Published in final edited form as:
Laryngoscope. 2008 July ; 118(7): 1228–1232. doi:10.1097/MLG.0b013e318170f8ac.

Maintenance Repetitive Transcranial Magnetic Stimulation Can Inhibit the Return of Tinnitus

Mark Mennemeier, PhD, **Kenneth C. Chelette, MS**, **Jeffery Myhill, MD**, **Patricia Taylor-Cooke, MS**, **Twyla Bartel, DO**, **William Triggs, MD**, **Timothy Kimbrell, MD**, and **John Dornhoffer, MD**

Department of Neurobiology and Developmental Sciences (M.M., K.C.C., P.T.-C., J.D.), the Department of Otolaryngology–Head and Neck Surgery (J.M., J.D.), and the Department of Radiology, Division of Nuclear Medicine (T.B.), University of Arkansas for Medical Sciences, Little Rock, Arkansas; the Department of Neurology (W.T.), University of Florida, Gainesville, Florida; and the Department of Psychiatry (T.K.), University of Arkansas for Medical Sciences and Mental Health Service, Central Arkansas Veterans Healthcare System, North Little Rock, Arkansas, U.S.A

Abstract

Objectives/Hypothesis—A single patient was tested to examine the safety and feasibility of using maintenance sessions of low-frequency repetitive transcranial magnetic stimulation (1 Hz rTMS) to reduce tinnitus loudness and prevent its return over time.

Study Design—Interrupted time series with multiple replications.

Methods—Tinnitus loudness was assessed using a visual analogue rating (VAR) with 0 = no tinnitus, and 100 = loudest tinnitus experienced; 1,800 TMS pulses delivered at 1 Hz and 110% of motor threshold were administered over the posterior, superior lateral temporal gyrus of the subject's right hemisphere until subjective tinnitus fell to a VAR of 25. TMS was reapplied as tinnitus returned to a VAR of 25 or higher. Cerebral metabolism was measured using positron emission tomography before and after treatment.

Results—In this patient, tinnitus could be reduced to a VAR of 6 or lower each time it reoccurred using one to three maintenance sessions of rTMS. Tinnitus loudness remained at or below a VAR of 25 and was reported to be unobtrusive in daily life when last assessed 4 months after the third and final round of maintenance treatment. Asymmetric increased cerebral metabolism in the right hemisphere reduced following treatment and as tinnitus improved. Maintenance treatment was well tolerated with no side effects.

Conclusions—Although a case study cannot establish treatment efficacy, this study demonstrates for the first time that it is feasible to use maintenance rTMS to manage chronic tinnitus. Maintenance rTMS might impede cortical expansion of the tinnitus frequency into adjacent cortical areas, but group studies are necessary to confirm this speculation.

Keywords

Transcranial magnetic stimulation; maintenance TMS; tinnitus; reaction time; positron emission tomography imaging

Send correspondence to Dr. Mark Mennemeier, Department of Neurobiology and Developmental Sciences, University of Arkansas for Medical Sciences, 4301 W. Markham Slot #826, Little Rock, AR 72205. msmennemeier@uams.edu.

This study was performed at the University of Arkansas for Medical Sciences, Little Rock, Arkansas, U.S.A.

INTRODUCTION

Subjective tinnitus (phantom perception of sound) affects 17% of the general population in the United States, and 25% of all tinnitus patients seek treatment. Antidepressants and benzodiazepines are most commonly prescribed for tinnitus, but no pharmaceutical is more effective at reducing tinnitus than placebo.[1] Tinnitus is theorized to involve some form of central nervous system dysfunction even when a peripheral injury is the inciting event.[2] Peripheral injury can lead to maladaptive cortical reorganization of the auditory cortex, which may amplify tinnitus.[3] Tonotopic mapping with magnetic source imaging in tinnitus patients demonstrated an expansion of cortical areas activated by the tinnitus frequency and an associated increases in tinnitus loudness.[3] Imaging studies of tinnitus patients revealed asymmetric cortical excitability (ACE) localized most frequently in the primary and secondary auditory cortices (Brodmann's areas 40, 41, 22, and 39).[4]

