



## Experimental Use of Transcranial Magnetic Stimulation (TMS) to Treat Tinnitus in a Deaf Patient

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### Abstract

A 28-year-old deaf female patient underwent 10 sessions of repetitive Transcranial Magnetic Stimulation (rTMS) as a participant in a placebo-controlled clinical trial for treatment of tinnitus. Trial participants received 2000 pulses of rTMS per session at a stimulation rate of 1 Hz. The neural target for rTMS was auditory cortex within Heschl's gyrus. The primary outcome measure was the Tinnitus Functional Index (TFI); secondary outcome measures included a Visual Numeric Scale (VNS) for self-rated tinnitus loudness, Beck Depression Inventory II (BDI-II) and State Anxiety Inventory (SAI). Assessments were conducted at baseline, immediately after the last (10<sup>th</sup>) rTMS session, and 1, 2, 4, 13 and 26 weeks after the last rTMS session. At baseline, the patient's TFI score was 27.6, which indicates that tinnitus was not a severe problem for her. After 10 rTMS sessions, her scores on the TFI, BDI and SAI increased (worsened), while the VNS score for tinnitus loudness decreased from 5.1 at baseline to 3.5. Her TFI score remained elevated at all follow-up assessments until week 26 when this score returned to its baseline level. Approximately half of the tinnitus patients in the clinical trial who received active rTMS (18 of 35) exhibited significant reductions in TFI scores that were sustained throughout the follow-up period. The fact that this patient did not benefit from rTMS might be attributed to the following factors: Low TFI baseline score; sub-optimal TMS stimulus intensity; sub-optimal neural target for TMS. Although this patient did not benefit from rTMS, additional participants with profound hearing loss + bothersome tinnitus should be tested to determine if some of them do benefit from the procedure. Because many forms of sound therapy for tinnitus management are not practical for patients with profound hearing loss, rTMS might be a potential treatment option for this population.

### Keywords

Tinnitus, Transcranial magnetic stimulation, TMS, Deaf, Profound hearing loss

### Abbreviations

BDI-II: Beck Depression Inventory II, NCRAR: National Center for Rehabilitative Auditory Research, rMT: resting Motor Threshold, rTMS: repetitive TMS, SAI: State Anxiety Inventory, TMS: Transcranial Magnetic Stimulation, THI: Tinnitus Handicap Inventory, VNS: Visual Numeric Scale

### Introduction

Chronic tinnitus, the perception of sound in the absence of external acoustic stimuli, affects 10-15% of the adult population [1] and is a major clinical problem that negatively affects quality of life [2-5]. A positive correlation exists between self-rated tinnitus loudness and tinnitus severity [6]. Therefore, a treatment capable of reducing the perceived loudness of tinnitus would be invaluable.

Currently there is no "cure" for tinnitus. Different clinical management strategies are available, but there are no procedures that consistently offer relief for all individuals with tinnitus. Tinnitus rehabilitation encompasses a wide variety of methods, many of which show little evidence-based support of effectiveness [7]. Also, there is a lack of understanding as to why some tinnitus patients report benefit from one treatment over another. Perhaps certain populations or certain forms of tinnitus respond better to specific interventions.

Many tinnitus interventions use sound-based methods to provide relief for patients [8]. These can include music or pleasant environmental sounds produced by iPhone apps, iPods, MP3 players or table-top sound systems; in-the-ear sound generators; hearing aids or other devices that improve hearing and also reduce the perception of tinnitus. Unfortunately, most of these sound-based therapies cannot be implemented by deaf patients.

While the prevalence of tinnitus among deaf individuals is unknown, the percentage is probably high because tinnitus is more likely to occur in people who experience significant hearing loss [1]. In a survey of 808 deaf patients who were referred for cochlear implantation, 72% experienced tinnitus [9]. For deaf individuals who are not interested in cochlear implantation and yet are bothered by their tinnitus, a tinnitus therapy that is not dependent on sound-based methods would be beneficial.

