Transcranial magnetic stimulation for severe depression

1 Guidance

1.1 Current evidence suggests that there are no major safety concerns associated with transcranial magnetic stimulation (TMS) for severe depression. There is uncertainty about the procedure’s clinical efficacy, which may depend on higher intensity, greater frequency, bilateral application and/or longer treatment durations than have appeared in the evidence to date. TMS should therefore be performed only in research studies designed to investigate these factors.

1.2 Future research should aim to address patient selection criteria, the optimal use of this procedure in relation to other treatments, and the duration of any treatment effect. Clinicians should collaborate to ensure that studies are sufficiently large to be adequately powered. The Institute may review the procedure upon publication of further evidence.

2 The procedure

2.1 Indications

2.1.1 Depression is characterised by low mood, loss of interest and enjoyment, and a range of associated emotional, cognitive, physical and behavioural symptoms. People with severe depression may develop psychotic symptoms. Depression is associated with risk of suicide and attempted suicide.

2.1.2 Diagnosis of depression and assessment of its severity are based on various criteria, including the persistence and severity of mood changes, the presence of other symptoms and the degree of functional and social impairment.

2.1.3 Conventional treatments for depression include antidepressant medication, psychological therapy or a combination of these. If depression is severe and resistant to other treatments, electroconvulsive therapy (ECT) may be used.

2.2 Outline of the procedure

2.2.1 The procedure aims to stimulate specific regions of the cerebral cortex by using a magnetic field generated by an electromagnet placed over the skull to induce electric currents. However, there is some uncertainty about the mechanism by which TMS operates.

2.2.2 TMS does not require anaesthesia and can be performed on an outpatient basis. The patient usually wears ear plugs to diminish the noise from the discharging coil. Magnetic resonance imaging can be used to facilitate precise targeting of selected brain regions, which can be unilateral or bilateral. For treatment of depression, a variant of TMS called repetitive TMS (rTMS) is used. This delivers rhythmic pulses of electromagnetism, rather than a single pulse, using a cut-off of 1 Hz; high or low frequency can be used. The intensity of rTMS is usually set as a percentage of the patient’s motor threshold (MT), defined as the minimum stimulus strength required to evoke involuntary muscle movements (usually in the hand) five times out of ten. Depending on intensity parameters, the patient may experience involuntary spasms of scalp muscles. Treatment with rTMS usually involves daily sessions lasting about 30 minutes for 2–4 weeks and possibly longer.

2.3 Efficacy

2.3.1 A meta-analysis of 11 studies (n = 197) showed a statistically significant improvement in depression according to the Hamilton Depression Rating Scale (HDRS) after 2 weeks of treatment with high-frequency rTMS over the left dorsolateral prefrontal cortex, compared with sham treatment (p = 0.03). Three of these studies reported that the difference was no longer statistically significant at 2-week follow-up. Seven of
the 11 studies (n = 145) used Beck Depression Inventory measurements, indicating no significant difference between active and sham rTMS.

2.3.2 A meta-analysis of 33 studies, including 877 patients, reported that reductions in depressive symptoms, as measured by the HDRS and Montgomery-Asberg Depression Rating Scale (MADRS), ranged from −10.4% to 59.4% for active rTMS and from 15% to 54% for sham rTMS at the end of treatment. A randomised controlled trial (RCT) of 301 patients (not included in either meta-analysis) reported that 18% of patients in the active TMS group achieved response at 4 weeks (MADRS scale) compared with 11% of patients in the sham TMS group (p < 0.05). There were no significant differences in the remission rates at 4 weeks (7% compared with 6% in the active TMS and sham groups respectively, p > 0.10). An RCT of 54 patients reported that 61% (11/18) of patients receiving rTMS at 100% MT and 28% (5/16) of patients receiving rTMS at 80% MT responded to treatment, compared with 6% (1/16) of patients in the sham group (p = 0.0008 for 100% MT versus sham, p = 0.1 for 80% MT versus sham, p = 0.044 for 100% versus 80% MT).

2.3.3 An RCT of 46 patients reported that significantly more patients responded to ECT compared with rTMS (59% [13/22] compared with 17% [4/24 respectively]; p = 0.006). A second RCT of 35 patients reported that 50% (10/20) of patients treated with rTMS responded to treatment and 10% (2/20) achieved remission, compared with 40% (6/15) and 20% (3/15), respectively, of patients treated with ECT (p = 0.6 for both results). For more details, refer to the ‘Sources of evidence’ section.

2.3.4 The Specialist Advisers raised concerns about its efficacy and considered it important to establish the optimal treatment parameters for the procedure.

2.4 Safety

2.4.1 The RCT of 130 patients reported that one patient developed a hypomanic episode soon after completion of the initial phase of treatment. Two case reports described a total of three patients with either mixed depression or induction of manic symptoms associated with TMS treatment. One case report described the development of a self-limited complex partial seizure in a patient after high-frequency rTMS treatment.

2.4.2 Two RCTs reported headache in 10% (6/60) and 11% (2/18 at 100% of MT and 2/19 at 80% of MT), respectively, of patients receiving rTMS. In a case series of 249 patients, headache after high-frequency rTMS was more common when it was administered over the right dorsolateral prefrontal cortex compared with the left (26% [5/19] and 5% [9/187], respectively).

2.4.3 In an RCT, the proportions of patients who reported site discomfort or pain were 0% (0/19) at 80% of MT and 17% (3/18) at 100% of MT, respectively. In two other RCTs, the proportions were 11% (7/60) at 100% of MT and 40% (14/35) (MT level not specified). For more details, refer to the ‘Sources of evidence’ section.

2.4.4 The Specialist Advisers stated that potential adverse events include induction of seizure, local scalp discomfort, headache, nausea, neck stiffness, hearing loss and induction of mania.

3 Further information

3.1 NICE has issued technology appraisal guidance on the use of electroconvulsive therapy (www.nice.org.uk/TA059) and computerised cognitive behaviour therapy (www.nice.org.uk/TA097), and clinical guidelines on the management of depression in adults (www.nice.org.uk/CG023, currently under review) and in children and young people (www.nice.org.uk/CG028).

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Information for patients

NICE has produced information describing its guidance on this procedure for patients and their carers (‘Understanding NICE guidance’). It explains the nature of the procedure and the decision made, and has been written with patient consent in mind. This information is available from www.nice.org.uk/IPG242publicinfo

Sources of evidence

The evidence considered by the Interventional Procedures Advisory Committee is described in the following document.


Available from: www.nice.org.uk/ip346overview

Ordering information

Copies of this guidance can be obtained from the NHS Response Line by telephoning 0870 1555 455 and quoting reference number N1418. ‘Understanding NICE guidance’ can be obtained by quoting reference number N1419.

The distribution list for this guidance is available at www.nice.org.uk/IPG242distributionlist