IN REVIEW

Transcranial Magnetic Stimulation in the Treatment of Mood Disorder: A Review and Comparison With Electroconvulsive Therapy

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Objective: *To review repetitive transcranial magnetic stimulation (rTMS) as a mode of therapy for depression.*

Method: *The following aspects of rTMS were reviewed and compared with electroconvulsive therapy (ECT): history, basic principles, technical considerations, possible mode of action, safety, adverse effects, and effects on mood in both healthy individuals and those suffering from bipolar disorder (BD) or depression.*

Results: *rTMS may selectively increase or decrease neuronal activity over discrete brain regions. As a result of this focused intervention with TMS, the potential for unwanted side effects is substantially reduced, compared with ECT. In open trials, rTMS and ECT are reported to be equally efficacious for patients having depression without psychosis, but the therapeutic benefits reported in double-blind sham-rTMS controlled trials are more modest.*

Conclusion: *The antidepressant and antimanic effects of rTMS depend on technical considerations such as stimulus frequency, intensity, and magnetic coil placement, which may not yet be optimized. Biological heterogeneity among the patients treated with rTMS may also contribute to differing efficacy across clinical trials. rTMS may possess tremendous potential as a treatment for mood disorder, but this has not yet been realized. rTMS must still be regarded as an experimental intervention requiring further refinement.*

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Key Words: *transcranial magnetic stimulation, depression, electroconvulsive therapy*

Any discussion of electroconvulsive therapy (ECT) inevitably involves the use of superlatives. ECT is the oldest of all biological treatments for psychopathology, the most effective for severe depression, and the most controversial. Since ECT was introduced in 1938, major advances in our understanding of neurophysiology and psychopathology, together with some serendipity, have led to many new pharmacologic treatments for depression. Nevertheless, as many as 1 in 5 patients with depression fail to respond to antidepressant medication (1,2). While ECT may be effective for these patients, its cognitive side effects and invasive nature make ECT unacceptable to many. New approaches to treating severe medication-resistant depression are needed.

Apart from psychotherapy, which may not be appropriate for patients with the most severe depression, few nonpharmacologic alternatives to antidepressant medications exist. Vagus nerve stimulation (VNS), an experimental adjunctive treatment for epilepsy (3,4), has been reported to have antidepressant effects in an open trial (5). The device requires surgical implantation, however, and double-blind controlled clinical trials demonstrating antidepressant efficacy are still lacking. Another new technology that holds promise as a treatment for mood disorder, and is somewhat better-studied than VNS, is transcranial magnetic stimulation (TMS). TMS, which employs magnetic energy to alter cortical neuronal activity, has been shown to have significant antidepressant efficacy in several randomized, double-blind, sham-controlled TMS trials (6–8).

TMS Background

Brief History

Although attempts to create an electromagnetic brain stimulator date back to the 19th century, an effective TMS device was first built in 1985 by Anthony Barker at the University of Sheffield. Designed to function as a neurodiagnostic tool, the TMS prototype could produce an evoked potential in muscle tissue by activating neurons in the motor cortex. Newer coil

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designs created more focused magnetic fields that were then used to map regions of cortical involvement in functions such as memory (9), vision (10), and muscle control (11). In 1993, Hoflich and others were the first to use TMS as a therapeutic modality in an open trial of TMS for depression (12).

Basic Principles

The TMS device consists of a stimulation coil made up of wire loops encased in insulated plastic and connected through a cable to one or more powerful capacitors capable of passing a large electrical current through the coil over 100 to 200 microseconds. As the current flows through the coil, a very short-lived magnetic field of up to 1 or 2 tesla intensity is generated. The large electromagnetic field "flux" that is created alters the electrochemical functioning of nearby neurons through the process of Faraday induction. Faraday's principle, commonly employed in electricity generation, states that a time-varying magnetic field will induce a voltage in a nearby conductor (in this case, cortical neurons) such that the induced current is proportional to the rate of change of the magnetic field. If the voltage induced in cortical neurons is sufficient, and properly oriented with respect to the neuronal axon, an action potential will be induced in that neuron. This, in its essence, is little different from ECT. However, since the hair, skin, skull, and meninges are not good electrical conductors, to reach brain tissue very large currents must pass through skin surface electrodes during ECT. In addition, the path taken by this current can only be very roughly controlled through the choice of electrode placement. By contrast, the skull and other tissues are transparent to the magnetic field created by a TMS coil, and much lower energy is required to alter neuronal activity. Further, the magnetic field can be highly focused, thereby reducing the side effects caused by the large currents that probably flow diffusely through neuronal structures during ECT.