Research has shown that regardless of the pathology associated with tinnitus onset (e.g., damage to peripheral auditory structures), the continued perception of tinnitus is generated by neural activity within in the central auditory system [10]. Many studies concluded that tinnitus is associated with neuroplastic changes in the central auditory system, such as increased spontaneous activity of auditory neurons [11], tonotopic reorganization of auditory cortex [12,13],

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and increased neural synchrony [14]. A common theme across all of these neurophysiological models is altered neural processing associated with tinnitus. Results from neuroimaging studies suggest that tinnitus is associated with abnormal neural activity in auditory cortex. Both positron emission tomography [15-17] and functional magnetic resonance imaging studies [18-20] have shown increased neural activity in auditory cortical regions in individuals with tinnitus compared to a control group.

These findings point to auditory cortex as a possible neural generator for tinnitus. A procedure that can suppress neural activity in regions associated with tinnitus perception would offer a means to treat the condition. Such a procedure exists in the form of Transcranial Magnetic Stimulation (TMS), a non-invasive intervention that delivers electromagnetic pulses through a coil placed in contact with the patient's scalp. Energy from the coil is transmitted through the skull, inducing an electric current in underlying neural tissue and thereby affecting neuronal activity. Results of previous studies suggest that TMS might be an effective treatment for tinnitus (see Theodoroff & Folmer [21] for a review), although most of these studies were conducted in relatively small research populations.

TMS represents a potential treatment option for deaf patients who are bothered by tinnitus, but who are not interested in cochlear implantation. The case presented here involves a profoundly hearing-impaired individual who participated in a clinical trial of repetitive TMS (rTMS) as a treatment for tinnitus at the National Center for Rehabilitative Auditory Research (NCRAR) located at the VA Portland Health Care System in Portland, Oregon. To our knowledge, this is the first published report of rTMS being used to treat tinnitus in a deaf patient.

## Methods

The rTMS clinical trial at NCRAR was a randomized, double-blind, placebo-controlled study. Eligible participants were randomized according to a stratified 2 x 2 design into active or placebo arms and left- or right-side of the head TMS coil placement. Participants received rTMS for ten consecutive business days. Outcomes were measured prior to receiving treatment and immediately post-treatment (i.e., following the final rTMS session). Follow-up evaluations were conducted 1, 2, 4, 13, and 26 weeks post-treatment.

### Repetitive transcranial magnetic stimulation procedure

A Magstim Rapid<sup>2</sup> (Magstim Company Ltd, Whitland, Carmarthenshire, Wales, UK) transcranial magnetic stimulator system was used in this study. Coil temperature was monitored by a system built into the Magstim Air Film coil. The coil was placed in an adjustable stand that held it against the subject's head in a fixed location. During rTMS sessions, subjects sat in a comfortable chair with head and neck supports which helped them to minimize movements. Prior to conducting rTMS sessions, each participant's resting motor threshold (rMT) was obtained by recording electromyography from the contralateral first dorsal interosseous muscle according to procedures described by Silbert et al. [22]. This threshold is used to determine the stimulus level for TMS sessions and for safety purposes (rMT helps to establish the stimulus level not to exceed during TMS sessions). For the clinical trial, TMS stimulus intensity was set to 110% (or lower) of the individual's rMT. Participants received 2000 pulses of low-frequency (1 Hz) rTMS during each of 10 sessions. Our target for TMS was auditory cortex, so the center of the coil was positioned just above the top of the subject's pinna (outer ear) according to a procedure described by Langguth et al. [23]. In this case study, the subject received active rTMS at this target location on the left side of her head.

