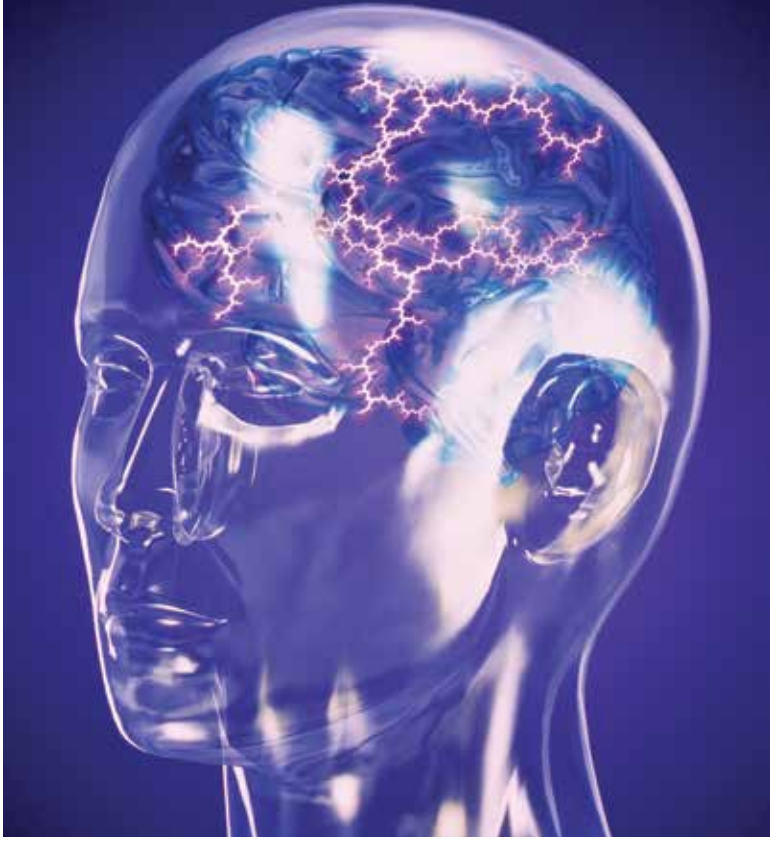
Brain stimulation treatments for depression



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Electroconvulsive therapy and repetitive transcranial magnetic stimulation are treatment options for people with depression, with or without concomitant pharmacotherapy. Several other neurostimulation techniques are considered experimental for depression although some are used for other indications.

Brain stimulation therapies are an emerging new field in psychiatry and offer potentially safe and efficacious treatments for the major health problem of depression, which is the second leading worldwide cause of disability.[1] Current pharmacological treatments for depression have the two main difficulties of treatment resistance (up to one-third of patients with depression do not remit despite treatment with up to four trials of antidepressant medications) and treatment intolerance (some patients are not able to tolerate side effects from antidepressants).[2,3] In this context, brain stimulation therapies offer an important additional treatment option for depression.

Repeated sessions of brain stimulation are usually given to modulate brain activity, with or without concomitant pharmacotherapy. There is some evidence suggesting that brain stimulation combined with pharmacotherapy might present better efficacy outcomes in treating depression than pharmacotherapy alone.[4-6]

In Australia, current approved neurostimulation treatments for depression are electroconvulsive therapy (ECT) and repetitive transcranial magnetic stimulation (rTMS). Transcranial direct current stimulation (tDCS), vagus nerve stimulation (VNS), magnetic seizure therapy (MST) and deep brain stimulation (DBS) are still considered experimental therapies (Table).

Established treatments

Electroconvulsive therapy

ECT involves the passage of a pulsed current through the brain to generate a controlled therapeutic seizure while the patient is under general anaesthesia. ECT is a highly specialised but short procedure. The current is typically applied for a few seconds (up to 8 s), and the patient recovers from anaesthesia minutes after. A course of ECT typically comprises eight to 12 sessions given at a frequency of two or three times per week.[7] Although most patients maintain clinical improvement after ECT with pharmacotherapy, a small proportion only respond to ECT and may be maintained with intermittent ECT treatments, once every month or six weeks, to prevent relapse.

