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Safety and tolerability of repetitive transcranial magnetic stimulation in patients with pathologic positive sensory phenomena: a review of literature

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Abstract

BACKGROUND—Repetitive transcranial magnetic stimulation (rTMS) is emerging as a valuable therapeutic and diagnostic tool. rTMS appears particularly promising for disorders characterized by positive sensory phenomena attributable to alterations in sensory cortex excitability. Among these are tinnitus, auditory and visual hallucinations, and pain syndromes.

OBJECTIVE—Despite studies addressing rTMS efficacy in suppression of positive sensory symptoms, the safety of stimulation of potentially hyperexcitable cortex has not been fully addressed. We performed a systematic literature review and metanalysis to describe the rTMS safety profile in these disorders.

METHODS—Using the PubMed database, we performed an English-language literature search from January 1985 to April 2011 to review all pertinent publications. Per study, we noted and listed pertinent details. From these data we also calculated a crude per-subject risk for each adverse event.

RESULTS—106 publications (n = 1815 subjects) were identified with patients undergoing rTMS for pathologic positive sensory phenomena. Adverse events associated with rTMS were generally mild and occurred in 16.7% of subjects. Seizure was the most serious adverse event, and occurred in three patients with a 0.16% crude per-subject risk. The second most severe adverse event involved aggravation of sensory phenomena, occurring in 1.54%.

CONCLUSIONS—The published data suggest rTMS for the treatment or diagnosis of pathologic positive sensory phenomena appears to be a relatively safe and well-tolerated procedure. However, published data are lacking in systematic reporting of adverse events, and safety risks of rTMS in these patient populations will have to be addressed in future prospective trials.

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aul Muller reports no biomedical financial interest or potential conflicts of interest. Alvaro Pasual-Leone serves on the scientific advisory board for Codman-Johnson & Johnson, Nexstim, Neuronix, Starlab, and Neosync, and holds intellectual property for various aspects of TMS technology and the combination of TMS with EEG and MRI. Alexander Rotenberg does not currently serve on any advisory board, but does hold intellectual property for TMS technology and the combination of TMS with EEG.

Keywords

repetitive transcranial magnetic stimulation; rTMS; tinnitus; auditory hallucinations; visual hallucinations; neuropathic pain; visceral pain; migraine; fibromyalgia; safety; seizure

1. Introduction

Repetitive transcranial magnetic stimulation (rTMS), a well-tolerated method for focal modulation of cortical excitability, is emerging as a therapeutic tool for a variety of neurologic conditions (1–4). In experimental protocols, rTMS can also be used to study cortical plasticity in healthy and disease states (1–7). Although rTMS modulatory mechanisms are not completely known, the durable functional changes induced by low-frequency (≤1Hz; LF rTMS) or high-frequency rTMS (≥10Hz; HF rTMS) resemble those of long-term depression (LTD) and long-term potentiation (LTD) respectively (8–11). Additionally, patterned rTMS delivered as either continuous or intermittent bursts of high frequency trains, such as theta burst stimulation (TBS), can also induce LTD-like or LTP-like changes in regional cortical excitability (12).

Therapeutic rTMS might be particularly beneficial for patients with disorders of regional cortical excitability (13–17). Epilepsy is one such example where LF rTMS has been applied over a cortical seizure focus to suppress seizures (18–21). Another broad category of disorders are those characterized by positive sensory phenomena that may involve pathologic activation of sensorimotor cortical areas along with related cerebral networks. Among these are tinnitus, auditory hallucinations (AH), visual hallucinations (VH), and pain syndromes such as somatic pain, visceral pain, migraine, and fibromyalgia. – all syndromes where functional imaging data show excess regional sensory cortex activity (22–37).

In some of these disorders, cortical hyperactivity may be directly attributable to cortical de-afferentation, resulting in disinhibition of excitatory cortical connections. Among these are phantom limb pain, tinnitus, and the VH associated with Charles Bonnet Syndrome (CBS) (37–39). In others, such as AH in schizophrenia, migraine or fibromyalgia, the anatomy of aberrant regional cortical activity is less clear. However, functional imaging data in these disorders support excess sensorimotor cortex activation (24, 33,35,36,40) and a number of studies have been aimed to test whether rTMS can interfere with symptom physiology by altering activity in hyperactive cortex. (41–43)

Although rTMS is generally safe when following guidelines, seizure induction remains the most serious safety concern (44–46). Analogous to the risks of rTMS in epilepsy (46), such concern is warranted with positive sensory symptoms where stimulation targets may be excessively excitable at baseline. While the assumption that hyperactivity corresponds to hyperexcitability and lowered threshold for seizure and other adverse events remains to be verified, the potential for excess risk in this patient population warrants consideration. Accordingly, we assess the available published data regarding seizures, symptom exacerbation or other adverse events when rTMS is applied over a sensori-motor cortex in chronic pain syndromes as well as in AH, VH, and tinnitus.

2. Methods

2.1 Literature Review

Using PubMed, we reviewed publications from January 1985 to April 2011 using the following keywords: “TMS,” ”transcranial magnetic stimulation,” “rTMS,” “repetitive transcranial magnetic stimulation,” “auditory hallucinations,” “visual hallucinations,”

"chronic," "pain," "visceral pain," "migraine," "fibromyalgia," and "tinnitus." Relevant information concerning patient characteristics, rTMS protocol, adverse events, and study outcomes were recorded (Tables 1–7) (13–17,41–43,47–144).

A secondary PubMed search from January 1985 through April 2011 used keywords: "TMS", "transcranial magnetic stimulation", "rTMS", "repetitive transcranial magnetic stimulation", "seizure", and "epilepsy." This was performed to assure that published reports of seizures were not missed. As necessary, we contacted the corresponding author for clarification of details that were not available in the publication.

2.2 Statistical Analysis

Each case of reported adverse event that occurred either during or immediately after rTMS was factored into the risk analysis. Our analysis was limited to the crude per-person risk with a 95% confidence interval (95% CI), truncated when appropriate to remain within natural limits when approaching 0 or 100%. The rationale for restricting the analysis to crude risk was the high variability in sample size (1–164 subjects) and rTMS protocol (0.2–50 Hz, 120–5200 stimuli per day, study duration 1 day–8 weeks).

3. Results

3.1 Literature Review

Subject characteristics, rTMS protocols and outcomes per publication are summarized in Tables 1–7. For the present analysis we distinguish between tinnitus, AH, neuropathic pain, visceral pain, migraine, fibromyalgia, and VH cases. Of 106 publications (n_S (n of subjects) = 1815) identified by literature review, there were 38 publications (n_S = 393) related to AH, 37 publications (n_S = 877 subjects) related to tinnitus, 18 publications (n_S = 311) related to neuropathic pain, five publications (n_S = 165) where rTMS was applied to patients with migraine, four publications (n_S = 53) address fibromyalgia, two publications (n_S = 14) concerning visceral pain, and two publications (n_S = 2) describing rTMS in patients with VH. One publication (71) was counted for tinnitus and AH, due to its inclusion of patients with both symptoms.

A total of 101 studies (n_S = 1653) described rTMS intensity as a percentage of motor threshold (MT), while six (n_S = 181) utilized only a specific machine output (MO). There were two publications (n_S = 103) in which a measure of rTMS intensity was not reported. Of AH studies, 11 (n_S = 86) used rTMS at or above MT (≥ MT; range 100–120%), and 26 (n_S = 306) utilized rTMS at sub-MT levels (< MT; range 80–90%). In one publication (76;n_S = 1) rTMS intensity was not described. For the studies involving tinnitus, 29 (n_S = 454) used rTMS with ≥MT intensity, while nine (n_S = 417) made use of rTMS with <MT intensity, and there were two publications (n_S = 128) in which percent of MT was not given, rather stimulation was fixed at 50% MO. Of studies on neuropathic pain six (n_S = 38) used rTMS with ≥MT intensity, and 12 (n_S = 273) used rTMS with <MT intensity. Two studies describing rTMS in migraine (n_S = 15) used ≥MT intensity, one (n_S = 6) used <MT intensity, one (n_S = 42) used a fixed MO of 30 or 50%, and one (98;n_S = 102) did not state the intensity at which rTMS was performed. Fibromyalgia studies had 2 publications (n_S = 18), which used ≥MT intensity, and two publications (n_S = 35), which used <MT intensity. The two studies on visceral pain had one (n_S = 5) which used <MT intensity, and the second (n_S = 9) utilized a set 70% MO. For two VH studies (n_S = 2), rTMS intensity was 80% MO, and involved two subjects.

There were 77 publications (n_S = 1202) using low frequency (LF; ≤1 Hz) protocols, 39 publications using a high frequency (HF; >1Hz) protocol (n_S = 804), and three publications

using combined LF and HF rTMS (n_s = 177). Based upon stimulation paradigm, these studies were binned to both LF and HF or classified as combined.

Thirty-five publications (n_s = 373) on AH made use of LF and four studies (n_s = 21) utilized HF. For tinnitus, 28 studies (n_s = 584) used LF rTMS and 13 studies (n_s = 433) used HF alone, while three studies (n_s = 177) used HF in combination with LF rTMS. Within those studies involving neuropathic pain, five (n_s = 54) utilized LF rTMS, while 17 (n_s = 302) used HF rTMS. Migraine publications had three studies (n_s = 157) that used LF rTMS, and two (n_s = 8) studies that used HF rTMS. Published reports for fibromyalgia had two studies (n_s = 18) using LF rTMS, and two studies (n_s = 35) using HF rTMS. Visceral pain reports had two studies (n_s = 14) with LF rTMS and one (n_s = 5) with HF rTMS. Both studies (n_s = 2) concerned with VH used LF rTMS at 1 Hz.

Sixty-five studies reported the incidence of adverse events. Of 1815 subjects receiving stimulation, across all 106 publications reviewed, the reported adverse events and numbers of patients are listed in Table 9. There were eight studies where adverse events were described, yet were not quantified in terms of number of patients. (16,75,77,100,103,110,128,129). Finally, there were 38 studies where adverse events were not reported (Tables 1–7).

Of 106 publications, 39 did not include placebo or sham stimulation (Tables 1–7). The remaining 67 studies included sham rTMS as part of either a cross-over or a group comparison design.

3.2 Risk Assessment

For purposes of analysis, we sorted adverse rTMS-related events into five categories as follows: (1) seizure induction, (2) other serious adverse events, (3) symptom exacerbation, (4) mild adverse events, and (5) no adverse events. Analysis of specific adverse events, categorized by separate positive sensory symptoms, is detailed in Table 9.

a) Seizure induction—Seizures during rTMS were documented in three of 1815 patients (Table 8): in one patient with tinnitus after 1 Hz rTMS over left primary auditory cortex (111), and in two with complex regional pain syndrome (CRPS) after 10 Hz rTMS over motor area (113,122). This approximates a 0.16% (95% CI: 0 – 0.19%) crude risk per subject. The seizure in a tinnitus patient was one in 877 subjects undergoing rTMS, translating to a 0.11% (95% CI: 0 – 0.22%) crude per subject risk of seizure during rTMS for tinnitus. Considering the risk of seizure induction according to rTMS frequency within tinnitus subjects: zero out of 477 patients had a seizure induced by HF rTMS while one out of 584 patients had a seizure induced by LF rTMS. These equate a 0.17% (95% CI: 0 – 0.33%) crude risk for LF rTMS in patients with tinnitus. The other two seizures occurred in two out of 311 patients with chronic pain giving a 0.64% (95% CI: 0 – 0.89%) crude risk. Both seizures were induced by HF-rTMS, equating to a 0.66% (95% CI: 0 – 0.92%) crude risk. None of the 54 patients with neuropathic pain undergoing LF rTMS had a seizure.

In all three patients, there was no previous history of seizure. One patient (122) had surgical neurovascular decompression by supraclavicular approach for thoracic outlet syndrome, while the other two patients had otherwise unremarkable medical histories. Only one patient was on medication at the time (113), which consisted of an antidepressant (amitriptyline) and an anticonvulsant (carbamazepine). In all three cases, a generalized seizure occurred with post-ictal confusion. Follow-up did not indicate changes in EEG, MRI, or any motor deficits.

b) Other serious adverse events—In one study (13), a patient was removed from the study because of ischemic chest pain. The authors note that this individual had a history of hypertension, smoking, and diabetes mellitus, and thus assumed that rTMS did not play a causal role in the ischemic event.

One incidence of optic neuritis was described (98) during a study aimed to test LF rTMS in migraine treatment. The event arose before the treatment with TMS, and was thought by the authors to also not be a result of the treatment.

c) Aggravation of sensory symptoms—Aggravation of underlying sensory symptoms was reported in 28 out of 1815 subjects across all studies. The crude risk per subject of symptom aggravation was 1.54% (95% CI: 0.97 – 2.11%). When categorized by underlying diagnosis, we found that in the tinnitus group 19 out of 877 patients had a worsening of symptoms, which gives a 2.17% (95% CI: 1.21 – 3.13%) crude risk. There were 11 patients out of 584 for LF rTMS, seven out of 433 patients for HF rTMS, and one out of 177 patients with combined HF and LF rTMS who experienced an increase in tinnitus. Symptom aggravation in AH occurred in four out of 39 subjects, which equates to a crude risk of 1.02% (95% CI: 0.03 – 2.01%). The crude risk per subject for aggravated tinnitus by LF rTMS is 1.88% (95% CI: 0.78 – 2.98%), with HF rTMS it is 1.61% (96% CI: 0 – 2.8%), and the combination of HF and LF rTMS gives 0.56% (96% CI: 0 – 1.66%). Four out of 373 patients reported aggravated AH with LF rTMS and zero out of 21 patients who were treated with HF rTMS. Crude risk per subject for aggravated AH was 1.07% (95% CI: 0.03 – 2.11%) using LF rTMS and 0% for HF rTMS. Last, among patients with migraine there were three out of 165 who had an aggravation of migraine including both headache and aura, equating to a 1.81% (95% CI: 0 – 3.85%) crude risk. If the data are restricted only to those patients who were treated with LF rTMS, then aggravation of migraine occurred in three out of 157 patients or a 1.91% (95% CI: 0 – 4.05%) crude risk.

Only studies involving tinnitus, AH, and migraine reported symptom aggravation either following or during stimulation. Two studies (13,76; $n_s = 23$ and $n_s = 1$, respectively), reported an increase of AH from baseline during rTMS in four patients with LF rTMS. In one study (13), increase in AH after stimulation of the temporo-parietal cortex was divided into one reported case for active-blind rTMS and two reported instances for active non-blind rTMS. Duration and level of AH aggravation was not detailed. The case report (76), describes a single patient experiencing an increase in AH for one month, described as “tolerable,” following the final LF rTMS session to the left tempoparietal cortex (LTC).

For tinnitus studies, there were 19 patients, 11 receiving LF rTMS, seven receiving HF rTMS, and one who received combined HF and LF rTMS, who experienced tinnitus exacerbation. We note that symptom exacerbation in patients with tinnitus undergoing rTMS requires a specialized definition, as even patients who improved after treatment have experienced transient tinnitus worsening. For instance one study (125) reported that “most” patients in this study experienced a 2–3 day increase in tinnitus symptoms, followed by a clinical improvement afterward. We have chosen to include all instances of aggravated tinnitus, as even in reports where some patients tolerated this increase there were others who exited the study (47).

The authors of one LF rTMS tinnitus study (62; $n_s = 3$) reported a single patient with worsening tinnitus after the first two days of 1 Hz rTMS over auditory cortex (AC). Following this transient increase, the patient had a reduction of tinnitus sensations for 1 week. One other patient (89; $n_s = 1$) had a similar experience in which tinnitus after 1 Hz to the AC increased for two days and then led to a significant reduction. In one LF rTMS study (118; $n_s = 9$) one patient reported an increase in tinnitus volume after only five minutes of

stimulation to an area of increased PET signal. The patient returned to their baseline tinnitus volume after resting for five minutes. LF rTMS in this patient was discontinued. Two patients (90; $n_s = 28$) reported a mild increase in tinnitus during 1 Hz rTMS which was performed for 33 minutes per day for 10 days.