The voltage of the electrical current flowing through the coil and the geometry of the coil itself (13,14) determine the strength and shape of the magnetic field and therefore the induced current in the cortex. A round coil generates a relatively unfocused torus, or doughnut-shaped field. A figure-8 coil, essentially 2 round coils with a region of overlap, generates a more highly focused magnetic field.

Stimulus intensity is typically defined as a function of the motor threshold (MT), which is the stimulator output intensity required to induce a motor-evoked potential of a given size in a target muscle, usually the abductor pollicis brevis muscle (of the thumb), when the stimulator coil is situated at the optimal site overlying the motor cortex (M1). Stimulus intensity is expressed as a percentage of the MT.

The first TMS instruments were limited technically, and the maximum rate of stimulation was less than one pulse per second (1 Hz). With technological advances, modern repetitive TMS (rTMS) devices are capable of delivering a series or "train" of magnetic pulses at 50 Hz or more. The capacity to stimulate either at high or low frequency is of extreme importance, because high-frequency rTMS (for example, 20 Hz) may increase cerebral blood flow, and increase neuronal "excitability" in the region of the cortex underlying the rTMS coil (15,16), while low-frequency rTMS (≤ 1 Hz) may have the reverse effect (16,17).

TMS and Mood in Healthy Subjects

Pascual-Leone and others (18) and, independently, George and others (19) were the first to show that rTMS could alter subjective mood state in healthy subjects. They were also the first to demonstrate that the effect of rTMS upon mood depends on the side of the brain stimulated. Using similar rTMS settings in 10 healthy control subjects, Pascual-Leone (18) and George (19) found that high-frequency rTMS increased sadness scores, when administered to the left prefrontal cortex, but increased happiness scores if administered to the right prefrontal area. The duration of the mood effects was at least 5 hours. Treatment of other brain regions including the midfrontal cortex, the occipital cortex, or the cerebellum did not change mood.

TMS may also affect anxiety levels. Martin and others administered high-frequency rTMS or sham rTMS to the prefrontal cortex in 9 healthy control subjects (20). Like George (19) and Pascual-Leone (18), they noted decreased self-rated happiness scores with left prefrontal stimulation; however, they also observed elevated anxiety scores after right prefrontal rTMS. Mood and anxiety ratings were unchanged after sham stimulation.

TMS as a Treatment for Depression

Low-Frequency or Single-Stimulation TMS

Because the rapid rTMS stimulator had not yet been developed, the earliest studies of TMS as therapy for depression employed low frequency stimulation (0.25 to 1.0 Hz). These studies were further limited by lack of awareness of the prefrontal site's importance for coil placement. Hoflich and others treated 2 "drug-resistant major depressive psychotic patients" with a total of 250 TMS stimuli administered to the vertex over 10 days (12). They noted a 21% decrease in the Hamilton Depression Rating Scale (HDRS) score (21) in one patient but no change in the other. Using a larger number of pulses (1250) or sham rTMS in 15 patients with major depressive disorder (MDD), this same group (22) observed a 34% improvement in HDRS scores in a low-stimulus intensity (sub-MT) subgroup, a 15% improvement in a high-intensity (supra-MT) subgroup, but no change in a sham-rTMS group. Although clinically meaningful, these differences did not reach statistical significance.