ECT is the brain stimulation method with the largest clinical experience available, and is considered the most effective proven biological treatment currently available for depression.[7] ECT is superior to pharmacotherapy, both in efficacy (60 to 90% response rates with ECT *vs* 30 to 50% response rates with

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TABLE. BRAIN STIMULATION THERAPIES FOR DEPRESSION

Technique	Clinically approved for depression*	Anaesthesia requirement	Focality	Seizure involved	Efficacy *vs* antidepressant medications	Common side effects
Electroconvulsive therapy (ECT)	Yes	Yes	Diffuse	Yes	Superior	Cognitive (mostly transient), headache
Repetitive transcranial magnetic stimulation	Yes	No	Focal	No	Similar	Pain at stimulation site during treatment, headache
Transcranial direct current stimulation	No	No	Relatively diffuse	No	Probably similar	Tingling, itching, mild burning sensation, erythema at stimulation site
Vagus nerve stimulation	No	Yes	Relatively focal	No	Superior (?)	Stimulation side effects: voice alteration, dyspnoea
Magnetic seizure therapy	No	Yes	Relatively focal	Yes	Superior (?)	Cognitive (less than ECT)
Deep brain stimulation	No	Yes	Very focal	No	Superior	Stimulation side effects: paraesthesias, mood changes, autonomic effects

* Clinically approved for depression in Australia.

pharmacotherapy) and onset of action, and has higher efficacy than rTMS.[8-10] For this reason, ECT is prescribed for severe or treatment-resistant depression, especially in patients who present with high severity, psychotic symptoms, refusal to eat or high suicide risk.[7] ECT is effective in both unipolar and bipolar depression, with faster onset of response in the latter.[11-14] Evidence suggests that patients with personality disorders or substance abuse may respond less well to ECT.[15]

When performed by appropriately qualified specialists, ECT is a safe procedure that can be given even to patients with severe medical comorbidities.[7] ECT is used in adults and the elderly and also can be used during pregnancy and in children and adolescents.[7,16] Patients may experience some cognitive side effects, including immediate post-treatment disorientation and anterograde and retrograde amnesia, although the severity and duration of these vary widely. Cognitive side effects are usually temporary and contingent on individual and treatment parameters (e.g. the type of ECT, the anaesthetic used and the patient's age and prior cognitive reserve).[8,17-19] Clinical data and studies in animal models have repeatedly demonstrated that ECT does not produce brain damage.[20,21]

Several important advances in treatment approach in the past 25 years have led to improved clinical outcomes with ECT. These include the individualisation of ECT dose based on the patient's seizure threshold, electroencephalographic monitoring of seizure quality for dose adjustment over the treatment course, bifrontal placement of stimulating electrodes and ultrabrief pulse stimulation.[22-30] The latter two developments have been shown to cause fewer cognitive side effects, through lesser stimulation of the temporal lobe, while maintaining the high efficacy of ECT.[31,32]

ECT is used worldwide, and despite its proven efficacy and safety is still associated with stigma.[33] However, studies exploring satisfaction rates have reported that more than 80% of patients are satisfied with the treatment.[34] Studies containing large samples have shown that self-ratings of quality of life significantly improve after a course of ECT in depressed individuals.[35]

Repetitive transcranial magnetic stimulation

Repetitive TMS uses an electromagnetic coil placed on the scalp to generate a strong magnetic field that crosses the skull and induces electrical currents in superficial cortical layers, depolarising neurons (Figure 1). It is a more focal brain stimulation method than ECT, as the magnetic field penetrates the skull without being dispersed. Repetitive TMS treatment is typically given every weekday over a period of four to six weeks. It is non-convulsive and does not require anaesthesia. For treatment of depression, rTMS has been targeted at the dorsolateral prefrontal cortex (DLPFC), activating subcortical and limbic areas implicated in depression pathophysiology.[36,37]