Two patients dropped out of their active rTMS trials to the LTC or AC (125; $n_s = 16$) after a two to three day increase in tinnitus. Their tinnitus rating recovered to basal values after two days. Two patients (47; $n_s = 26$) failed to complete the study due to worsening of tinnitus after LF stimulation of the left auditory cortex (LAC). The same study reported a common complaint of transient tinnitus increase during active stimulation. In the last LF rTMS study reporting tinnitus exacerbation (114; n = 14), two patients reported a worsening of tinnitus after rTMS to the tempoparietal junction (TPJ), however the details of this worsening are not reported possibly due to the author's classification of this adverse event as "moderate."

With theta burst stimulation (TBS) to the LTC, three patients (119; $n_s = 33$) complained of worsening tinnitus after their first experience with one of three TBS protocols. A single patient, (116; $n_s = 14$), had an increase in tinnitus lasting for two weeks following one day of 10 Hz rTMS at various scalp locations. Three patients (101; $n_s = 10$) reported a very loud tinnitus after individual alpha frequency (IAF) rTMS, which lasted for several hours up to a few days.

The combined HF and LF rTMS study (99; $n_s = 13$), reports one patient experiencing aggravated tinnitus symptoms immediately after stimulation and lasting for 10 days. The rTMS protocol utilized a brief 10 Hz pulse followed by longer 1Hz stimulation. The rTMS target was posterior to the fMRI determined auditory cortex. This patient completed the entire study.

Among migraine publications, there was one (98; $n_s = 102$), which reported three patients experiencing migraine during or following treatment of LF rTMS over occipital cortex. One of these migraine attacks was considered severe, however relevant details are not provided in the text.

d) Other adverse events—271 out of 1815 patients reported adverse events other than seizure or primary symptom aggravation, which are listed in Table 9. This translates into a 14.93% (95% CI: 13.29 – 16.57%) crude risk for the remaining symptoms. The majority of adverse events (208 out of 271 reported) were noted in tinnitus and AH groups.

e) Adverse events during placebo rTMS—Of the 67 publications ($n_s = 1275$) in which included a placebo condition, there were 67 out of 1275 subjects that reported adverse events. This equates to a 5.25% (95% CI: 4.03 – 6.47%) crude risk for adverse events in the placebo rTMS condition. The most severe adverse event reported was deterioration of psychological clinical state in 3 patients (64,75), which carries a crude risk of 0.23% (95% CI: 0 – 0.49%). The second most severe adverse event, symptom exacerbation, was reported in two AH studies (13,75; $n_s = 12$, $n_s = 23$). Another report (47) indicated an increase in tinnitus in some patients, but the number of subjects for this adverse event was not quantified. The most common adverse event was headache in 24 out of 1275 patients, equating to a crude risk of 1.88% (95% CI: 1.13 – 2.63%). A single study (114) did not clarify which adverse events corresponded to placebo or real rTMS.

4. Discussion

The published data suggest that rTMS is generally well tolerated in patients with positive sensory symptoms. Seizure, the most serious reported adverse event was rare, occurring only

in three of 1815 subjects: in one during LF rTMS for tinnitus and two during HF rTMS for chronic pain (Table 8; 111,113,122). However that the data for patients experiencing seizure during rTMS are derived from two case reports and one larger treatment trial, and should be interpreted with caution. In particular there is published debate as to whether one of the cases (111), an instance of seizure during LF rTMS in a patient with tinnitus, was indeed seizure or convulsive syncope (147,149). Previous surgical intervention in one patient (122) or concurrent use of antidepressant and anticonvulsant medication in another (113) should also be considered important risk factors for increased seizure risk.

We note that 27 case reports are included in our safety review, of which only eight report the occurrence of unwanted side effects (71,76,89,111,122,136,138,144). This was necessary as two out three instances of seizure in this patient population were reported in case report form. (111,122). The reader should recognize that inclusion of case reports may skew metanalysis results towards a higher proportion of adverse events, and should be interpreted with caution. For instance, three out of 25 reports were published explicitly to describe an adverse event occurrence: either seizure ($n_S = 2$) or increased "passivity" ($n_S = 1$) (111,122,136).

Although statistically sound conclusions cannot be made from these limited data, the likelihood of seizure induction by rTMS in patients with positive sensory symptoms may approximate that of the general population. According to a review of the literature incorporated into the 2009 TMS application guidelines, the risk of seizure in healthy subjects is <1% with either LF rTMS or HF rTMS (44). With the conservative assumption that all three reported instances were indeed seizures induced by rTMS, the crude per subject risk in this group also appears <1% (0.08% (95% CI: 0 – 0.24%) for LF rTMS and 0.25% (95% CI: 0 – 0.59%) for HF rTMS). In contrast, patients with epilepsy have a considerably greater likelihood of seizure induction during rTMS (>1.4%) (14,28). Thus, although alterations in regional cortical excitability may predispose patients with positive sensory symptoms toward seizures, the published data do not support a markedly heightened risk relative to other disease states (44,45,145).

Along similar lines as seizure induction in patients with epilepsy, positive sensory symptom exacerbation is another theoretical adverse effect of rTMS in the studied patient population. As these syndromes are associated with pathologic alterations in regional cortical activity, modulation of cortical excitability induced by rTMS may theoretically alter how the patient perceives his or her symptom. However, here also, the risk of symptom exacerbation appears to be relatively low 1.16% (95% CI: 0.61 – 1.71%). There were several studies in which aggravation of disease state was described, but was not classified as an adverse event (47,89,90,125,128).

It is interesting to point out that in several studies an increase in tinnitus was reported as an adverse event, however its increase was not durable (47,62,89,91,116,117,119,125). In addition, this symptom exacerbation would sometimes be preceded a significant reduction in tinnitus severity (47,62,89,125). In cases reporting dropouts, patients never made it past the two-day increase that was described. It may be that the auditory cortex has an inherent threshold for activation that must be reached before stimulation becomes of therapeutic benefit.

It is worth considering that neurologic rTMS effect may result from an interaction between applied current and ongoing brain activity. Thus, in cases of seizure or symptom exacerbation following rTMS in patients with positive sensory phenomena, state dependent effect of rTMS might be playing an important role (151). In patients with positive sensory phenomena, the targeted cortical may be characterized either by abnormal excitability or

abnormal plasticity, and this will condition the effects of rTMS. Thus, the effects might be opposite, in part due to metaplasticity mechanisms.

Pharmacotherapy is another important confounding factor that can contribute to the likelihood of adverse events during rTMS. While the disease state provides an initial change in the cortical steady state activity, the introduction of drugs either past or present can have a lasting impact on cortical activity and simultaneously alter the effect of rTMS.

Upon examining adverse effects other than seizure or symptom exacerbation, we find that the type and frequency of minor of adverse events are similar to rTMS studies on other neuropsychiatric disorders (54,145,146,148,150). In our review these additional adverse events were reported most often in AH studies, followed by tinnitus and were less frequently observed in neuropathic pain and migraine (with only two VH and fibromyalgia cases published, an absence of reported adverse events is of little statistical value). This may be attributed to distinct pathophysiology of these symptoms. However, discrepancy in the apparent rate of adverse events may also reflect differences in experimental design, symptom surveys, or underreporting of adverse events that are considered less severe than seizure. It is important to highlight that future prospective trials characterizing rTMS safety and tolerability should incorporate detailed questionnaires, which may capture, in greater detail, symptoms other than those relating to the chief complaint. Particularly, among plausible adverse events, loss (or lack thereof) of normal function is not regularly mentioned in rTMS clinical literature, and necessitates inclusion in adverse events records of future trials.

Side effects were more frequent in active stimulation versus the placebo condition, 16.7% to 5.25%. In particular there was no report of seizure with placebo stimulation. However, the range of adverse events was the similar to active stimulation, including aggravation of positive sensory symptoms, but excluding seizure occurrence. The published data are lacking a consistent controlled experimental design, and consistent report reporting of adverse events during sham rTMS.

As rTMS gains acceptance in management of neuropsychiatric symptoms, further studies of its safety will be necessary. The published data to date support that in appropriate circumstances the risk:benefit ratio may favor rTMS use for treatment of symptoms characterized by positive sensory phenomena and likely regional cortical hyperxcitability, but certainly warrants further investigation. It is the suggestion of these authors that all reports include a section indicating presence or lack of adverse events and all pertinent details. In particular, reports of seizure and symptom exacerbation make the case for future studies aimed to characterize the overall safety and tolerability of a treatment paradigm, which has the potential to alter cortical excitability.

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References

1. Kobayashi M, Pascual-Leone A. Transcranial magnetic stimulation in neurology. Lancet Neurol. 2003; 2:145–156. [PubMed: 12849236]
2. Frye RE, Rotenberg A, Ousley M, Pascual-Leone A. Transcranial magnetic stimulation in child neurology: current and future directions. J Child Neurol. 2008; 23:79–96. [PubMed: 18056688]

3. Hallett M. Transcranial magnetic stimulation: a primer. Neuron. 2007; 55:187–199. [PubMed: 17640522]
4. Rossini PM, Rossi S. Transcranial magnetic stimulation: diagnostic, therapeutic, and research potential. Neurology. 2007; 68:484–488. [PubMed: 17296913]
5. Ziemann U, Paulus W, Nitsche MA, et al. Consensus: Motor cortex plasticity protocols. Brain Stimul. 2008; 1:164–182. [PubMed: 20633383]
6. Cazzoli D, Muri RM, Hess CW, Nyffeler T. Horizontal and vertical dimensions of visual extinction: a theta burst stimulation study. Neuroscience. 2009; 164:1609–1614. [PubMed: 19782729]
7. Gangitano M, Mottaghy FM, Pascual-Leone A. Release of premotor activity after repetitive transcranial magnetic stimulation of prefrontal cortex. Soc Neurosci. 2008; 3:289–302. [PubMed: 18979382]
8. Bliss TV, Lomo T. Long-lasting potentiation of synaptic transmission in the dentate area of the anaesthetized rabbit following stimulation of the perforant path. J Physiol. 1973; 232:331–356. [PubMed: 4727084]
9. Dudek SM, Bear MF. Homosynaptic long-term depression in area CA1 of hippocampus and effects of N-methyl-D-aspartate receptor blockade. Proc Natl Acad Sci U S A. 1992; 89:4363–7. [PubMed: 1350090]
10. Kandel ER. The molecular biology of memory storage: a dialogue between genes and synapses. Science. 2001; 294:1030–1038. [PubMed: 11691980]
11. Hodgson RA, Ji Z, Standish S, Boyd-Hodgson TE, Henderson AK, Racine RJ. Training-induced and electrically induced potentiation in the neocortex. Neurobiol Learn Mem. 2005; 83:22–32. [PubMed: 15607685]
12. Huang YZ, Edwards MJ, Rounis E, Bhatia KP, Rothwell JC. Theta burst stimulation of the human motor cortex. Neuron. 2005; 45:201–206. [PubMed: 15664172]
13. Hoffman RE, Hawkins KA, Gueorguieva R, et al. Transcranial magnetic stimulation of left temporoparietal cortex and medication-resistant auditory hallucinations. Arch Gen Psychiatry. 2003; 60:49–56. [PubMed: 12511172]
14. Poulet E, Brunelin J, Bediou B, et al. Slow transcranial magnetic stimulation can rapidly reduce resistant auditory hallucinations in schizophrenia. Biol Psychiatry. 2005; 57:188–191. [PubMed: 15652879]
15. Marcondes RA, Sanchez TG, Kii MA, et al. Repetitive transcranial magnetic stimulation improve tinnitus in normal hearing patients: a double-blind controlled, clinical and neuroimaging outcome study. Eur J Neurol. 2009
16. Fregni F, Potvin K, Dasilva D, et al. Clinical effects and brain metabolic correlates in non-invasive cortical neuromodulation for visceral pain. Eur J Pain. 2011; 15:53–60. [PubMed: 20822942]
17. Passard A, Attal N, Benadhira R, et al. Effects of unilateral repetitive transcranial magnetic stimulation of the motor cortex on chronic widespread pain in fibromyalgia. Brain. 2007; 130:2661–2670. [PubMed: 17872930]
18. Fregni F, Otachi PT, Do Valle A, et al. A randomized clinical trial of repetitive transcranial magnetic stimulation in patients with refractory epilepsy. Ann Neurol. 2006; 60:447–455. [PubMed: 17068786]
19. Rotenberg A, Bae EH, Takeoka M, Tormos JM, Schachter SC, Pascual-Leone A. Repetitive transcranial magnetic stimulation in the treatment of epilepsia partialis continua. Epilepsy Behav. 2009; 14:253–257. [PubMed: 18832045]
20. Theodore WH, Hunter K, Chen R, et al. Transcranial magnetic stimulation for the treatment of seizures: a controlled study. Neurology. 2002; 59:560–562. [PubMed: 12196649]
21. Cantello R, Rossi S, Varrasi C, et al. Slow repetitive TMS for drug-resistant epilepsy: clinical and EEG findings of a placebo-controlled trial. Epilepsia. 2007; 48:366–374. [PubMed: 17295632]
22. Kazui H, Ishii R, Yoshida T, et al. Neuroimaging studies in patients with Charles Bonnet Syndrome. Psychogeriatrics. 2009; 9:77–84. [PubMed: 19604330]
23. Lanting CP, de Kleine E, van Dijk P. Neural activity underlying tinnitus generation: results from PET and fMRI. Hear Res. 2009; 255:1–13. [PubMed: 19545617]

24. Marti-Bonmati L, Lull JJ, Garcia-Marti G, et al. Chronic auditory hallucinations in schizophrenic patients: MR analysis of the coincidence between functional and morphologic abnormalities. Radiology. 2007; 244:549–556. [PubMed: 17641373]
25. Moisset X, Bouhassira D. Brain imaging of neuropathic pain. Neuroimage. 2007; 37 (Suppl 1):S80–88. [PubMed: 17512757]
26. Stephane M, Hagen MC, Lee JT, et al. About the mechanisms of auditory verbal hallucinations: a positron emission tomographic study. J Psychiatry Neurosci. 2006; 31:396–405. [PubMed: 17136217]
27. Dornhoffer JL, Mennemeier M. Transcranial magnetic stimulation and tinnitus: implications for theory and practice. J Neurol Neurosurg Psychiatry. 2007; 78:113. [PubMed: 17229742]
28. Oertel V, Rotarska-Jagiela A, van de Ven VG, Haenschel C, Maurer K, Linden DE. Visual hallucinations in schizophrenia investigated with functional magnetic resonance imaging. Psychiatry Res. 2007; 156:269–273. [PubMed: 17976960]
29. Pirotte B, Voordecker P, Neugroschl C, et al. Combination of functional magnetic resonance imaging-guided neuronavigation and intraoperative cortical brain mapping improves targeting of motor cortex stimulation in neuropathic pain. Neurosurgery. 2005; 56:344–359. discussion 344–359. [PubMed: 15794831]
30. Fontaine D, Hamani C, Lozano A. Efficacy and safety of motor cortex stimulation for chronic neuropathic pain: critical review of the literature. J Neurosurg. 2009; 110:251–256. [PubMed: 18991496]
31. Dunckley P, Aziz Q, Wise RG, Brooks J, Tracey I, Chang L. Attentional modulation of visceral and somatic pain. Neurogastroenterol Motil. 2007; 19:569–577. [PubMed: 17593138]
32. Patrizi F, Freedman SD, Pascual-Leone A, Fregni F. Novel therapeutic approaches to the treatment of chronic abdominal visceral pain. ScientificWorldJournal. 2006; 6:472–490. [PubMed: 16633700]
33. Afridi SK, Goadsby PJ. Neuroimaging of migraine. Curr Pain Headache Rep. 2006; 10:221–224. [PubMed: 18778577]
34. Chiapparini L, Ferraro S, Grazzi L, Bussone G. Neuroimaging in chronic migraine. Neurol Sci. 2010; 31 (Suppl 1):S19–22. [PubMed: 20464577]
35. Clauw DJ. Fibromyalgia: an overview. Am J Med. 2009; 122:S3–S13. [PubMed: 19962494]
36. Cutrer FM. Pathophysiology of migraine. Semin Neurol. 2010; 30:120–130. [PubMed: 20352582]
37. Menon GJ, Rahman I, Menon SJ, Dutton GN. Complex visual hallucinations in the visually impaired: the Charles Bonnet Syndrome. Surv Ophthalmol. 2003; 48:58–72. [PubMed: 12559327]
38. Roberts LE, Eggermont JJ, Caspary DM, Shore SE, Melcher JR, Kaltenbach JA. Ringing ears: the neuroscience of tinnitus. J Neurosci. 2010; 30:14972–14979. [PubMed: 21068300]
39. Weeks SR, Anderson-Barnes VC, Tsao JW. Phantom limb pain: theories and therapies. Neurologist. 2010; 16:277–286. [PubMed: 20827116]
40. Latremoliere A, Woolf CJ. Central sensitization: a generator of pain hypersensitivity by central neural plasticity. J Pain. 2009; 10:895–926. [PubMed: 19712899]
41. Merabet LB, Kobayashi M, Barton J, Pascual-Leone A. Suppression of complex visual hallucinatory experiences by occipital transcranial magnetic stimulation: a case report. Neurocase. 2003; 9:436–440. [PubMed: 14972758]
42. Brighina F, Piazza A, Vitello G, et al. rTMS of the prefrontal cortex in the treatment of chronic migraine: a pilot study. J Neurol Sci. 2004; 227:67–71. [PubMed: 15546593]
43. Rollnik JD, Wustefeld S, Dauper J, et al. Repetitive transcranial magnetic stimulation for the treatment of chronic pain - a pilot study. Eur Neurol. 2002; 48:6–10. [PubMed: 12138303]
44. Rossi S, Hallett M, Rossini PM, Pascual-Leone A. Safety of TMSCG. Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. Clin Neurophysiol. 2009; 120:2008–2039. [PubMed: 19833552]
45. Machii K, Cohen D, Ramos-Estebanez C, Pascual-Leone A. Safety of rTMS to non-motor cortical areas in healthy participants and patients. Clin Neurophysiol. 2006; 117:455–471. [PubMed: 16387549]