The antidepressant effects of low-frequency rTMS may be considerably greater when the coil is held over the prefrontal region. Geller and others reported nearly immediate

antidepressant effects in 3 of 10 patients with depression after a single day of low-frequency rTMS delivered over the right and left prefrontal cortex (23). Conca and others randomly assigned 24 patients with MDD to receive either antidepressant medication alone or combined with rTMS (24). Conca observed significantly greater improvement in the rTMS-treated group by the third rTMS session. Neither Conca nor Geller, however, employed a sham condition to control for the potentially powerful "placebo" effect.

More recently, Klein and others compared low-frequency rTMS delivered over the right prefrontal cortex with sham rTMS in 70 patients with MDD, using a randomized, double-blind design (8). Of those receiving true low-frequency rTMS, 49% improved (50% reduction in HDRS score), compared with 25% of those receiving the sham condition. This effect was statistically significant.

High-Frequency rTMS

Technically, any stimulation at frequencies in excess of 1 Hz would be called "high frequency," but most published studies to date report using frequencies in the range of 5 to 20 Hz. George and others (25) published the first report describing the application of high-frequency rTMS in patients with depression. In this open trial in 6 medication-resistant patients, with depression, rTMS was administered to the left dorsolateral prefrontal cortex (DLPFC) at 20 Hz for at least 5 consecutive days. Two patients were unchanged, 2 improved slightly, and 2 showed major improvement, with 1 patient experiencing complete remission. In another open study, Figiel and others (26) found that 21 out of 50 treatment-refractory patients with depression showed at least a 60% reduction in their HDRS score after 10 Hz rTMS for 5 days, administered over the left prefrontal cortex.

The first sham-controlled blind study of high-frequency rTMS was conducted by Pascual-Leone and others (6). They treated 17 patients suffering from medication-resistant psychotic MDD with genuine 10 Hz rTMS and with sham stimulation over the left DLPFC, the right DLPFC, and the vertex. Eight of the 17 tolerated withdrawal of antidepressant medications. Each patient received 5 consecutive days of each treatment, with the order of conditions randomized and counterbalanced across patients. They observed significantly greater reduction in HDRS scores after left frontal true rTMS, compared with the other conditions. Although the beneficial effects lasted for only 2 weeks following the end of the rTMS course, a more recent study involving 45 patients with MDD (27) suggests that higher stimulus intensity (110% vs 90% MT) may lead to longer-lasting improvement.

Using a double-blind cross-over design, George and others compared 2 weeks of active 20 Hz rTMS with 2 weeks of sham rTMS in 12 subjects with depression (7). Nine of the 12 subjects had their antidepressant medications withdrawn. These patients showed a small but statistically significant decrease in HDRS scores after receiving active rTMS to the left DLPFC, compared with the sham-rTMS phase.

Not all controlled studies have fully supported the antidepressant efficacy of rTMS. Padberg and others compared the antidepressant effects of high- and low-frequency rTMS with sham rTMS in 18 patients with medication-refractory unipolar disorder (28). Although the difference between active and sham rTMS was significant for the HDRS, it was not for the Montgomery-Asberg Depression Rating Scale (MADRS) (29) or for subjects' depression self-rating scores.

It might be argued that this poor outcome was a function of the very low number of stimulations (1250) used by Padberg, compared with Pascual-Leone and others (10 000 stimulations) (6) and George and others (8000 stimulations) (7); however, Loo and others also failed to find a significant difference in treatment response to true or sham rTMS in 18 patients with depression, despite using a high total number of rTMS stimulations (15 000) (30). Depression scores improved by 35% to 39% in Loo's treatment-resistant patients, suggesting either efficacy of the concurrently administered antidepressant drugs, a powerful "placebo" effect, or significant biological activity for the sham-rTMS condition used. Studies in primates indicate that "sham" rTMS, with the coil angulated at 45 degrees away from the head (as used by Loo and others), may produce measurable changes in intracerebral voltage (31). It is also possible that the sample size in this and most other rTMS studies is too small to control adequately for unrecognized biological heterogeneity among the study subjects. It has, for example, been shown that patients who do not respond to high-frequency rTMS may improve after low-frequency rTMS (32). Our own (unpublished) data indicate that patients with a particular pretreatment quantitative electroencephalography (QEEG) pattern may respond to high-frequency rTMS, while those lacking this pattern may not.