There is good evidence for the efficacy of rTMS in the treatment of unipolar depression in adult populations, with comparable effect sizes to antidepressant medications.[38,39] Repetitive TMS is generally recommended as a second-line treatment, when there is moderate resistance or intolerance to antidepressants.[40]

Greater antidepressant response has been described in relatively young individuals (e.g. less than 65 years), patients with shorter depressive episode duration (less than a year) and patients with less treatment resistance (one or two antidepressant medications failed).[41,42] Comparative trials of ECT and rTMS showed that rTMS is less efficacious than ECT in the treatment of depression, especially in the case of depression with psychotic features.[9,10,43,44] More research is needed regarding the efficacy of rTMS in patients with bipolar depression, as current evidence is not conclusive and studies targeting exclusively bipolar depression are scarce.[45]

Repetitive TMS has consistently been shown to be a safe procedure that is well tolerated. The most common side effects are local (e.g. discomfort at the area of stimulation, headaches).[46,47] In contrast to ECT, rTMS has shown no detrimental effects on cognition.[46] Seizures have been reported with rTMS, although the risk is low if safety recommendations are followed.[47] Induction of mania has been associated with the use of rTMS, especially in patients with bipolar disorder, although the risk is low.[47]

Figure 1. Transcranial magnetic stimulation. (Demonstrated by members of the Sydney Neurostimulation Centre at the Black Dog Institute, Sydney.)

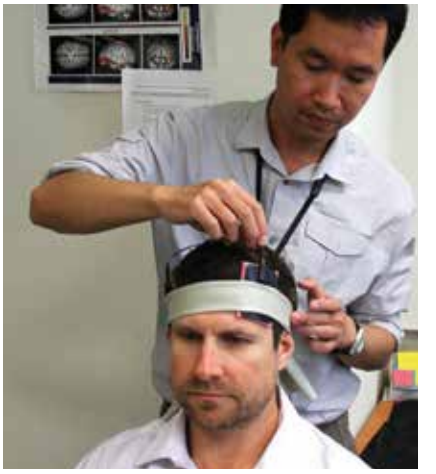

Figure 2. Transcranial direct current stimulation. (Demonstrated by members of the Sydney Neurostimulation Centre at the Black Dog Institute, Sydney.)

Experimental treatments

Transcranial direct current stimulation

Transcranial DCS is a relatively diffuse, noninvasive, neuromodulatory technique that uses a mild current applied through two electrodes to modify brain excitability.[48] The current is 'direct' in that it flows in one direction from the excitatory electrode (anode) to the inhibitory electrode (cathode). The treatment approach is similar to that for rTMS, with both stimulation electrodes applied to the DLPFC and a treatment course involving several weeks. Transcranial DCS has shown promising results in the treatment of patients with depression, with the most recent meta-analyses reporting active tDCS to be more effective than sham.[49,50] Effect sizes have been shown to be moderate and comparable to rTMS (0.37 *vs* 0.39, respectively).[49,51]

Transcranial DCS has an excellent safety profile, with no major side effects reported to date. Typical side effects are minor and localised to the site of stimulation (e.g. itching, burning sensation and redness).[52,53] Switches to mania are rare.[54-56] Transcranial DCS has several advantages over other brain stimulation techniques, such as anaesthesia is not required, there is no risk of seizure and it may exert positive effects on cognition.[57] Further, the equipment is relatively economical and the device is portable, which augurs well for widespread clinical translation and possibly home-based tDCS administration in the future.[58] However, given the limited number of patients treated in placebo-controlled trials in depression, more research is needed before tDCS is recommended in clinical practice.