46. Bae EH, Schrader LM, Machii K, et al. Safety and tolerability of repetitive transcranial magnetic stimulation in patients with epilepsy: a review of the literature. Epilepsy Behav. 2007; 10:521–528. [PubMed: 17493877]
47. Anders M, Dvorakova J, Rathova L, et al. Efficacy of repetitive transcranial magnetic stimulation for the treatment of refractory chronic tinnitus: a randomized, placebo controlled study. Neuro Endocrinol Lett. 2010; 31:238–249. [PubMed: 20424590]
48. Andre-Obadia N, Mertens P, Gueguen A, Peyron R, Garcia-Larrea L. Pain relief by rTMS: differential effect of current flow but no specific action on pain subtypes. Neurology. 2008; 71:833–840. [PubMed: 18779511]
49. Andre-Obadia N, Peyron R, Mertens P, Mauguiere F, Laurent B, Garcia-Larrea L. Transcranial magnetic stimulation for pain control. Double-blind study of different frequencies against placebo, and correlation with motor cortex stimulation efficacy. Clin Neurophysiol. 2006; 117:1536–1544. [PubMed: 16753335]
50. Bagati D, Nizamie SH, Prakash R. Effect of augmentatory repetitive transcranial magnetic stimulation on auditory hallucinations in schizophrenia: randomized controlled study. Aust N Z J Psychiatry. 2009; 43:386–392. [PubMed: 19296295]
51. Borckardt JJ, Smith AR, Reeves ST, et al. A pilot study investigating the effects of fast left prefrontal rTMS on chronic neuropathic pain. Pain Med. 2009; 10:840–849. [PubMed: 19594842]
52. Carretero B, Martin MJ, Juan A, et al. Low-frequency transcranial magnetic stimulation in patients with fibromyalgia and major depression. Pain Med. 2009; 10:748–753. [PubMed: 19460131]
53. Chibbaro G, Daniele M, Alagona G, et al. Repetitive transcranial magnetic stimulation in schizophrenic patients reporting auditory hallucinations. Neurosci Lett. 2005; 383:54–57. [PubMed: 15936511]
54. Clarke BM, Upton AR, Kamath MV, Al-Harbi T, Castellanos CM. Transcranial magnetic stimulation for migraine: clinical effects. J Headache Pain. 2006; 7:341–346. [PubMed: 17058041]
55. Cosentino G, Giglia G, Palermo A, et al. A case of post-traumatic complex auditory hallucinosis treated with rTMS. Neurocase. 2010; 16:267–272. [PubMed: 20104391]
56. d'Alfonso AA, Aleman A, Kessels RP, et al. Transcranial magnetic stimulation of left auditory cortex in patients with schizophrenia: effects on hallucinations and neurocognition. J Neuropsychiatry Clin Neurosci. 2002; 14:77–79. [PubMed: 11884659]
57. de Jesus DR, Gil A, Barbosa L, et al. A pilot double-blind sham-controlled trial of repetitive transcranial magnetic stimulation for patients with refractory schizophrenia treated with clozapine. Psychiatry Res. 2010
58. De Ridder D, van der Loo E, Van der Kelen K, Menovsky T, van de Heyning P, Moller A. Theta, alpha and beta burst transcranial magnetic stimulation: brain modulation in tinnitus. Int J Med Sci. 2007; 4:237–241. [PubMed: 17952199]
59. De Ridder D, Verstraeten E, Van der Kelen K, et al. Transcranial magnetic stimulation for tinnitus: influence of tinnitus duration on stimulation parameter choice and maximal tinnitus suppression. Otol Neurotol. 2005; 26:616–619. [PubMed: 16015156]
60. Dollfus S, Larmurier-Montagne A, Razafimandimby A, et al. Treatment of auditory hallucinations by combining high-frequency repetitive transcranial magnetic stimulation and functional magnetic resonance imaging. Schizophr Res. 2008; 102:348–351. [PubMed: 18501564]
61. Eberle MC, Wildgruber D, Wasserka B, Fallgatter AJ, Plewnia C. Relief from chronic intractable auditory hallucinations after long-term bilateral theta burst stimulation. Am J Psychiatry. 2010; 167:1410. [PubMed: 21041260]
62. Eichhammer P, Langguth B, Marienhagen J, Kleinjung T, Hajak G. Neuronavigated repetitive transcranial magnetic stimulation in patients with tinnitus: a short case series. Biol Psychiatry. 2003; 54:862–865. [PubMed: 14550687]
63. Favalli G, Gil A, Lobato MI, Marcolin MA, Belmonte-de-Abreu P. Repeated transcranial magnetic stimulation effect over treatment-resistant auditory hallucinations in a female patient with schizophrenia. Rev Bras Psiquiatr. 2007; 29:291–292. [PubMed: 17891262]
64. Fitzgerald PB, Benitez J, Daskalakis JZ, et al. A double-blind sham-controlled trial of repetitive transcranial magnetic stimulation in the treatment of refractory auditory hallucinations. J Clin Psychopharmacol. 2005; 25:358–362. [PubMed: 16012279]

65. Fitzgerald PB, Benitez J, Daskalakis JZ, De Castella A, Kulkarni J. The treatment of recurring auditory hallucinations in schizophrenia with rTMS. World J Biol Psychiatry. 2006; 7:119–122. [PubMed: 16684685]
66. Fitzgerald PB, Sritharan A, Benitez J, et al. A preliminary fMRI study of the effects on cortical activation of the treatment of refractory auditory hallucinations with rTMS. Psychiatry Res. 2007; 155:83–88. [PubMed: 17398078]
67. Folmer RL, Carroll JR, Rahim A, Shi Y, Hal Martin W. Effects of repetitive transcranial magnetic stimulation (rTMS) on chronic tinnitus. Acta Otolaryngol Suppl. 2006:96–101. [PubMed: 17114152]
68. Frank E, Landgrebe M, Kleinjung T, Hajak G, Langguth B. Burst transcranial magnetic stimulation for the treatment of tinnitus. CNS Spectr. 2010; 15:536–537. [PubMed: 20703200]
69. Fregni F, DaSilva D, Potvin K, et al. Treatment of chronic visceral pain with brain stimulation. Ann Neurol. 2005; 58:971–972. [PubMed: 16315281]
70. Fregni F, Marcondes R, Boggio PS, et al. Transient tinnitus suppression induced by repetitive transcranial magnetic stimulation and transcranial direct current stimulation. Eur J Neurol. 2006; 13:996–1001. [PubMed: 16930367]
71. Garcia-Toro M, Vazquez MJ, Quevedo BC, Martinez MC, Beltran TJ, Herrera BM. Transcranial magnetic stimulation, tinnitus and auditory hallucinations. Actas Esp Psiquiatr. 2009; 37:54–56. [PubMed: 19267269]
72. Hirayama A, Saitoh Y, Kishima H, et al. Reduction of intractable deafferentation pain by navigation-guided repetitive transcranial magnetic stimulation of the primary motor cortex. Pain. 2006; 122:22–27. [PubMed: 16495011]
73. Hoffman RE, Boutros NN, Berman RM, et al. Transcranial magnetic stimulation of left temporoparietal cortex in three patients reporting hallucinated “voices”. Biol Psychiatry. 1999; 46:130–132. [PubMed: 10394483]
74. Hoffman RE, Boutros NN, Hu S, Berman RM, Krystal JH, Charney DS. Transcranial magnetic stimulation and auditory hallucinations in schizophrenia. Lancet. 2000; 355:1073–1075. [PubMed: 10744097]
75. Hoffman RE, Gueorguieva R, Hawkins KA, Varanko M, Boutros NN, Wu YT. Temporoparietal transcranial magnetic stimulation for auditory hallucinations: safety, efficacy and moderators in a fifty patient sample. Biol Psychiatry. 2005; 58:97–104. [PubMed: 15936729]
76. Hong N, Jung MH, Seok JH, Hong HJ, Jon DI. Effects of repetitive transcranial magnetic stimulation on late-onset hallucinations: A case report. Prog Neuropsychopharmacol Biol Psychiatry. 2010
77. Horacek J, Brunovsky M, Novak T, et al. Effect of low-frequency rTMS on electromagnetic tomography (LORETA) and regional brain metabolism (PET) in schizophrenia patients with auditory hallucinations. Neuropsychobiology. 2007; 55:132–142. [PubMed: 17641545]
78. Jandl M, Steyer J, Weber M, et al. Treating auditory hallucinations by transcranial magnetic stimulation: a randomized controlled cross-over trial. Neuropsychobiology. 2006; 53:63–69. [PubMed: 16511336]
79. Kang BS, Shin HI, Bang MS. Effect of repetitive transcranial magnetic stimulation over the hand motor cortical area on central pain after spinal cord injury. Arch Phys Med Rehabil. 2009; 90:1766–1771. [PubMed: 19801069]
80. Khedr EM, Kotb H, Kamel NF, Ahmed MA, Sadek R, Rothwell JC. Longlasting antalgic effects of daily sessions of repetitive transcranial magnetic stimulation in central and peripheral neuropathic pain. J Neurol Neurosurg Psychiatry. 2005; 76:833–838. [PubMed: 15897507]
81. Khedr EM, Rothwell JC, Ahmed MA, El-Atar A. Effect of daily repetitive transcranial magnetic stimulation for treatment of tinnitus: comparison of different stimulus frequencies. J Neurol Neurosurg Psychiatry. 2008; 79:212–215. [PubMed: 18202212]
82. Khedr EM, Abo-Elfetoh N, Rothwell JC, El-Atar A, Sayed E, Khalifa H. Contralateral versus ipsilateral rTMS of temporoparietal cortex for the treatment of chronic unilateral tinnitus: comparative study. Eur J Neurol. 2010; 17:976–983. [PubMed: 20236173]

83. Kleinjung T, Eichhammer P, Landgrebe M, et al. Combined temporal and prefrontal transcranial magnetic stimulation for tinnitus treatment: a pilot study. Otolaryngol Head Neck Surg. 2008; 138:497–501. [PubMed: 18359361]
84. Kleinjung T, Eichhammer P, Langguth B, et al. Long-term effects of repetitive transcranial magnetic stimulation (rTMS) in patients with chronic tinnitus. Otolaryngol Head Neck Surg. 2005; 132:566–569. [PubMed: 15806046]
85. Kleinjung T, Steffens T, Sand P, et al. Which tinnitus patients benefit from transcranial magnetic stimulation? Otolaryngol Head Neck Surg. 2007; 137:589–595. [PubMed: 17903575]
86. Kleinjung T, Steffens T, Landgrebe M, et al. Levodopa does not enhance the effect of low-frequency repetitive transcranial magnetic stimulation in tinnitus treatment. Otolaryngol Head Neck Surg. 2009; 140:92–95. [PubMed: 19130969]
87. Lai IC, Yang CC, Kuo TB, Shieh KR. Transcranial magnetic stimulation for auditory hallucination in severe schizophrenia: partial efficacy and acute elevation of sympathetic modulation. Psychiatry Clin Neurosci. 2010; 64:333–335. [PubMed: 20408989]
88. Landgrebe M, Binder H, Koller M, et al. Design of a placebo-controlled, randomized study of the efficacy of repetitive transcranial magnetic stimulation for the treatment of chronic tinnitus. BMC Psychiatry. 2008; 8:23. [PubMed: 18412944]
89. Langguth B, Eichhammer P, Wiegand R, et al. Neuronavigated rTMS in a patient with chronic tinnitus. Effects of 4 weeks treatment. Neuroreport. 2003; 14:977–980. [PubMed: 12802186]
90. Langguth B, Eichhammer P, Zowe M, Marienhagen J, Spiessl H, Hajak G. Neuronavigated transcranial magnetic stimulation and auditory hallucinations in a schizophrenic patient: monitoring of neurobiological effects. Schizophr Res. 2006; 84:185–186. [PubMed: 16624530]
91. Langguth B, Zowe M, Landgrebe M, et al. Transcranial magnetic stimulation for the treatment of tinnitus: a new coil positioning method and first results. Brain Topogr. 2006; 18:241–247. [PubMed: 16845596]
92. Lee SH, Kim W, Chung YC, et al. A double blind study showing that two weeks of daily repetitive TMS over the left or right temporoparietal cortex reduces symptoms in patients with schizophrenia who are having treatment-refractory auditory hallucinations. Neurosci Lett. 2005; 376:177–181. [PubMed: 15721217]
93. Lee SL, Abraham M, Cacace AT, Silver SM. Repetitive transcranial magnetic stimulation in veterans with debilitating tinnitus: a pilot study. Otolaryngol Head Neck Surg. 2008; 138:398–399. [PubMed: 18312892]
94. Lefaucheur JP, Drouot X, Keravel Y, Nguyen JP. Pain relief induced by repetitive transcranial magnetic stimulation of precentral cortex. Neuroreport. 2001; 12:2963–2965. [PubMed: 11588611]
95. Lefaucheur JP, Drouot X, Menard-Lefaucheur I, et al. Neurogenic pain relief by repetitive transcranial magnetic cortical stimulation depends on the origin and the site of pain. J Neurol Neurosurg Psychiatry. 2004; 75:612–616. [PubMed: 15026508]
96. Lefaucheur JP, Drouot X, Nguyen JP. Interventional neurophysiology for pain control: duration of pain relief following repetitive transcranial magnetic stimulation of the motor cortex. Neurophysiol Clin. 2001; 31:247–252. [PubMed: 11601430]
97. Lefaucheur JP, Hatem S, Nineb A, et al. Somatotopic organization of the analgesic effects of motor cortex rTMS in neuropathic pain. Neurology. 2006; 67:1998–2004. [PubMed: 17159107]
98. Lipton RB, Dodick DW, Silberstein SD, et al. Single-pulse transcranial magnetic stimulation for acute treatment of migraine with aura: a randomised, double-blind, parallel-group, sham-controlled trial. Lancet Neurol. 2010; 9:373–380. [PubMed: 20206581]
99. Londero A, Lefaucheur JP, Malinvaud D, et al. Magnetic stimulation of the auditory cortex for disabling tinnitus: preliminary results. Presse Med. 2006; 35:200–206. [PubMed: 16493347]
100. Loo CK, Sainsbury K, Mitchell P, Hadzi-Pavlovic D, Sachdev PS. A sham-controlled trial of left and right temporal rTMS for the treatment of auditory hallucinations. Psychol Med. 2010; 40:541–546. [PubMed: 19656432]
101. Lorenz I, Muller N, Schlee W, Langguth B, Weisz N. Short-term effects of single repetitive TMS sessions on auditory evoked activity in patients with chronic tinnitus. J Neurophysiol. 2010; 104:1497–1505. [PubMed: 20592125]

