A practical guide to the use of repetitive transcranial magnetic stimulation in the treatment of depression

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Background
Repetitive transcranial magnetic stimulation (rTMS) is currently emerging as a new treatment for patients with mood disorders. Research into the use of rTMS for the treatment of patients with depression has been conducted now for a period of greater than 15 years and a considerable body of knowledge has accumulated informing its use.

Objective
The aim of this paper was to review the use of various rTMS techniques for the treatment of depression and to provide practical suggestions to address the common issues encountered in the prescribing and administration of rTMS treatment.

Methods
These suggestions have been informed both by a review of the relevant literature and the experience of the authors in the treatment of many patients with depression with rTMS over a period of 10 years.

Results and Conclusions
High-frequency rTMS applied to the left dorsolateral prefrontal cortex, using a set of parameters very similar to those originally described in the mid-1990s, is an effective treatment for patients with major depressive disorder. Other forms of stimulation, such as low-frequency stimulation applied to the right prefrontal cortex and bilateral approaches, may prove valuable but require evaluation in larger trials. Significant benefit appears likely to accumulate through the use of methods that involve a more reliable targeting of prefrontal brain regions. Suggestions are also made around the use of rTMS treatment as a maintenance therapy and in specific illness subgroups.

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Repetitive transcranial magnetic stimulation (rTMS) has been developed in the last 15 years as a potential treatment for patients with depressive disorders. In recent years it has been approved for clinical use in a number of countries, including the United States in 2008. The aim of this paper is to review a number of practical issues concerning the provision of rTMS treatment to patients with depression in clinical settings, and to provide guidance to clinicians in the choice of a range of clinical TMS parameters. The paper addresses these issues from the viewpoint of the authors; it is not a consensus statement and it has not been commissioned by a specific medical body. In regard to a number of issues such as the credentialing of staff, emergency and consent procedures, local laws and regulations will override the recommendations contained within these guidelines.

General overview

rTMS involves the repeated application of a rapidly time variable magnetic field to a local restricted area of the cortex to try and modulate local and distal brain activity.\(^1\) When an electrical current passes through a TMS coil, it generates a magnetic field that passes into the brain without resistance. This magnetic field acts via induction to produce electrical activity in the underlying cortical neurones.\(^1\) If the stimulation is provided above a certain threshold, these neurones will be induced to fire. The repeated firing of local cortical neurones will progressively change their activity over time. High-frequency stimulation is known to produce an increase in local cortical excitability, and low-frequency stimulation the opposite effect.\(^2\) The effects of rTMS are likely to extend further than local areas, as the coordinated firing of a group of cortical neurones is likely to change activity in connected brain regions and possibly the strength of connections between brain regions. This has been confirmed in a series of integrated TMS-functional magnetic resonance imaging (fMRI) experiments.\(^3\)

rTMS treatment for depression has generally followed protocols set in the early treatment studies. It is mostly provided at high frequency to the left dorsolateral prefrontal cortex (DLPFC) at between 5 and 20 Hz. Treatment sessions are provided on a daily basis 5 days per week for between 2 and 9 weeks. However, a number of other stimulation methods have been used, including low-frequency stimulation provided to the right prefrontal cortex and bilateral approaches. There are also several more experimental approaches, such as theta burst stimulation, that are undergoing ongoing evaluation.