In general it should be appreciated that the optimal rTMS stimulus parameters for treating depression, including frequency, number, intensity, and neuroanatomic treatment site are not known and that differences across clinical rTMS trials may contribute to the variance in outcome.

Frequency, Laterality, and the Antidepressant Effect

The earliest studies suggested that high-frequency rTMS may be more efficacious for depression than low-frequency treatment, but this may reflect the tendency for these pioneer low-frequency projects to employ coil placement over the vertex rather than over the more effective DLPFC site. More recently, however, Padberg found that low-frequency rTMS over the left DLPFC may be at least as effective as high-frequency rTMS in patients with depression, (28), and Klein and others reported a very robust and clinically significant antidepressant response to low-frequency rTMS when administered to the right DLPFC (8).

The hemisphere treated may also be highly relevant to the therapeutic effect achieved. In healthy volunteers, the reversed direction of the mood changes seen after high-frequency rTMS to the left and right DLPFC (18,19) suggests that both the left and right hemisphere are involved in mood regulation and that their influence may be opposite in "valence." This is supported by evidence that unilateral cortical lesions in the right hemisphere are associated with mania, while left-hemisphere lesions are associated with depression (33). Because high- and low-frequency rTMS may also exert neurophysiological effects that are opposite in direction (15–17), it may be possible to treat both mania and depression. It has been reported, for example, that depression may respond to either high-frequency rTMS to the left prefrontal cortex (6,7) or low-frequency rTMS to the right prefrontal cortex (8). Further, high-frequency right prefrontal rTMS lessens mania, while left prefrontal high-frequency treatment may make it worse (34).

Davidson and others (35) postulated that an imbalance of left-to-right prefrontal activity conveys heightened vulnerability to depression, a hypothesis supported by the reported correlation between left–right prefrontal alpha-EEG symmetry and depression severity (36) and by our own pilot data (unpublished) demonstrating that rTMS responders show a shift in the left-to-right ratio of alpha-EEG power with recovery. We might speculate that rTMS improves mood in patients with depression by restoring the left-to-right balance of cerebral activity. There may, however, be considerable biological heterogeneity among patients with depressive symptoms, and the response to rTMS may vary widely, depending upon the pathophysiology affecting the individual patient. For example, Kimbrell and others showed that patients with depression and baseline cerebral hypometabolism tended to improve with high-frequency prefrontal rTMS, while those with baseline cerebral hypermetabolism responded to low-frequency rTMS (32).

rTMS and Bipolar Disorder

So far, the largest study of rTMS in patients with bipolar disorder (BD) is an open trial of rTMS as an adjunct to medications in the treatment of mania. Grisaru treated 16 patients suffering from mania with high-frequency rTMS to either the right or the left DLPFC in addition to stable doses of mood stabilizers and neuroleptics (37). Consistent with the proposed interhemispheric valence effect, high-frequency stimulation of the left DLPFC (which is antidepressant in patients with unipolar depression), produced worsening of mania, while rTMS to the right prefrontal region was antimanic. Others have also reported the emergence of hypomania in some patients with depression after treatment of the left DLPFC with high-frequency rTMS (25,38).

Although many studies of rTMS for depression may include a very small number of patients with BD, none address the possibility of a differential response in bipolar and unipolar depression. George and others (39) and Kimbrell and others (32) noted an antidepressant response to low-frequency, but not high-frequency, left DLPFC rTMS in 3 patients in the depressed phase of BD. This is the reverse of the usual experience with patients having unipolar depression.

rTMS and Mood Stabilizers

Michelucci and others demonstrated that anticonvulsant drugs reversibly raise the rTMS threshold intensity required to elicit a motor-evoked potential (40). This suggests that rTMS may work less well, or that higher-intensity rTMS may be necessary, in patients on anticonvulsants. Patients with BD and depression who are on stable doses of anticonvulsant mood stabilizers are, however, reported to respond to low-frequency rTMS (32,39), and there is some evidence that the anticonvulsant gabapentin may even prolong the duration of the antidepressant effect of rTMS (27).