102. Marcondes RA, Sanchez TG, Kii MA, et al. Repetitive transcranial magnetic stimulation improve tinnitus in normal hearing patients: a double-blind controlled, clinical and neuroimaging outcome study. Eur J Neurol. 2010; 17:38–44. [PubMed: 19614962]
103. McIntosh AM, Semple D, Tasker K, et al. Transcranial magnetic stimulation for auditory hallucinations in schizophrenia. Psychiatry Res. 2004; 127:9–17. [PubMed: 15261700]
104. Meeus O, Blaivie C, Ost J, De Ridder D, Van de Heyning P. Influence of tonic and burst transcranial magnetic stimulation characteristics on acute inhibition of subjective tinnitus. Otol Neurotol. 2009; 30:697–703. [PubMed: 19623097]
105. Mennemeier M, Chelette KC, Myhill J, et al. Maintenance repetitive transcranial magnetic stimulation can inhibit the return of tinnitus. Laryngoscope. 2008; 118:1228–1232. [PubMed: 18475211]
106. Mennemeier M, Chelette KC, Allen S, et al. Variable changes in PET activity before and after rTMS treatment for tinnitus. Laryngoscope. 2011; 121:815–822. [PubMed: 21287564]
107. Meppelink AM, de Jong BM, van der Hoeven JH, van Laar T. Lasting visual hallucinations in visual deprivation; fMRI correlates and the influence of rTMS. J Neurol Neurosurg Psychiatry. 2010; 81:1295–1296. [PubMed: 20547615]
108. Mhalla A, Baudic S, de Andrade DC, et al. Long-term maintenance of the analgesic effects of transcranial magnetic stimulation in fibromyalgia. Pain. 2011
109. Minami SB, Shinden S, Okamoto Y, et al. Repetitive transcranial magnetic stimulation (rTMS) for treatment of chronic tinnitus. Auris Nasus Larynx. 2010
110. Montagne-Larmurier A, Etard O, Razafimandimby A, Morello R, Dollfus S. Two-day treatment of auditory hallucinations by high frequency rTMS guided by cerebral imaging: a 6 month follow-up pilot study. Schizophr Res. 2009; 113:77–83. [PubMed: 19505799]
111. Nowak DA, Hoffmann U, Connemann BJ, Schonfeldt-Lecuona C. Epileptic seizure following 1 Hz repetitive transcranial magnetic stimulation. Clin Neurophysiol. 2006a; 117:1631–1633. [PubMed: 16679059]
112. O'Reardon JP, Fontecha JF, Cristancho MA, Newman S. Unexpected reduction in migraine and psychogenic headaches following rTMS treatment for major depression: a report of two cases. CNS Spectr. 2007; 12:921–925. [PubMed: 18163038]
113. Picarelli H, Teixeira MJ, de Andrade DC, et al. Repetitive Transcranial Magnetic Stimulation Is Efficacious as an Add-On to Pharmacological Therapy in Complex Regional Pain Syndrome (CRPS) Type I. J Pain. 2010; 11:1203–1210. [PubMed: 20430702]
114. Piccirillo JF, Garcia KS, Nicklaus J, et al. Low-frequency repetitive transcranial magnetic stimulation to the temporoparietal junction for tinnitus. Arch Otolaryngol Head Neck Surg. 2011; 137:221–228. [PubMed: 21422304]
115. Pleger B, Janssen F, Schwenkreis P, Volker B, Maier C, Tegenthoff M. Repetitive transcranial magnetic stimulation of the motor cortex attenuates pain perception in complex regional pain syndrome type I. Neurosci Lett. 2004; 356:87–90. [PubMed: 14746870]
116. Plewnia C, Bartels M, Gerloff C. Transient suppression of tinnitus by transcranial magnetic stimulation. Ann Neurol. 2003; 53:263–266. [PubMed: 12557296]
117. Plewnia C, Reimold M, Najib A, et al. Dose-dependent attenuation of auditory phantom perception (tinnitus) by PET-guided repetitive transcranial magnetic stimulation. Hum Brain Mapp. 2007; 28:238–246. [PubMed: 16773635]
118. Plewnia C, Reimold M, Najib A, Reischl G, Plontke SK, Gerloff C. Moderate therapeutic efficacy of positron emission tomography-navigated repetitive transcranial magnetic stimulation for chronic tinnitus: a randomised, controlled pilot study. J Neurol Neurosurg Psychiatry. 2007; 78:152–156. [PubMed: 16891384]
119. Poreisz C, Paulus W, Moser T, Lang N. Does a single session of theta-burst transcranial magnetic stimulation of inferior temporal cortex affect tinnitus perception? BMC Neurosci. 2009; 10:54. [PubMed: 19480651]
120. Poulet E, Brunelin J, Kallel L, et al. Is rTMS efficient as a maintenance treatment for auditory verbal hallucinations? A case report. Schizophr Res. 2006; 84:183–184. [PubMed: 16580181]
121. Richter GT, Mennemeier M, Bartel T, et al. Repetitive transcranial magnetic stimulation for tinnitus: a case study. Laryngoscope. 2006; 116:1867–1872. [PubMed: 17016213]

122. Rosa MA, Picarelli H, Teixeira MJ, Rosa MO, Marcolin MA. Accidental seizure with repetitive transcranial magnetic stimulation. J ECT. 2006; 22:265–266. [PubMed: 17143158]
123. Rosa MO, Gattaz WF, Rosa MA, et al. Effects of repetitive transcranial magnetic stimulation on auditory hallucinations refractory to clozapine. J Clin Psychiatry. 2007; 68:1528–1532. [PubMed: 17960967]
124. Rosenberg O, Roth Y, Kotler M, Zangen A, Dannon P. Deep transcranial magnetic stimulation for the treatment of auditory hallucinations: a preliminary open-label study. Ann Gen Psychiatry. 2011; 10:3. [PubMed: 21303566]
125. Rossi S, De Capua A, Ulivelli M, et al. Effects of repetitive transcranial magnetic stimulation on chronic tinnitus: a randomised, crossover, double blind, placebo controlled study. J Neurol Neurosurg Psychiatry. 2007; 78:857–863. [PubMed: 17314192]
126. Saitoh Y, Hirayama A, Kishima H, et al. Reduction of intractable deafferentation pain due to spinal cord or peripheral lesion by high-frequency repetitive transcranial magnetic stimulation of the primary motor cortex. J Neurosurg. 2007; 107:555–559. [PubMed: 17886555]
127. Sampson SM, Rome JD, Rummans TA. Slow-frequency rTMS reduces fibromyalgia pain. Pain Med. 2006; 7:115–118. [PubMed: 16634724]
128. Sampson SM, Kung S, McAlpine DE, Sandroni P. The use of slow-frequency prefrontal repetitive transcranial magnetic stimulation in refractory neuropathic pain. J ECT. 2011; 27:33–37. [PubMed: 21336050]
129. Schonfeldt-Lecuona C, Gron G, Walter H, et al. Stereotaxic rTMS for the treatment of auditory hallucinations in schizophrenia. Neuroreport. 2004; 15:1669–1673. [PubMed: 15232304]
130. Schreiber S, Dannon PN, Goshen E, Amiaz R, Zwas TS, Grunhaus L. Right prefrontal rTMS treatment for refractory auditory command hallucinations - a neuroSPECT assisted case study. Psychiatry Res. 2002; 116:113–117. [PubMed: 12426038]
131. Slotema CW, Blom JD, de Weijer AD, et al. Can Low-Frequency Repetitive Transcranial Magnetic Stimulation Really Relieve Medication-Resistant Auditory Verbal Hallucinations? Negative Results from a Large Randomized Controlled Trial. Biol Psychiatry. 2010
132. Smith JA, Mennemeier M, Bartel T, et al. Repetitive transcranial magnetic stimulation for tinnitus: a pilot study. Laryngoscope. 2007; 117:529–534. [PubMed: 17334317]
133. Soekadar SR, Arfeller C, Rilk A, Plontke SK, Plewnia C. Theta burst stimulation in the treatment of incapacitating tinnitus accompanied by severe depression. CNS Spectr. 2009; 14:208–211. [PubMed: 19407732]
134. Sommer IE, de Weijer AD, Daalman K, et al. Can fMRI-guidance improve the efficacy of rTMS treatment for auditory verbal hallucinations? Schizophr Res. 2007; 93:406–408. [PubMed: 17478084]
135. Sperling W, Kornhuber J, Biermann T. Bilateral Temporal 1 Hz rTMS (Repetitive Transcranial Magnetic Stimulation) Treatment in a Left-Handed Patient with Imperative Auditory Hallucinations. Pharmacopsychiatry. 2010 [Epub ahead of print].
136. Subramanian P, Burhan A. Worsening of “passivity” symptoms with low-frequency bilateral temporo-parietal repetitive transcranial magnetic stimulation used to treat refractory auditory hallucinations: a case report. Schizophr Res. 2010; 116:291–292. [PubMed: 19926454]
137. Teepker M, Hotzel J, Timmesfeld N, et al. Low-frequency rTMS of the vertex in the prophylactic treatment of migraine. Cephalalgia. 2009; 30:137–144. [PubMed: 19515124]
138. Thirthalli J, Bharadwaj B, Kulkarni S, Gangadhar BN, Kharawala S, Andrade C. Successful use of maintenance rTMS for 8 months in a patient with antipsychotic-refractory auditory hallucinations. Schizophr Res. 2008; 100:351–352. [PubMed: 18252271]
139. Topper R, Foltys H, Meister IG, Sparing R, Boroojerdi B. Repetitive transcranial magnetic stimulation of the parietal cortex transiently ameliorates phantom limb pain-like syndrome. Clin Neurophysiol. 2003; 114:1521–1530. [PubMed: 12888036]
140. Vanneste S, Plazier M, van der Loo E, Ost J, Van de Heyning P, De Ridder D. Burst transcranial magnetic stimulation: which tinnitus characteristics influence the amount of transient tinnitus suppression? Eur J Neurol. 2010; 17:1141–1147. [PubMed: 20374277]

141. Vanneste S, Plazier M, Van de Heyning P, De Ridder D. Repetitive transcranial magnetic stimulation frequency dependent tinnitus improvement by double cone coil prefrontal stimulation. J Neurol Neurosurg Psychiatry. 2011

142. Vercammen A, Knegtering H, Bruggeman R, et al. Effects of bilateral repetitive transcranial magnetic stimulation on treatment resistant auditory-verbal hallucinations in schizophrenia: a randomized controlled trial. Schizophr Res. 2009; 114:172–179. [PubMed: 19679450]

143. Vercammen A, Knegtering H, Liemburg EJ, den Boer JA, Aleman A. Functional connectivity of the temporo-parietal region in schizophrenia: effects of rTMS treatment of auditory hallucinations. J Psychiatr Res. 2010; 44:725–731. [PubMed: 20189190]

144. Zaghi S, DaSilva AF, Acar M, Lopes M, Fregni F. One-year rTMS treatment for refractory trigeminal neuralgia. J Pain Symptom Manage. 2009; 38:e1–5. [PubMed: 19713068]

145. Avery DH, Isenberg KE, Sampson SM, et al. Transcranial magnetic stimulation in the acute treatment of major depressive disorder: clinical response in an open-label extension trial. J Clin Psychiatry. 2008; 69:441–451. [PubMed: 18294022]

146. Cohen H, Kaplan Z, Kotler M, Kouperman I, Moisa R, Grisaru N. Repetitive transcranial magnetic stimulation of the right dorsolateral prefrontal cortex in posttraumatic stress disorder: a double-blind, placebo-controlled study. Am J Psychiatry. 2004; 161:515–524. [PubMed: 14992978]

147. Epstein CM. Seizure or convulsive syncope during 1-Hz rTMS? Clin Neurophys. 2006; 117:2566–2568.

148. Lisanby SH, Husain MM, Rosenquist PB, et al. Daily left prefrontal repetitive transcranial magnetic stimulation in the acute treatment of major depression: clinical predictors of outcome in a multisite, randomized controlled clinical trial. Neuropsychopharmacology. 2009; 34:522–534. [PubMed: 18704101]

149. Nowak DA, Hoffmann U, Connemann BJ, Schonfeldt-Lecuona C. Reply to “Seizure or convulsive syncope during 1-Hz rTMS?”. Clin Neurophys. 2006b; 117:2566–2568.

150. Osuch EA, Benson BE, Luckenbaugh DA, Geraci M, Post RM, McCann U. Repetitive TMS combined with exposure therapy for PTSD: a preliminary study. J Anxiety Disord. 2009; 23:54–59. [PubMed: 18455908]

151. Silvanto J, Pascual-Leone A. State dependency of transcranial magnetic stimulation. Brain Topogr. 2008; 21:1–10. [PubMed: 18791818]

Table 1

Literature review summary of auditory hallucinations (AH) treatment or investigation by rTMS

All studies used a Figure of 8 TMS coil except for Loo et al (2009), which used a circular coil and Rosenberg et al (2011), which used an H-coil. AC, auditory cortex; AH, auditory hallucinations; AHRS, auditory hallucination rating scale; AVH, auditory visual hallucinations; BPRS, 18-item brief psychiatric rating scale; CGI, clinical global impression scale; cTBS, continuous theta burst (3 50Hz pulses at 5Hz); D, diagnostic; DVR, daily voices ratings questionnaire; fMRI, functional magnetic resonance imaging; HCS, hallucination change scale; ITI, intertrain interval; LORETA, low-resolution brain electromagnetic tomography; LTC, left tempoparietal cortex; MRI; magnetic resonance imaging; MT, motor threshold; NR, not reported; PANAS, positive and negative affect scale; PANNS (H), positive and negative syndrome scale hallucinations subscale; PET, positron emission tomography; PSYRATS (AH), pyschotic symptom ratings scale auditory hallucinations subscale; QLS, quality of life scale; RMT, resting motor threshold; SPECT, single photon emission computed tomography; STG, superior temporal gyrus; RTC, right tempoparietal cortex; rTMS, repetitive transcranial magnetic stimulation; SAH, scale for assessment of auditory hallucinations; SANS, scale for assessment of negative symptoms; SAPS, scale for assessment of positive symptoms; t, therapeutic; TPJ, tempo-parietal junction; VAS, analog scale of auditory hallucinations

Author (Year)	# of Subjects (Age Range)	Drug Therapy *details*	rTMS Protocol [Therapeutic or Diagnostic]	Coil Position	MRI Navigation	Sham Method	Adverse Events *details*	AH Outcome Measure	# Responders (% total) *comments*
Hoffman RE, et al. (1999)	3 (30–54)	Yes *Maintained medication with no change in dose (antipsychotic)*	[LF] 4 days/week × 2 weeks of (1 Hz × 4min (Day 1), 8min (Day 2), 12min (Day 3), 16min (Day 4)) = 240–960 pulses/day @ 80% MT [T]	Halfway between T3 and P3 based on 10–20 EEG system	No	Coil tilted 45° from the skull	None	Individualized composite score	3 (100%)
Hoffman RE, et al. (2000)	12 (32–50)	Yes *Maintained medication with no change in dose (anticonvulsant, antipsychotic)*	[LF] 4 days/week × 2 weeks of (1 Hz × 4min (Day 1), 8min (Day 2), 12min (Day 3), 16min (Day 4)) = 240–960 pulses/day @ 80% MT [T]	Halfway between T3 and P3 based on 10–20 EEG system	No	Coil tilted 45° from the skull	Headache (n = 2)	Individualized composite score	NR *Symptom improvements relative to baseline were significant for 12 and 16min stimulation.*
d'Alfonso AA, et al. (2002)	9 (19–43)	Yes *Maintained medication with no change in dose (antipsychotic)*	[LF] 8 days of (1 Hzx 20min) = 1800 pulses/day @ 80% MT [T]	2cm above T3 based on 10–20 EEG system	No	None	NR	Topography of Voices Rating Scale	NR *Statistically significant effect on hallucination severity ratings. 7 out of 8 patients had severity improvement at week 2.*
Schreiber S, et al. (2002)	1 (49)	Yes *Maintained medication with no change in dose (antipsychotic)*	[LF] 5 days/week × 4 weeks of (20 trains (10 Hz × 6s (w/1 min ITI))) = 1200 pulses/day @ 90% MT [T]	RDLPFC chosen using documentation of right hypofrontality in pre-treatment SPECT	No	None	NR	VAS BPRS PANSS SPECT	0 (0%)
Hoffman RE, et al. (2003)	21 (18–60)	Yes	[LF] 9 days of (1 Hz × 8min (Day 1), 12min (Day 2), 16min (Day	LTC based on 10–20 EEG system	No	Coil tilted 45° from the skull	Headache (n = 6) Lightheaded (n = 4)	AHRS	9 (75%)