Treatment intensity/dosing and motor threshold

The intensity of rTMS treatment provided is usually relative to the measurement of an individual patient’s resting motor threshold (RMT). This is established by the application of single TMS pulses to the motor cortex and determining the lowest stimulation intensity required to consistently induce a motor response in a peripheral muscle, usually the abductor pollicis brevis (APB) in the contralateral hand. Typically, the RMT is defined as the minimum intensity required to produce a prespecified motor response on a certain number of occasions (e.g., on 3 of 5 or 5 of 10 stimulations). The type of motor response is usually assessed either visually (by seeing a muscle twitch) or via the measurement of a motor evoked response of a specific size (often greater than 50 μV) using electromyographic equipment (EMG). The former method is simpler and does not require the knowledge needed to set up EMG monitoring. However, the measurement of EMG allows the operator to be sure the patient has maintained a state of muscle relaxation that may not otherwise be known. This is important, as a relatively low level of muscle contraction, which might be expected in some anxious patients undertaking rTMS for the first time, will reduce the measured threshold, potentially leading to an “underdosing” of treatment. Several studies have investigated the relationship between RMT values produced by these differing methods. Although the results of these studies are not completely consistent,\(^4,5\) the RMT values are likely to be similar when measured with EMG or when assessed with a visualisation of motor response in any hand muscle but higher if assessed as the visualised motor response in a single muscle. Other methods for the measurement of the RMT have been developed, including the use of software algorithms to estimate the RMT from the size and presence of motor responses at varied stimulation intensities,\(^6,7\) although there remains some dispute about the accuracy of some of these.\(^8\) Future developments may modify the dosing based on RMT assessments to take into account individual differences in scalp-cortex distance comparing motor and prefrontal regions.

Conclusion and suggestion

rTMS dosing should be based on individual measurement of the RMT. Although there is no clear consensus on the optimal method for measurement of the RMT, assessment of the minimum intensity required to produce a EMG measured motor response in 5 of 10 trials or the visualization of a motor response in any hand muscle would

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produce values most equivalent to those used in most rTMS trials and the safety studies. Algorithms to simplify the procedure would seem sensible but should be compared with one or both of these approaches.

Patient selection and treatment indications

Depression and treatment resistance

Depression is clearly a highly prevalent disorder with substantial impact on patients, their health carers, and on society in general. Although recent times have seen a significant increase in the number of evidence based treatments for depression, it is clear that a substantial proportion of patients does not respond to, or have trouble tolerating, standard treatment that conventionally includes antidepressant medications and psychotherapy. For example, approximately 30% of patients with depression will not respond to several antidepressant trials. A sizable percentage of these patients will remain depressed for prolonged periods despite multiple courses of treatment. These patients, who are conventionally regarded as having treatment resistant depression (TRD), have few other treatment options. The main treatment option for TRD is electroconvulsive therapy (ECT), although a significant percentage of patients will choose not to have ECT because of concerns about potential side effects, fear, or associated stigma. Also, in mild-to-moderate TRD, ECT may not be regarded as offering an appropriate risk-benefit. It is in a number of these patient groups that rTMS has been most extensively assessed. However, device registration for rTMS in the United States was based on data from a comparison of antidepressant response between TMS and sham stimulation in patients who had only failed to respond to one antidepressant medication. The current US Food and Drug Administration (FDA) approval in the United States is therefore for adults with depression who have only failed a single antidepressant trial in the current depressive episode (http://dev.neuronetics.com/pdf/Prescribing%20Information.pdf). In contrast, the majority of studies have focused on patients with more treatment resistant illness; many of the published metaanalyses confirming the antidepressant efficacy of rTMS are comprised of such studies. A relationship has been seen in a number of studies between the degree of treatment resistance and antidepressant efficacy, but this has not been confirmed in all large TMS trials.

Conclusion and suggestion

It seems likely that response to rTMS treatment in depression may be greater in patients with fewer failed medication trials. However, there is evidence of response in patients with a greater degree of treatment resistance and this should not be considered a potential exclusion criterion from rTMS treatment.