Vagus nerve stimulation

In VNS, a surgically implanted lead with several electrodes is placed over the left vagus nerve in its trajectory through the neck. The lead and associated stimulator is connected to a battery implanted subcutaneously in the chest area. This generates electrical pulses that stimulate the vagus nerve, which has up-connections to the brainstem and other cortical areas involved in depression.[59]

VNS, a treatment for uncontrolled epilepsy, was controversially approved as an adjunctive treatment for patients with treatment resistant chronic or recurrent depression in the USA in 2005. However, the evidence-base for VNS antidepressant efficacy is unclear. Although initial open-label studies reported response rates of around 30% and patients continued to improve after the initial acute phase, a large multicentre study failed to demonstrate that active VNS was more efficacious than sham.[59-62]

Adverse effects from VNS include uncommon complications of the surgical procedure (e.g. infection of the wound, pain, temporary asystole) and side effects from stimulation, which are more frequent (10 to 60%; e.g. voice alteration, dyspnoea). Hypomania and mania have also been reported, mostly in patients with bipolar disorders, but they are considered infrequent (1 to 3%).[63] VNS does not seem to have a detrimental effect on cognition.[59] Although the literature suggests that VNS can have long-term benefits for patients who are highly treatment resistant, more randomised controlled trials are necessary to elucidate its efficacy.[64-66]

Magnetic seizure therapy

MST has evolved from TMS technology; in MST, a much stronger magnetic field is used to induce a seizure while the patient is under general anaesthesia. MST is, therefore, a convulsive therapy, but differs from ECT in that it uses magnetic fields to transfer energy into brain tissue rather than a direct electrical current.[67]

The limited randomised data available on MST suggest the efficacy may be close to that of unilateral forms of ECT, with response rates of 40 to 60% and relatively minimal cognitive side effects.[68,69] It is still considered an experimental treatment and research is needed to assess its effectiveness, tolerability and role relative to ECT.

Deep brain stimulation

In DBS, fine electrodes inserted in specific deep brain areas under stereotaxic guidance and connected to a stimulator unit and battery implanted under the skin deliver constant stimulation over a period of years.[70,71] DBS has been used successfully to treat patients with Parkinson's disease and is under research for the treatment of patients with refractory severe depression that has failed to respond to ECT, essentially as a replacement to psychosurgical ablative therapy.[71,72] Potential although infrequent serious cerebral side effects include bleeding (0.2 to 5%), infection and seizures. Side effects repeatedly reported in clinical trials are those related with stimulation (paraesthesias, mood changes, autonomic effects).[63]

Trials to date of DBS for patients with treatment-resistant unipolar and bipolar depression have shown encouraging results, although efficacy and safety need to be further tested.[73] DBS is currently only offered in research studies for the treatment of depression.

Conclusion

The science of brain stimulation treatments for depression is developing rapidly. In modern ECT, cognitive side effects are reduced and the therapy remains an important treatment for severe, refractory depression. Repetitive TMS can be used when there is moderate treatment resistance or intolerance to antidepressants. Experimental brain stimulation techniques (tDCS, VNS, MST and DBS) show promising results and may emerge as clinical treatment options for depression in the near future. MT

References

A list of references is included in the website version of this article (www.medicinetoday.com.au).

