Brain stimulation in psychiatry and its effects on cognition

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Abstract | From the advent of electroconvulsive therapy in the 1930s to the emergence of magnetic seizure therapy in the 2000s, the refinement of brain stimulation in psychiatry has been largely motivated by a desire to achieve clinical efficacy and eliminate cognitive adverse effects. As a result of these efforts, a clinically efficacious brain stimulation technique that does not negatively affect cognition could soon be available. In the course of developing a 'cognitively safe' brain stimulation technique, potential methods to enhance various aspects of cognition have also emerged. In this article, we discuss the past, present and future of brain stimulation in psychiatry, and its effects on cognition.

Hoy, K. E. & Fitzgerald, P. B. *Nat. Rev. Neurol.* **6**, 267–275 (2010); published online 6 April 2010; doi:10.1038/nrneurol.2010.30

Introduction

Brain stimulation in psychiatry has come a long way since the introduction of electroconvulsive therapy (ECT) in 1938.[1] Over the past 20 years, a variety of brain stimulation techniques have been developed with the aim of producing effective clinical tools with minimal cognitive adverse effects (Figure 1). As well as considerable improvements to ECT itself in an attempt to reduce such adverse effects, we have witnessed a resurgence of interest in transcranial direct current stimulation (tDCS), the development and refinement of transcranial magnetic stimulation (TMS), the introduction of invasive brain stimulation techniques such as deep brain stimulation (DBS) and epidural cortical stimulation (EpCS) into psychiatry, and the emergence of magnetic seizure therapy (MST).[2] As a result, the availability of efficacious brain stimulation techniques has increased considerably, and several are potentially free from cognitive adverse effects. In addition, some of these techniques could have potential for enhancing aspects of cognition.[3]

This Review will discuss the past, present and immediate future of brain stimulation in psychiatry. In view of the breadth of the literature, we selected the most inclusive reviews and meta-analyses, along with research articles considered to be seminal contributions to the field, to provide a balanced overview of this large body of research.

Electroconvulsive therapy

Historical background

Following observations of a seemingly dichotomous relationship between the diagnoses of dementia praecox (subsequently termed schizophrenia) and epilepsy, the first therapeutic seizure in psychiatry was induced, via an injection of camphor, in 1934.[4] Following some initial success in the treatment of schizophrenia, this new form of therapy spread rapidly throughout the world, although camphor was replaced with metrazol to limit the adverse effects of treatment.[1] However, persistent problems were experienced with metrazol-based seizure induction, including bouts of terror preceding loss of consciousness, which led to considerable reluctance among patients to undergo treatment. Electrical seizure induction in the form of ECT was introduced as an alternative in the late 1930s, and this form of treatment, with refinement, continues to be used in psychiatric practice today.[5] Currently, ECT is generally reserved for severe and treatment-resistant depression, and is less commonly used to treat schizophrenia and other disorders.

Cognitive adverse effects

Although ECT is effective, with reported response rates of 60–90%, major problems with this treatment persist.[6] Despite superior acute effectiveness, evidence exists of high relapse rates following discontinuation of ECT, with reported rates as high as 50% within 6 months.[7] From a longer-term perspective, a retrospective chart review reported an 82% relapse rate over 5 years following an acute course of ECT with antidepressant therapy alone.[8,9] In addition, the use of ECT, both acutely and as maintenance therapy, is complicated by the production of marked cognitive adverse effects, especially memory impairment. Estimates of the prevalence of cognitive impairment following ECT vary considerably, with a figure as high as 79% being quoted in some studies.[10] The cognitive impairments seen after ECT are possibly the result of widespread electric current distribution throughout the brain, including stimulation of medial temporal lobe structures such as the hippocampus.[11]

Competing interests
P. B. Fitzgerald declares associations with the following companies: Brainsway, MagVenture, Neurontics. See the article online for full details of the relationships. K. E. Hoy declares no competing interests.