Unipolar and bipolar illness

The vast majority of studies of rTMS have focused on the treatment of unipolar major depressive disorder (MDD). However, a significant percentage of patients have included patients in the depressive phase of bipolar affective disorder, and a very small number of trials have focused specifically on this illness. In trials including both unipolar and bipolar subjects, there has been no indication of a poorer response in bipolar patients, and in at least one study, bipolar depression seemed to be a positive predictor of response. The trials conducted specifically on bipolar depression have been too limited at this stage to allow meaningful conclusions to be drawn. In the absence of this evidence, there is no reason to presume that bipolar depression will respond more poorly to rTMS than unipolar. rTMS may therefore be a reasonable treatment option for bipolar depression given the limited options available for these patients. There is a risk of switch to mania with rTMS, although this appears low. There is no evidence that concurrent mood stabilizing treatment interacts adversely with rTMS or lessens outcomes; the provision of mood stabilizers would therefore seem to be a sensible action in patients who have experienced particularly troublesome manic episodes in the past. However, it is also possible that the mechanism of action of rTMS may depend on some action, such as the spread of activation from the site of stimulation, that could be adversely affected by anti-convulsant medication: larger studies are required to more firmly establish whether treatment response may be affected by medication in this class. Unlike ECT, there is no evidence that standard rTMS has antimanic properties and as such, should be withheld or discontinued if there is evidence of switch to mania.

Conclusion and suggestion

Although supported by limited evidence at this stage, rTMS seems a reasonable treatment option for patients with bipolar depression. Concurrent mood stabilizers should be used in patients who have a history of difficult to treat or moderate-to-severe mania to reduce the risk of manic switch. rTMS should be discontinued if there is a switch to hypomania or mania.

Selection of treatment type

The largest group of rTMS trials conducted have tested the efficacy of high-frequency stimulation applied to the left DLPFC. This type of rTMS has been evaluated in numerous studies, including two multicenter trials, both of which yielded positive results. This type of stimulation has been shown to have greater antidepressant effects than sham in a number of metaanalyses, now with over 1000 randomized subjects.
There are, however, a number of alternative methods of rTMS administration. Low-frequency rTMS applied to the right DLPFC has been evaluated in a number of trials. It has been found to be efficacious when evaluated alone and in all the comparative trials conducted it has been shown to be as efficacious as the left sided approach. The efficacy of right-sided treatment has been confirmed in one recent metaanalysis. However, it is important to note that its efficacy has not been confirmed in any large multisite sham controlled trials, as is the case with high-frequency left-sided rTMS. Low-frequency stimulation has several possible advantages. It places less demand on equipment, including fewer problems of coil overheating that can occur with some rTMS systems. It is usually, but not always, better tolerated than high-frequency stimulation and has a considerably reduced risk of seizure induction. In fact, low-frequency stimulation has been assessed for potential anticonvulsant properties. In our experience, most patients experience the slow steady stimulation of low-frequency rTMS as more comfortable than the high-frequency bursts.

Another possibility is the sequential combination of low-frequency right-sided rTMS and high-frequency left-sided rTMS. It is not yet clear from the literature whether such bilateral stimulation is more effective than unilateral stimulation, though one study found higher efficacy rates with bilateral stimulation than those usually seen in sham controlled trials of unilateral stimulation alone. A number of other stimulation protocols are being assessed in clinical trials, including priming stimulation and theta burst rTMS. Further research is required before the role of these approaches in clinical practice is clear.

There is limited evidence that some patients may respond to rTMS applied to one hemisphere after nonresponse to treatment applied to the other. To date, no studies have assessed whether patients will respond to bilateral rTMS where there was no response to unilateral treatment.

Conclusion and suggestion

The literature does not clearly indicate the superior efficacy of any form of rTMS over other types described previously. The greatest body of literature, most importantly two large multisite sham controlled trials, supports high-frequency stimulation applied to the left DLPFC. However, right-sided stimulation is usually better tolerated and may be safer. It is a good second line option or possibly could be used first line in patients with high RMTs or low tolerance for discomfort associated with rTMS treatment. It may also be a sensible first line treatment option if there are any risk factors increasing seizure likelihood. The role of bilateral stimulation is not yet clear. A trial of stimulation of the opposite hemisphere is warranted in patients who have failed to respond to unilateral rTMS.

Treatment scheduling

Almost all rTMS studies have assessed treatment provided 5 days per week. One study supported the notion that treatment three times per week could be as effective as that provided five times per week. However, it is not yet clear if an equivalent number of total treatments, or an equivalent time and hence fewer treatments would be required. In the opposite direction, twice daily rTMS appears better than placebo but there is no indication to date that it is more effective than once daily treatment. In our limited experience, there appears to be no additional benefit of providing treatment 7 days per week. In a limited number of cases, patients did not seem to have responded faster and in some have required extra treatment sessions responding ultimately in a similar amount of time.