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References

1. Murray CJ, Vos T, Lozano R, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012; 380: 2197-2223.
2. Rush AJ. Star-D: lessons learned and future implications. Depress Anxiety 2011; 28: 521-524.
3. Warden D, Rush AJ, Trivedi MH, Fava M, Wisniewski SR. The STAR*D Project results: a comprehensive review of findings. Curr Psychiatry Rep 2007; 9: 449-459.
4. Sackeim HA, Dillingham EM, Prudic J, et al. Effect of concomitant pharmacotherapy on electroconvulsive therapy outcomes: short-term efficacy and adverse effects. Arch Gen Psychiatry 2009; 66: 729-737.
5. Berlim MT, Van den Eynde F, Tovar-Perdomo S, Chachamovich E, Zangen A, Turecki G. Augmenting antidepressants with deep transcranial magnetic stimulation (DTMS) in treatment-resistant major depression. World J Biol Psychiatry 2014; 15: 570-578.
6. Brunoni AR, Valiengo L, Baccaro A, et al. The sertraline vs. electrical current therapy for treating depression clinical study: results from a factorial, randomized, controlled trial. JAMA Psychiatry 2013; 70: 383-391.
7. Coffey CE, Fochtmann LJ, Greenberg RM, et al; American Psychiatric Association Committee on Electroconvulsive Therapy. The practice of electroconvulsive therapy: recommendations for treatment, training, and privileging: a task force report of the American Psychiatric Association. 2nd ed. Washington: American Psychiatric Association; 2001. pp. viii, 355.
8. UK ECT Review Group. Efficacy and safety of electroconvulsive therapy in depressive disorders: a systematic review and meta-analysis. Lancet 2003; 361: 799-808.
9. Slotema CW, Blom JD, Hoek HW, Sommer IE. Should we expand the toolbox of psychiatric treatment methods to include repetitive transcranial magnetic stimulation (rTMS)? A meta-analysis of the efficacy of rTMS in psychiatric disorders. J Clin Psychiatry 2010; 71: 873-884.
10. Berlim MT, Van den Eynde F, Daskalakis ZJ. Efficacy and acceptability of high frequency repetitive transcranial magnetic stimulation (rTMS) versus electroconvulsive therapy (ECT) for major depression: a systematic review and meta-analysis of randomized trials. Depress Anxiety 2013; 30: 614-623.
11. Fink M. What was learned: studies by the consortium for research in ECT (CORE) 1997-2011. Acta Psychiatr Scand 2014; 129: 417-426.
12. Daly JJ, Prudic J, Devanand DP, et al. ECT in bipolar and unipolar depression: differences in speed of response. Bipolar Disord 2001; 3: 95-104.
13. Sienaert P, Vansteelandt K, Demyttenaere K, Peuskens J. Ultra-brief pulse ECT in bipolar and unipolar depressive disorder: differences in speed of response. Bipolar Disord 2009; 11: 418-424.
14. Agarkar S, Hurt S, Lisanby S, Young RC. ECT use in unipolar and bipolar depression. J ECT 2012; 28: e39-40.
15. Rasmussen KG. Do patients with personality disorders respond differentially to electroconvulsive therapy? A review of the literature and consideration of conceptual issues. J ECT 2015; 31: 6-12.
16. Galvez V, Ho KA, Alonzo A, Martin D, George D, Loo CK. Neuromodulation therapies for geriatric depression. Curr Psychiatry Rep 2015; 17: 59.
17. Semkovska M, McLoughlin DM. Objective cognitive performance associated with electroconvulsive therapy for depression: a systematic review and meta-analysis. Biol Psychiatry 2010; 68: 568-577.
