RES MEDICA
Journal of the Royal Medical Society
Res Medica 2015, Volume 23, Issue 1

PERSPECTIVE ARTICLE

Transcranial direct current stimulation: a viable therapeutic option for depression

George Huntington[1]
[1]Medical student, University of Sheffield
Correspondence: ghuntington1@sheffield.ac.uk

ABSTRACT

Transcranial direct current stimulation (tDCS) is a form of neurostimulation that has recently regained popularity in its experimental use. tDCS utilizes a direct current applied to the scalp via electrodes to induce long-term changes to cortical excitability. A series of recent studies and reviews concluded its efficacy as a potential treatment for major depressive disorder. However, further research is required to establish effective montages and intensities of treatment to promote efficacy while reducing adverse effects. These potential future studies should include wider representative samples with more detailed reporting of adverse effects. Until then, this perspective piece argues that tDCS should continue to be considered as a potential addition to the therapies used to manage depression.

ISSN: 2051-7580 (Online) ISBN: 0482-3206 (Print)
Res Medica is published by the Royal Medical Society, 5/5 Bristo Square, Edinburgh, EH8 9AL

Res Medica, 2015, 23(1):82-85.
doi:10.2218/resmedica.v23i1.1190

Introduction

Depression is an illness affecting at least 9% of the British adult population.[1] It led to the loss of 10.4 million working days in 2012/3.[2] Currently, the standard treatment regimen involves the use of both selective serotonin reuptake inhibitor (SSRI) antidepressant drugs[3] and psychotherapy.[4]

Electroconvulsive therapy is well known to practitioners and the public alike as a form of psychiatric treatment. Lesser known is transcranial direct current stimulation (tDCS), which has yet to be adopted in a mainstream clinical setting. tDCS is a brain stimulation technique that uses a small direct current to stimulate targeted areas of the brain via a positive anode and a negative cathode. There has been historical interest in this area of research,[5] but it is only recently that developments have been made towards its inclusion in the treatment of conditions such as depression and stroke.[6]

The first recorded application of a direct current to the brain for therapeutic purposes can be found in the experiments of Mesmer and Aldini.[5] Interest was reawakened in the 1960s when it was shown that tDCS may affect neuroexcitability and improve cognitive performance, but this discovery was overlooked due to the development of effective psychopharmacy.[7] However, long-term treatment with psychopharmaceuticals is often associated with undesirable side effects and treatment resistance. In 2001, tDCS was further shown to produce changes in cortical neuronal excitability,[8] a discovery which led to a renewed interest in tDCS and investigation into its experimental and potential clinical applications.[6,7]

As to the mechanisms behind tDCS, the anode is thought to produce increased neuronal excitability at the targeted site while the cathode is thought to decrease it. These excitability changes do not lead to the production of an action potential directly but alter the probability of a neuron firing.[8]

Recent studies have suggested that tDCS is an effective therapeutic tool both as a monotherapy and in concert with psychopharmaceuticals in managing treatment-resistant depression. [9,10] However, tDCS has yet to be approved by NICE or any other governing body for use in a standard clinical setting, though guidelines are in development.[11] This article briefly attempts to justify its inclusion in future treatment guidelines.

Current experimental use of tDCS in depression

In current investigations into the use of tDCS towards in depression, the anode is placed over the left dorsolateral prefrontal cortex (DLPFC) and the cathode is placed over lateral aspect of the contralateral orbit.[9] Underactivity of the DLPFC is associated with depression,[8] and it is hoped that the excitatory activity of the anode can correct this. A weak current is passed through the brain, usually 0.5–2 mA for sessions lasting around 30 minutes.[7,9] Though the standard is several weeks of anodal 2 mA tDCS applied regularly, different parameters are being experimented with to ascertain the optimum intensity and montage.[12] This produces demonstrable changes to neuroexcitability[7] and the severity of depression.[9] Current understanding of neuroplasticity highlights that long-term changes in neuroexcitability may result from this stimulation. These changes and enhancements could last after the original stimulus is withdrawn[7] and may lead to increased spontaneous firing rates.

Several recent reviews and meta-analyses have investigated the use of tDCS in the treatment of depression.[7,13,14] They concluded that tDCS was more effective than sham for the treatment of depression, though some results were mixed and further randomized controlled trials with larger sample sizes and better reporting of side effects are needed.