Conclusion and suggestion

Treatment should be provided five times per week until further evidence is available. However, if patients are able to attend only three or four times per week, this may not undermine efficacy.

Treatment duration

Initial rTMS trials were only of 1 or 2 weeks duration but showed antidepressant effects. Increasingly longer trials have emerged over the last 10 years with periods of treatment up to 9 weeks. There certainly appears to be a progressive improvement in mood over longer treatment courses (e.g., see course of mood change). It is less clear how long a treatment course should continue in patients who have not responded to treatment. In our experience, the majority of treatment responders will begin to notice mood changes in the second or third week of treatment. Often these are initially very subtle changes, and may include improvement in attention and concentration. Some patients do eventually respond after a longer period of ongoing treatment. However, there is little data available on the number of patients who will respond later, or how long a maximum treatment course is reasonable. There is no evidence of an accumulation of side effects or adverse events with longer rTMS treatment durations; however, there is limited data on treatment beyond 6 weeks.

Conclusion and suggestion

There is no clear maximum treatment number or duration for responders to rTMS. It would seem reasonable to continue treatment for at least 6 weeks, and potentially longer, in a patient who is continuing to improve with rTMS. There is also no well-defined duration for an adequate trial of rTMS treatment: in our practice we would not commonly
progress beyond 4 weeks unless there was a clear prior history of previous treatment response. Failure to respond after 3 or 4 weeks of treatment should potentially lead to a change in stimulation type, for example from unilateral to bilateral treatment or from right to left hemisphere, or a consideration of non-rTMS options.

**Concurrent treatments**

Although several of the larger rTMS trials have only included patients free of antidepressant medication, many trials have also included patients on concurrent treatment. The most common approach has been to include patients on stable ongoing medication with medication increases disallowed to avoid confounding study results. These patients were presumably either nonresponders or partial responders to existing treatment. A smaller number of trials have concurrently commenced medication treatment and rTMS. These have mostly failed to show any benefit of rTMS over sham. Although one early study of rTMS treatment of auditory hallucinations in schizophrenia reported a poorer response to treatment in patients receiving mood stabilizers, no effect of this or any other medication class on response to rTMS treatment in depression has been systematically demonstrated. It is possible that medication changes during a course of rTMS may alter the RMT and therefore either predispose the patient to a higher risk of seizures or lessen efficacy. Therefore, if substantial changes in medication doses are made, RMT levels should be remeasured and the prescribed rTMS intensity adjusted accordingly.

**Conclusion and suggestion**

rTMS treatment may be provided in patients who are medication free, or in nonresponders or partial responders where the treatment is continued during rTMS provision. There appears to be no benefit of the concurrent commencement of antidepressant medication and rTMS. Medication changes during treatment should result in retitration of rTMS dose.

**Coil positioning**

The original provision of rTMS to the DLPFC involved the use of the “5-cm method.” This involves locating the ideal position, or “hot spot” for the stimulation of a peripheral hand muscle, usually the APB, in the cortex ipsilateral to the proposed site of stimulation. This is marked on the scalp, and 5 cm measured anteriorly in a sagittal plane. The forward site is marked as the target for stimulation. However, Herwig et al. in 2001 demonstrated that this technique results in the accurate localization of DLPFC (defined as Brodmann areas 9 and 46) in only a minority of subjects. An alternative method of localization, neuronavigation, was assessed in a subsequent clinical trial. This study demonstrated that rTMS applied to the junction of areas 9 and 46, located using MRI-based neuronavigation, resulted in a superior antidepressant response to that seen with the 5-cm method. However, neuronavigation may not be necessary for greater accuracy in DLPFC localization. The main limitations of the 5-cm method appear to be that it locates treatment too posteriorly, and does not consider variation in head size. These factors can be overcome by increasing the distance measured forward and/or using a method that takes head size into account. The system of measurement used for the 10-20 EEG system can do the latter and is widely understood. EEG coordinates may be reliably correlated with cortical areas. The site stimulated in the trial comparing neuronavigation with the 5-cm method appears to be anterior to the F3 EEG point. This is considerably further forward than the location usually established with the 5-cm method. Given that the majority of trials have evaluated efficacy of rTMS localized with the 5-cm method, it may not be appropriate to move to such an anterior position without replication of the Fitzgerald et al. trial. However, the F3 EEG point itself seems a good alternative as it will locate treatment more anteriorly, while taking variation of head size into account. A simple guide for the measurement of these sites have been recently published.