rTMS and ECT

ECT and rTMS both use electrical energy to induce neuropsychiatric change, and this naturally invites their comparison. Studies in animals have indicated that rTMS can produce qualitatively similar behavioural and biological effects, although they are less robust than those seen after electroconvulsive shock (ECS). For example, both ECS and rTMS significantly enhanced apomorphine-induced stereotypy, reduced immobility in the Porsolt swim test and increased seizure threshold (41,42).

Fujiki and Steward reported that rTMS increased expression of the gene for glial fibrillary acidic protein in the amygdala in animals, an effect similar to that seen after a seizure. Elevated mRNA levels for this marker of increased neuronal activity persisted for at least 8 days after rTMS, indicating that rTMS may cause lasting changes in brain activity (43).

To date, there are few trials comparing ECT with rTMS. Grunhaus and others randomly assigned 40 subjects with severe MDD to groups receiving open treatment with either left prefrontal rTMS or right unilateral ECT (44). Patients who had not responded by the 7th unilateral treatment were switched to bilateral electrode placement for the remainder of the course. They observed marked improvement in patients without psychosis in both the ECT- and rTMS-treated groups, with no significant differences in response. ECT, however, was significantly more effective than rTMS for patients with psychotic depression. Pridmore treated 22 patients suffering from depression with either 2 weeks of standard nondominant right unilateral ECT (3 ECT per week) or 2 weeks of combined ECT and rTMS. The combined group received a single unilateral ECT followed by daily left prefrontal rTMS treatments (4 per week). He observed a similar robust antidepressant effect in both groups, but fewer side effects in the combined ECT–rTMS group (45).

If these results can be confirmed through further investigation, this will represent a tremendous therapeutic advance, because rTMS is dramatically less intimidating to patients and has few, if any, obvious cognitive side effects.

Mechanism of Action

The mechanism by which rTMS may alter neuropsychiatric functioning is unknown. Some studies, however, suggest that rTMS may downregulate beta adrenoreceptors (42) and increase dopamine and serotonin levels in the striatum, frontal cortex, and hippocampus (46).

In human volunteers, high- and low-frequency rTMS may respectively induce increases (15) and decreases (17) in neuronal electrochemical activity in a manner analogous to the phenomena of long-term potentiation or kindling and long-term depression or quenching reported after high- and low-frequency electrical stimulation of the cortex in rats (47–49). In accordance with these findings, Speer and others observed increased cerebral blood flow in the left DLPFC after high-frequency rTMS (20 Hz), and reduced flow after low-frequency (1 Hz) treatment, in subjects with depression (16). However, the cortical response to rTMS is also affected by stimulus intensity (47), coil orientation (50), and the brain region being treated (10), and others describe results that differ from Speer's (51,52).

rTMS and Brain activity in Mood Disorder

The literature describing changes in brain activity in patients with mood disorders is immense and beyond the scope of this review. Several general observations regarding frontal lobe functioning, however, appear very relevant to the use of rTMS as a treatment for depression. Several, if not most, imaging studies have found "hypofrontality"—reduced prefrontal cortical metabolism and blood flow—in patients with depression (53,54) (see also the comprehensive review of Soares and Mann [55]). This is important because most TMS studies demonstrating antidepressant efficacy used coil placement over the frontal lobes, and increased prefrontal metabolism has been documented in individual patients with depression who have responded to high-frequency rTMS (25,36). The literature, however, also points toward considerable biological heterogeneity among patients with depression (56–62).

The key to antidepressant effectiveness across large numbers of patients with depression may therefore be recognition of a specific subtype of cerebral dysfunction, followed by an appropriate corrective intervention. To date, rTMS is the only treatment capable of producing a highly focused and directional change in cerebral functioning.