### Outcome measures

The primary outcome measure for the clinical trial was the Tinnitus Functional Index, a 25-item questionnaire that assesses tinnitus severity [24]. The TFI has a 0-to-10 response format for each of its items allowing for finer scaling of tinnitus severity compared to

other questionnaires. Another advantage of the TFI is its sensitivity to treatment-related change. Secondary outcome measures included: Self-rated tinnitus loudness reported on a Visual Numeric Scale (VNS); Tinnitus Handicap Inventory (THI), a 25-item questionnaire that is widely-used in both clinical and research settings as a self-assessment measure of tinnitus severity [25]; and two questionnaires assessing psychological status: the Beck Depression Inventory II (BDI-II), a 21-item questionnaire used to assess depression [26], and the State Anxiety Inventory (SAI), a 20-item self-report instrument developed by Spielberger [27]. The THI, TFI, BDI-II, and SAI questionnaires were also administered pre-TMS treatment (baseline), post-TMS treatment, and at each of the follow-up visits. An American Sign Language interpreter was present for all sessions (including the informed consent process) attended by the deaf participant who is the subject of this report. Otherwise, procedures conducted with this subject were identical to those implemented with all other participants in the clinical trial.

## Results

This case study presents data from a 28 year-old profoundly hearing-impaired female subject. The patient's hearing loss was caused by scarlet fever at age 4 years. Hearing loss worsened during childhood and adolescence to reach the current profound levels in adulthood. Neurological status was otherwise normal. The patient's medical history includes depression, anxiety and irritable bowel syndrome. She reported hearing tinnitus for 17 years and described its perception as "in the head" – not localized to one side or the other. Prior to starting the TMS procedure, all participants completed a tinnitus history questionnaire. One of the questions asked, "How much of a problem is your tinnitus?" with possible responses: "Not a problem"; "a small problem"; "a moderate problem"; "a big problem"; or "a very big problem". The subject responded her tinnitus was "a small problem" for her. A different question asked, "Which is more of a problem for you, hearing difficulty or tinnitus?" The subject's response: "They are equally bothersome." It is interesting that the subject considers tinnitus and hearing loss as "small problems" although she is deaf and chose to participate in a clinical trial for tinnitus treatment.

Table 1 displays audiometric results for this subject for pure-tone frequencies 0.25-1.5 kHz (no measurable thresholds could be obtained for test frequencies above 1.5 kHz). Table 2 displays her scores on the primary and secondary outcome measures at baseline and all follow-up assessments.

After baseline assessments were completed, the subject's rMT was measured at 60%, but she could not tolerate the sensations produced by the TMS coil at a stimulus intensity of 60%. This subject needed to have the stimulus intensity reduced to 40% initially, and then she could tolerate rTMS intensities of 45-50% in subsequent

**Table 1:** Audiometric thresholds in dB HL for right ear (RE) and left ear (LE) for frequencies 0.25-1.5 kHz)

Audiometry	.25 kHz	.5 kHz	.75 kHz	1 kHz	1.5 kHz	2 – 8 kHz
RE	80	90	95	105	110	NR
LE	75	85	90	95	110	NR

NR: No Response

**Table 2:** Scores on primary and secondary outcome measures

VISIT	TFI	THI	BDI-II	SAI	VNS
<i>Baseline</i>	27.6	18	13	36	5.1
<i>Post-TMS</i>	44.0	18	19	42	3.5
FOLLOW-UP	TFI	THI	BDI-II	SAI	VNS
<i>1 week</i>	35.2	18	26	59	4.5
<i>2 week</i>	56.0	36	24	50	3.0
<i>4 week</i>	34.4	20	34	53	4.0
<i>13 week</i>	38.0	18	8	36	7.1
<i>26 week</i>	25.2	14	15	35	4.0

TFI: Tinnitus Functional Index, THI: Tinnitus Handicap Inventory, BDI-II: Beck Depression Inventory-II, SAI: State Anxiety Inventory, VNS: Visual Numeric Scale for tinnitus loudness

**Table 3:** Stimulus intensity for each TMS session; Sessions with "\*" indicate when the coil was moved from the original scalp target to reduce subject discomfort.

Stimulus Intensity for Each TMS Session									
1	2	3	4	5	6	7	8	9	10
40%*	45%	45%	50%	50%	50%	50%	50%*	50%*	45%

sessions (Table 3). After the stimulus intensity was reduced, she was able to tolerate the entire presentation of 2000 pulses per session. In the clinical trial, five other subjects requested the TMS intensity to be reduced by 5 or 10%. During three TMS sessions with the deaf participant, the TMS coil was moved a few millimeters away from the original scalp target location to reduce her discomfort by decreasing the temporalis muscle response (contraction) to the magnetic field.