**Conclusion and suggestion**

rTMS treatment is usually located 5 cm anterior to the hand motor hot spot. Locating treatment more anteriorly (e.g., 6-7 cm) is a sensible and easily adoptable modification to this method. Clinicians should also consider the use of the F3 (and F4 on the right) EEG points as locations for treatment, especially in patients with smaller or larger than average head size.

**Treatment of relapse**

Depression is clearly a relapsing disorder and patients remain at risk of relapse after successful rTMS treatment. For example, 99 patients who responded or achieved partial response (> 25% reduction in depression severity) to rTMS were followed for 24 weeks after transition back onto antidepressant medication. Ten percent relapsed in the 24 weeks and 38.4% experienced “symptom worsening” as defined by a Clinical Global Impressions Severity of Illness (CGI-S) score increase of 1 point or greater. A limited number of studies have explored the retreatment of subsequent depressive episodes, using the same parameters as the previously successful course of rTMS. This literature suggests that in the majority of cases, patients will respond to rTMS treatment when applied in...
subsequent episodes. For example, in the study of Janicak et al. discussed previously, 38 patients were retreated during the 24 weeks of follow-up and 32 (84.2%) subsequently improved. This is also the case in our experience, although treatment nonresponse can occur on the second, or any subsequent treatment occasion.

**Conclusion and suggestion**

The provision of rTMS treatment using the same treatment parameters is a reasonable option on the occurrence of depressive relapse after previously successful rTMS treatment.

**Maintenance treatment**

Maintenance rTMS has only been explored to a very limited degree, and there are no sham controlled studies supporting its efficacy to date. The most commonly reported maintenance model has been the provision of weekly or 2 weekly single rTMS sessions, often with a progressive decrease in session frequency over time. This is often performed with maintenance ECT. Another possibility is the more intensive provision of multiple sessions. Over a number of years, we have provided maintenance rTMS by administering five individual treatment sessions over a 3-day period, usually a weekend, once per month, in patients who have had several depressive episodes successfully treated with rTMS. This has been successful in some patients, although several have required more frequent periods of treatment (e.g., every 2 weeks). Continued or newly commenced antidepressant medication treatment seems a sensible option at the end of an acute rTMS treatment course.

**Conclusion and suggestion**

As the duration of clinical response after a successful acute course of rTMS treatment is unpredictable, it seems reasonable to provide patients with continued medication and psychological support after an initial treatment episode. Maintenance rTMS should not be automatically provided. In patients who relapse frequently despite these measures, a defined individual trial of maintenance rTMS may be pursued. To justify ongoing maintenance treatments, comparison of time-to-relapse during maintenance with previous patterns should be made on a patient by patient basis.

**Safety and monitoring**

rTMS treatment is generally very well tolerated. It is notable that the overall discontinuation rate is markedly lower that that usually seen in depression treatment trials, especially of medication. For example, in the two large multisite rTMS trials, the drop out rate in the active groups was 12% and <10% and it is often less than 5% in single site studies. The main side effects experienced are discomfort at the site of stimulation and a headache during, and immediately after treatment. These are produced through stimulation of nerves and muscles in the scalp. Stimulation related discomfort may be reduced in several ways. First, small modifications of coil position or orientation may reduce the sensation produced with stimulation. Although it has not been systematically assessed, there is no reason to believe that small modifications should substantially affect treatment efficacy. Second, a reduction in stimulation intensity will reduce discomfort in most patients. Given that there seems to be a relationship between stimulation intensity and efficacy, this reduction should be limited. However, antidepressant effects of rTMS have been seen from 90% to 120% of the RMT, and may well still be produced if intensity is reduced down from the higher stimulation levels. The intensity of rTMS related discomfort does seem to relate to patient anxiety; in patients with higher thresholds or substantial anxiety, it is often prudent to begin treatment at a lower stimulation intensity to allow them to become comfortable with the sensation. Stimulation intensity should then be progressively increased over one or several sessions.