In contrast to pharmacologic treatments for tinnitus, a week-long course of low-frequency, repetitive transcranial magnetic stimulation (1 Hz rTMS) applied to the auditory cortex can reduce or eliminate tinnitus temporarily in over 50% of patients.[5–10] During TMS, a brief, focused magnetic field is created beneath a stimulating coil placed over the scalp. The magnetic field induces direct electrical stimulation of cortical neurons to a depth of up to 2 cm.[11] Low-frequency rTMS inhibits cortical activity beneath the coil, which may also affect activity in functionally linked cortical regions.[12,13] Five studies used positron emission tomography (PET) images to target 1-Hz rTMS over areas of ACE in either the left or right temporal lobe.[5–9] Partial and complete remissions of tinnitus were found after active but not sham rTMS in 50–83% of patients. One study also examined changes on PET following treatment and found a tendency for reduced ACE as tinnitus improved.[8] Another study found changes in TMS parameters after treatment consistent with decreased cortical excitability.[14] A major limitation of all these studies, however, is that tinnitus returns within 1 to 2 weeks after treatment. Increasing the number of initial rTMS treatments from 5 to 10 days does little to extend the duration of the treatment effect.[9]

We hypothesized that if tinnitus signals an expansion of cortex representing the tinnitus frequency, then applying rTMS as symptoms return (maintenance rTMS) might prolong the treatment effect by inhibiting cortical expansion. Maintenance rTMS has some demonstrated efficacy in studies of depression,[15] but it has not been applied to tinnitus. In addition, the reliability of the rTMS treatment effect for tinnitus has not been examined. The feasibility of using maintenance rTMS to treat tinnitus was tested for the first time in a single patient with chronic tinnitus who demonstrated an initial positive response to a weeklong course of 1-Hz rTMS.

MATERIALS AND METHODS

Subject

The subject was a 44-year-old white male with a 15-year history of bilateral tinnitus that worsened over 3 years preceding this study. He described the tinnitus as a high-pitched ringing sound of equal intensity in both ears. He had a 20-year history of exposure to loud music and complained of mild hearing loss (HL), but had no other significant auditory or vestibular complaints. He was not taking medication routinely. An audiogram revealed a mild to moderate, down-sloping, sensorineural HL symmetrical in both ears to a maximum loss at 4,000 Hz of 55 dB, with 100% speech discrimination in both ears. A magnetic resonance image of the head with contrast was read as normal. The patient provided written informed consent, in the presence of witnesses, to participate in an rTMS treatment study for tinnitus, which had been approved by the local Institutional Review Board for Research Involving Human Subjects. Exclusionary criteria for the study included a history positive for

epilepsy, significant head injury, stroke, aneurysm, previous cranial neurosurgery, pacemaker or other metal implants, acoustic neuroma, glomus tumor, brain tumor, profound HL (>90 dB threshold at 4,000 Hz), active Ménière's disease, or medications that alter seizure threshold. Detailed results of that study have been reported elsewhere[8] and are described briefly below.

Initial rTMS Treatment Study

The subject received 5 days of active rTMS (1800 pulses delivered at 1 Hz and 110% of motor threshold [MT]) followed by 5 days of sham stimulation (i.e., a 45-degree tilt of the TMS coil with the maximum stimulator output [MSO] set at 55% without regard to MT; the MT was recorded during sham stimulation simply to mimic procedures of active stimulation). MT, defined as the lowest percentage of MSO required to elicit a visible twitch of the thumb or fingers in 3 of 6 trials when the coil was placed over the contralateral motor cortex, was not significantly different between the week of active (57% of MSO) and sham stimulation (63% of MSO). A baseline F-18-fluorodeoxyglucose (FDG)-PET/computed tomography (CT) scan revealed increased metabolic activity in a region of interest (ROI) in the anterior aspect of the superior temporal gyrus (STG) in the right hemisphere. TMS was applied directly over this ROI using a stereotaxy system.

The patient's total score on the tinnitus severity index questionnaire[16] was lowest after active rTMS (a score of 26) than at baseline (a score of 29), postsham rTMS (29), and at 3-month (27) and 6-month follow-up periods (28). His VAR of tinnitus loudness, which used a magnitude scale from 0 to 100 (0 = no tinnitus; 100 = loudest tinnitus experienced), was also lowest after active rTMS (a VAR of 20) than at baseline (44), after sham rTMS (38), and at 3-month (53) and 6-month follow-up periods (70). Cognitive tests of executive function (the digit symbol test), sensory-motor performance (the finger tapping test), and memory (the three words at 5 minutes test) were conducted as a safety precaution before and after each rTMS session. Other than improvement due to practice, the subject's cognitive test scores did *not* change in association with rTMS; however, his mean reaction time (RT) to auditory stimulation on the psychomotor vigilance test (PVT) was quickest following active rTMS (mean RT = 300 ms) than at baseline (324 ms), after sham rTMS (314 ms), and at 3-month (311 ms) and 6-month follow-up periods (310 ms). The order of the PVT findings negated a simple practice effect.

