

# Repetitive transcranial magnetic stimulation: beyond the treatment of depression



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“It is now time to extend the therapeutic applications of [rTMS] beyond the treatment of depression, and even more urgently, to make it more available to depressed patients who have not improved with standard interventions.”

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Repetitive transcranial magnetic stimulation (rTMS) is an effective and well tolerated antidepressant treatment. There is also increasing evidence of its usefulness in other psychiatric and neurological disorders.

In the UK, rTMS is officially recommended by NICE, the relevant reviewing body attached to the NHS, for the treatment of migraine [1] and depression [2]. The effectiveness of rTMS in these conditions is very well established, particularly in the case of depression, but the evidence supporting its effectiveness in other conditions is increasing. Given that rTMS is a very safe treatment [3] and its putative mode of action is well known [4], and given the common pathophysiological factors involved in a number of psychiatric and neurological disorders, there is a drive to expand the use of rTMS beyond its current recognized indications.

## Psychiatric uses

A number of meta-analyses have demonstrated the effectiveness of real high frequency over sham rTMS in depression [5].

It is normally used for treatment-resistant depression, although it could be argued that given its safety, tolerability and effectiveness profile, it should be used more extensively, particularly when tablets are best avoided, like in depressed pregnant or nursing women.

There is also mounting evidence that rTMS is likely to be effective in other psychiatric disorders. Given that anxiety is almost always present as a comorbid factor in depression, it seems intuitive that rTMS should help with anxiety, and indeed there is evidence of this. A meta-analysis failed to demonstrate a superior effect of real versus sham rTMS in anxiety, but many of the randomized controlled trials (RCTs) included in the review studied specific anxiety modalities, such as obsessive compulsive disorder (OCD) (see below), that were treated with low doses and using treatment protocols that we now know not to be necessarily effective in these specific disorders [6]. The preferred modality for the treatment of anxiety is low frequency, typically 1 Hz, rTMS over the right prefrontal cortex [7].

## KEYWORDS

- anxiety • depression • migraine
- OCD • rTMS • stroke • tinnitus

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A number of different treatment protocols have been postulated for OCD. A meta-analysis conducted in 2013 concluded that low frequency rTMS and protocols targeting the orbitofrontal cortex or the supplementary motor area seemed to be the most promising in the treatment of OCD [8].

There is also some evidence that rTMS can be useful in post-traumatic stress disorder (PTSD). This is not surprising, since we know that depression and anxiety, two crucial components of PTSD, respond to rTMS. A case series of 12 patients with PTSD were treated in an open-label study. These patients reported a diminution in symptoms of depression and anxiety after treatment with rTMS [9].

The auditory hallucinations in schizophrenia have been identified as another possible target for treatment with rTMS [10]. Researchers in this area have found that sham rTMS tends to induce a large placebo effect in randomized controlled trials. While this casts some doubt on the size of the effectiveness of real rTMS in treating auditory hallucinations in schizophrenia, it should not detract from the overall potential usefulness of this intervention.

A randomized controlled trial of real and sham rTMS found that a single session of rTMS transiently reduced core symptoms of anorexia nervosa and the patients considered rTMS to be a viable treatment option [11].

The affective dysregulation that characterizes a borderline personality disorder was the target of treatment with very high-frequency rTMS (20 Hz and intermittent Theta burst stimulation [iTBS]) in a two-case report published this year [12]. Both patients improved significantly after 20 sessions.

A meta-analysis of clinical trials on the use of rTMS in Alzheimer's disease, published in 2015, concluded that high-frequency rTMS had a significant therapeutic effect on cognitive function in patients with mild to moderate Alzheimer's disease [13].

### Nonpsychiatric uses

A randomized trial of real high frequency versus sham rTMS found that the real stimulation was more effective than sham in reducing headache

frequency and functional disability and that the treatment was well tolerated. The authors concluded that this study provided evidence of the efficacy and safety of 10 Hz rTMS in migraine prophylaxis [14].

A systematic literature review and meta-analysis on the effect of real rTMS compared with sham in chronic tinnitus patients found real rTMS to be associated with a significant medium to large therapeutic effect size, although the authors also noted a high degree of variability in the studies design and reported outcomes [15].

Low-frequency (1 Hz) rTMS has also been used to treat poststroke chronic nonfluent aphasia. A relatively small clinical trial found positive changes in the stimulation group when compared to the placebo control group at 2 months poststimulation on naming performance, as well as other aspects of expressive language and auditory comprehension [16].

### Conclusion

The effectiveness of rTMS as an antidepressant treatment is already widely recognized and extensively researched, although it is yet to become a mainstream intervention outside North America. It is a safe and noninvasive neurostimulation technology that allows us to access specific targets in the brain for specific clinical purposes, either stimulating or inhibiting that part of the brain, depending on the treatment frequency chosen.

It is now time to extend the therapeutic applications of this safe and effective technology beyond the treatment of depression, and even more urgently, to make it more available to depressed patients who have not improved with standard interventions.

### Financial & competing interests disclosure

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