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Key points

- Numerous advances have been made in the field of brain stimulation in psychiatry since the introduction of electroconvulsive therapy in 1938
- The motivation to maintain the superior efficacy of electroconvulsive therapy while avoiding its cognitive adverse effects has driven much of the research
- The past 10 years have seen rapid progress, and a number of brain stimulation techniques with varying efficacy and side-effect profiles are currently under investigation
- In light of recent developments in the field, the future role of brain stimulation in psychiatry, and its effects on cognition, must be considered

ECT has been shown to induce postictal disorientation, anterograde amnesia (inability to form new memories) and retrograde amnesia (loss of past memories).[12] Disorientation following ECT is not uncommon and can be prolonged, with reports of durations ranging from 11–40 min depending on stimulation parameters.[13] Longer durations of disorientation are associated with greater degrees of retrograde amnesia, as measured at 2 months post-ECT.[13] Disruption to memory was originally thought to be transient and to relate only to events occurring around the time of the ECT, but more-recent research suggests that some impairment can persist over time.[14] In the case of anterograde amnesia, acute impairment can last for up to 4 weeks, with reports of further improvements in this memory function occurring over a period of up to 6 months.[14] These findings are not universal, and studies comparing ECT patients with controls have reported no impairment in anterograde memory persisting for more than 4 weeks.[12,15] Recovery from retrograde amnesia has been reported to be considerably slower than recovery from anterograde amnesia, and may not always be absolute.[14] Such reports, however, contrast with the findings of the UK ECT Group study, which found no longitudinal evidence for persistent cognitive effects of ECT, although the authors acknowledged a considerable lack of randomized evidence on the potential longer-term cognitive adverse effects of ECT.[15] With respect to the qualities of retrograde amnesia, a suggestion has been made that impersonal memory (knowledge of public events) is more profoundly affected than autobiographical memory (knowledge about oneself).[16] Also, events closest in time to ECT administration and less-salient personal events are thought to be particularly vulnerable to disruption.[16] These amnestic effects of ECT are found to occur independently of response to treatment.[14–16]

While memory impairment is the most commonly reported cognitive adverse effect of ECT, one cannot safely assume that the treatment does not adversely affect other cognitive domains. As reviewed by Ingram *et al.*,[14] the research that has been conducted into non-memory cognitive impairment (including attention, information processing, visuospatial ability, executive functioning and language) has resulted in highly variable findings, mostly due to methodological limitations.

Research advances

The presence of memory deficits following ECT has motivated research into modified ECT treatment procedures that produce minimal memory-related adverse effects while maintaining efficacy. Both the positive and negative effects of ECT could be affected by a variety of treatment parameters, including electrode placement, electrical dose, pulse width, and the pattern of seizure initiation and spread.[11]

Studies of ECT modifications have been underway since the 1960s. A study by d'Elia and Raotma published in 1975 showed that nondominant temporal lobe unilateral ECT (RUL ECT) had the potential to be as effective as bilateral temporal lobe ECT (BL ECT), and produced less cognitive impairment.[17] More recently, Sackeim *et al.*[18,19] have found that if RUL ECT is delivered at a sufficiently high stimulus intensity (five times above seizure threshold), equivalent efficacy to standard temporal lobe-focused BL ECT can be obtained, with a concomitant reduction in the severity of cognitive adverse effects. Studies investigating the use of bifrontal ECT indicate that this technique could be as efficacious as temporal BL ECT while producing less-severe cognitive impairment.[20–23] Such findings suggest that ECT may exert its primary therapeutic effect in the frontal lobes; however, an insufficient number of high-quality studies have adequately addressed this question to date.[24]

The most recently investigated ECT modification involves shortening the width of the electrical pulse delivered. By reducing the overall charge required, this 'ultra-brief ECT' technique could stimulate neurons more efficiently than standard ECT, and could result in less spread of electrical current and, thus, a more focal seizure.[25] The research to date indicates that ultra-brief ECT reduces cognitive adverse effects, but a greater number of treatment sessions seem to be required to produce an equivalent therapeutic effect when compared with standard ECT.[25–28]

Research into ECT modification has yet to find a cognitively safe approach, but an important conclusion from this body of research is that the therapeutic efficacy of ECT can potentially be dissociated from its cognitive adverse effects, thereby providing motivation for the development of alternative brain stimulation treatments.