A follow up FDG-PET/CT scan obtained immediately after the last day of active treatment showed reduced metabolic activity in the ROI targeted for treatment, consistent with an inhibitory effect of low-frequency rTMS. Eighteen months after completing this first treatment study, the patient was rerecruited and reconsented to participate in a follow-up study to examine the effects of maintenance rTMS. This study was also approved by the local Institutional Review Board and is described below.

Maintenance rTMS

Apparatus—The maintenance study protocol differed from that of the first study in three ways. First, to reduce patient burden, the VAR was the only repeated measure of tinnitus loudness; tests of cognitive function and the PVT were readministered only at the end of maintenance treatment; and there was no sham stimulation condition. Sham stimulation was not included because the subject failed to report any change in tinnitus during 5 days of sham stimulation in the first study, sham stimulation does not typically alter tinnitus perception in treatment studies,[5–10] and because the follow-up study focused on replication as a means of demonstrating the rTMS effect. Second, the MT was defined electrophysiologically rather than visually as the percentage of MSO necessary to elicit a motor evoked potential of 50 μvolts from the thenar muscle of the hand contralateral to TMS

in three of six stimulus trials. Third, due to the variability in PET activation associated with tinnitus, TMS was delivered over a standard treatment site corresponding to Brodmann's areas 22 and 39 located in the posterior aspect of the STG of either 1) the temporal lobe showing asymmetric increased metabolic activity, 2) the temporal lobe contralateral to the ear with loudest tinnitus, or 3) the left temporal lobe when no clear metabolic asymmetry or tinnitus imbalance is present. For this subject, the coil was positioned over the right temporal lobe owing to PET findings from the first study.

A third FDG-PET/CT scan was obtained 2 weeks after maintenance treatment had ended using the same Biograph 6 PET/CT scanner (Siemens Medical Systems, Malvern, PA) and methods as in the first study.[8] The CT portion was a six-slice Siemens Sensation helical CT scanner, and the PET portion had "Hi-Rez" lutetium silicate oxime 4-mm crystals arranged in a full-ring gantry with high-speed Pico Electronics (Pelham, NY). All images were obtained 30 minutes after the intravenous administration of 12 mCi (444 MBq) FDG. TMS was also applied using the same equipment (MagStim SuperRapid 200 Series Stimulator with an air-cooled figure-of-eight coil) and the same stimulation parameters as the first study (1,800 pulses at 1 Hz and 110% of MT). The patient's CT scan was used to navigate the TMS coil over the posterior portion of the STG in the right hemisphere using the Brainsight Frameless Stereotaxy system (Rouge Research, Montreal, Canada).

Procedures—The subject rated tinnitus loudness for both ears using the VAR. His VAR ratings for each ear were averaged because he could not discern a difference between ears. Maintenance rTMS was repeated on consecutive days (not to exceed five in a row) until the subject reported tinnitus at or below a VAR of 25, which was reported to be tolerable and unobtrusive. He was instructed to notify the examiner immediately if and when his tinnitus returned to a louder level. He was also contacted during the week via e-mail to rate his tinnitus loudness. Maintenance treatment was reinstated either the same day or the day after he reported a return of tinnitus to a level that exceeded a VAR of 25. At this point, he received one rTMS treatment per day until tinnitus fell below a VAR of 25.

Changes in PET activity across the three scans were examined using the NeuroQ Display and Analysis Program (Cardinal Health, Dublin, Ohio, Version 2.0). The subject's mean, normalized pixel counts in predefined regions of the baseline, posttreatment, and postmaintenance-treatment scans were expressed as standard deviations of the mean value for the same regions of the database of 50 normal PET scans (Table I). The registration algorithm for fitting the patient's brain scan to the normal template was a robust spatial transformation method.[17] The predefined regions encompassed two in the temporal lobes (one involving the superior temporal gyrus where the treatment ROI from the first study was located and another involving the inferior temporal gyrus) and two outside the temporal lobe, including the visual cortex in the occipital lobe and the somatosensory cortex from the postcentral gyrus to the prefrontal cortex. The latter regions were selected to examine a wide area and type of cortex.