Author (Year)	# of Subjects (Age Range)	Drug Therapy *details*	rTMS Protocol [Therapeutic or Diagnostic]	Coil Position	MRI Navigation	Sham Method	Adverse Events *details*	AH Outcome Measure	# Responders (% total) *comments*
		Maintained medication with no change in dose (antipsychotic)	3–9)) = 480–960 pulses/day @ 90% MT [T]				Concentration difficulty (n = 3) Memory difficulty (n = 1) Aggravation of AH (n = 3) Racing thoughts (n = 1) Visual hallucination (n = 1) Ischemic chest pain (n = 1) *Chest pain caused by factors such as smoking, diabetes, and hypertension.*		
Schonefeldt-Lecuona C, et al. (2004)	11 (26–58)	Yes *Maintained medication with no change in dose (antipsychotic)*	[LF] 5 days of (1 Hz × 16 min) =960 pulses/day @ 90% MT [T]	LSTG and Broca's area based on fMRI	Yes	Coil placed over the parieto-occipital transition	*Stimulation over the temporal muscle when targeting superior temporal gyrus or Broca's area was generally reported as uncomfortable.*	Haddock self-rating scale	3(27%)
Lee SH, et al. (2004)	25 (18–60)	NR	[LF] 8 days of (1 Hz × 20min) = 1200 pulses/day @ 100% MT [T]	LTC or RTC based on 10–20 EEG system	No	Coil perpendicular to head	Headache (n = 5) Dizziness (n = 2) Amnesia (n = 1)	AHRS	NR *Significant improvements in frequency of AHs, positive symptoms of PANSS, and CGI-I scores.*
McIntosh AM, et al. (2004)	16 (22–65)	NR	[LF] 4 days/week × 2 weeks of (1 Hz × 4min (Day 1), 8min (Day 2), 12min (Day 3), 16min (Day 4)) w/15s interval between each minute of stimulation = 240–960 pulses/day @ 80% MT [T]	LTC based on 10–20 EEG system	No	Coil tilted 45° from the skull	*Many patients complained of headache during active treatment.*	VAS	NR *No significant effects of TMS on symptom measures were found.*
Chibbaro G, et al. (2005)	8 (21–53)	Yes *Maintained medication with no change in dose (antipsychotic)*	[LF] 4 days out of 8 weeks of (1 Hz × 15min) = 900 pulses/day @ 90% MT [T]	LTC based on 10–20 EEG system	No	Coil tilted 45° from the skull	NR	SAPS SANS SAH	NR *Significant improvement in SAPS, SANS, and SAH scores for real rTMS versus sham.*
Fitzgerald PB, et al. (2005)	17 (16–65)	Yes *Maintained medication with no change in dose (antidepressant, antipsychotic)*	[LF] 8 days of (1 Hz × 15min) w/ 30s break at halfway point = 900 pulses/day @ 90% MT [T]	TP3 marking based on 10–20 EEG system	No	Coil tilted 45° from the skull	None	PSYRATS (AH) PANNS (H)	NR *No clinically significant reduction in loudness of voices.*
Hoffman RE, et al. (2005)	27 (18–60)	Yes *Maintained medication with no change in dose (antipsychotic)*	[LF] 9 days of (1 Hz × 8min (Day 1), 12min (Day 2), 16min (Day 3–9)) = 480–960 pulses/day @ 90% MT	Halfway between T3 and P3 based on 10–20 EEG system	No	Coil tilted45° from the skull	Memory difficulty (n = 2) *Headache, lightheadedness, and concentration difficulty all reported.*	HCS AHRS PANNS (H)	14 (51.9%)

Author (Year)	# of Subjects (Age Range)	Drug Therapy *details*	rTMS Protocol [Therapeutic or Diagnostic]	Coil Position	MRI Navigation	Sham Method	Adverse Events *details*	AH Outcome Measure	# Responders (% total) *comments*
			[T]						
Poulet E, et al. (2005)	10 (25–51)	Yes *Maintained medication with no change in dose (antipsychotic)*	[LF] 15 days of (1 Hz × 33min) = 2000 pulses/day @ 90% MT) [T]	Halfway between T3 and P3 based on 10–20 EEG system	No	Sham Coil	Headache (n = 1)	AHRS	7 (70%) *7 responders at 1-month follow-up; 5 (50%) at 2 month follow-up*
Fitzgerald PB, et al. (2006)	2 (18–47)	Yes *Maintained medication with no change in dose (antipsychotic)*	[LF] 10 days of (1 Hz × 15min) = 900 pulses/day @ 90% RMT [T]	TP3 marking based on 10–20 EEG system	No	None	NR	HCS PANSS	2(100%)
Jandl M, et al. (2006)	16 (19–70)	Yes *Maintained medication with no change in dose (antipsychotic)*	[LF] 15 days of (1 Hz × 15min) = 900 pulses/day @ 100% MT [T]	Left posterior portion of STG, right posterior portion of STG, and midway based on to 10–20 EEG setup	No	Coil midway T4-P4	Headache (n = 1) Clicking noise persistence (n = 1)	PSYRATS (AH)	6 (38%) *5 (31%) with right hemisphere stimulation; 1 (6%) with left hemisphere stimulation*
Langguth B, et al. (2006)	1 (25)	Yes *Maintained medication with no change in dose (antipsychotic)*	[LF] 20 days of (1 Hz × 33min) = 2000 pulses/day @ 110% MT [T]	LTC based on PET/ MRI	Yes	None	NR	AHRS	1 (100%)
Poulet E, et al. (2006)	1 (50)	Yes *Maintained medication with no change in dose (antipsychotic)*	[LF] 10 days of (1 Hz × 16.6min) =1000 pulses/day @ 100% MT followed by: Maintenance with 1 day of (1 Hz × 16.6 min) = 1000 pulses/day @ 100% MT [T]	Halfway between T3 and P3 based on 10–20 EEG system	No	None	NR	AHRS SAPS	1(100%)
Favalli G, et al. (2007)	1 (59)	NR	[LF] 20 days of (1Hz × 20min) = 1200 pulses/day @ 90% MT [T]	Halfway between T3 and P3 based on 10–20 EEG system	No	None	NR	AHS BPRS	1(100%)
Fitzgerald PB, et al. (2007)	3 (23–61)	Yes *Maintained medication with no change in dose (anticonvulsant, antipsychotic)*	[LF] 10 days of (1 Hz × 15min) = 900 pulses/day @ 90% RMT [D]	TP3 marking based on 10–20 EEG system	No	None	NR	PANSS PSYRATS (AH) HCS	3(100%)
Horacek J, et al. (2007)	12 (25–44)	Yes *Maintained medication with no change in dose (antipsychotic)*	[LF] 10 days of (0.9 Hz × 20min) = 1080 pulses/day @ 100% MT [D]	LTC based on 10–20 EEG system	No	None	*Mild Headache*	AHRS HCS PANSS PET LORETA	NR *Significant decrease in Hallucination item and positive PANSS score.*
Rosa MO, et al. (2007)	6 (18–50)	Yes	[LF] 8 days of (1 Hz × 16min) = 960 pulses/day @ 90% MT	LTC based on 10–20 EEG system	No	Sham Coil	Headache (n = 1)	AHRS VAS	NR

Author (Year)	# of Subjects (Age Range)	Drug Therapy *details*	rTMS Protocol [Therapeutic or Diagnostic]	Coil Position	MRI Navigation	Sham Method	Adverse Events *details*	AH Outcome Measure	# Responders (% total) *comments*
		Maintained medication with no change in dose (antipsychotic)	[T]						*Weak reduction in auditory hallucinations.*
Sommer IEC, et al. (2007)	15 (27–45)	Yes *Maintained medication with no change in dose (antipsychotic)*	[LF] 15 days of (1 Hz × 20min) = 1200 pulses/day @ 90% MT) [T]	Based on fMRI data or halfway between T3 and P3 based on 10–20 EEG system	Yes	None	Increased Anxiety/Suspicion (n = 2)	AHRS PANSS	NR *There was a significant decrease in AVH during the study.*
Thirthalli J, et al. (2008)	1 (22)	Yes *Maintained medication with no change in dose (antipsychotic)*	[LF] Sessions of (1 Hz × 15 min) = 900 pulses/day @ 100% MT [T]	LTC based on 10–20 EEG system	No	None	Headache (n = 1)	PANSS (AH)	1 (100%)
Bagati D, et al. (2009)	40 (18–37)	Yes *Maintained medication with no change in dose (antipsychotic)*	[LF] 10 days of 1 Hz @ 90% MT [T]	LTC based on 10–20 EEG system	No	None	NR	AHRS PSYRATS (AH)	NR *Significant reduction of AH parameters of AHRS scores.*
Garcia-Toro M, et al. (2009)	1 (26)	Yes *Maintained medication with no change in dose (antipsychotic)*	[LF] 34 pulse trains (1 Hz × 60s) = 2040 pulses/day at 100% MT [T]	LTC based on 10–20 EEG system	No	None	Facial twitching (n = 1)	PSYRATS (AH)	1 (100%)
Montagne-Larmurier A, et al. (2009)	11 (24–57)	Yes *Maintained medication with no change in dose (antipsychotic)*	[HF] 2 days with 2 sessions of 13 trains (20 Hz × 10s (w/50s ITI)) = 5200 pulses/day @ 80% RMT [T]	STS using fMRI and frameless stereotaxic TMS system	Yes	None	Headache (n=2) *Slight contractions of temporal and facial muscles were reported*	AHRS CGI	7 (63.8%)
Vercammen A, et al. (2009)	24 (19–48)	Yes *Maintained medication with no change in dose (antipsychotic)*	[LF] 6 days with 2 sessions of (1 Hz × 20min) = 2400 pulses/day @ 90% MT [T]	RTC and LTC based on 10–20 EEG system	No	Sham Coil	Headache (n = 8) Tingling sensation (n = 1) Restless legs (n = 1) Light-headedness (n = 1) Transient earache (n = 1) Twitching of facial muscles (n = 7)	AHRS PANAS PANSS	*8 (33%) immediately after rTMS;* *6 (28.6%) after 1 week*
Consentino G, et al. (2010)	1 (63)	NR	[LF] 10 days of (1 Hz × 20min) = 1200pulses/day @ 90% MT [T]	Right posterior temporal lobe as determined by MRI and PET	Yes	None	NR	Self-rated scale from 1 to 10	1(100%)
de Jesus DR, et al. (2010)	8 (18–65)	Yes *Maintained medication with no change in dose (antipsychotic)*	[LF] 20 days of (Day 1 (1 Hz × 8 mins), Day 2 (1 Hz × 16 mins), and Days 3–20 (1 Hz × 20 mins) =480–1200 pulses/day @ 90% MT [T]	LTC based on 10–20 EEG system	No	Coil tilted 45° from the skull	Headache (n=2)	BPRS QLS CGI AHRS	NR *There was no significant effect observed on AHs.*

Author (Year)	# of Subjects (Age Range)	Drug Therapy *details*	rTMS Protocol [Therapeutic or Diagnostic]	Coil Position	MRI Navigation	Sham Method	Adverse Events *details*	AH Outcome Measure	# Responders (% total) *comments*
Dollfus S, et al. (2010)	1 (56)	Yes *Maintained medication, however a new regimen was started during treatment(antipsychotic)*	[LF]-[HF] 10 days of (1 Hz × 20min) = 1200pulses/day @ 90% MT 2 days of (2 sessions of 13 trains (20 Hz × 10s)) = 5200 pulses/day @ 80% RMT [T]	TP3 marking based on 10–20 EEG system or left superior temporal sulcus based on fMRI	Yes	None	None	AHRS	1(100%) *Patient responded with HF stimulation, but not with LF stimulation.*
Eberle MC, et al. (2010)	1 (52)	Yes *Maintained medication with no change in dose (antipsychotic)*	[HF] 45 days of (40s (3 pulses at 50 Hz every 200 msec)) =600 pulses/day @ 80% AMT [T]	TP3 and TP4 marking based on 10–20 EEG system	No	None	None	HCS	1(100%)
Hong N, et al. (2010)	1 (79)	Yes *Maintained medication with no change in dose (antipsychotic)*	[LF] 15 days of (1Hz) [T]	LTC, but method of locating NR	No	None	Aggravation of AH (n = 1) *Persisted for one month after rTMS.*	PSYRATS (AH)	1(100%)
Lai I, et al. (2010)	8 (34–48)	Yes *Maintained medication with no change in dose (antipsychotic)*	[HF] 11 days of (1 Hz × 16 min) = 960 pulses/day @ 90% MT [T]	LTC, method of location NR	No	Yes, but method not reported	None	CGI HCS	*3 (37.5%) with 50% reduction* *2 (25%) with 20% reduction* *1 (12.5%) with 10% reduction*
Loo CK, et al. (2010)	18 (20–74)	Yes *Maintained medication with no change in dose (antidepressant, antipsychotic)*	[LF] 3 days of (1 Hz × 16 min) = 960 pulses/day @ 110% MT [T]	Posterior half of the LSTG and RSTG based on MRI	Yes	Coil tilted 45° from the skull	Increase in auditory threshold (n = 2) *Eight participants reported experiencing side-effects during the active treatment (right or left), with the most commonly reported side-effect being twitching*	AHRS DVR	5 (27%)
Slotema CW, et al. (2010)	42 (26–51)	Yes *Maintained medication with no change in dose (antipsychotic)*	[LF] 15 days of (1 Hz × 20 mins) = 1200 pulses/day @ 90% MT [T]	Halfway between T3 and P3 based on 10–20 EEG system Site of maximal fMRI activation during AVHs	Yes	Coil tilted 90° from the skull	Facial twitching (n = 7) Increased psychosis (n = 2) Scalp discomfort (n = 1) Headache (n = 9) Nausea (n = 1) Dizziness (n = 1) Abdominal pain (n = 1) Fatigue (n = 1)	AHRS PSYRATS (AH) HCS PANSS	*rTMS was not able to significantly reduced AVH as compared to sham.*
Sperling W, et al. (2010)	1 (37)	No	[LF] 4 days of (1 Hz × 10 min) × 2 hemispheres =1200 pulses/day (600/hemisphere) @ 90% MT [T]	Halfway between T3 and P3 based on 10–20 EEG system on Left and Right side	No	None	NR	SAPS	1 (100%)
Subramanian P, et al. (2010)	1 (24)	Yes	[LF]	LTC and RTC based on 10–20 EEG system	No	None	Increased passivity experiences of volition and impulse (n = 1)	VAS	1 (100%)