Alternative forms of stimulation

Currently, ECT is the only established therapy for patients with treatment-resistant mental illness, who represent a substantial population given that a large proportion of patients fail to respond to medication.[1] This fact holds particularly true for antidepressant medication, as highlighted by the findings of the recent STAR*D (Sequenced Treatment Alternatives to Relieve Depression) study, in which monotherapy (citalopram) remission rates were 28% and lessened with each subsequent intervention.[29] Consequently, a considerable research effort has been dedicated to the development of alternative therapies for people with treatment-resistant mental illness; in particular, the development of a cognitively safe and clinically effective form of brain stimulation. From the early applications of tDCS in the 1960s to the development of 100 Hz MST in the mid to late 2000s, considerable progress has been made towards this goal.

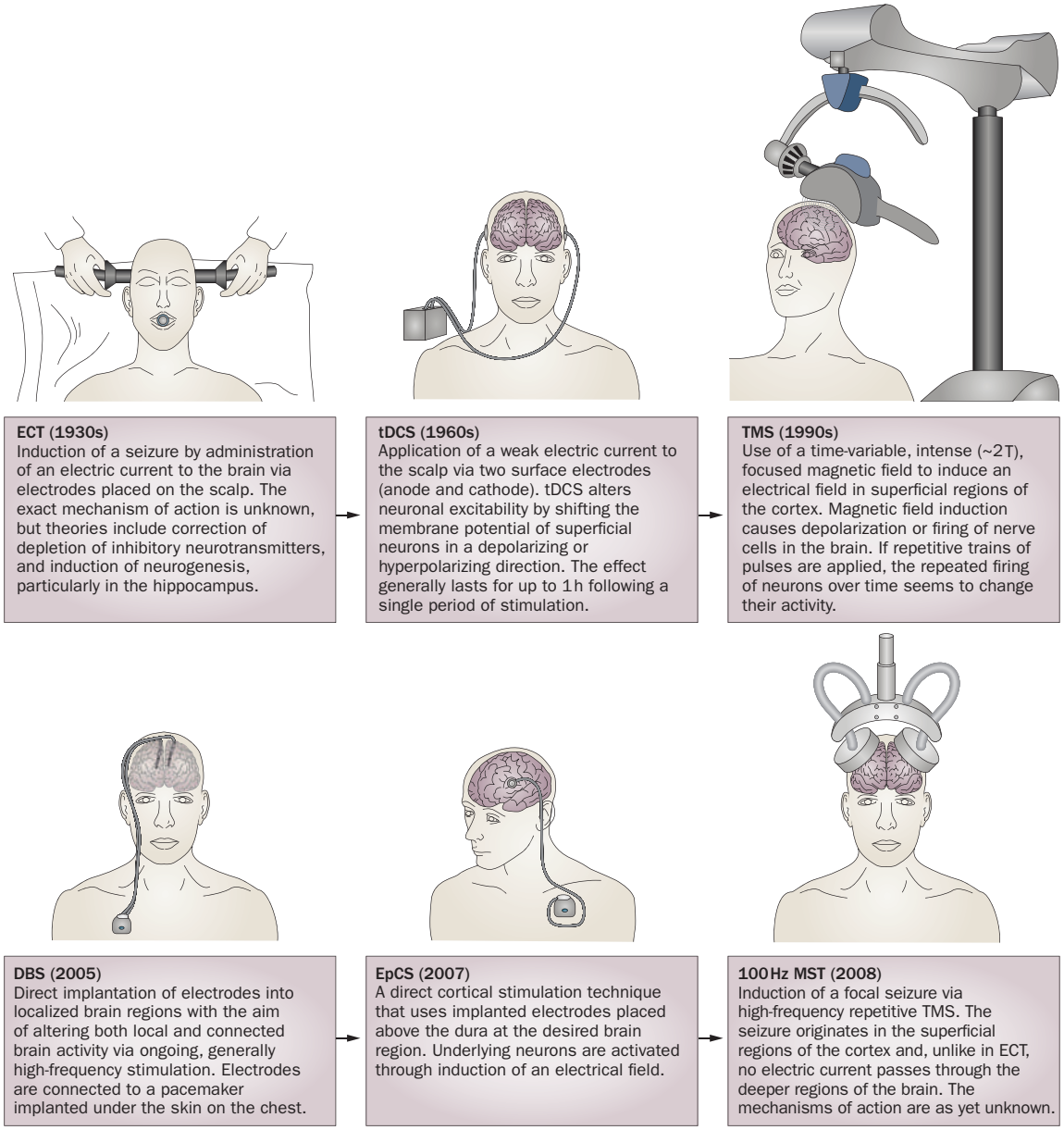

Figure 1 | Timeline of introduction of brain stimulation techniques. Abbreviations: DBS, deep brain stimulation; ECT, electroconvulsive therapy; EpCS, epidural cortical stimulation; MST, magnetic seizure therapy; tDCS, transcranial direct current stimulation; TMS, transcranial magnetic stimulation.

Transcranial direct current stimulation

tDCS was the first of a range of alternative forms of brain stimulation to be investigated for their application in neuropsychiatric disorders. This technique was initially investigated in the 1960s as a possible treatment for schizophrenia; however, researchers at this time had a relatively rudimentary understanding of its mechanism of action, and it was applied in a manner quite different from how it is utilized today. As a consequence, few conclusions can be drawn from these initial reports.[30] With the recent growth in brain stimulation research and techniques, interest in tDCS has undergone a substantial revival.

tDCS is a nonconvulsive process that involves the application of a small electric current (usually 1–2 mA) between anode and cathode electrodes that are placed on the scalp.[31] The technique seems to act by making nerve cells in the cortex more or less likely to fire (owing to hyperpolarization under the anode and depolarization under the cathode, respectively).[31–34] Over the past few years, tDCS has been investigated for its therapeutic potential in a number of neurological and neuropsychiatric disorders.[31,32] Of five sham-controlled studies of tDCS applied to the dorsolateral prefrontal cortex in patients with treatment-resistant depression, all but one demonstrated significant therapeutic effects of tDCS