Compared to baseline, the subject's TFI score increased 16.4 points post-TMS, which indicates increased tinnitus severity (Table 2). Her TFI score remained higher than baseline at all follow-up assessments until 26 weeks, when the score returned to the pre-TMS level. The subject's self-rated tinnitus loudness (VNS score) decreased 1.6 points post-TMS compared to her baseline score. However, follow-up VNS scores tended to fluctuate according to the subject's usual pre-treatment pattern of perceptual variation in tinnitus. BDI-II and SAI scores both increased post-treatment, but returned to baseline levels at the 26-week assessment.

## Discussion

A majority of tinnitus patients have some degree of hearing loss [1]. Many patients with tinnitus and significant hearing loss can use hearing aids to reduce the perception of tinnitus and improve their communication abilities [28,29]. In cases of profound hearing-impairment with tinnitus, cochlear implantation often reduces the perception or severity of tinnitus (for a review of this literature, see Baguley & Atlas [30]).

Andersson et al. [31] mailed questionnaires to 151 cochlear implant (CI) recipients who had been profoundly hearing-impaired. Although 74% of respondents experienced tinnitus, only 17% of them were severely distressed by their tinnitus; this percentage increased only to 25% when individuals with moderate tinnitus-related distress were included in the calculation.

Data presented in this case study indicate that the subject's baseline self-reported tinnitus severity (TFI score) was low, consistent with the findings of Andersson et al. [31] that many individuals with profound hearing loss also experience tinnitus, but are not distressed by it. Results of this case study also indicate that the subject did not benefit from rTMS treatment. One explanation is that increases in TFI, BDI and SAI scores the patient exhibited post-TMS could be due to her usual patterns of fluctuations in these symptoms. Another possibility is the changes are a direct result of rTMS treatment. Multiple factors probably contributed to this subject not being a "responder" to TMS treatment: 1) Low TFI baseline score – results from our rTMS clinical trial for tinnitus indicate that treatment responders often have significantly higher TFI scores at baseline compared to non-responders [32]; 2) Sub-optimal TMS stimulus intensity – Table 3 shows that rTMS stimulation intensity was reduced from the initial 60% value to 40-50% during different sessions at the subject's request due to her complaints of discomfort; and 3) Sub-optimal neural target for TMS, which was left auditory cortex for this subject. Factor 3 might have occurred for the following reasons: a) a different target, perhaps in the opposite hemisphere, might have been more effective; b) in response to subject complaints of discomfort (involving her jaw/ temporalis muscle), the TMS coil was sometimes moved a few millimeters away from the initial target. Research has yet to definitively establish an optimal target for TMS coil placement for treating tinnitus patients who have relatively normal central auditory systems. Because long-term deafness often results in abnormal organization of auditory cortex and other neural structures, it is possible that the optimal target for rTMS treatment of tinnitus in this population is different from the one used for this subject.

Results from our clinical trial indicate that approximately

half of the tinnitus patients who received active (as opposed to placebo) rTMS exhibited significant reductions in TFI score post-treatment compared to baseline values [32]. These reductions in tinnitus severity were sustained by the "responder" group during the 6-month follow-up period. Therefore, rTMS shows promise as a potential tinnitus treatment. Although the subject of this case study did not benefit from rTMS treatment, additional research should be conducted to determine if other deaf or profoundly hearing-impaired individuals with tinnitus might benefit from this procedure. Because such patients are, for the most part, unable to use external sound therapy for tinnitus management, rTMS treatment might be a viable alternative for some of them.

## Ethical Statement

The VA Portland Health Care System Institutional Review Board reviewed and approved the study protocol. All participants provided informed written consent prior to implementation of any study procedures. The parent study was registered at www.ClinicalTrials.gov (Identifier: NCT01104207).

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