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Chronic neuropathic pain alleviation after transcranial direct current stimulation to the dorsolateral prefrontal cortex

Abraham P. Arul-Anandam, Colleen Loo, MBBS, MD, FRANZCP, Donel Martin, BSci(Psych), PhD, Philip B. Mitchell, MBBS, MD, FRANZCP, FRCPsych

University of New South Wales, School of Psychiatry, Black Dog Institute, Sydney, Australia

We report on the case of a 51-year-old woman who experienced significant alleviation of chronic neuropathic pain, while participating in a clinical trial using transcranial direct current stimulation (tDCS) for the treatment of major depressive disorder (MDD).[1] tDCS is a noninvasive brain stimulation technique that applies weak direct currents via scalp surface electrodes to the underlying cerebral cortex.[2] Increased neuronal activity has been shown in cortical regions underlying the anode, whereas reduced neuronal activity occurs in areas underlying the cathode.[3]

Two recent double-blinded, sham-controlled clinical trials have shown anodal tDCS to be efficacious in the treatment of MDD when applied to the left dorsolateral prefrontal cortex (DLPFC).[4,5] The theory is that tDCS exerts its antidepressant response by enhancing prefrontal activity, which is underactive in MDD.[6]

There is also interest in using tDCS for the treatment of chronic pain, though the majority of studies have targeted the motor cortex.[7,8] However, Boggio et al[9,10] have reported increased pain threshold and decreased response to aversive visual stimuli after anodal tDCS to the DLPFC in healthy subjects. The DLPFC modulates pain networks, including the amygdala and anterior cingulate cortex,[11] possibly accounting for these findings. Recently reported effects of prefrontal tDCS on appetite further suggest modulation of reward pathways.[12] However, to our knowledge, there have been no reports of tDCS to the DLPFC alleviating chronic neuropathic pain.

Our group is examining the efficacy of 20 minutes of 1 mA anodal tDCS to the left DLPFC for the treatment of MDD for 10 sessions on alternate days in a double-blind sham-controlled study. Direct currents were administered using $7 \times 5\ cm^2$ rubber electrodes, separated from the scalp by saline-soaked sponges (total surface area = $35\ cm^2$). The anode was placed over the F3 position (electroencephalographic [EEG] 10/20 system), corresponding to the left DLPFC, while the cathode was placed over the contralateral supraorbital area. In active and sham conditions, the current was gradually increased to the level of 2 mA, over a 30-second period. In the sham condition, the current was turned off after 30 seconds, although the subject continued to remain seated for 20 minutes; in the active condition, the current was maintained for the full 20 minutes. Subjects were informed that some of the first 10 treatment sessions may be sham, but were not aware which sessions these involved. The blind was maintained for the first 10 sessions. Before the breaking of the blind, subjects were asked to guess whether they had received active or sham tDCS. The difference in

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Correspondence: Prof. Collen Loo, University of New South Wales, School of Psychiatry,Black Dog Institute, Hospital Road Randwick, Sydney, NSW2031, Australia.

E-mail address: colleen.loo@unsw.edu.au

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active/sham guesses between the active and sham treatment groups was not significant ($\chi^2 = 0.00$; $df = 1$; $P = 0.98$; n = 40). Subjects were equally likely to base their guesses on either their change in mood or side effects experienced.

Case report

The patient was a 51-year-old woman with a 5-year history of neurologic symptoms, including chronic radicular pain, caused by bilateral facet joint arthropathy and a broad-based central and right paracentral posterior disc/osteophyte complex at C4/5, causing moderate encroachment on the C5 nerve root in the right exit foramen and C7 nerve root in the left exit foramen. She described solely left-sided symptoms, including sharp pain in the posterior left upper arm and shoulder and numbness and paresthesia in the lateral half of her left hand. Magnetic resonance imaging (MRI) of the cervical spine reported findings consistent with the patient's clinical syndrome.

The patient was managed with frequent traction, massage therapy, and hydrotherapy, but avoided oral analgesics. She received a single course of spinal block analgesia 3 years ago, which alleviated pain levels for approximately 6 months. Her specialist had advised a foraminectomy in the near future.

Independent of her pain syndrome, the patient also had a 4-year DSM-IV major depressive episode without melancholic features. At the time of entering our clinical trial, she was not taking any antidepressant medications.

The patient was randomly assigned to commence with sham treatment. She received five sessions of sham treatment, followed by 10 sessions of active treatment, on alternate weekdays. She described "significant improvement" in her pain soon after commencing active treatment (although she was still blind to treatment allocation) but not while she was in the sham condition. On a rating of 1 (no pain)-10 (worst pain), the patient reported that her pain severity changed from 7 (before commencing active tDCS) to 4 (after five sessions of active tDCS). This is a degree of change that she compared to the effect of the spinal block analgesia she received 3 years ago. The improvements were maintained at 1-month follow-up. She did not require any specific pain treatment while in the tDCS trial and reported that her sleep was uninterrupted by pain.

The patient's depression also responded significantly to the tDCS treatment, which she rated as "much improved." Her scores on the Montgomery Asberg Depression Rating Scale (rated by a psychiatrist blind to treatment condition) changed from 33 at study entry to 9 at the end of the trial. Self-rating scores further suggested significant improvement with her Beck Depression Inventory score falling from 38 to 1. A battery of cognitive tests administered throughout the trial found no significant deficits after treatment.

Comment

Chronic pain is defined by the International Association for the Study of Pain as "pain that persists beyond normal tissue healing time, which is assumed to be 3 months."[13]

This case report suggests that tDCS to the prefrontal cortex may help alleviate chronic pain caused by nerve root compression. Although no clinical trials have assessed tDCS to the DLPFC in the treatment of chronic pain, electrical stimulation of fibers connecting the prefrontal cortex to the midbrain in rodents has demonstrated antinociceptive effects.[14-16] Moreover, fibromyalgia pain has been reduced by transcranial magnetic stimulation to the DLPFC,[17] though tDCS to the DLPFC appears to have lower efficacy for fibromyalgia pain compared with motor cortex stimulation.[18,19] Neuroimaging studies in the last decade, especially positron emission tomography (PET) and functional MRI (fMRI), have further implicated the frontal cortex in the cognitive and attentional processing of pain.[11]

The significance of these findings is limited, as it is confined to one case. Moreover, it is difficult to differentiate the subject's pain alleviation from the dramatic improvement in her depressive symptoms, a factor which in itself can modulate pain perception.[20] However, given the involvement of prefrontal cortical activity in pain processing, and the antinociceptive effects of various forms of prefrontal brain stimulation in animals and humans, further research in this area may be worthwhile.

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