over sham,[35–38] with Loo *et al.*[39] reporting equivalent improvements in mood in both the active and sham conditions. All the studies except for Loo *et al.*[39] included small patient samples. Rigonatti *et al.*[38] reported a persistence of antidepressant effects for 4 weeks, but the long-term efficacy of tDCS is largely unknown and requires further investigation. In summary, the data relating to efficacy of tDCS in depression should be considered to be preliminary, as a considerable amount of research remains to be conducted with respect to the optimal treatment durations, stimulation parameters, and degree and duration of effects.[40]

Initial studies investigating the effects of tDCS on cognition have yielded interesting results. Not only does tDCS seem to be cognitively safe, but evidence exists that it might enhance cognitive functioning independently of its effects on psychopathology.[31,41] A series of studies has shown that anodal tDCS applied to the left dorsolateral prefrontal cortex may enhance working memory performance in patients with depression[42] or Parkinson disease,[43] as well as in healthy individuals.[44,45] Cognitive symptoms of such disorders are not easily remedied with standard treatments, and tDCS could have valuable applications as an adjunct to existing cognitive remediation programs or medication therapies.

Repetitive transcranial magnetic stimulation

One of the more extensively researched brain stimulation therapies in psychiatry is repetitive transcranial magnetic stimulation (rTMS).[46] rTMS involves the production of a magnetic field via an alternating electric current. This magnetic field passes into the brain and stimulates electrical activity in neurons in a focused field of stimulation. High-frequency rTMS increases brain activity, whereas low-frequency stimulation decreases brain activity.[46]

Many rTMS trials have been conducted in patients with depression—mostly of a treatment-resistant type—over the past 15 years.[6,47–50] Most of these trials used high-frequency stimulation applied to the left dorsolateral prefrontal cortex (HFL-TMS). The results of this type of stimulation have been subjected to numerous meta-analyses, with most clearly showing greater antidepressant effects with a 2 week course of HFL-TMS than with sham treatment.[51–57] However, the average percentage improvements seen in scores on standard rating scales have been moderate.[53] Clinically modest results were also seen in the largest study conducted to date, a multisite trial of the efficacy and safety of left prefrontal rTMS undertaken by a private TMS manufacturer.[58]