18. Martin DM, Gálvez V, Loo CK. Predicting retrograde autobiographical memory changes following electroconvulsive therapy: relationships between individual, treatment, and early clinical factors. Int J Neuropsychopharmacol 2015; 18(12). Available online at: http://dx.doi.org/10.1093/ijnp/pyv067 (accessed December 2015).
19. Sackeim HA, Prudic J, Fuller R, Keilp J, Lavori PW, Olfson M. The cognitive effects of electroconvulsive therapy in community settings. Neuropsychopharmacology 2007; 32: 244-254.
20. Dwork AJ, Arango V, Underwood M, et al. Absence of histological lesions in primate models of ECT and magnetic seizure therapy. Am J Psychiatry 2004; 161: 576-578.
21. Johanson A, Gustafson L, Risberg J, Rosen I, Sjobeck M, Silfverskiold P. Long-term follow-up in depressed patients treated with electroconvulsive therapy. J ECT 2005; 21: 214-220.
22. Sackeim HA, Prudic J, Devanand DP, et al. Effects of stimulus intensity and electrode placement on the efficacy and cognitive effects of electroconvulsive therapy. N Engl J Med 1993; 328: 839-846.
23. Sackeim HA, Decina P, Portnoy S, Neeley P, Malitz S. Studies of dosage, seizure threshold, and seizure duration in ECT. Biol Psychiatry 1987; 22: 249-268.
24. McCall WV, Reboussin DM, Weiner RD, Sackeim HA. Titrated moderately suprathreshold vs fixed high-dose right unilateral electroconvulsive therapy: acute antidepressant and cognitive effects. Arch Gen Psychiatry 2000; 57: 438-444.
25. Weiner RD, Krystal AD. EEG monitoring of ECT seizures. In: Coffey CE, ed. The clinical science of electroconvulsive therapy. Washington: American Psychiatric Press; 1993. pp. 93-109.
26. Kellner CH, Knapp R, Husain MM, et al. Bifrontal, bitemporal and right unilateral electrode placement in ECT: randomised trial. Br J Psychiatry 2010; 196: 226-234.
27. Dunne RA, McLoughlin DM. Systematic review and meta-analysis of bifrontal electroconvulsive therapy versus bilateral and unilateral electro-convulsive therapy in depression. World J Biol Psychiatry 2012; 13: 248-258.
28. Sackeim HA, Prudic J, Nobler MS, et al. Effects of pulse width and electrode placement on the efficacy and cognitive effects of electroconvulsive therapy. Brain Stimul 2008; 1: 71-83.
29. Loo CK, Katalinic N, Smith DJ, et al. A randomized controlled trial of brief and ultrabrief pulse right unilateral electroconvulsive therapy. Int J Neuropsychopharmacol 2014; 18(1). Available online at: http://dx.doi.org/10.1093/ijnp/pyu045 (accessed December 2015).
30. Tor PC, Bautovich A, Wang MJ, Martin D, Harvey SB, Loo C. A systematic review and meta-analysis of brief versus ultrabrief right unilateral electroconvulsive therapy for depression. J Clin Psychiatry 2015; 76: e1092-e1098.
31. Bai S, Loo C, Al Abed A, Dokos S. A computational model of direct brain excitation induced by electroconvulsive therapy: comparison among three conventional electrode placements. Brain Stimul 2012; 5: 408-421.
32. Bai S, Loo C, Dokos S. Effects of electroconvulsive therapy stimulus pulsewidth and amplitude computed with an anatomically-realistic head model. Conf Proc IEEE Eng Med Biol Soc 2012; 2012: 2559-2562.
33. Leiknes KA, Jarosh-von Schweder L, Hoie B. Contemporary use and practice

