RESEARCH ARTICLE

Repetitive transcranial magnetic stimulation for tinnitus: influence of loudness and frequency of tinnitus on tinnitus suppression

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Abstract

Background and Aim: Tinnitus is a distressing symptom for which few treatments exist. Low-frequency repetitive transcranial magnetic stimulation (rTMS) of the temporal cortex has been proposed as a treatment for chronic tinnitus. This study determined relationship between psychoacoustic parameters such as loudness and frequency of tinnitus and outcome with rTMS treatment.

Methods: Twenty six patients (22 male, 4 female) with chronic tinnitus received low frequency (1 Hz) rTMS at intensity 110% motor threshold and 1200 stimuli on three subsequent days to the left auditory cortex. The treatment outcome was assessed with loudness balance test and Tinnitus Handicap Inventory (THI).

Results: There was a significant difference between loudness of tinnitus and THI scores before and after rTMS. There was no correlation between psychoacoustic parameters loudness and frequency of tinnitus and rTMS treatment outcome.

Conclusion: Our data suggest that repetitive transcranial magnetic stimulation, regardless of loudness and frequency of tinnitus, can be used as a therapeutical tool for the treatment of tinnitus.

Keywords: Transcranial magnetic stimulations; repetitive; tinnitus

Introduction

Tinnitus is a phantom sound that one hears in the ears or in the head with no external source. It is a common symptom of disorders of the auditory system [1]. Epidemiological data indicate that its prevalence in the adult population is over 10%. Approximately one percent of the general population is severely affected by tinnitus with major negative impact on quality of life and is seeking medical advice for their tinnitus [2]. It is estimated that in Western Europe and in the United States of America more than 13 million patients are suffering from tinnitus. No treatment, either pharmacological or nonpharmacological, has proved efficacy in tinnitus [3]. The complete pathophysiology of this symptom is still unknown. A wide range of peripheral disorders such as hearing loss, anxiety, insomnia or depression is often associated with tinnitus [4].
In recent years, it has become widely accepted that maladaptive changes of central information processing are critically involved in tinnitus perception and generation [5]. Recently human brain imaging studies for tinnitus have elucidated various neural networks engaging in tinnitus perception [6]. It seems patient’s conscious thinking about tinnitus result in activity in both cortical and sub-cortical areas of the brain, which includes the limbic and autonomic nervous systems [7]. Some studies exhibited relationship between dysfunction of outer hair cells and tinnitus in patients with normal hearing [8]. It now generally is accepted that some forms of tinnitus are auditory phantom phenomena similar to central neuropathic pain or other forms of pain [9]. These phantom phenomena are considered to be the results of reorganization of central nervous system (CNS) structures [10].

It has been shown that, the normal tonotopic map is altered in tinnitus and the subjective tinnitus strength is correlated with the amount of shift of the tinnitus frequency in the auditory cortex [11]. This is similar to the phantom limb phenomenon where there is a strong correlation between the amount of reorganization of the somatosensory cortex and the amount of phantom limb pain. The tonotopic map can become reorganized in reaction to any abnormal or even normal pattern of neural activity from the periphery through expression of neural plasticity [12]. Functional imaging, using both functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) scanning has supported the hypothesis of cortical reorganization in tinnitus patients [13,14].

The fact that tinnitus may persist after total cochlear and auditory nerve removal, for example after vestibular schwannoma surgery, prompts the view of tinnitus as a central phenomenon [15]. The report of total disappearance of long-lasting tinnitus in a patient after stroke also endorses this central hypothesis [15]. Other aspects of central disturbances related to tinnitus include cognitive and affective repercussions of tinnitus perception, attention deficit, sleep disorders, anxiety and depression [16].

Transcranial magnetic stimulation (TMS) is a noninvasive technique that allows brain excitability to be transiently modified. This method uses a coil placed on the scalp that generates magnetic pulses of very short duration. Taking advantage of the fact that magnetic fields pass largely undistorted through the scalp and skull, TMS induces an electrical current in the brain that can excite or inhibit neuronal activity depending on the stimulation frequency [17].

The objective of this study is to determine effects of using repetitive transcranial magnetic stimulation (rTMS) aimed at the left auditory cortex in patients with chronic tinnitus. We aimed to investigate the potential prognostic factors in patients with tinnitus that predict a beneficial outcome of low-frequency rTMS treatment.

**Methods**

Twenty six patients (4 women, 22 men with mean age 49.03 with SD 14.36 years) with chronic tinnitus where included in the study. The protocol was approved by the local ethics committee in Hamadan University of Medical Sciences (I Registration ID in IRCT IRCT-201403189014N32). 26 patients, 5 had bilateral tinnitus and 20 had unilateral tinnitus (12 left, 8 right) and one had tinnitus in head. Bilateral tinnitus was defined as a sound with the same frequency and loudness in both ears. The duration of tinnitus was longer than six months for all patients. Patients with history of severe neurologic disorders, epilepsy and cardiac pacemaker were excluded from the study.

Before treatment, all otological and audiological examinations, including otoscopy, tympanometry, pure tone audiometry, and tinnitus evaluation had been done for all subjects. Each patient was assessed with the Persian version of validated questionnaires Tinnitus Handicap Inventory (THI) before and after rTMS. The scores were then graded into four categories not handicapped (0-16), mildly handicapped (18-36), moderately handicapped (38-56), and severely handicapped (58-100) [18].

Repetitive transcranial magnetic stimulation (rTMS) was applied using a super rapid...
stimulator, with the circular coil placed over the left auditory cortex. Patients received stimulation on three subsequent working days. The stimulation protocol consisted of 1200 stimulations at frequency 1 kHz and intensity of 110% of the individual resting motor threshold, over the left auditory cortex. All patients tolerated rTMS well. None of the patient developed seizures or other serious side effects or adverse effects.