To date, eight randomized trials have been conducted to compare HFL-TMS with ECT in patients with depression or bipolar disorder.[59–66] Three of these trials reported significantly higher response rates with ECT, with the remaining five reporting no significant difference in response. Interestingly, one study found ECT to be superior to rTMS for psychotic but not nonpsychotic patients.[59] These head-to-head studies have been somewhat biased towards finding a benefit of ECT, in that many compared an unrestricted number of either unilateral or bilateral ECT treatments with a fixed number of unilateral rTMS treatments. So far, research into relapse rates after rTMS has been limited, although the available data suggest that they are likely to be quite high.[67,68] In the most substantive study to date, only 22.6% of a large sample of 204 patients who achieved remission during rTMS treatment remained in remission at 6 months.[69]

Several attempts have been made to improve the efficacy of rTMS. For example, some studies have investigated the effects of low-frequency rTMS applied to the right dorsolateral prefrontal cortex (LFR-TMS),[70–73] with a review of LFR-TMS concluding that this technique might be as effective as HFL-TMS but with greater tolerability.[73] Studies have also been performed to investigate bilateral rTMS,[49,74,75] although most have not demonstrated greater response rates than those seen with HFL-TMS. However, one study that used sequentially administered bilateral rTMS with greater treatment duration (6 weeks) than in most previous studies found a >50% response rate at the end of the study.[49] Currently, a number of other methods are under active investigation that could potentially improve the response rate to TMS for depression, including the use of neuronavigational targeting (individualized localization of the dorsolateral prefrontal cortex treatment site using structural MRI and a neuronavigational system), priming (providing a priming stimulation of 6 Hz immediately before LFR-TMS), and theta burst stimulation (consisting of short bursts of high-dose rTMS; specifically, 50 Hz at 5 s intervals).[76–78] Approval for use of rTMS has been obtained in several countries including the US, but much work still needs to be done to optimize its efficacy.

rTMS has also been studied for the potential treatment of a number of other disorders. The most extensive of these research efforts has focused on schizophrenia; in particular, the treatment of two prominent symptom types—persistent auditory hallucinations and negative symptoms. Several studies have investigated the use of low-frequency rTMS administered to the left temporoparietal region for the treatment of auditory hallucinations, and a meta-analysis (10 studies, $n = 212$) found a positive effect of treatment over placebo.[79] However, the results of the studies included in this meta-analysis showed considerable heterogeneity, and further studies, preferably with much larger samples and more-unified methods, are required to confirm this effect. A smaller group of studies, with mixed and currently inconclusive results, used high-frequency frontal rTMS in an attempt to treat negative symptoms such as lack of motivation and interest in activities.[79–82] rTMS has also been investigated for the treatment of post-traumatic stress disorder,[83] generalized anxiety disorder,[84] and obsessive–compulsive disorder (OCD),[85] but a substantive body of research has not yet been collected for any of these indications.

Clinical trials of rTMS in psychiatric illness have frequently included cognitive assessments, which have demonstrated that rTMS does not adversely affect cognitive function.[6] In fact, a number of these clinical trials have shown improvements in cognition—most commonly in attention, concentration, working memory, and processing speed[64,86]—and probable flow-on effects

leading to improvements in learning, memory and aspects of executive functioning. These beneficial effects are seen primarily among patients who experience clinical improvement, so they are most likely to be related to the neuropsychological gains seen in patients with depression when their symptoms are relieved. Clear evidence exists that rTMS results in favorable cognitive outcomes relative to ECT, with a direct comparison study reporting no evidence of anterograde or retrograde amnesia following rTMS, in contrast to the acute negative cognitive outcomes following ECT.[64,86] Trials have also demonstrated improvement in certain cognitive functions in response to rTMS outside the treatment of psychiatric disorders,[87] but major trials of the effects of TMS on cognition are lacking.

