

## NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

### Interventional procedure consultation document

## Transcranial direct current stimulation (TDCS) for depression

Depression causes low mood or sadness that can last for weeks or months. People with depression often feel hopeless and lose interest in things they used to enjoy. Other symptoms include sleeping badly, and having no appetite or sex drive. Transcranial direct current stimulation aims to treat depression by applying a very weak electric current to the head for several minutes at a time, using electrodes placed on the scalp.

The National Institute for Health and Care Excellence (NICE) is examining transcranial direct current stimulation (TDCS) for depression and will publish guidance on its safety and efficacy to the NHS. NICE's Interventional Procedures Advisory Committee has considered the available evidence and the views of specialist advisers, who are consultants with knowledge of the procedure. The Advisory Committee has made provisional recommendations about TDCS for depression.

This document summarises the procedure and sets out the provisional recommendations made by the Advisory Committee. It has been prepared for public consultation. The Advisory Committee particularly welcomes:

- comments on the provisional recommendations
- the identification of factual inaccuracies
- additional relevant evidence, with bibliographic references where possible.

**Note that this document is not NICE's formal guidance on this procedure. The recommendations are provisional and may change after consultation.**

The process that NICE will follow after the consultation period ends is as follows.

- The Advisory Committee will meet again to consider the original evidence and its provisional recommendations in the light of the comments received during consultation.

- The Advisory Committee will then prepare draft guidance which will be the basis for NICE's guidance on the use of the procedure in the NHS.

For further details, see the [Interventional Procedures Programme process guide](#), which is available from the NICE website.

Through its guidance NICE is committed to promoting race and disability equality, equality between men and women, and to eliminating all forms of discrimination. One of the ways we do this is by trying to involve as wide a range of people and interest groups as possible in the development of our interventional procedures guidance. In particular, we aim to encourage people and organisations from groups who might not normally comment on our guidance to do so.

In order to help us promote equality through our guidance, we should be grateful if you would consider the following question:

Are there any issues that require special attention in light of NICE's duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations between people with a characteristic protected by the equalities legislation and others?

Please note that NICE reserves the right to summarise and edit comments received during consultations or not to publish them at all where in the reasonable opinion of NICE, the comments are voluminous, publication would be unlawful or publication would otherwise be inappropriate.

Closing date for comments: 31<sup>st</sup> March 2015

Target date for publication of guidance: June 2015

## **1 Provisional recommendations**

- 1.1 The evidence on transcranial direct current stimulation (TDCS) for depression raises no major safety concerns. There is some evidence of efficacy but there are uncertainties about the specific mode of administration, the number of treatments needed and the duration of effect. Therefore, this procedure should only be used with special arrangements for clinical governance, consent and audit or research.

1.2 Clinicians wishing to undertake TDCS for depression should take the following actions:

- Inform the clinical governance leads in their NHS trusts.
- Ensure that patients understand the uncertainty about the procedure's efficacy and provide them with clear written information. In addition, the use of NICE's [information for the public](#) *[[URL to be added at publication]]* is recommended.
- [Audit](#) *[[URL to audit tool to be added at publication]]* and review clinical outcomes of all patients having TDCS for depression (see section 7.2).

1.3 NICE encourages further research into TDCS for depression which should document how patients were selected and any other treatments they were having. It should describe the precise method and regime used for administering TDCS. Outcome measures should include the duration of effect. NICE may update the guidance on publication of further evidence.

## **2 Indications and current treatments**

2.1 Depression is a common disorder, characterised by persistent sadness, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep, appetite and libido, feelings of tiredness and poor concentration. Depression is often accompanied by feelings of hopelessness and suicidal thoughts. Depression can last from weeks to years, and can be recurrent, substantially impairing an individual's ability to function at work or cope with daily life.

2.2 Treatments for depression include a range of psychological therapies and antidepressant medications.

- 2.3 In severe depression electroconvulsive therapy is sometimes used.