of electroconvulsive therapy worldwide. Brain Behav 2012; 2: 283-344.
34. Rose D, Fleischmann P, Wykes T, Leese M, Bindman J. Patients' perspectives on electroconvulsive therapy: systematic review. BMJ 2003; 326: 1363.
35. McCall WV, Prudic J, Olfson M, Sackeim H. Health-related quality of life following ECT in a large community sample. J Affect Disord 2006; 90: 269-274.
36. Loo CK, Sachdev PS, Haindl W, et al. High (15 Hz) and low (1 Hz) frequency transcranial magnetic stimulation have different acute effects on regional cerebral blood flow in depressed patients. Psychol Med 2003; 33: 997-1006.
37. Nobler MS, Teneback CC, Nahas Z, et al. Structural and functional neuroimaging of electroconvulsive therapy and transcranial magnetic stimulation. Depress Anxiety 2000; 12: 144-156.
38. Berlim MT, van den Eynde F, Tovar-Perdomo S, Daskalakis ZJ. Response, remission and drop-out rates following high-frequency repetitive transcranial magnetic stimulation (rTMS) for treating major depression: a systematic review and meta-analysis of randomized, double-blind and sham-controlled trials. Psychol Med 2014; 44: 225-239.
39. Brunelin J, Jalenques I, Trojak B, et al. The efficacy and safety of low frequency repetitive transcranial magnetic stimulation for treatment-resistant depression: the results from a large multicenter French RCT. Brain Stimul 2014; 7: 855-863.
40. RANZCP. Position Statement 79. Repetitive transcranial magnetic stimulation. Available online at: https://www.ranzcp.org/Files/Resources/College_Statements/Position_Statements/PS-79-PPC-Repetitive-Transcranial-Magnetic-Stimula.aspx (accessed December 2015).
41. Lisanby SH, Husain MM, Rosenquist PB, et al. Daily left prefrontal repetitive transcranial magnetic stimulation in the acute treatment of major depression: clinical predictors of outcome in a multisite, randomized controlled clinical trial. Neuropsychopharmacology 2009; 34: 522-534.
42. Kedzior KK, Azorina V, Reitz SK. More female patients and fewer stimuli per session are associated with the short-term antidepressant properties of repetitive transcranial magnetic stimulation (rTMS): a meta-analysis of 54 sham-controlled studies published between 1997-2013. Neuropsychiatr Dis Treat 2014; 10: 727-756.
43. Grunhaus L, Dannon PN, Schreiber S, et al. Repetitive transcranial magnetic stimulation is as effective as electroconvulsive therapy in the treatment of nondelusional major depressive disorder: an open study. Biol Psychiatry 2000; 47: 314-324.
44. Ren J, Li H, Palaniyappan L, et al. Repetitive transcranial magnetic stimulation versus electroconvulsive therapy for major depression: a systematic review and meta-analysis. Prog Neuropsychopharmacol Biol Psychiatry 2014; 51: 181-189.
45. Nahas Z, Kozel FA, Li X, Anderson B, George MS. Left prefrontal transcranial magnetic stimulation (TMS) treatment of depression in bipolar affective disorder: a pilot study of acute safety and efficacy. Bipolar Disord 2003; 5: 40-47.
46. Loo CK, McFarquhar TF, Mitchell PB. A review of the safety of repetitive transcranial magnetic stimulation as a clinical treatment for depression. Int J Neuropsychopharmacol 2008; 11: 131-147.
47. Rossi S, Hallett M, Rossini PM, Pascual-Leone A, Safety of TMS Consensus Group. Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. Clin Neurophysiol 2009; 120: 2008-2039.
48. Arul-Anandam AP, Loo C. Transcranial direct current stimulation: a new tool for the treatment of depression? J Affect Disord 2009; 117: 137-145.
49. Shiozawa P, Fregni F, Bensenor IM, et al. Transcranial direct current stimulation for major depression: an updated systematic review and meta-analysis. Int J Neuropsychopharmacol 2014; 17: 1443-1452.
50. Brunoni A, Moffa A, Fregni F, et al. Transcranial direct current stimulation for the acute major depressive episode: a meta-analysis of individual patient data. Br J Psychiatry In press.
51. Schutter DJ. Antidepressant efficacy of high-frequency transcranial magnetic stimulation over the left dorsolateral prefrontal cortex in double-blind sham-controlled designs: a meta-analysis. Psychol Med 2009; 39: 65-75.