Invasive stimulation methods

Deep brain stimulation

Invasive forms of brain stimulation that were initially developed for neurological applications have now been investigated in psychiatric illnesses. DBS involves the direct implantation of electrodes into localized brain regions, with the aim of altering both local and connected brain activity via ongoing, generally high-frequency stimulation.[88] The electrodes are connected to a pacemaker-like device, which is implanted under the skin on the chest. DBS has a number of established applications in neurology, including severe Parkinson disease.

OCD and treatment-refractory depression are the main psychiatric disorders in which DBS has been investigated to date.[89] In OCD, DBS has been targeted to either the anterior capsule or the subthalamic nucleus, with some reports of stimulation to the caudate nucleus and the inferior peduncle.[90] The most notable study to date reported on the outcomes of 10 patients in an open-label trial of DBS administered to the anterior limb of the internal capsule.[91] Four of eight patients who were followed up for 3 years achieved a >35% reduction in OCD symptoms, which translated into improved functioning and quality of life. Neuropsychological assessment after 10 months showed no significant changes from baseline at an individual level, and a significant improvement in verbal recall (as measured by prose passages) was observed when performances were analyzed at a group level.

DBS studies are increasingly focusing on treatment-resistant depression, with two main sites—the subgenual anterior cingulate cortex, and the ventral internal capsule and nucleus accumbens—currently being targeted.[89] Mayberg *et al.* reported on the outcomes of a group of 20 patients treated by means of DBS delivered to the white matter adjacent to the subgenual anterior cingulate cortex.[92,93] 60% of the patients met response criteria and 35% were in remission 6 months following the surgery. Neuropsychological outcomes were assessed at 3, 6 and 12 months on a subsample, and no evidence of impaired cognition was found.[94] Malone *et al.* recently reported findings from 15 patients who underwent DBS to the ventral capsule–ventral striatum region for treatment-resistant depression.[95] At their final follow-up (>12 months after surgery), 53.3% of the patients met response criteria and 40% met remission criteria. Comprehensive neuropsychological testing again revealed no negative effects of DBS on general intellectual ability, processing speed, learning and memory, language, or executive functioning.

Interest is emerging in the potential role of DBS in the enhancement of cognition; in particular, memory formation and recall.[96] A small body of research has reported vivid autobiographical memory recollections following both depth electrode recordings in the temporal lobe—especially following stimulation of the entorhinal cortex—and DBS of the hypothalamus.[96] In addition, stimulation of regions of the basal ganglia in rhesus monkeys, specifically the anterior caudate and putamen, were reported to result in enhanced memory formation; in particular, markedly improved associative learning.[96] Research in this area is complicated by considerable ethical implications, and the ultimate gains of using invasive stimulation methods will need to be balanced against the risks of the procedure. These issues are more acutely apparent when considering the potential of such a technique to enhance normal cognition, as opposed to improving cognition in a disorder such as dementia.

Epidural cortical stimulation

EpCS is a direct stimulation technique that uses implanted electrodes placed above the dura at the desired brain region, which thereby remain separated from the underlying cortex by the arachnoid space.[97] EpCS has been used to treat pain and the motor symptoms of Parkinson disease, and as an aid to stroke recovery,[98–100] and is now being investigated in the treatment of depression. In an initial study, which to date has only been reported in abstract form, results from 11 patients seemed to demonstrate an advantage of active stimulation over sham stimulation, with a relatively modest reduction in depression scores being observed beyond the blind phase (mean reduction of 26% on Hamilton Depression Rating Scale).[101] In a second pilot study of five patients, three achieved clinical remission at 7 months after stimulation onset, and no cognitive side effects were reported following a brief cognitive screen that looked primarily at attention, working memory and executive functioning.[97] At this stage, limited data are available on which to draw conclusions regarding the efficacy and/or duration of effect of EpCS.