The major risk with rTMS treatment is the induction of seizure activity. A number of seizures were reported with TMS before the delineation of safety guidelines defining safe stimulation parameters. Since then, there have been sporadically published seizure reports, mainly in conditions other than depression. Two seizures have been reported in bipolar disorder, suggesting that this may be a higher risk factor for seizure induction.

Because of the potential seizure risk associated with rTMS treatment, it has previously been considered a medical procedure that should only be prescribed by a physician and administered by a trained physician or nurse. We are aware that this standard has not been universally adopted and some consider that treatment could be provided by a trained technician. At a minimum, we believe that the treatment should be prescribed by a physician who has been specifically trained in the use of rTMS. This training at a minimum should provide the physician with an understanding of the principles of rTMS stimulation and treatment, the clinical indications and contraindications, the range of potential patient response to treatment (therapeutic and side effects) and the potential for interactions between rTMS and other treatment types.

In the physician prescription of treatment, the stimulation parameters should be individually determined. Patients’ stimulation intensity should be prescribed relative to their RMT, that should be measured by the prescribing physician or a highly trained individual. Regular measurement of the RMT is required to maintain an appropriate skill base. Treatment should be provided by trained medical
or nursing staff or under close supervision of these: the individual providing treatment should be trained in “first responder” first aid, including the maintenance of airway patency, and medical response should be close at hand. There should be ready access to support if required, and established and clearly posted emergency response protocols. Syncopal episodes are also possible with rTMS treatment and may complicate the diagnosis in the case of loss of consciousness.

The main contraindication to the use of rTMS treatment is the presence of intracranial nonremovable ferromagnetic material or the use of a magnetically programmed medical device where disruption of this use may prove dangerous (e.g., a pacemaker). A number of conditions increase the risk of seizure induction necessitating avoidance of the procedure or use with considerable caution. These include a past history of epilepsy or seizures or a currently active brain disorder. The presence of unstable cardiac disease also requires caution because of the increased demands that could be placed on the cardiovascular system in the event of a seizure. A history of ongoing problematic alcohol misuse is a contraindication, especially given the increased risk of seizures during withdrawal stages of use. Patients taking benzodiazepines should be advised not to discontinue their use during treatment because of the increased risk of seizure during benzodiazepine withdrawal.

Other safety issues with rTMS treatment include the possible induction of changes in auditory thresholds. In a large group of patients receiving relatively high dose rTMS, no change in auditory thresholds was detected. Because of this risk, although not supported by any systematic research, it seems sensible to recommend that patients and any practitioner remaining in close proximity to the rTMS treatment wear appropriate ear protection such as disposable ear plugs or noise protection ear coverings. Reports of manic switching in patients receiving rTMS treatment, predominantly patients with bipolar disorder, have also been published. Patients with a bipolar illness, especially those not receiving a mood stabiliser, should be monitored carefully during an rTMS course.

The safety of rTMS in adolescent patients, during pregnancy, or during lactation has not been systematically studied, although some case reports have been published. rTMS would seem to be an ideal treatment for depression during pregnancy and lactation as there are no systemic effects of medication or risks as associated with ECT and little likelihood that the magnetic field would reach the fetus in sufficient strength to produce any deleterious effects. However, it is possible that hormonal changes induced by rTMS could have adverse effects and this will require systematic research. In addition, provision of rTMS during pregnancy may require the more careful monitoring of motor thresholds and dose as hormonal fluctuations may affect cortical excitability over time. A recent case series carefully assessed mother and child outcomes in 10 pregnant women who received rTMS treatment and found no adverse events (7 of the 10 patients responded).