52. Loo CK, Alonzo A, Martin D, Mitchell PB, Galvez V, Sachdev P. Transcranial direct current stimulation for depression: 3-week, randomised, sham-controlled trial. Br J Psychiatry 2012; 200: 52-59.
53. Brunoni AR, Amadera J, Berbel B, Volz MS, Rizzerio BG, Fregni F. A systematic review on reporting and assessment of adverse effects associated with transcranial direct current stimulation. Int J Neuropsychopharmacol 2011; 14: 1133-1145.
54. Galvez V, Alonzo A, Martin D, Mitchell PB, Sachdev P, Loo CK. Hypomania induction in a patient with bipolar II disorder by transcranial direct current stimulation (tDCS). J ECT 2011; 27: 256-258.
55. Brunoni AR, Valiengo L, Zanao T, de Oliveira JF, Bensenor IM, Fregni F. Manic psychosis after sertraline and transcranial direct-current stimulation. J Neuropsychiatry Clin Neurosci 2011; 23: E4-5.
56. Arul-Anandam AP, Loo C, Mitchell P. Induction of hypomanic episode with transcranial direct current stimulation. J ECT 2010; 26: 68-69.
57. Loo CK, Martin DM. Could transcranial direct current stimulation have unexpected additional benefits in the treatment of depressed patients? Expert Rev Neurother 2012; 12: 751-753.
58. Charvet LE, Kasschau M, Datta A, et al. Remotely-supervised transcranial direct current stimulation (tDCS) for clinical trials: guidelines for technology and protocols. Front Syst Neurosci 2015; 9: 26.
59. Sackeim HA, Rush AJ, George MS, et al. Vagus nerve stimulation (VNS) for treatment-resistant depression: efficacy, side effects, and predictors of outcome. Neuropsychopharmacology 2001; 25: 713-728.
60. Rush AJ, George MS, Sackeim HA, et al. Vagus nerve stimulation (VNS) for treatment-resistant depressions: a multicenter study. Biol Psychiatry 2000; 47: 276-286.
61. Schlaepfer TE, Frick C, Zobel A, et al. Vagus nerve stimulation for depression: efficacy and safety in a European study. Psychol Med 2008; 38: 651-661.
62. Rush AJ, Marangell LB, Sackeim HA, et al. Vagus nerve stimulation for treatment-resistant depression: a randomized, controlled acute phase trial. Biol Psychiatry 2005; 58: 347-354.
63. Schlaepfer TE, George MS, Mayberg H; WFSBP Task Force on Brain Stimulation. WFSBP guidelines on brain stimulation treatments in psychiatry. World J Biol Psychiatry 2010; 11: 2-18.
64. Marangell LB, Rush AJ, George MS, et al. Vagus nerve stimulation (VNS) for major depressive episodes: one year outcomes. Biol Psychiatry 2002; 51: 280-287.
65. George MS, Rush AJ, Marangell LB, et al. A one-year comparison of vagus nerve stimulation with treatment as usual for treatment-resistant depression. Biol Psychiatry 2005; 58: 364-373.
66. Nahas Z, Marangell LB, Husain MM, et al. Two-year outcome of vagus nerve stimulation (VNS) for treatment of major depressive episodes. J Clin Psychiatry 2005; 66: 1097-1104.
67. Lisanby SH, Schlaepfer TE, Fisch HU, Sackeim HA. Magnetic seizure therapy of major depression. Arch Gen Psychiatry 2001; 58: 303-305.
68. Cretaz E, Brunoni AR, Lafer B. Magnetic seizure therapy for unipolar and bipolar depression: a systematic review. Neural Plast 2015; 2015: 521398.
69. Kayser S, Bewernick BH, Grubert C, Hadrysiewicz BL, Axmacher N, Schlaepfer TE. Antidepressant effects, of magnetic seizure therapy and electroconvulsive therapy, in treatment-resistant depression. J Psychiatr Res 2011; 45: 569-576.
70. Morishita T, Fayad SM, Higuchi MA, Nestor KA, Foote KD. Deep brain stimulation for treatment-resistant depression: systematic review of clinical outcomes. Neurotherapeutics 2014; 11: 475-484.
71. Cleary DR, Ozpinar A, Raslan AM, Ko AL. Deep brain stimulation for psychiatric disorders: where we are now. Neurosurg Focus 2015; 38: E2.
72. Delaloye S, Holtzheimer PE. Deep brain stimulation in the treatment of depression. Dialogues Clin Neurosci 2014; 16: 83-91.
73. Holtzheimer PE, Kelley ME, Gross RE, et al. Subcallosal cingulate deep brain stimulation for treatment-resistant unipolar and bipolar depression. Arch Gen Psychiatry 2012; 69: 150-158.