NICE guidance

# Transcranial direct current stimulation (tDCS) for depression

Interventional procedures guidance
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## Your responsibility

This guidance represents the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, healthcare professionals are expected to take this guidance fully into account, and specifically any special arrangements relating to the introduction of new interventional procedures. The guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful

discrimination, advance equality of opportunity, and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties. Providers should ensure that governance structures are in place to review, authorise and monitor the introduction of new devices and procedures.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

# 1 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 do tDCS for depression should:

- 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 is recommended.
- Audit and review clinical outcomes of all patients having tDCS for depression (see section 7.1).

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, low self-worth, tiredness, poor concentration, and disturbed sleep, appetite and libido. It is often accompanied by feelings of hopelessness and suicidal thoughts. Depression can last from weeks to years, and can be recurrent. It can substantially impair a person'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. In severe depression that has not responded to other treatments, 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 under the scalp electrodes. It is thought to work by 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-strength direct current to 2 saline-soaked sponge electrodes placed on the scalp. Treatment sessions typically last for about 20–30 minutes, and are repeated daily for several weeks. Treatment is usually delivered by a trained clinician, but it can also 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.

4.1 A systematic review and meta-analysis of 7 randomised controlled trials (RCTs) including 259 patients treated by active transcranial 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 against the sham tDCS group. An RCT of 120 patients treated by active tDCS plus sertraline (n=30), active tDCS plus placebo (n=30), sham tDCS plus sertraline (n=30), or sham tDCS plus 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 plus sertraline compared against patients treated by sham tDCS plus 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 plus placebo compared against patients treated by sham tDCS plus 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 plus sertraline, 40% (12/30) for patients treated by active tDCS plus placebo, 30% (9/30) for patients treated by sham tDCS plus sertraline and 13% (4/30) for patients treated by sham tDCS plus placebo (p=0.03 between groups).

4.4 A follow-up study of 42 patients whose depression had responded ('responders') to tDCS treatment in the RCT of 120 patients reported a sustained response rate at 24 weeks in these 'responders' of 47% (95% CI, 27 to 64, measured by

Kaplan–Meier survival analysis). 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). The same study reported a mean response duration (for 'responders', n=42) of 11.7 weeks.

4.5 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).

4.6 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.

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 active transcranial direct current stimulation (tDCS) plus sertraline, active tDCS plus placebo, sham tDCS plus sertraline, or sham tDCS plus placebo. Five episodes (including 2 manic episodes) were from the active tDCS plus sertraline 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 of 42 patients whose depression had responded to tDCS treatment in the RCT of 120 patients.

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 of 42 patients whose depression had responded to tDCS treatment in the RCT of 120 patients.

5.7 Light-headedness was reported in 40% of patients when tDCS was administered weekly and in 17% when tDCS was administered once every 2 weeks in a case series of 26 patients treated by tDCS for up to 6 months after an acute course of tDCS (absolute numbers not reported).

5.8 Somnolence was reported in 16% (7/42) of patients in the follow-up study of 42 patients whose depression had responded to tDCS treatment in the RCT of 120 patients. Fatigue was reported in 10% of patients when tDCS was administered weekly in the case series of 26 patients treated by tDCS for up to 6 months after an acute course of tDCS (absolute numbers not reported).

5.9 Blurred vision was reported in 7% of patients when tDCS was administered weekly and in 11% when tDCS was administered once every 2 weeks in the case series of 26 patients treated by tDCS for up to 6 months after an acute course of tDCS (absolute numbers not reported).

5.10 Panic attacks were reported in a single case report 5 days after starting tDCS treatment. It was hypothesised that the patient, who was left-handed and dyslexic, had right hemispheric dominance.

5.11 Nausea was reported in 10% of patients when tDCS was administered weekly and in 6% when tDCS was administered once every 2 weeks in the case series of 26 patients treated by tDCS for up to 6 months after an acute course of tDCS (absolute numbers not reported).

5.12 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 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 This guidance requires that clinicians doing the procedure make special arrangements for audit. NICE has identified relevant audit criteria and has developed an audit tool (which is for use at local discretion).

## Information for patients

NICE has produced information on this procedure for patients and carers (information for the public). It explains the nature of the procedure and the guidance issued by NICE, and has been written with patient consent in mind.

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# Endorsing organisation

This guidance has been endorsed by Healthcare Improvement Scotland.