Author (Year)	# of Subjects (Age Range)	Drug Therapy *details*	rTMS Protocol [Therapeutic or Diagnostic]	Coil Position	MRI Navigation	Sham Method	Adverse Events *details*	AH Outcome Measure	# Responders (% total) *comments*
		Maintained medication with no change in dose (antipsychotic)	20 days of 1 Hz stimulation =Unknown # of pulses @ 100% RMT [T]						
Vercammen A, et al. (2010)	9 (21–52)	Yes *Maintained medication with no change in dose (antipsychotic)*	[LF] 6 days of (1 Hz × 20 min) for a total of 12 sessions. =2400 pulses/day @ 90% MT [D]	Halfway between T3 and P3 based on 10–20 EEG system	No	Sham Coil	NR	PANSS	NR *Left TPJ active stimulation showed significant decrease in PANSS score.*
Rosenberg O, et al. (2011)	8 (28–62)	Yes *Maintained medication with no change in dose (antipsychotic)*	[LF] 10 or 20 days of (1 Hz × 10 min) =600 pulses/day @ 110% MT [T]	LTC based on H-coil magnetic field modeling.	No	None	Headache (n = 1)	AHRS SAPS CGI SANS	7(87.5%) *Improvement in both 10 and 20 day treatment regimens. This improvement was less in 20 days, but upon follow-up the reduction in AH was markedly more as compared to 10 days of treatment.*

Table 2

Literature review summary of tinnitus treatment or investigation by rTMS

Note all studies used a Figure of 8 TMS coil except for De Ridder et al. (2005), which used a circular coil and Vanneste et al. (2011), which used a double cone coil. AC, auditory cortex; AMT, active motor threshold; B, bilateral tinnitus; BDI, Beck depression inventory; BDI-II, Beck depression inventory, second edition; BSI-18, 18-item brief symptom inventory; CGI, clinical global impression scale; CT, computed tomography; cTBS, continuous theta burst (3 50Hz pulses at 5Hz); D, diagnostic; fMRI, functional magnetic resonance imaging; IAF, individual alpha frequency (50, frequency ranging between 8 and 12 Hz); imTBS, intermediate theta burst (75 50Hz pulses at 0.06Hz); iTBS, intermittent theta burst (3 50Hz pulses at 0.1Hz); ITI, intertrain interval; L, left-sided tinnitus; LAC, left auditory cortex; LTA, left tempoparietal area; LTC, left tempoparietal cortex; LTG, left temporal gyrus; MEG, magnetoencephalography; MPA, mesial parietal area; MRI, magnetic resonance imaging; MT, motor threshold; NR, not reported; PET, positron emission tomography; PET-CT, positron emission tomography-computed tomography; R, right-sided tinnitus; RAC, right auditory cortex; RMT, resting motor threshold; RSTG, right superior temporal gyrus; RTC, right tempoparietal cortex; rTMS, repetitive transcranial magnetic stimulation; SPECT, single photon emission computed tomography; T, therapeutic; THQ, tinnitus handicap score; TPJ, tempo-parietal junction; TSIQ, tinnitus severity index questionnaire; TQ, tinnitus questionnaire; U, unilateral tinnitus; VARL, ear-specific visual analogue rating of tinnitus loudness; VAS, visual analog scale

Author (Year)	**# of Subjects (Age Range)**	**Tinnitus Laterality**	**Drug Therapy *details***	**rTMS Protocol [Therapeutic or Diagnostic]**	**Coil Position**	**MRI Navigation**	**Sham Method**	**Adverse Events *details***	**Tinnitus Outcome Measure**	**# Responders (% total) *comments***
Eichhammer P, et al. (2002)	3 (48–62)	2B 1 L	No	[LF] 5 days of (1Hz × 33.3 min) = 2000 pulses/day @ 110% MT [D]	AC based on PET	Yes	Sham Coil	Aggravation of tinnitus (n = 1) *Two days of tinnitus worsening followed by a dramatic reduction in tinnitus.*	TQ PET	3(100%)
Plewnia C, et al. (2003)	14 (35–59)	12 B 2 L	NR	[HF] 1 day of (10 Hz × 3s × 5 per each of 12 scalp positions) w/30s inter train interval = 1800 pulses @ 120% MT [D]	12 scalp positions based on 10–20 EEG setup	No	None	NR Aggravation of tinnitus (n = 1)	Self-rating scale (1– 4)	8 (57%) *with left temporal or temporoparietal stimulation*
Langguth B, et al. (2003)	1 (62)	1 B	No	[LF] 20 days of (1Hz × 33.3 min) = 2000 pulses/day @ 110% MT [D]	AC based on PET	Yes	Sham Coil	NR Aggravation of tinnitus (n = 1) *Two days of tinnitus worsening followed by a dramatic reduction in tinnitus.*	TQ	1(100%)
De Ridder D, et al. (2005)	114 (Not Reported)	106 U 8 B	NR	[LF/HF] 1 day with 200 pulses of 1, 3, 5, 10, and 20 Hz = 1000 pulses @ 90% MT [T]	AC contralateral to tinnitus site based on fMRI	Yes	Coil positions, coil perpendicular to the skull	NR	VAS	28 (24.5%) *32 (28%) additional had a partial response*

Author (Year)	# of Subjects (Age Range)	Tinnitus Laterality	Drug Therapy *details*	rTMS Protocol [Therapeutic or Diagnostic]	Coil Position	MRI Navigation	Sham Method	Adverse Events *details*	Tinnitus Outcome Measure	# Responders (% total) *comments*
Kleinjung T, et al. (2005)	14 (20–62)	2 B 6 L 6 R	No	[LF] 5 days of (1 Hz × 33min) = 2000 pulses @ 110% MT [T]	12 LAC and 2 RAC based on PET	Yes	Sham Coil	None	TQ	8 (57%)
Fregni F, et al. (2006)	7 (44–68)	7 B	NR	[HF] 1 day of (10 Hz × 3s × 9 trains) w/5min inter train interval =270 pulses @ 120% MT [T]	LTA and MPA based on 10–20 EEG system	No	Sham Coil	None	Self-rating scale (1– 4)	3 (42%) *with LTA stimulation*
Folmer RL, et al. (2006)	15 (44–71)	7 L 8 R	No	[HF] 1 day of (10 Hz × 3s × 5 sessions w/57s intertrain interval) = 150 pulses @ 100% MT [D]-[T]	LTC and RTC based on 10–20 EEG system	No	Coil with recorded sounds of actual TMS	NR	Self-rating scale (1– 10)	6 (40%) *5 (33.3%) with LTC stimulation,* *1 (6.6%) with RTC stimulation*
Richter GT, et al. (2006)	1 (43)	1 B	NR	[LF] 5 days of (1 Hz × 30s w/1 day inter train interval) = 1800 pulses @ 110% MT [D]-[T]	RAC based on PET-CT	No	None	None	PET-CT Tinnitus severity questionnaire with analogue scale	1 (100%)
Londero A, et al. (2006)	13 (22–64)	10 L 3 R	No *Patients had undergone previous treatment with antiepileptics.*	[LF/HF] 1 day of (10 Hz × 3s followed by 1 Hz × 20min) = 1230 pulses @ 120% MT [T]	AC contralateral to tinnitus site based on fMRI	No	None	NR Aggravation of tinnitus (n = 1) *Aggravation lasting for10 days*	THQ	*6(46%) with 1 Hz stimulation* *1(7.7%) with 10 Hz stimulation*
Langguth B, et al. (2006)	28 (38–65)	13 B 9 L 6 R	NR	[LF] 10 days of (1 Hz × 33min) = 2000 pulses/day @ 110% MT [T]	LAC based on 10–20 EEG system	No	None	Aggravation of tinnitus (n = 2)	TQ	19 (67%)
Nowak DA, et al. (2006)	1 (27)	1 U	No	[LF] 5 days of (1 Hz × 18min) = 1080 pulses/day @ 90% MT	LAC	No	None	GTC seizure (n = 1)	NR	0 (0%)

Author (Year)	# of Subjects (Age Range)	Tinnitus Laterality	Drug Therapy *details*	rTMS Protocol [Therapeutic or Diagnostic]	Coil Position	MRI Navigation	Sham Method	Adverse Events *details*	Tinnitus Outcome Measure	# Responders (% total) *comments*
				[T]						
De Ridder D, et al. (2007)	46 (>18)	46 U	NR	[HF] 1 day of tonic rTMS with 200 pulses at5, 10, and 20 Hz = 600 pulses followed by a second day of burst rTMS at 5, 10, and 20 Hz Hz both @ 90% MT [T]	AC contralateral to tinnitus site	No	Coil positions, coil perpendicular to the skull	NR	VAS TQ	14 (30.4%) *5 (10.9%) with 5Hz* *2 (4.3%) with 10Hz* *7 (15.2%) with 20Hz*
Plewnia C, et al. (2007a)	9 (49–68)	8 B 1 R	Yes *Lidocaine (1.5 mg/kg) i.v.*	[LF] 2 days of (1 Hz × 5, 15, and 30min w/30 min inter train interval) = 3000 pulses/day @ 120% MT [D]-[T]	Based on PET scan results	Yes	Occipital control position	Aggravation of tinnitus (n = 1) *Tinnitus increased after 5 minutes stimulation and returned to baseline after 30 mins.*	VAS	6 (66%)
Plewnia C, et al. (2007b)	6 (49–68)	6 B	No	[LF] 20 days of (1 Hz × 30min) = 1800 pulses/day @ 120% MT [T]	Based on PET scan results	Yes	Occipital control position	None	TQ	5 (83%)
Kleinjung T, et al. (2007)	45 (20–69)	30 B 8 L 7 R	NR	[LF] 10 days of (1 Hz × 33 mins) = 2000 pulses/day @ 110% MT [T]	AC based on fMRI	Yes	None	NR	TQ	18 (40%)
Rossi S, et al. (2007)	16 (only 14 completed) (35–72)	7 B 4 L 3 R	No	[LF] 5 days of (4 trains of (1Hz × 6.66 mins w/ITI of 30s)) = 1200 pulses/day @ 120% MT [T]	LTC based on PET or AC based on 10–20 EEG system	Yes	Coil positioned 45° from the skull	Aggravation of tinnitus (n = 2) *Slight headache or tongue paraesthesia*	VAS	8(57%)
Smith JA, et al. (2007)	4 (30–60)	4 B	No	[LF] 5 days of (1 Hz × 30 mins) = 1600 pulses/day @ 110% MT [D]	Primary AC based on PET/CT	Yes	Coil positioned 45° from the skull	None	PET TSIQ VAS	NR *TSIQ and VAS scores decreased, but were not considered*

Author (Year)	# of Subjects (Age Range)	Tinnitus Laterality	Drug Therapy *details*	rTMS Protocol [Therapeutic or Diagnostic]	Coil Position	MRI Navigation	Sham Method	Adverse Events *details*	Tinnitus Outcome Measure	# Responders (% total) *comments*
										statistically significant.
Lee SL, et al. (2008)	8 (57–85)	8 B	NR	[LF] 5 days of (0.5 Hz × 20 min) = 600 pulses/day @ 100% MT [T]	LTC, but method of finding area NR	No	None	Jaw Soreness (n =1) Photophobia (n=1) Restlessness (n=1) Imbalance (n=1)	THI	1 (12.5%)
Mennemeir M, et al. (2008)	1 (44)	1 B	No	[LF] 10 days of (1 Hz × 30 min) = 1800 pulses/day @ 110% MT [T]	Anterior RSTG based on PET	Yes	Coil positioned 45° from the skull	None	PET-CT VAR	1 (100%)
Kleinjung T, et al. (2008)	16 (41–60)	27 B 3 L 2 R	NR *Patients had previously been on vasodilators and anti-depressesants as possible tinnitus treatment.*	[LF]-[HF] 1 day of (1 Hz × 33 min) = 2000 pulses/day @ 110% MT 1 day of (20 Hz × 50s) followed by (1 Hz × 16min) = 2000 pulses/day @ 110% MT [D]	Neuronavigation to LAC	Yes	None	None	TQ	*3 (18.75%) with 1Hz* *8 (50%) with 50Hz/1Hz*
Khedr EM, et al. (2008)	50 (6 mo – 25yrs)	12 B 22 R 32 L	No	[LF]-[HF] 10 days of either 1, 10, 25 Hz @ 100% RMT (90% RMT for 25 Hz) [T]	LTC based on 10– 20 EEG system	No	Occipital control position	NR	THI	38 (76%) *13 (26%) with 1Hz* *13 (26%) with 10Hz* *12 (24%) with 25Hz*
Garcia-Toro M, et al. (2009)	1 (73)	1 B	Yes *Trimetazidine (60mg daily) although period of treatment NR.*	[LF] 34 pulse trains (1 Hz × 60s) = 2040 pulses/day at 100% MT [T]	LTC based on 10– 20 EEG system	No	None	Facial twitching (n =1)	Self Rating Scale (0–100) HDS	1 (100%)
Kleinjung T, et al. (2009)	32 (35–56)	12 B 9 L 11 R	Yes *16 patients received levodopa (100mg) and benserazide (25mg)*	[LF] 10 days of (1 Hz × 33.3 mins) =2000 pulses/day @ 110%MT [D]-[T]	Neuronavigation to LAC	Yes	None	None	TQ	NR *TQ scores in both control and levodopa groups. No significant difference between groups and only the*

Author (Year)	# of Subjects (Age Range)	Tinnitus Laterality	Drug Therapy *details*	rTMS Protocol [Therapeutic or Diagnostic]	Coil Position	MRI Navigation	Sham Method	Adverse Events *details*	Tinnitus Outcome Measure	# Responders (% total) *comments*
										control group had a significant lasting suppression during the follow-up period
Marcondes RA, et al. (2009)	10 (>18)	NR	No	[LF] 5 days of (1 Hz × 17min) = 1020 pulses/day @110% MT [D]-[T]	LTC based on 10– 20 EEG system	No	Sham Coil	None	THI VAS SPECT	NR *Active rTMS showed significant reduction in tinnitus outcome measures as compared to Sham rTMS.*
Meeus O, et al (2009)	50 (22–78)	26 B 24 U	NR	[LF/HF] 1 day of 1, 5, 10, and 20 Hz tonic stimulation for 200 pulses followed by 5, 10, or 20 Hz burst stimulation (50 or 100 Hz bursts with either 3, 5, or 10 pulses) for 200 pulses = 400 pulses/day @ 50% MO [D]	AC contralateral to the tinnitus, 5 cm above the entrance of the external auditory meatus on straight line to the vertex	No	Coil positioned 45° from the skull	NR	VAS	NR *Active rTMS showed a significant reduction in tinnitus outcome measures as compared to Sham rTMS. 1 Hz stimulation was significantly better at reducing tinnitus than high frequency stimulation.*
Poreisz C, et al. (2009)	33 (only 20 completed the trial) (35–60)	12 B 4 L 4 R	No	[HF] cTBS, iTBS, or imTBS separated by 5 days for 600 pulses at 80% AMT (6 patients) or 80% RMT (14 patients) [D]	LTC based on 10– 20 EEG system	No	None	Headache (n = 2) Unpleasant feeling (n = 5) Aggravation of tinnitus (n = 3)	TQ VAS	11 (55%)
Soekadar SR, et al. (2009)	1 (54)	1B	Yes *Prior treatment with antidepressants. Mirtazapine 45 mg/ day started 4 weeks before treatment and maintained through treatment.*	[HF] 15 days of ((cTBS × 40s train) × 30 mins) × 1 or 2 times/ day =18,000 – 36,000 pulses/ day @ 80% AMT	LTC and/or RTC based on 10–20 EEG system	No	None	NR	TQ VAS	1(100%)