Magnetic seizure therapy

Post-ECT research into brain stimulation techniques in psychiatry has seen the development of a number of promising cognitively safe or even cognition-enhancing treatments; however, the clinical efficacy of these techniques needs to be improved. Similarly, the substantial research into ECT modification has not resulted in a cognitively safe and efficacious treatment. A recently developed form of brain stimulation—MST—is one of the more promising techniques to date. MST is an alternative form of convulsive therapy to ECT, and it uses very high-frequency rTMS rather than an electric

Table 1 | Comparison of brain stimulation techniques used in psychiatry

Technique	Advantages	Disadvantages	Future challenges
Electroconvulsive therapy (ECT)	Superior efficacy Rapid rate of response	Cognitive adverse effects Requires anesthetic	Further establishing optimal stimulation methods to decrease cognitive adverse effects while maintaining superior efficacy
Transcranial direct current stimulation (tDCS)	Noninvasive and nonconvulsive High tolerability Low cost and potential applicability in developing countries No cognitive adverse effects; possibly enhances cognition	Lacks evidence for degree of efficacy compared with other techniques A considerable amount of further research required	Establishing the optimal stimulation protocols and parameters for delivery of the technique
Repetitive transcranial magnetic stimulation (rTMS)	Noninvasive and nonconvulsive Some evidence for efficacy in treatment-resistant depression No evidence of cognitive adverse effects	Produces only modest clinical results Lacks evidence of efficacy for other psychiatric indications Further research required to optimize response Definitive evidence required of efficacy in treatment-resistant depression	Developing ways to enhance response rates to rTMS
Deep brain stimulation (DBS)	Provides continual stimulation Provides direct and targeted stimulation of deep brain structures No evidence of cognitive adverse effects	Invasive surgical procedure Restricted to treatment-refractory patients	Establishing optimal site for electrode placement Establishing optimal stimulation parameters Studies with larger sample size to establish efficacy
Epidural cortical stimulation (EpCS)	Provides continual stimulation Provides direct and targeted stimulation of cortical brain regions Seems to be cognitively safe	Invasive surgical procedure A considerable amount of further research required to establish treatment efficacy	Establishing clinical efficacy in a large sample size Establishing optimal placement and stimulation parameters of paddle leads
Magnetic seizure therapy (MST)	Noninvasive Seems to lack cognitive adverse effects	Requires anesthetic Head-to-head trials with ECT required to establish efficacy	Establishing clinical efficacy of 100 Hz MST Development of the optimal stimulation parameters for seizure induction

current as the mechanism of seizure induction.[102] The seizure produced by MST originates in the superficial regions of the cortex, and is more focal than the seizure produced by ECT. Unlike in ECT, no electrical current passes through the deeper regions of the brain. Consequently, MST could, theoretically, produce similar therapeutic benefits to ECT without inducing memory-related adverse effects.

The first MST-induced seizure was produced in non-human primates in the late 1990s.[103] Initial studies showed that MST did not produce identifiable histological lesions in the brains of primates,[104] and MST seemed to produce fewer cognitive adverse effects than electroconvulsive shock (ECS, the animal equivalent of ECT) in this animal model.[105] Human studies of MST for the treatment of depression began in 2000. The first patient received MST stimulation over four sessions and a second successfully received a full treatment course.[106,107] The patients, both of whom were treated with stimulation at 40 Hz, tolerated the treatment well and responded clinically. In a subsequent study, 10 patients with treatment-resistant depression received two MST sessions within a course of ECT.[108] The MST sessions were better tolerated and resulted in fewer acute adverse effects than the ECT.

Following these safety and feasibility investigations of MST in humans, a controlled efficacy investigation was undertaken. In a two-site study, 20 patients with major depressive disorder were treated with a full course of MST using a 50 Hz device.[102,109] The MST treatment course produced mood improvement, and was associated with fewer adverse effects than were observed in an ECT comparison group, including a dramatically more rapid reorientation. The magnitude of improvement, however, seemed lower than is generally seen with ECT, with only 53% of patients achieving a ≥50% improvement following MST. The authors speculated that as the stimulation dose was only on average 1.3 times above magnetic seizure threshold, substantially greater responses could have been achieved with higher stimulation intensity, especially given that ECT response rates are highly sensitive to dose relative to seizure threshold.[19] The MST stimulators used at that time, however, could only produce short trains (8 s) of 50 Hz stimulation at high intensity. Alternatively, the lower antidepressant effect of 50 Hz MST may have been due to differences in the method of seizure induction and, consequently, the less widespread seizure activity, compared with ECT.