RESULTS

The subject's VAR fell from 30 to 6 after his first maintenance rTMS session (Table II). He contacted the experimenter 7 days later to report an increase in the VAR to 63. His VAR rating fell to 5 following three additional maintenance treatments. His tinnitus was reduced for 10 days, after which he reported a sudden increase to a VAR of 82. His VAR fell again to a 5 after three more maintenance treatments. He reported a VAR of 23 when contacted 18 days postmaintenance treatment and a VAR of 25 when contacted 35 days postmaintenance treatment. The subject reported at that time that his tinnitus was barely noticeable. He returned to the clinic to see his treating physician (J.D.) 4 months after his last rTMS

treatment. He rated his tinnitus as a 17 using the VAR. Moreover, he said he was no longer aware of his tinnitus on a daily basis. A repeat audiogram showed no change from the first audiogram completed 2 years earlier. Statistical comparisons revealed that the mean VAR averaged over treatment days (47.9 [standard error = 7.9]) was significantly higher than the average VAR on days immediately following treatment (5.3 [standard error = 0.33], $t = 5.3$, degrees of freedom [df] = 6.01, $P < .001$, equal variance not assumed). Additionally, the mean VAR for treatment days was significantly higher than the mean VAR for days 18 and 35 postmaintenance treatment (24 [standard error = 1], $t = 3.0$, df = 6.1, $P < .02$, equal variance not assumed). Due to procedural differences, the patient's mean MT was higher during the maintenance study (74.7% of the MSO) than during the first treatment study (56.8% of the MSO, $t = 7.7$, df = 10, $P < .001$). As a result, the mean intensity of rTMS was also higher during the maintenance study than during the first treatment study (81.8% of MSO vs. 62.6% of MSO, respectively, $t = 7.6$, df = 10, $P < .001$).

Regarding the PET data, pixel counts for ROIs in both of the patient's temporal lobes consistently fell below the mean value for normal subjects (i.e., a negative standard deviation in 10 of 12 comparisons spanning three PET scans; $P < .01$ binomial test). The two exceptions involved the superior lateral temporal cortex in the right hemisphere of the patient's baseline scan, which was targeted for rTMS treatment, and a homologous region in the left hemisphere of the postmaintenance-treatment scan. Further, pixel counts in the right superior lateral temporal cortex showed a steady decrease relative to normal values with each successive posttreatment scan, whereas pixel counts in a homologous region of the left hemisphere showed a steady increase in each posttreatment scan. Pixel counts for the regions lying outside the temporal lobes tended to fall above the mean value for normal subjects (i.e., a positive standard deviation in 10 of 12 comparisons across the three patient scans; $P < .01$ binomial test). The two exceptions, which involved the visual cortex, were not evident in the postmaintenance treatment scan.

All rTMS sessions were well tolerated, and the subject exhibited no alteration in cognitive or audiologic function when assessed 18 days after maintenance rTMS ended. The mean RT on the PVT was faster than in any previous assessment of the PVT (293 ms).

DISCUSSION

Four findings of this study suggest it is feasible to use maintenance rTMS to manage chronic tinnitus. First, the effect of rTMS on tinnitus loudness was reliable. Tinnitus loudness could be reduced each time it reoccurred after only one to three maintenance rTMS sessions. Second, the time interval separating each successive maintenance session increased until tinnitus remained at a low and tolerable level 35 days after the last maintenance session. Third, a PET scan obtained 2 weeks after the last maintenance session showed the level of metabolic activity in the ROI initially targeted for treatment was reduced from baseline to a level commensurate with activity in the rest of the temporal lobe. Fourth, maintenance rTMS did not have an adverse effect on cognitive or audiologic function. In fact, RT improved over time.