Author (Year)	# of Subjects (Age Range)	Tinnitus Laterality	Drug Therapy *details*	rTMS Protocol [Therapeutic or Diagnostic]	Coil Position	MRI Navigation	Sham Method	Adverse Events *details*	Tinnitus Outcome Measure	# Responders (% total) *comments*
				[T]						
Anders M, et al. (2010)	26 (20–69)	13 B 3 L 6 R	No	[LF] 10 days of (1 Hz × 25 mins) =1500 pulses/ day @ 110% RMT [T]	Neuronavigation to LAC	Yes	Coil positioned 45° from the skull	Aggravation of tinnitus (n = 2) Neck muscle contractions (n = 1) *Transient headache, mild tongue paresthesia, transient worsening of tinnitus, and changes in sleep quality also reported.*	THI TQ VAS	NR *Active rTMS was capable of significantly reducing the total baseline score of basic scales that measure tinnitus severity.*
Frank E, et al. (2010)	1 (61)	1 R	NR	[LF]-[HF] 10 days of (1Hz × 16min) = 2000 pulses/day @ 110% MT 1 day of: −5 Hz tonic; 10 Hz tonic; 20 Hz tonic = 100 pulses/day @ 110% MT−cTBS for 100 pulses/ day @ 110% MT −10 Hz burst (3 stimuli with a frequency of 100 Hz) = 100 pulses/day @ 110% MT −20 Hz burst (5 stimuli with a frequency of 500 Hz) = 100 pulses/day @ 110% MT 10 days of (40 trains of 50 bursts (5 stimuli at 500Hz) w/ITI 25s) = 2000 pulses/day @ 110% MT [T]	Based on PET scan results	Yes	Yes, but not detailed.	NR	TQ CGI	1(100%) *With 1 Hz and 20 Hz burst stimulation.*
Khedr EM, et al. (2010)	62 (26–55)	30 L 32 R	No	[LF]-[HF] 10 days of either ipsilateral or contralateral stimulation using:	LTC or RTC based on 10–20 EEG system	No	None	*LF* Headache (n = 21) Neck Pain (n = 14) Jaw Pain (n = 16) *HF* Headache (n = 19)	THI VAS	*43 (69%) for both HF and LF rTMS with THI 40 (64%) for both HF and LF*

Author (Year)	# of Subjects (Age Range)	Tinnitus Laterality	Drug Therapy *details*	rTMS Protocol [Therapeutic or Diagnostic]	Coil Position	MRI Navigation	Sham Method	Adverse Events *details*	Tinnitus Outcome Measure	# Responders (% total) *comments*
				−1 Hz =2000 pulses/day @ 100% RMT −25 Hz for 40 trains × 50 pulses w/5s ISI = 2000 pulses/day @ 90% RMT [T]				Neck Pain (n = 10) Jaw Pain (n = 7)		*rTMS with Loudness 40 (64%) for both HF and LF rTMS with Annoyance 38 (61%) for both HF and LF rTMS with Awareness*
Lorenz I, et al. (2010)	10 (21–70)	5 B 4 L 1 R	No	[LF]-[HF] 1 day of either 1 Hz, IAF (20 trains with 25s ITI), iTBS (10 trains with 8s ITI), or cTBS = 1000 pulses/day @110 %RMT for 1 Hz/IAF or 80% RMT for iTBS/cTBS [D]	AC contralateral to tinnitus site based on 10–20 EEG system	No	Coil positioned 45° from the skull	Aggravation of tinnitus with IAF (n = 3)	MEG VAS	NR *1 Hz, iTBS, and cTBS all showed a reduction in tinnitus, while IAF caused an increase in tinnitus.*
Marcondes RA, et al. (2010)	10 (>18)	NR	No	[LF] 5 days of (1 Hz × 17min) = 1020 pulses/day @110% MT [T]	LTC based on 10– 20 EEG system	No	Sham Coil	None	THI VAS SPECT	NR *Significant reduction in tinnitus with Active stimulation versus Sham. Reduction in cortical activity shown by SPECT with Active stimulation.*
Minami SB, et al. (2010)	16 (23–79)	4 B 7 L 5 R	NR	[LF] 1 day of (1 Hz × 20 mins) = 1200 pulses/day @ 110% RMT [T]	LAC based on 10–20 EEG system	No	None	None	VAS THI	NR *Significant reduction in VAS scores, but not in THI scores.*
Vanneste S, et al. (2010)	100 (38–63)	25 B 23 U 52 NR	NR	[LF]-[HF] 1 day of (1, 5, 10, 20 Hz w/5 pulse bursts) = 800 pulses/day @ 90%MT [D]-[T]	AC, method of locating NR	No	Coil positioned 45° from the skull	NR	VAS TQ	48(48%) *48 patients were described as placebo free responders.*

Author (Year)	# of Subjects (Age Range)	Tinnitus Laterality	Drug Therapy *details*	rTMS Protocol [Therapeutic or Diagnostic]	Coil Position	MRI Navigation	Sham Method	Adverse Events *details*	Tinnitus Outcome Measure	# Responders (% total) *comments*
Mennemeir M, et al. (2011)	21 (28–75)	21 B	No	[LF] 5 days of (1 Hz × 30 mins) =1800 pulses/ day @ 110%MT [D]-[T]	MRI-guided using PET asymmetry, posterior one third of the STG that lies opposite to ear with tinnitus if no asymmetry but lateralized tinnitus, or left hemisphere STG if no asymmetry/later alized tinnitus	Yes	Sham Coil w/electrical scalp stimulation	NR *Only looked at results of neuropsychological tests as a reporter of detrimental effects.*	VARL PET	9(43%)
Piccirillo JF, et al. (2011)	14 (42–59)	9 B 3 R 2 L	Yes *Maintained medication with no change in dose (antidepressant)*	[LF] 10 days of (6 trains of (1 Hz × 5.5 minutes for 5 trains and 6 minutes for last train w/90s ITI)) = 2000 pulses/ day @ 110%MT [D]-[T]	TPJ based on 10– 20 EEG system or neuronavigation	Yes	Sham Coil	Jaw twitch (6) Neck/Shoulder Twitch (5) Facial twitch (4) Headache (2) Eye twitching (1) Facial tingling (1) Jaw pain (1) Arm twitch (1) Lightheadedness (1) Temple pain (1) Aggravation of tinnitus (2)	THI BDI-II BSI-18	2(14%)
Vanneste S, et al. (2011)	78 (22–81)	55 B 25 U	NR	[LF]-[HF] 1 day of (1, 3, 5, 10, 20 Hz w/200 pulses per frequency) =1000 pulses/ day @ 50%MO [D]-[T]	Medial frontal cortex defined as 1.5cm anterior to one-third distance from nasion inion.	No	Coil positioned 45° from the skull	NR	VAS	31(59.61%) *52 out of 78 patients (66.67%) were non responders to sham and were used to calculate the percent of responders/non-responders.*

Table 3

Literature review summary of somatic pain treatment or investigation by rTMS

Note all studies used a figure-of-8 TMS coil except for Rollnik et al. (2002), which used a circular coil. bid, twice daily; BPI, brief pain inventory; CNP, chronic neuropathic pain; D, diagnostic; NRS, numeric rating scale; CRPS, complex regional pain syndrome; HF, high frequency; HRSD, Hamilton rating scale for depression; ITI, intertrain interval; LANSS, Leeds assessment of neuropathic symptoms and signs; LF, low frequency; LPC, left prefrontal cortex; MEP, motor evoked potential; MPQ, McGill pain questionnaire; MRI, magnetic resonance imaging; MT, motor threshold; NPS, neuropathic pain scale; NPSI, neuropathic pain symptom inventory; NR, not reported; PIQ, pain impact questionnaire; qd, once daily; RMT, resting motor threshold; rTMS, repetitive transcranial magnetic stimulation; T, therapeutic; THQ, tinnitus handicap score; TQ, tinnitus questionnaire; VAS, visual analog scale; VNS, visual numeric scale

Author (Year)	**# of Subjects (Age Range)**	**Drug therapy *details***	**Pain Type**	**rTMS Protocol [Therapeutic or Diagnostic]**	**Coil Position**	**MRI Navigation**	**Sham Method**	**Adverse Events *details***	**Pain Outcome Measure**	**#of Responders (% total) *comments***
Lefaucheur JP, et al. (2001a)	18 (28–75)	NR	Lesional	[LF]-[HF] 1 day of (20 trains (10Hz × 5s w/55s ITI) = 1000 pulses/day @ 80% RMT 1 Day of (0.5 Hz × 20 min) =600 pulses/day @ 80% RMT [T]	Motor cortex as defined by maximal contralateral MEP amplitude	No	Coil tilted 45° from the skull	None	VAS	7 (38.9%)
Lefaucheur JP, et al. (2001b)	14 (34–80)	NR	Varied	[HF] 2 days of (20 trains (10Hz × 5s w/55s ITI) = 1000 pulses/day @ 80% RMT [T]	Motor cortex as defined by maximal contralateral MEP amplitude	No	Sham Coil	None	VAS	8 (57%)
Rollnik JD, et al. (2002)	12 (33–67)	NR	Varied	[HF] 1 day of (20 trains (20 Hz × 5s) over 20 min) = 800 pulses/day @ 80% MT [T]	Motor cortex as definedby maximal contralateral MEP amplitude	No	Coil tilted 45° from the skull	Headache (n=1)	VAS	6 (50%)
Topper R, et al. (2003)	2 (29–37)	Yes *Maintained medication with no change in dose (analgesic, NSAIDs)*	Phantom- Limb	[LF]-[HF] 15 Hz × 2s for multiple stimulation sites 15 days of (20trains (10Hz × 2s) w/1min ITI) = 400 pulses/ day @ 110% RMT 15 days of (1Hz × 12min) = 720 pulses/day @ 110% RMT [D]-[T]	Motor cortex as defined by maximal contralateral MEP amplitude F3, F4, Fz, C3, C4, Cz, P3, P4, Pz, T5, T6, O1 and O2, all according to the International 10–20 System	No	None	NR	VAS	2 (100%)
Lefaucheur JP, et al. (2004)	60 (27–69)	NR	Lesional	[HF] 1 day of (20 trains (10Hz × 5s w/55s ITI) = 1000 pulses/day @ 80% RMT [D]	Motor cortex as defined by maximal contralateral MEP amplitude	No	Sham Coil	None	Thermal sensory threshold VAS	39 (65%)
Pleger B, et al. (2004)	10 (29–72)	No	CRPS I	[HF]	Motor cortex as defined by maximal	No	Coil tilted 45° from the skull	Hemihyperther-maesthesy (n = 2)	VAS	7 (70%)

Author (Year)	# of Subjects (Age Range)	Drug therapy *details*	Pain Type	rTMS Protocol [Therapeutic or Diagnostic]	Coil Position	MRI Navigation	Sham Method	Adverse Events *details*	Pain Outcome Measure	#of Responders (% total) *comments*
				1 day of (10 trains (10 Hz × 1.2s w/10s ITI)) = 120 pulses/ day @ 110% MT [T]	contralateral MEP amplitude			Tingling sensation in limb (n = 2) Drowsiness (n = 1) Dizziness (n = 1) Headache (n = 1)		
Khedr EM, et al. (2005)	48 (39–63)	NR	Varied CNP	[HF] 5 days of (10 trains (20 Hz × 10s) w/50s ITI)) =2000 pulses/ day @ 80% RMT [T]	Motor cortex as defined by maximal contralateral MEP amplitude	No	Coil tilted 45° from the skull	NR	VAS LANSS	LANSS responders *21(43.75%) immediately after rTMS* *15(31.25%) Two weeks after rTMS* VAS responders *21(43.75%) immediately after rTMS* *17(35.4%) Two weeks after rTMS*
Andre-Obadia N, et al. (2006)	12 (31–66)	Yes *Maintained medication with no change in dose (analgesic, anticonvulsant, antidepressant, antipsychotic, antispastic)*	Lesional	[LF]-[HF] 2 days of (1 Hz × 26min) =1560 pulses/day @ 90% MT 1 day of (20 trains of 80 pulses at 20 Hz with ITI of 84s) = 1600 pulses/day @ 90% MT [T]	Motor cortex as defined by maximal contralateral MEP amplitude	Yes	Coil tilted 45° from the skull	None	VAS Global subjective assessment	*1 (8.3%) with 1Hz* *5 (41.6%) with 20Hz*
Hirayama A, et al. (2006)	20 (28–72)	Yes *Maintained medication with no change in dose(antianxiety, anticonvulsant, antidepressant, NSAIDs)*	Lesional	[HF] 2 days of 20 Trains (5 Hz × 10s with ITI of 50s @ 90% RMT) = 500 pulses/day [D]	Motor cortex as defined by maximal contralateral MEP amplitude	Yes	Coil tilted 45° from the skull	None	VAS	10 (50%)
Lefaucheur JP, et al. (2006)	36 (30–79)	Yes *Maintained medication with no change in dose (analgesics, anti- anxiety, anti- convulsants, anti- depressants)*	Varied	[HF] 1 day of (20 trains (10Hz × 10s w/50s ITI) = 2000 pulses/day @ 90% RMT [D]	Motor cortex as defined by maximal contralateral MEP amplitude	No	None	None	VAS CGI	*Varied by pain location and stimulation site*
Rosa MA, et al. (2006)	1 (24)	NR	CRPS	[HF] 1 day of (25 trains (10Hz × 10s w/20s ITI)) = 2500 pulses/day @ 100% MT [T]	Motor cortex as defined by maximal contralateral MEP amplitude	No	None	Seizure (n=1)	VAS MPQ	0 (0%)
Saitoh Y, et al. (2007)	13 (29–76)	Yes	Lesional	[LF]-[HF]	Motor cortex as defined by maximal	Yes	Coil tilted 45° from the skull	None	VAS MPQ	NR

Author (Year)	# of Subjects (Age Range)	Drug therapy *details*	Pain Type	rTMS Protocol [Therapeutic or Diagnostic]	Coil Position	MRI Navigation	Sham Method	Adverse Events *details*	Pain Outcome Measure	#of Responders (% total) *comments*
		Maintained medication with no change in dose (anticonvulsants, antidepressants, NSAIDs)		1 day of (10 trains (10Hz × 5s w/50s ITI)) 1 day of (5 trains (10Hz × 10s w/50s ITI)) = 500 pulses/day @ 90% RMT 1 day of (1Hz × 500s) = 500 pulses/day @ 90% RMT [D]	contralateral MEP amplitude					*Pain reduced significantly in the entire treatment group relative to control*
Andre-Obadia N, et al. (2008)	28 (31–72)	Yes *Maintained medication (analgesic, anticonvulsant, antidepressant)*	Varied	[HF] 1 day of (20 trains (20Hz × 4s w/84s ITI)) = 1600 pulses/day @ 90% MT [D]-[T]	Motor cortex as defined by maximal contralateral MEP amplitude	No	Coil tilted 45° from the skull	None	NPSI VNS	14 (50%)
Borckardt JJ, et al. (2009)	4 (33–58)	Yes *Maintained medication with no change in dose (analgesic, antidepressant, anti-anxiety, anti-spastic)*	Varied	[HF] 3 days of (40 trains (10Hz × 10s w/20s ITI)) = 4000 pulses/day @ 100% RMT [D]	Motor cortex as defined by maximal contralateral MEP amplitude LPC using frameless stereotactic system	Yes	Sham Coil	NR	Pain Diary NPS BPI Cutaneous and Mechanical Pain Assessment	3 (75%)
Kang BS, et al. (2009)	11 (33–75)	Yes *Maintained medication (anticonvulsant, antidepressant, NSAIDs)*	Varied CNP	[HF] 1 day of (20 trains (10 Hz × 5s w/55s ITI)) = 1000 pulses/day @ 80% RMT [T]	Motor cortex as defined by maximal contralateral MEP amplitude	No	Coil tilted 45° from the skull	NR	NRS BPI	0 (0%)
Zhagi S, et al. (2009)	1 (62)	Yes *Maintained medication with no change in dose (analgesic, anticonvulsant)*	CNP	[HF] 35 days of (30 trains (10 Hz × 4s w/26s ITI)) =1200 pulses/day @ 80% RMT [T]	Motor cortex as defined by maximal contralateral MEP amplitude	No	None	Headache (n=1) Neck Pain (n = 1)	Self-reported overall daily pain	1(100%)
Picarelli H, et al. (2010)	12 (22–65)	Yes *All patients were washed out of their previous treatment and started on a standardized pharmacological treatment based on the best evidence available for 30 days (naproxen 250 mg bid, amitriptyline 50 mg qd, and carbamazepine 200 mg bid)*	CRPS I	[HF] 10 days of (25 trains (10 Hz × 10s w/60s ITI) = 2500 pulses/day @ 100% RMT [T]	Motor cortex as defined by maximal contralateral MEP amplitude	No	Sham Coil	Seizure (n = 1) Headache (n = 6) Neck Pain (n = 2) Scalp Tingling (n = 4) Dizziness (n = 1)	VAS MPQ PIQ	7 (58%)
Sampson SM, et al. (2011)	9 (18–65)	Yes *Maintained medication with no change in dose (analgesic)*	Varied CNP	[LF] 15 days of (1 Hz × 26.67 mins) =1600 pulses/day @ 110% MT [D]-[T]	RDLPC defined as area 5cm anterior to MC for activation of ABP	No	None	NR *Treatment site discomfort* *Transient mild headeche*	HRSD VAS Likert pain ratings	4 (44.4%)