Although rTMS appears initially unacceptable as a treatment option to depressed pregnant women, this can potentially be altered with appropriate education.

All units administering rTMS should have a clear local protocol regarding management of a seizure or loss of consciousness, available to all staff. The initial response required is to move the patient into a semiprone lying position and ensure patency of the airway. The pulse should be checked. Seizures are likely to terminate fairly rapidly and not require medication treatment: emergency response medical units should potentially be summoned if the seizure does not terminate in several minutes. Appropriate follow-up may include a postictal EEG and brain scan.

**Conclusion and suggestion**

TMS treatment is generally well tolerated and with few risks. However, as it does entail a risk of seizure induction, it needs to be appropriately prescribed (by a trained specialist medical practitioner), administered, and monitored (by a medical practitioner or a trained nurse). Prescription of stimulation parameters should follow established safety guidelines.

**Personnel**

Because of the possibility of seizure induction, rTMS treatment is considered a medical procedure that requires appropriate assessment and monitoring. As discussed previously, international guidelines indicate that rTMS should be prescribed by an appropriately trained medical practitioner and administered by a trained medical practitioner or nurse, although it is possible that a technician may be used as discussed. Individuals providing rTMS treatment should have up-to-date “first responder” life support training, including in the maintenance of an airway. There is no evidence that the availability of medication for the treatment of a seizure is likely to enhance safety as personnel involved in rTMS treatment are unlikely to have up-to-date experience in the provision of this medication in an emergency situation. It is highly likely that privileging and credentialing will remain the local responsibility of medical administration authorities within health care provision bodies, although it would seem sensible that the guidelines for this are informed by individuals with experience in the use of rTMS.

**Conclusion and suggestion**

rTMS should be prescribed by an appropriately trained medical practitioner and administered by trained medical or nursing staff.
Patient consent and education

Patients should be provided with sufficient verbal and written information as to the nature of rTMS treatment, its risks and potential benefits to allow them to provide informed consent in a manner similar to that required for equivalent procedures. At this stage this should include, at a minimum, a discussion of the short-term nature of the research trials from which rTMS treatment has evolved; the potential risk of seizure induction, and the need to inform the rTMS treatment team should there be any change in the individual’s medical status or medication treatment during the course of rTMS therapy.

Other special groups

Limited data has been published on the use of rTMS in a number of special groups. Case reports or small series have suggested that rTMS may be effective in patients with depression that has developed in the context of Parkinson’s disease,61,62 a stroke,63 or traumatic brain injury.64 Further research is required to establish the indications for rTMS treatment in these populations. rTMS may well prove to be a sensible option on some occasions with some patients in these groups given that other therapeutic possibilities are often problematic.

Choice of equipment

There are a limited number of TMS equipment manufacturers; availability may also be limited by local regulatory approval and device distribution. As well as regulatory status, choice of equipment should consider a number of other factors. These include the capacity of the stimulator to stimulate at sufficient power and frequency, and the availability of coils that do not overheat with the duration of typical treatment sessions (and will cool sufficiently between tightly scheduled treatment sessions if required), the availability of accessories such as coil stands and devices to ensure the repeatability of coil positioning, the easy manipulation of the coil during the measurement of motor threshold, the flexibility of the stimulation protocols provided, the ease of use of the software interface, the potential requirement for multiple power sources and the local provision of service, training, and support. As rTMS equipment is technically complex, in planning service provision, the user should make contingency plans for equipment down times for breakdown/repair and service requirements.

Conclusions

rTMS treatment is a viable alternative treatment for patients with TRD. There are a variety of methods of rTMS administration and adequate prescribing and administration of rTMS requires an understanding of these techniques, the potential complications of rTMS treatment, and the clinical variables that may modulate rTMS response. There is a substantive baseline level of knowledge required to underpin the administration of rTMS in clinical practice.

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