Two weaknesses of this study limit conclusions about the efficacy of maintenance rTMS for treating tinnitus. It is unclear how well the findings from one patient will generalize to groups of subjects. Any decisions regarding treatment efficacy await replication in group studies. It will be important to learn, for example, which patients respond to maintenance rTMS as half of all tinnitus patients appear to fail initial treatment. One study found "responders" were more likely than "non-responders" to have preserved hearing and a shorter duration of tinnitus,[18] but others have not supported this relationship.[6,8,10] Even responders can react differently to rTMS. Some patients report an absence of tinnitus

following rTMS, while others, such as our patient, report a decrease but not an absence. Assessments of tinnitus can also evolve during treatment. Many patients are in the habit of ignoring tinnitus. They may not be well prepared to assess change when it occurs. For example, the patient in this study showed greater fluctuation in his VAR ratings during maintenance treatment than during his first trial of rTMS. This could be due to a greater potency of the maintenance rTMS, which was delivered at a higher intensity than in the first study, or his tinnitus may have only seemed louder when it returned after a relatively long period of reduced tinnitus. The 45-degree coil tilt method used for sham stimulation in our first study may also limit decisions about efficacy. While a coil tilt is the most commonly used form of sham stimulation for TMS, it is problematic because the magnetic field can still activate cortical neurons to some degree; in which case, a treatment effect might be observed during sham stimulation. Subjects can also tell the coil is in a different position, which might contaminate a blind. To avoid these problems, our ongoing studies now employ a method of sham stimulation that uses a sham coil, which attenuates the magnetic field to only 2.25% of MSO, and electrical stimulation of the scalp to replicate muscles twitching associated with active rTMS. However, no subject tested in our laboratory has reported a change in tinnitus perception during sham stimulation. Given these findings, the follow-up study used replication rather than sham stimulation to demonstrate an effect of rTMS on tinnitus. We observed a reduction in tinnitus loudness four of the four times that active rTMS was applied over the auditory cortex.

While interpretation is only speculative when based on a case study, our findings are at least consistent with the theory that tinnitus is *amplified* by an expansion of the cortical representation of the tinnitus frequency into areas that represent other sound frequencies.[3] We observed a relative excess of cortical activity in our patient's baseline PET scan that was used to target 1 Hz rTMS over auditory processing areas in the temporal lobe of the right hemisphere. Low-frequency TMS has been shown to inhibit neural activity.[13] The PET studies showed a steady reduction in cortical metabolism following treatment that co-occurred with reduced tinnitus. Low-frequency rTMS may reduce tinnitus loudness by inhibiting neural activity in cortical areas where the tinnitus frequency has expanded. Tinnitus may not be eliminated entirely if the tinnitus frequency is generated outside the cortex, such as in the case of loss or absence of sensory input secondary to damage to the peripheral nervous system. Peripheral injury is thought to promote and maintain tinnitus.[2] In fact, the effect of a one-time application of rTMS might be short lived precisely because the tinnitus frequency generator continues to promote cortical expansion. Maintenance rTMS may extend the duration of the rTMS effect by impeding cortical expansion of the tinnitus frequency, and prolonged inhibitory conditioning via maintenance rTMS could render the adjacent cortex less susceptible to reorganization.

CONCLUSION

This study demonstrates the feasibility and safety of using maintenance rTMS to reduce tinnitus chronically. Low-frequency rTMS also had the effect of reducing increased, asymmetric cortical metabolism in areas targeted for treatment. Maintenance rTMS appeared to extend this effect.

Acknowledgments

This study was supported by the National Institutes of Health, National Center for Research Resources Centers of Biomedical Research Excellence (COBRE) grant number RR20146; National Institute of Neurological Disorders and Stroke NS39348; National Institute of Child Health and Human Development HD040631 and HD055269; and by a Tinnitus Research Consortium grant-in-aid.