### **3 The procedure**

- 3.1 Transcranial direct current stimulation (TDCS) is a non-invasive method of electrical stimulation of the brain using a weak direct current applied to the scalp through electrodes. The aim is to modify cortical excitability and activity in the brain areas underlying the scalp electrodes. The method of action is proposed to be through the depolarisation and hyperpolarisation of cortical neurons.
- 3.2 The patient, who remains awake and alert during the procedure, is usually seated while a portable battery-operated stimulator delivers a constant low-amplitude (typically 1–2 mA) direct current to 2 saline-soaked sponge electrodes placed on the scalp. The anode is usually positioned over the left frontal cortex and the cathode over the right frontal cortex.
- 3.3 Treatment sessions typically last for about 20–30 minutes, and are repeated daily for several weeks. The treatment can be self-administered by the patient. TDCS may be used alone or in addition to other treatments for depression.

### **4 Efficacy**

This section describes efficacy outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the [interventional procedure overview](#) *[add URL]*.

- 4.1 A systematic review and meta-analysis of 7 randomised controlled trials (RCTs) including 259 patients treated by active transcranial IPCD: Transcranial direct current stimulation (TDCS) for depression

direct current stimulation (TDCS, n=137) or sham TDCS (n=122) reported a significantly greater improvement in depressive symptoms in the active TDCS group using Hedges' g as the measure of the effect size, which standardises studies using different depression scales (Hedges' g=0.37; 95% confidence interval [CI] 0.04 to 0.7) compared to the sham TDCS group. An RCT of 120 patients treated by either active TDCS and sertraline (n=30), active TDCS and placebo (n=30), sham TDCS and sertraline (n=30) or sham TDCS and placebo (n=30) reported significantly lower Montgomery–Åsberg Depression Rating Scale (MADRS) scores (10 items measured on a scale of 0 to 6 with low values indicating less depression) after 6 weeks in patients treated by active TDCS and sertraline compared against patients treated by sham TDCS and sertraline (mean difference 8.5 points; 95% CI 2.96 to 14.03; p=0.002). Significantly lower MADRS scores after 6 weeks were also reported in patients treated by active TDCS and placebo compared against patients treated by sham TDCS and placebo (mean difference 5.6 points; 95% CI 1.30 to 10.01; p=0.01).

4.2 The systematic review of 7 RCTs including 259 patients reported significantly better treatment response rates (defined as an improvement greater than 50% in depression scores from baseline to end point) in the active TDCS group compared against the sham TDCS group (odds ratio [OR] 1.63, 95% CI 1.26 to 2.12).

4.3 The systematic review of 7 RCTs including 259 patients reported significantly better remission rates in the active TDCS group compared against the sham TDCS group, with scores lower than 8 in the Hamilton Depression Rating Scale (several variables assessed and measured on 5-point or 3-point scales, with low

values indicating less depression), or lower or equal to 10 in the MADRS (OR 2.5, 95% CI 1.26 to 4.99). In the RCT of 120 patients, remission rates (according to MADRS scores) after 6 weeks were 47% (14/30) for patients treated by active TDCS and sertraline, 40% (12/30) for patients treated by active TDCS and placebo, 30% (9/30) for patients treated by sham TDCS and sertraline and 13% (4/30) for patients treated by sham TDCS and placebo ( $p=0.03$  between groups).

- 4.4 A follow-up study ( $n=42$ ) of the RCT of 120 patients treated by TDCS (every other week for 3 months and then once a month for the following 3 months), reported a sustained response rate of 47% (95% CI, 27 to 64, measured by Kaplan–Meier survival analysis) at 24 weeks. Patients with treatment-resistant depression had a much lower 24-week sustained response rate than patients with non-refractory depression (10% versus 77%, OR 5.52;  $p<0.01$ ).
- 4.5 The follow-up study ( $n=42$ ) of the RCT of 120 patients treated by TDCS reported a mean response duration of 11.7 weeks.
- 4.6 The systematic review of 7 RCTs including 259 patients reported dropout rates of 8% (12/137) in the active TDCS group and 11% (15/122) in the sham TDCS group, with no difference in treatment acceptability (OR 0.73, 95% CI 0.32 to 1.69).
- 4.7 The specialist advisers listed key efficacy outcomes as improvement in depressive symptoms, remission, reduction in anxiety, effectiveness in treatment resistance and improvement in other parameters including cognitive function, pain and neurological symptoms.

