDCS work?” but also explores the potential of tDCS as an adjunct to another common therapeutic approach.

The results of the trial are convincingly negative. Relative to sham stimulation, active tDCS had no effect on any of the primary or secondary outcome measures at any time point. A course of tDCS equivalent to that delivered in existing small positive trials did not reduce pain and disability or influence the outcome of the rehabilitation programme that followed. The data were conclusive.

How might we interpret these findings? This is the first substantial trial of tDCS for chronic low back pain. Could tDCS fail to work for that chronically painful condition but remain a valuable treatment option in others? This is a possibility, though broadly at odds with the current evidence. Systematic reviews already suggested that effect sizes declined over time,[8] as early promise of benefit faded with additional trials.[9] The new results fit that picture. Arguably, tDCS is an exemplar of the well known decline effect whereby evidence of benefit gets weaker as trials get stronger. Studies to date have been mostly small and underpowered with short follow-up periods, commonly used blinding strategies were suboptimal,[10] and there were signs of selective outcome reporting.[8] [11]

The theoretical and mechanistic foundations of tDCS as a treatment for pain are also worth closer scrutiny. As Luedtke and colleagues point out, evidence from experimental pain studies is not compelling.[11] Moreover, a recent systematic review of the physiological effects of tDCS in healthy participants concluded that, of 30 separate neurophysiological measures that have been reported by more than one research group, tDCS was found to have an effect on just one—the amplitude of motor evoked potentials. Post hoc analyses

suggest that even those effect sizes might be declining over time.[12] There may be substantial problems with both replication and rigour in this specialty.

In the broader literature, and in the media, tDCS has been the subject of much recent attention and considerable hype[13] because of its various purported clinical applications and its potential role as a form of “neuro-enhancement.” The attention seems to have run some way ahead of the research findings. Brain stimulation can induce a transient physiological effect, but at this point the evidence of a reliable effect on any aspect of cognitive performance is unconvincing,[14] and, as Walsh recently pointed out, effects are usually short lived, often small, and hard to replicate and have a tendency to disappear in the noise of real life.[13] Perhaps then, we should not be surprised by the disappearing benefits of tDCS for chronic pain.

Patients with chronic pain are currently faced with a large and confusing choice of treatment options. While we acknowledge the possibility that further research may yet indicate a role for tDCS in the treatment of pain, we must be absolutely confident that it represents genuine benefit before recommending it to patients. Luedtke and colleagues should be congratulated on their important contribution to this process. The rigour of their research and the transparency of their reporting should serve as a template for researchers continuing to investigate the effects of non-invasive brain stimulation on chronic pain.

Competing interests: We have read and understood the BMJ Group policy on declaration of interests and declare the following interests: None.

Provenance and peer review: Commissioned; not externally peer reviewed.

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Cite this as: *BMJ* 2015;350:h1774