BIBLIOGRAPHY

1. Dobie RA. A review of randomized clinical trials in tinnitus. Laryngoscope 1999;109:1202–1211. [PubMed: 10443820]
2. Jeanmonod D, Magnin M, Morel A. Low-threshold calcium spike bursts in the human thalamus. Common physiopathology for sensory, motor and limbic positive symptoms. Brain 1996;119:363–375. [PubMed: 8800933]
3. Muhlnickel W, Elbert T, Taub E, Flor H. Reorganization of auditory cortex in tinnitus. Proc Natl Acad Sci U S A 1998;95:10340–10343. [PubMed: 9707649]
4. Marcondes R, Fregni F, Pascual-Leone A. Tinnitus and brain activation: insights from transcranial magnetic stimulation. Ear Nose Throat J 2006;85:233–234. 236–238. [PubMed: 16696357]
5. 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]
6. 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]
7. Richter GT, Mennemeier M, Bartel T, et al. Repetitive transcranial magnetic stimulation for tinnitus: a case study. Laryngoscope 2006;116:1867–1872. [PubMed: 17016213]
8. Smith JA, Mennemeier M, Bartel T, et al. Repetitive transcranial magnetic stimulation for tinnitus: a pilot study. Laryngoscope 2007;117:529–534. [PubMed: 17334317]
9. Plewnia C, Reimold M, Najib A, Reischl G, Plontke S, Gerloff C. Moderate therapeutic efficacy of positron emission tomography-navigated repetitive transcranial magnetic stimulation against chronic tinnitus: a randomized, controlled pilot study. J Neurol Neurosurg Psychiatry 2007;78:152–156. [PubMed: 16891384]
10. 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]
11. Bohning, DE. Introduction and Overview of TMS Physics. Washington, DC: American Psychiatric Press; 2000. p. 13-44.
12. Kimbrell TA, Dunn RT, George MS, et al. Left prefrontal-repetitive transcranial magnetic stimulation (rTMS) and regional cerebral glucose metabolism in normal volunteers. Psychiatry Res 2002;115:101–113. [PubMed: 12208488]
13. Chen R, Classen J, Gerloff C, et al. Depression of motor cortex excitability by low-frequency transcranial magnetic stimulation. Neurology 1997;48:1398–1403. [PubMed: 9153480]
14. Langguth B, Kleinjung T, Marienhagen J, et al. Transcranial magnetic stimulation for the treatment of tinnitus: effects on cortical excitability. BMC Neurosci 2007;8:45. [PubMed: 17605764]
15. O'Reardon JP, Blumner KH, Peshek AD, Pradilla RR, Pimiento PC. Long-term maintenance therapy for major depressive disorder with rTMS. J Clin Psychiatry 2005;66:1524–1528. [PubMed: 16401152]
16. Folmer RL, Griest SE, Martin WH. Chronic tinnitus as phantom auditory pain. Otolaryngol Head Neck Surg 2001;124:394–400. [PubMed: 11283496]
17. Tai Y-C, Lin K, Hoh CK, Huang S, Hoffman E. Utilization of 3-D elastic transformation in the registration of chest x-ray CT and whole body PET. IEEE Trans Nuclear Sci 1997;4:1606–1612.
18. 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]

TABLE I

Patient's PET Data Expressed as Standard Deviations of Normal Values*.

	Predefined ROI							
PET Scan	**Left sLT**	**Right sLT**	**Left iLT**	**Right iLT**	**Left SM**	**Right SM**	**Left PVC**	**Right PVC**
Baseline	−.37	.15†	−.78	−1.06	.21	.48	−.05	.24
3-1-06								
Postactive Tx	−.37	−.26†	−1.79	−.79	.45	.17	.15	−.15
3-13-06								
Postmaintenance Tx	.06	−.67†	−1.03	−1.62	.45	.17	.35	.24
11-07-07								

*From the NeuroQ database of 50 PET scans of normal subjects. Left and right refer to the left and right hemispheres, respectively.

†Includes the PET ROI targeted for treatment in the first study.

PET = positron emission tomography; ROI = region of interest; sLT = superior lateral temporal cortex; iLT = inferior lateral temporal cortex; SM = sensory motor cortex; PVC = primary visual cortex; Tx = 1 Hz rTMS.

TABLE II

Ratings of Tinnitus Loudness and TMS Intensities During Maintenance Treatment.

	Chronology of Study													
	M1	**F1**	**M2**	**M3**	**M4**	**F2**	**M5**	**M6**	**M7**	**F3**	**Third PET**	**F4**	**F5**	**F6**
Variables	**9-24-07**	**9-25-07**	**10-9-07**	**10-10-07**	**10-11-07**	**10-12-07**	**10-22-07**	**10-23-07**	**10-24-07**	**10-25-07**	**Scan 11-07-07**	**11-16-07**	**12-05-07**	**2-22-08**
VAR	30	6	63	51	29	5	82	50	40	5		23	25	17
MT	74		74	81	74		72	74	77					
SI	81		81	89	81		79	81	85					

M refers to a day of maintenance treatment. F refers to a day of follow-up assessment.

TMS = transcranial magnetic stimulation; VAR = visual analogue rating from 0 to 100, with 0 = no tinnitus and 100 = loudest tinnitus experienced; MT = motor threshold based on a motor evoked potential of 50 μvolts or greater in 3/6 single TMS pulse trials; SI = stimulation intensity calculated as 110% of the MT.