Safety

Seizures

Comparisons with the kindling phenomenon reported in animals raise issues of possible epileptogenesis with rTMS. Kindled seizures, however, have never been conclusively observed in humans, even in those who have received long-term electrical cortical stimulation (63) or frequent ECT over many years. Because low-frequency rTMS may actually decrease cortical excitability and increase the seizure threshold (64), only high-frequency rTMS may be capable of inducing a seizure. High-frequency rTMS has caused intratreatment seizures in 5 normal volunteers and 1 subject with depression (65). For the most part, these seizures occurred during early studies using stimulation parameters outside current safety guidelines; however, an interaction between rTMS and some psychotropic medications may also be possible. In one instance, a seizure occurred in a patient with depression who, unknown to the investigator, started taking amitriptyline and haloperidol during the course of high-frequency rTMS (65).

Prior personal and family medical history is also relevant. At least 1 control subject who experienced a seizure during rTMS had a family history of seizure disorder (personal communication, Pascual-Leone 1998), and an individual who developed paroxysmal epileptiform discharges on EEG, recorded during rTMS, had demonstrated EEG slowing in the same region prior to his first rTMS (66). Given the small number of seizures reported in the literature, and the large numbers of subjects receiving rTMS internationally, it is likely that the risk of seizures in properly screened patients is not appreciably different from that of antidepressant medication.

Recently, high-frequency rTMS has been used as an alternative to ECT to repeatedly induce seizures in patients with depression. To do this reliably, a specially designed high-power rTMS device is required (personal communication, SH Lisanby). The extreme difficulty encountered in intentional seizure induction using standard rTMS devices further supports the safety of rTMS when used in properly screened patients at usual stimulus intensities.

Cognitive Effects

In terms of potential cognitive impairment, rTMS seems to be a dramatically more favourable treatment than does ECT. No deficits in short-term spatial memory were detectable in monkeys given up to 7000 high-intensity magnetic pulses (67). In healthy human control subjects, transient, very subtle inhibition of implicit procedural learning has been reported (9), but in general no clinically apparent ill effects have been noted (68).

Other studies suggest that rTMS may actually enhance some aspects of cognitive functioning. Padberg and others demonstrated an increase in verbal memory performance in patients

receiving high- but not low-frequency rTMS (28). Avery and others (69) and Little and others (70) reported improved brief auditory attention span, complex psychomotor speed, rote verbal learning, and list recall in patients with depression after rTMS).

Adverse Effects

Studies have demonstrated permanent elevation in the auditory thresholds of animals (71) and transient increases in humans (72) following TMS. Using foam earplugs during rTMS, however, prevents changes in hearing threshold (72). In susceptible individuals (about one-third of the subjects in our laboratory), rTMS can cause muscle-tension–type headaches that persist after the end of the stimulation session. In our experience, these have responded well to mild analgesics. Although rTMS does not require anesthesia, some patients find the stimulations uncomfortable or even painful, especially when a round coil is used.

In our laboratory, we have seen transient dysphasia in 2 right-handed women during high-frequency (10 Hz) rTMS. Both were petite individuals with small head size. In these women, standard coil placement 5 cm anterior to M1 resulted in one wing of the figure-8 coil being held over what may be Broca's area in the inferior frontal lobe. The dysphasia disappeared entirely at the end of the stimulus train, without sequelae. When the coil was moved slightly higher for subsequent stimulations, there was no recurrence.

The issue of long-term adverse effects has not been resolved. rTMS has been used since 1983, and there are no reports of long-term adverse effects; however, rTMS has only recently been widely used, and the number of patients who received treatment years ago is still small. Some studies in populations exposed to extremely low-intensity electromagnetic fields, such as those surrounding electrical power transmission lines or electrical appliances, suggest some potential for carcinogenesis, but this is controversial (73). The high-energy, but extremely short-lived, magnetic field created during rTMS is very different from low-energy continuous environmental exposure, and one cannot confidently extrapolate between these areas. Further, exposure to magnetic resonance imaging (MRI) scanners, which create intense magnetic fields that approximate those of rTMS, is not associated with cancer (74).