Psychoacoustic pitch and loudness matching were determined before and after treatment (immediately after treatment and one week later). To investigate which patients with tinnitus benefit from rTMS treatment, we relied on patient’s statements and compared the percentage of change with loudness matching and Tinnitus Handicap Inventory scores.

Results
Twenty-six patients were studied. TMS had a partial effect in 13 of the patients studied (50%), no effect in twelve (46.2%) patients, and in one case (3.8%) worsened (negative). Pure tone audiometry showed normal hearing in five individuals; in the remainder, seven had mild, eleven moderate and three of patients had severe hearing loss. The audiograms after rTMS did not differ from before rTMS audiograms. Loudness matching test reveal the loudness of tinnitus ranged between 1-20 dBSL. There is significant difference between loudness of tinnitus before and after treatment (p<0.05) (Table 1).

Direct comparison indicates a reduction in THI score after rTMS compared with baseline. There is significant difference between scores of THI before and after rTMS (Table 1). The present findings also suggest that there is no correlation between loudness of tinnitus and outcome of treatment according to patients’ statements regarding effect of rTMS (Table 2). Our finding highlights, there is no significant correlation between frequency of tinnitus and effect of rTMS treatment (Table 3).

Discussion
The results of the present study show that tinnitus can be transiently suppressed partially by rTMS. We obtained that 50% of patients showed decreased tinnitus after rTMS that lasted for one month. Shapiro et al. reported suppression of tinnitus in 44% of their cases. They used a single session of rTMS. These results are in agreement with Hallet study that demonstrated reduction of tinnitus in 57% of their cases [17]. This small difference (44% vs. 50%) might be a result of the small sample sizes of these studies. Theodoroff and Folmer, and Plewnia et al. reported an overall proportion of success to be 51% and 64%, respectively [19,20]. Given the relatively small number of subjects in most of these studies, as well as the broad range of percentage of success, the reported benefit of rTMS for tinnitus may be overestimated.

We stimulated all cases in the left auditory cortex with rTMS 1 Hz for 20 minutes for three days, because investigations have been reported abnormal asymmetry in auditory cortex of tinnitus patients, with higher levels of spontaneous

Table 1. Mean (standard deviation) of loudness of tinnitus and Tinnitus Handicap Inventory scores before and after treatment in patients with tinnitus

<table>
<thead>
<tr>
<th>Test</th>
<th>Before (n=26)</th>
<th>After (n=26)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loudness</td>
<td>6.23 (3.62)</td>
<td>4.57 (2.88)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>THI score</td>
<td>2.88 (1.21)</td>
<td>2.46 (1.06)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

THI; Tinnitus Handicap Inventory

Table 2. Correlation between loudness of tinnitus and outcome of repetitive transcranial magnetic stimulation

<table>
<thead>
<tr>
<th>Treatment outcome</th>
<th>&lt;2dB</th>
<th>2-5dB</th>
<th>&gt;5dB</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partial</td>
<td>7.70</td>
<td>30.80</td>
<td>61.50</td>
<td>0.466</td>
</tr>
<tr>
<td>No-effect</td>
<td>33.30</td>
<td>16.70</td>
<td>50.00</td>
<td>0.408</td>
</tr>
</tbody>
</table>

rTMS; repetitive transcranial magnetic stimulation
neural activity on the left side and rTMS can induce a tinnitus suppression and it has been shown that it results in tinnitus suppression for longer periods [21,22]. The result of this study reveal that mean of loudness of tinnitus after treatment was less than before and this difference was statistically significant. Also, the results of present study are in agreement with Khedr et al. and Plewnia et al. who both reported self-assessment scales for tinnitus loudness and tinnitus annoyance showed a tendency towards a benefit of rTMS [20,23].

Our results showed a significant difference in the tinnitus questionnaire score after rTMS compared with baseline. These results are an extension of our earlier studies showing the short-term effects of low-frequency rTMS on tinnitus [24].

In this study, two psychoacoustic parameters, loudness and pitch of tinnitus, were not significantly related with treatment outcome. In our study, since no similar research has been done on the mentioned parameters, the results are not comparable.

**Conclusion**

Repetitive transcranial magnetic stimulation is a promising technique in the management of chronic tinnitus. There are still important questions about this method. According to these results the effect of rTMS on tinnitus reduction did not relate to loudness and frequency of tinnitus. Thus rTMS can be used as a treatment for tinnitus regardless of loudness and frequency of tinnitus. This finding needs to be studied in larger samples.

**Table 3. Correlation between frequency of tinnitus and effect of repetitive transcranial magnetic stimulation**

<table>
<thead>
<tr>
<th>Treatment outcome</th>
<th>Tinnitus frequency</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;1 KHz</td>
<td></td>
</tr>
<tr>
<td>Partial</td>
<td>53.80</td>
<td></td>
</tr>
<tr>
<td>No-effect</td>
<td>41.70</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2-6 KHz</td>
<td></td>
</tr>
<tr>
<td>Partial</td>
<td>38.50</td>
<td>0.180</td>
</tr>
<tr>
<td>No-effect</td>
<td>41.70</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;6 KHz</td>
<td></td>
</tr>
<tr>
<td>Partial</td>
<td>7.70</td>
<td></td>
</tr>
<tr>
<td>No-effect</td>
<td>16.70</td>
<td>0.329</td>
</tr>
</tbody>
</table>

**Acknowledgements**

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**REFERENCE**