Table 4

Literature review summary of migraine treatment or investigation by rTMS

Note all studies used a figure-of-8 TMS coil except for Teepker M et al. (2009), which used a circular coil. A, migraine with aura; D, diagnostic; FDI, first dorsal interosseous; HF, high-frequency; LDLPC, left dorsolateral prefrontal cortex; LF, low-frequency; M, migraine without aura; MASQ, measuring and assessing suffering questionnaire; MC, motor cortex; MEP, motor evoked potential, MO, machine output; MPQ, McGill pain questionnaire; MT, motor threshold; NR, not reported; NSAID, non-steroidal anti-inflammatory drug; NVA, migraine with non-visual aura; RMT, resting motor threshold; rTMS, repetitive transcranial magnetic stimulation; SSRI, selective serotonin reuptake inhibitors; T, therapeutic; TCA, tricyclic antidepressant

Author (Year)	**# of Subjects (Age Range)**	**Type of Migraine**	**Drug therapy *details***	**rTMS Protocol [Therapeutic or Diagnostic]**	**Coil Position**	**MRI Navigation**	**Sham Method**	**Adverse Events *details***	**Migraine Outcome Measure**	**#of Responders (% total) *comments***
Brighina F, et al. (2004)	6 (40–54)	6 M	Yes *Maintained medication with no change in dose(anticonvulsant, β-blockers, calcium channel-blocker, SSRI)*	[HF] 12 days of (10 trains (20 Hz × 2s w/30s ITI)) =400 pulses/day @ 90% MT [D]-[T]	LDLPC defined as area 5cm anterior to MC for activation of FDI	No	Coil tilted 45° from the skull	None	Self-rating scale	NR *rTMS had a significant long-lasting effect in reducing headache attack frequency, headache index, and the number of abortive pills.*
Clarke BM, et al. (2006)	42 (30–53)	32 M 10 A	Yes *Maintained medication with no change in dose. (analgesics, antiemetics)*	[LF] 1–3 days of (0.2 Hz × 5s) =2 pulses/day @ 30% or 50% MO [T]	NR	No	None	Dizziness (n = 1) Drowsiness (n = 3)	5- point Likert scale MASQ	*29(69%) improved with 1 trial* *19(87%) improved with 2 trials* *9(82%) improved with 3 trials*
O'Reardon JP, et al. (2007)	2 (51–66)	2 M	NR *Both patients used varying pharmacologic methods of treating migraines, but no mention of use during trial, including anticonvulsants and analagesics.*	[HF] 30 days of (10 Hz × 5 mins) =3000 pulses. day @ 120% MT [T]	LDLPC defined as area 5cm anterior to MC for activation of FDI	No	None	NR	Self-rating scale	2(100%)
Teepker M, et al. (2009)	13 (20–63)	6 M 7 A	No	[LF] 5 days of (2 trains (1 Hz × 8.3 mins w/1 min ITI)) =1000 pulses/day @ 100% RMT [T]	Vertex, method of locating stimulation site not specified.	No	Sham Coil	Drowsiness (n = 1) Amyostasia (n = 1) Irritability (n = 1) Phonophobia (n = 1) Vigorous dreams (n = 1)	Self-reporting Self-rating scale	NR *Significant reduction in migraine occurrence with active rTMS.*
Lipton RB, et al. (2010)	102 (27–50)	37 VA 45 NVA *Additional patient data missing.*	Yes *Maintained medication with no change in dose (β-adrenergic antagonists, SSRI, calcium-channel blockers)*	[LF] 1 day of (0.03 Hz × variable time) =max 120 pulses/day @ MO NR [T]	Occiput just below the occipital bone, location method not specified.	No	Sham Coil	Headache (n = 3) Migraine (n = 3) Sinusitis (n = 2) Optic neuritis (n = 1) Nausea (n = 1)	Self-reporting Self-rating scale	34(42.7%)

Table 5

Literature review summary of fibromyalgia treatment or investigation by rTMS

Note all studies used a figure-of-8 TMS coil. ABP, abductor pollicis brevis; BDI, Beck depression inventory; BPI, brief pain inventory; CGI, clinical global impression; D, diagnostic; FIQ, fibromyalgia impact questionnaire; GAF, global assessment of function; HAD, hospital anxiety and depression scale; HF, high-frequency; HRSD, Hamilton rating scale for depression; ICF, intracortical facilitation; LF, low-frequency; MADRS, Montgomery Asberg depression rating scale; MC, motor cortex; MEP, motor evoked potential; MPQ, McGill pain questionnaire; NR, not reported; NSAID, non-steroidal anti-inflammatory drug; PCS, pain catastrophizing RDLPC, right dorsolateral prefrontal cortex; rTMS, repetitive transcranial magnetic stimulation; SICI, short intracortical inhibition; T, therapeutic

Author (Year)	**# of Subjects (Age Range)**	**Drug therapy *details***	**rTMS Protocol [Therapeutic or Diagnostic]**	**Coil Position**	**MRI Navigation**	**Sham Method**	**Adverse Events *details***	**Fibromyalgia Outcome Measure**	**#of Responders (% total) *comments***
Sampson SM, et al. (2006)	4 (36–51)	Yes *Maintained medication with no change in dose (analgesic, anticonvulsant)*	[LF] 18–20 days of (2 trains (1 Hz × 13.3 mins w/60s ITI)) =1600 pulses/day @ 110% MT [T]	RDLPC defined as area 5cm anterior to MC for activation of ABP	No	Coil tilted 45° from the skull	NR	HRSD MADRS CGI GAF Self-rating scale	4(100%)
Passard A, et al (2007)	15 (44–60)	Yes *Maintained medication with no change in dose (analgesics, antidepressants, NSAIDS)*	[HF] 10 days of (25 trains (10 Hz × 8s w/52s ITI)) =2000 pulses/ day @ 80% RMT [T]	Motor cortex as defined by maximal contralateral MEP amplitude	No	Sham Coil	Headache (n = 4) Nausea (n = 1)	BPI MPQ FIQ manual tender point survey HDRS BDI HAD	NR *Active rTMS improved pain associated with fibromyalgia.*
Carretero B, et al. (2009)	14 (41–53)	Yes *Maintained medication with no change in dose (analgesic, antidepressant)*	[LF] 20 days of (20 trains (1 Hz × 1 min w/45s ITI)) =1200 pulses/ day @ 110% MT [T]	RDLPC defined as area 5cm anterior to MC for activation of ABP	No	Coil tilted 45° from the skull	Headache (n = 6) Neck Pain (n = 6) Aggravation of depression (n = 1)	HDRS CGI Likert pain scale FibroFatigue scale	NR *Active rTMS improved pain associated with fibromyalgia.*
Mhalla A, et al. (2011)	20 (40–62)	Yes *Maintained medication with no change in dose (analgesics, antidepressants)*	[HF] 14 days of (15 trains (10 Hz × 10s w/50s ITI)) =1500 pulses/ day @ 80% RMT [T]	Motor cortex as definedby maximal contralateral MEP amplitude	No	Sham Coil	Headache (n = 6) Dizziness (n = 1)	BPI MPQ FIQ HAD BDI PCS ICF SICI MEP RMT	NR *Active rTMS improved pain and quality of life associated with fibromyalgia. SICI and ICF were significantly higher after rTMS.*

Table 6

Literature review summary of visceral pain treatment or investigation by rTMS

Note all studies used a figure-of-8 TMS coil. BDI, Beck depression inventory; D, diagnostic; HF, high-frequency; LF, low-frequency; MMSE, mini-mental state examination; MRS, magnetic resonance spectroscopy; NR, not reported; rTMS, repetitive transcranial magnetic stimulation; SII, secondary somatosensory area; T, therapeutic; VAS, visual analog scale

Author (Year)	**# of Subjects (Age Range)**	**Drug therapy *details***	**rTMS Protocol [Therapeutic or Diagnostic]**	**Coil Position**	**MRI Navigation**	**Sham Method**	**Adverse Events *details***	**Visceral Pain Outcome Measure**	**#of Responders (% total) *comments***
Fregni F, et al. (2005)	5 (33–55)	NR	[LF]-[HF] 6 days of (1 or 20 Hz) =1600 pulses/day @ 90% RMT [D]-[T]	Left or right SII using MRI navigation	Yes	Sham Coil	None	VAS MMSE	NR *1 Hz active rTMS reduced pain when stimulating both left and right SII. 20 Hz worsened pain when stimulating left SII and improved pain when stimulating right SII.*
Fregni F, et al. (2011)	9 (30–52)	NR	[LF] 10 days of (1 Hz × 26.6 mins) =1600 pulses/day @ 70% MO [D]-[T]	Right SII using MRI navigation	Yes	Sham Coil	*Total number of adverse events was reported per treatment group. Numbers of patients with adverse events is not reported.*	VAS BDI MRS Biological markers	NR *Active rTMS significantly reduced visceral pain.*

Table 7

Literature review summary of visual hallucinations (VH) treatment or investigation by rTMS

Data from one case report are summarized. A figure-of-eight coil was employed. D, diagnostic; LF, low frequency; MO; Machine output; MRI, magnetic resonance imaging; rTMS, repetitive transcranial magnetic stimulation; T, therapeutic; VH, visual hallucinations

Author (Year)	**# of Subjects (Age)**	**Drug Therapy *details***	**rTMS Protocol [Therapeutic or Diagnostic]**	**Coil Position**	**MRI Navigation**	**Sham Method**	**Adverse Events *details***	**Outcome Measure**	**# Responders (% total) *comments***
Merabet LB, et al. (2003)	1 (52)	NR *Use of β-blockers, diabetes, and lipid controlling medication.*	[LF] 1 day of (1 Hz × 10 min) = 600 pulses/day @ 80% MO [T]	Striate cortex 2 cm above inion	None	Sham Coil	None	Self-report	1 (100%)
Meppelink AM, et al. (2010)	1 (50)	NR *Use of antipsychotic and antiepileptic medication.*	[LF] 1 day of (1Hz × 10 min) = 600 pulses/day @ 80% MO [T]	Based on fMRI activation	Yes	Yes, but method NR	NR	Self-report	1(100%)

Table 8

Seizures induced by rTMS in patients with positive sensory symptoms

Details of three case reports are summarized. ABP, abductor pollicis brevis; bid, twice daily; CRPS, complex regional pain syndrome; FDI, first dorsal interosseus muscle; GTC, generalized tonic clonic seizure; ITI, intertrain interval; MEP, motor evoked potential; MT, motor threshold; NR, not reported; qd, once daily

Reference	Age/Sex	Seizure Details	Coil Location	Stimulation	Medical History	Medications
Nowak DA, et al. (2006)	27y M	• Right versive seizure with epigastric aura (epigastricdiscomfort followed by loss of consciousness with head and eye version to right, for 5 secs, and generalized tonic stiffening for 10 secs) • No incontinence • 10 sec postictal unresponsiveness • Complete amnesia for event	Over left primary auditory cortex	5 days of 1 train per day (1 Hz × 18 min) = 1080 pulses/ day @ 90% MT	• Mono-auricular tinnitus • Otherwise unremarkable medical history	None
Rosa MA, et al. (2006)	24y F	• GTC (initial tonic phase for 8 seconds, followed by clonic movements for about 3 min). • Heart rate elevation. • No incontinence. • 10 min postictal confusion. • Complete amnesia for event. • Oxygenation was provided and intravenous medication access was achieved but occurred after seizure had ended. • Seizure occurred on the 5th day of stimulation during the 10th session.	Left motor cortex, as defined by optimal position for induction of MEPs in the ABP.	5 days of 25 trains per day (10 Hz × 10s; 20s ITI) = 2500 pulses/day @ 100% MT	• CRPS • Had previous surgical neurovascular decompression by supraclavicular approach for a thoracic outlet syndrome. • Otherwise unremarkable medical history	NR
Picarelli H, et al (2010)	>22y Sex NR	• GTC (no focal onset, lasting 15 seconds) • Mild post-ictal confusion lasting 15 minutes. • Following seizure there were no motor deficits, head CT and EEG were normal. • Seizure occurred on the 7th day of stimulation.	Left motor cortex, as defined by optimal position for induction of MEPs in the FDI.	10 days of (25 trains (10 Hz × 10s w/60s ITI) = 2500 pulses/day @ 100% RMT	• CRPS • Physical therapy program (kinesiotherapy plus low impact, aerobic, relaxation and stretching exercises) • No history of seizure or epileptic disorders.	• naproxen 250mg bid • amitriptyline 50mg qd • carbamazepine 200 mg bid

Table 9

rTMS adverse events by positive sensory symptom

Number of patients experiencing specified adverse events per positive sensory symptom. Total number patients with adverse event are given along with corresponding percentage of total patient population within positive sensory symptom.

	AH (n =393)	Tinnitus (n =877)	Neuropathic Pain (n = 311)	Migraine (n = 165)	Fibromyalgia (n = 53)
Abdominal Pain	**1 (0.25%)**	0	0	0	0
Clicking Noise Persistence	**1 (0.25%)**	0	0	0	0
Concentration Difficulty	**3 (0.76%)**	0	0	0	0
Dizziness	**3 (0.76%)**	0	**2 (0.64%)**	**1 (0.61%)**	**1 (1.89%)**
Earache	**1 (0.25%)**	0	0	0	0
Fatigue/Drowsiness	**1 (0.25%)**	0	**1 (0.32%)**	**4 (2.42%)**	0
Headache	**39 (9.92%)**	**44 (5.02%)**	**9 (2.89%)**	**3 (1.82)**	**16 (30.19%)**
Hearing Problems	**2 (0.51%)**	0	0	**1 (0.61%)**	0
Hot/Cold Sensitivity	0	0	**2 (0.64%)**	0	0
Imbalance	0	**1 (0.11%)**	0	0	0
Irritability	0	0	0	**1 (0.61%)**	0
Ischemic Chest Pain	**1 (0.25%)**	0	0	0	0
Jaw Soreness	0	**25 (2.85%)**	0	0	0
Light-Headedness	**5 (1.27%)**	**1 (0.11%)**	0	0	0
Memory Difficulty	**4 (1.02%)**	0	0	0	0
Muscle Twitching	**14 (3.56%)**	**19 (2.17%)**	0	**1 (0.61%)**	0
Nausea	**1 (0.25%)**	0	0	**1 (0.61%)**	**1 (1.89%)**
Neck Pain	0	**24 (2.74%)**	**3 (0.96%)**	0	**6 (11.32%)**
Optic Neuritis	0	0	0	**1 (0.61%)**	0
Pain in Shoulder	0	0	0	0	0
Photophobia	0	**1 (0.11%)**	0	0	0
Psychiatric Symptom Exacerbation	**6 (1.53%)**	0	0	0	**1 (1.89%)**
Restlessness	**1 (0.25%)**	**1 (0.11%)**	0	0	0
Seizure	0	**1 (0.11%)**	**2 (0.64%)**	0	0
Scalp Discomfort	**1 (0.25%)**	0	0	0	0

	AH (n =393)	Tinnitus (n =877)	Neuropathic Pain (n = 311)	Migraine (n = 165)	Fibromyalgia (n = 53)
Sinusitis	0	0	0	**2 (1.21%)**	0
Symptom Exacerbation	**4 (1.02%)**	**19 (2.17%)**	0	**4 (2.42%)**	0
Tingling Sensation	**1 (0.25%)**	**1 (0.11%)**	**5 (1.61%)**	0	0
Temple Pain	0	**1 (0.11%)**	0	0	0
Unpleasantness	0	**5 (0.57%)**	0	0	0
Vigorous Dreams	0	0	0	**1 (0.61%)**	0
Visual Hallucination	**1 (0.25%)**	0	0	0	0