Conclusions

TMS is, without question, an extremely useful and versatile tool for studying neurophysiology. rTMS may also prove to be an extremely valuable treatment for mood disorder and other psychopathology, but this is not yet definitively established. Many of the very favourable studies have been uncontrolled open trials, and the powerful antidepressant effects seen in some of the earlier sham-controlled studies have not been widely replicated. This could be due to differences in rTMS methodology or to underlying biological heterogeneity in the patients with depression studied.

In addition, the optimal treatment parameters for rTMS have not yet been clearly identified, and much current rTMS practice is arbitrarily defined. For example, the anatomic stimulation site for rTMS in most studies is determined by measuring out a fixed distance from the motor cortex. This does not allow for differences in skull size or brain shape, and strict adherence to this method could result in coil placement over widely different brain regions in different subjects.

One of the major advantages of rTMS over ECT is that magnetic energy can be delivered to discrete brain regions in a relatively controlled manner. This dramatically reduces unwanted side effects, compared with ECT. This specificity, however, also places rTMS at a potential disadvantage with respect to efficacy, in that coil placement even a few centimetres off the ideal site might be associated with loss of therapeutic benefit.

A great deal of work must be done before we can confidently identify the optimal site, stimulation frequency, and stimulation intensity for therapeutic applications of rTMS. Until this is done, we will likely continue to see negative studies or studies showing modest therapeutic efficacy. Neuroimaging, electroencephalography, or other techniques measuring brain function and structure may in future help to identify patients who could respond to rTMS and guide our choice of the appropriate rTMS stimulation site and frequency.

The unique capacity to selectively increase or decrease neuronal excitability in discrete brain regions endows rTMS with tremendous therapeutic potential; however, this potential is still to be realized, and rTMS should be seen as an experimental intervention at an early stage of development.

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Clinical Implications

- Repetitive transcranial magnetic stimulation (rTMS) may in the future prove to be an effective treatment for mood disorders.
- rTMS has fewer cognitive side effects and is medically safer than electroconvulsive therapy (ECT).
- ECT is currently more effective for treating depression than is rTMS.

Limitations

- Optimal treatment parameters such as pulse frequency and site of stimulation have not yet been determined for rTMS.
- Biological heterogeneity among patients with depression may reduce rTMS response rate.
- rTMS could precipitate seizures in some circumstances.

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Résumé : Stimulation magnétique transcrânienne : étude et comparaison avec les électrochocs dans le traitement des troubles de l'humeur

Objectif : *Examiner la stimulation magnétique transcrânienne répétitive (rTMS) comme mode de traitement de la dépression.*

Méthode : *Les aspects suivants de la rTMS ont été étudiés et comparés avec les électrochocs : historique, principes de base, considérations techniques, mode d'action possible, innocuité, effets nuisibles et effets sur l'humeur tant chez les personnes en santé que chez celles qui souffrent de trouble bipolaire (TB) ou de dépression.*

Résultats : *La rTMS peut sélectivement accroître ou diminuer l'activité neuronale sur des régions distinctes du cerveau. Par suite de cette intervention ciblée avec la TMS, le potentiel d'effets secondaires indésirables est considérablement réduit, comparativement aux électrochocs. Dans les essais ouverts, on constate que la rTMS et les électrochocs sont également efficaces pour les patients souffrant de dépression mais pas de psychose, mais les avantages thérapeutiques décrits dans les essais contrôlés à l'insu de rTMS fictive sont plus modestes.*

Conclusion : *Les effets antidépresseurs et antimaniaques de la rTMS reposent sur des considérations techniques qu'on ne peut encore optimiser comme la fréquence du stimulus, l'intensité et l'endroit où s'opère le blindage magnétique. L'hétérogénéité biologique des patients traités à la rTMS peut contribuer aux différences d'efficacité entre les essais cliniques. La rTMS peut détenir un potentiel énorme comme traitement des troubles de l'humeur, mais ce potentiel ne s'est pas encore réalisé. Elle doit être encore vue comme une intervention expérimentale qu'il faut raffiner davantage.*