When compared to pharmacological therapies, tDCS may be more effective than SSRIs for the treatment of depression. A randomized controlled trial investigating the use of tDCS to treat a major depressive episode produced a number needed to treat (NNT) of 2.6 after 6 weeks.[9] Given that the NNT of SSRIs is 7,[3] this demonstrates how potentially effective tDCS could be in the treatment of major depressive episodes. In addition to this, studies investigating the effects of tDCS in depressed subjects treated unsuccessfully with antidepressants found improvement.[9] Furthermore, reviews of the experimental treatment of depression with tDCS found that a reduction in depressive symptoms[7] and higher rates of remission[14] were observed in studies where the subjects were both taking and not taking antidepressants. The greater reductions were usually seen in subjects taking antidepressants. Finally, a study examining clinical response found greater changes in subjects undergoing tDCS in combination with antidepressants than in those taking antidepressants alone.[15] Thus, there is

evidence for the clinical use of tDCS, both as an adjunct to treatment and as a distal line monotherapy for depression and drug-resistant depression.

Potential advantages and disadvantages of tDCS

There are already other forms of brain stimulation used in the treatment of severe depression, so what are the advantages of tDCS over others? In comparison to alternative forms of brain stimulation, tDCS is more cost effective,[6] easier to use, less invasive,[7] and has potentially fewer side effects.[7] The devices used to administer tDCS are smaller and more portable so they are easier to store in a clinic or as part of a mobile service.

tDCS is not without its disadvantages: a review of adverse effects of tDCS found itching, tingling, and headache to be most common.[16] However, the increased incidence of these adverse effects in genuine tDCS compared to sham was not statistically significant. This demonstrates an advantage over pharmacotherapies, the long-term effects of which are undesirable and may impact treatment concordance. However, there is currently no data on its long-term side effects, if they do exist.

Transcranial magnetic stimulation (TMS) is an additional form of brain stimulation that is another potential treatment option. However, TMS is still expensive and difficult to utilize,[7] with uncertain efficacy due to the difficulties inherent in producing a sham alternative during studies.

The Improving Access To Psychological Therapies (IAPT) initiative was introduced as a result of the Depression Report,[4] which highlights that it is more cost-effective to provide psychotherapy to treat depression and anxiety compared to the number of working days lost to these problems. It follows that implementing a similar programme with brain stimulation (such as tDCS) may have a similar effect. tDCS is also thought to be more cost-effective than alternative pharmaceutical or neurostimulative programmes in treating depression.[6]

In the developing world, poor access to healthcare and the expense of drugs lead to poor continuity of treatment and difficulty maintaining therapeutic levels of pharmaceuticals.[6] With tDCS, this is less of a concern as the device need only be purchased once. The provision of, and the resources available to, psychiatric services in the developing world are in dire need of improvement.[6,17] tDCS is a treatment which could possibly assist in ameliorating some of these concerns.

Conclusion and summary

Recently, many major pharmaceutical companies have either reduced funding of their research into psychiatric treatments or closed their departments altogether[18] citing poor financial returns in these areas of research. Thus, there are fewer new treatments being developed that are likely to improve or contribute to psychiatric practice in the near future. With this in mind, it is important to continue investigating further treatment options if we are to continue to help a population of patients that is predicted to increase. Research should be focused on cost-effective, accessible treatments that produce viable results. These treatments could be used to combat the growing prevalence of depression worldwide and the difficulties of managing it in the developing world. With evidence suggesting its efficacy, tDCS could be considered one of those potential treatments.

tDCS is still in its experimental stages and much needs to be done to determine protocols for efficient clinical administration, such as further research into optimal current intensity and electrode placement. In addition to this, further data on side effects need to be researched, both to reduce short-term adverse effects and to investigate the occurrence of long-term adverse effects. Once these concerns are alleviated, tDCS could be made available for the management of depression, in addition to or as an adjunct to current treatments.

What is known already:	What this study adds/ highlights:
• Transcranial direct current stimulation (tDCS) is an experimental form of neurostimulation which has been demonstrated to produce changes in cortical excitability. • It is thought that these changes translate into alterations of behaviour and may help alleviate depression. • Reviews examining the efficacy of tDCS in the treatment of depression are hopeful, but larger studies with better reporting of side effects needs to be carried out. Also, an accepted protocol and montage for the administration of tDCS needs to be clarified before tDCS can be approved as an appropriate therapy.	• A supportive argument for the continuing investigation of tDCS as a clinical tool for the treatment of depression. • A commentary on the current state of treatment development in psychopharmacology, mentioning its stagnation, the limited accessibility of treatment in resource-poor countries, and the need to develop new therapies. • Contrasting tDCS with current therapies and discussing how it may solve the problems mentioned above.

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