Since these initial studies, the technology used to produce MST has advanced considerably. Several devices have been developed that are capable of stimulating continuously at 100 Hz for up to 10 s at full machine power. This type of stimulation has been shown in primate experiments to induce seizures much more reliably while still producing fewer cognitive adverse effects than ECS.[104] The first patients reported to have treatment with 100 Hz MST ($n = 11$) received the intervention in a single session during a regular course of ECT for treatment-resistant depression.[111] Seizures were elicited in 10 of the 11 patients. All patients showed rapid recovery of orientation (on average 15 min shorter than the recovery time after ECT) and reported less confusion than they experienced following ECT. The initial clinical outcome data with this type of high-dose 100 Hz MST are also promising. Of 10 patients in Bonn, Germany who were treated twice a week with 100 Hz MST at 100% for 1–6 s, 7 (70%) met the criteria for a clinical response without any adverse effects such as headache, nausea, dizziness, or cognitive or memory impairment.[112] Despite these promising data, much research remains to be done on the efficacy of 100 Hz MST and on the duration of the effects, both of which are unknown at this stage. Should future studies show MST to have similar efficacy to ECT but with fewer adverse effects, this technique is uniquely placed to be rapidly introduced into clinical practice using the existing ECT infrastructure.

Future prospects

Treatment of psychiatric disorders has predominately involved the use of pharmacological agents and various forms of psychotherapy, with ECT having a relatively restricted role. The progressive development of a wide range of alternative brain stimulation technologies, such as those discussed here, indicates that the future psychiatric treatment armamentarium will be a much broader one. The extent to which these treatments will be adopted, however, is currently unclear. The provision of rTMS or tDCS requires the development of new therapeutic infrastructure or programs, although MST could be implemented relatively easily using established ECT facilities. Several barriers are likely to hinder the widespread uptake of the more-invasive treatments, especially those involving some form of surgical intervention. However, given the high relapse rates with current standard treatments, and the likelihood of fairly high relapse rates with treatments such as TMS, which are acutely applied to induce remission but are not provided as a maintenance therapy, more-permanently implanted treatment options could gather support. A comprehensive demonstration of the safety of these techniques, especially with regard to cognitive outcomes, will be important. Combinations of stimulation methods that target different aspects of brain circuits, or combinations of these techniques with more-traditional approaches, could also prove to be highly useful. For example, cognitive behavioral therapy has been suggested to reduce relapse rates after ECT,[113] and a similar approach could be taken after a course of rTMS or tDCS. Less clear is whether brain stimulation techniques could ultimately be used to augment cognitive function beyond the primary treatment of psychiatric symptoms such as depression. Some promising but preliminary data have been obtained in this regard.

Conclusions

A substantive body of research is now emerging on the development and refinement of a range of old and new brain stimulation techniques that can be applied in psychiatric disorders (Table 1). The precise roles of many of these techniques within the spectrum of treatments for mental illness are currently unknown, but research that aims to ultimately provide patients with evidence-based treatment choices is ongoing. This research needs to demonstrate both the therapeutic efficacy and the safety of these techniques, as well as the potential benefits with regard to cognition.

Review criteria

OVID and MEDLINE databases were used to search for the relevant literature. Search terms used alone and in combination were "electroconvulsive therapy", "transcranial direct current stimulation", "epidural cortical stimulation", "deep brain stimulation", "transcranial magnetic stimulation", "magnetic seizure therapy", "psychiatry", "depression", "schizophrenia", "anxiety disorders" and "cognition". A manual search of papers referenced in this literature was also undertaken. Owing to the breadth of the literature, reviews, meta-analyses and other articles considered to be seminal in the field were selected to provide an overview of this large body of research. The most inclusive reviews and meta-analyses were selected to avoid bias, and for the purposes of discussing areas of well-known controversy the authors selected and reviewed papers presenting opposing views.

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