## 5 Safety

This section describes safety outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the [interventional procedure overview](#) *[add URL]*.

- 5.1 Six episodes of either treatment-emergent mania or hypomania (Young Mania Rating Scale score greater than 8) were reported in a randomised controlled trial (RCT) of 120 patients treated by either active transcranial direct current stimulation (TDCS) and sertraline, active TDCS and placebo, sham TDCS and sertraline or sham TDCS and placebo. Five episodes (including 2 manic episodes) were from the combined treatment group and 1 was from the TDCS-only group (no further details provided).
- 5.2 Skin lesions were reported in all (5/5) patients treated by 2 mA TDCS and in 1 (1/10) patient treated by 1 mA TDCS in a case series of 15 patients treated by 1 mA or 2 mA TDCS. Generally, the lesions occurred after the fourth or fifth stimulation, showed stable superficial extensions during further TDCS and healed without scars about 1–3 weeks after the end of the TDCS treatment.
- 5.3 A burning sensation was reported in 9% of the studies in the active TDCS group and in 10% of the studies in the sham TDCS group in a systematic review of 117 studies (p value not significant).
- 5.4 Skin redness 2 weeks after treatment was reported in 25% (13/60) of patients in the active TDCS group and in 8% (4/60) of patients in the sham TDCS group, in the RCT of 120 patients ( $p=0.03$ ). Skin redness was reported in 23% (10/42) of patients in a follow-up study ( $n=42$ ) of the RCT of 120 patients treated by TDCS every

other week for 3 months and then once a month for the following 3 months.

- 5.5 Itching was reported in 39% of the studies in the active TDCS group and in 33% of the studies in the sham TDCS group in the systematic review of 117 studies (p value not significant and no details of timing provided). Tingling was reported in 22% of the studies in the active TDCS group and in 18% of the studies in the sham TDCS group in the systematic review of 117 studies (p value not significant and no details of timing provided).
- 5.6 Headache was reported in 15% of the studies in the active TDCS group and in 16% of the studies in the sham TDCS group in the systematic review of 117 studies (p value not significant). Headache was reported in 19% (8/42) of patients in the follow-up study (n=42) of the RCT of 120 patients
- 5.7 Somnolence was reported in 16% (7/42) of patients in the follow-up study (n=42) of the RCT of 120 patients.
- 5.8 Panic attacks were reported in a single case report 5 days after starting TDCS treatment. It was hypothesised that the patient had a right hemispheric dominance, considering that he was left-handed and dyslexic.
- 5.9 In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never done so). For this procedure, specialist advisers reported induction of phosphenes ('flashing lights') with anterior stimulation positions as an anecdotal adverse event. They considered that the



following were theoretical adverse events: precipitation of seizures, 'exacerbation of depression', interference with implanted electrical devices (for example, brain stimulators or cardiac pacemakers), light headedness and twitching of facial muscles.

## **6 Committee comments**

- 6.1 The Committee was mindful that depression is a very common condition and that a range of other treatments is available. It considered that this increased the need for good evidence on transcranial direct current stimulation (TDCS).
- 6.2 The Committee noted the inconsistency of the outcomes reported after TDCS for depression between the various studies. Together with the uncertainties about the different modes of administration and number of treatments, this underpinned the recommendation for further research.

## **7 Further information**

- 7.1 For related NICE guidance, see the [NICE website](#).
- 7.2 This guidance requires that clinicians undertaking the procedure make special arrangements for audit. NICE has identified relevant audit criteria and is developing an audit tool (which is for use at local discretion), which will be available when the guidance is published.

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