

Case Series

One Hz low frequency repetitive transcranial magnetic stimulation to Heschl's gyrus and auditory cortex in patients of tinnitus: a case series and review of literature

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Received: 04 January 2025

Accepted: 03 April 2025

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ABSTRACT

Tinnitus affects as much as 10% of young adults at some point in their life. Most tinnitus is "sensorineural," meaning that it's due to hearing loss at the cochlea or cochlear nerve level but it may originate anywhere along the auditory pathway, from the outer or middle and inner ear to the brain's auditory cortex. There is no FDA-approved drug treatment for tinnitus as of now, and controlled clinical trials have not found any drug, supplement, or herb to be any more effective than a placebo. A new and innovative promising approach for the treatment of tinnitus is repetitive transcranial magnetic stimulation (TMS) as this directly affects tinnitus-related brain activity. We hereby report the three distinct cases of tinnitus which responded well to 1 Hz low frequency TMS to Heschl's gyrus and auditory cortex. The overarching goal is to enhance awareness, understanding, and management of chronic tinnitus using TMS neurostimulation therapy as there are no such reports of interventions in Indian clinical practice till date.

Keywords: Tinnitus, Transcranial magnetic stimulation, Low frequency, Effectiveness

INTRODUCTION

Tinnitus, a condition characterized by the perception of sound without an external auditory stimulus, affects up to 10% of young adults at some point in their lives and for about 25% of them, it can be distressing enough to have a substantial impact on their mental wellbeing, family, professional and social life.¹ It is primarily caused by damage to the hair cells in the cochlea, which disrupts normal auditory processing. This damage leads to abnormal electrical signals being sent to the brain via the auditory nerve, resulting in the perception of phantom sounds. Most tinnitus cases are 'sensorineural', originating from the cochlea or cochlear nerve, but the disorder can stem from any point along the auditory pathway, including the outer, middle, and inner ear or even the auditory cortex in the brain.² Currently, there is

no FDA-approved drug treatment for tinnitus, and clinical trials have not identified any significant pharmacological intervention, supplement, or herbal remedy that is more effective than a placebo. This lack of effective treatment options has led to the exploration of alternative therapies. One promising approach is repetitive TMS (rTMS), a non-invasive technique that modulates brain activity. rTMS has been found to target brain areas involved in tinnitus, specifically reducing abnormal neuronal activity in the auditory cortex, making it an innovative option for tinnitus management.³

Recent case reports have demonstrated the potential of low-frequency (1 Hz) rTMS, particularly applied to Heschl's gyrus and the auditory cortex, to alleviate tinnitus symptoms.^{4,5} These findings offer new hope for patients suffering from chronic tinnitus, particularly in

regions like India, where such interventions are not yet widely implemented in clinical practice. This case series aims to understand the effectiveness of 1 Hz low-frequency rTMS in tinnitus patients, providing valuable insights into its potential as a therapeutic strategy for managing persistent and often debilitating condition.

CASE SERIES

Case 1

A 45-year school teacher presented with a 3-year history of gradual-onset "ringing" in both ears. The tinnitus was constant and was more noticeable when he went to bed. He believed that his hearing may have slightly worsened during the past 3 years as well but was unsure. The patient denied otalgia, otorrhea, or vertigo. He had no history of otologic trauma or surgery, recreational or occupational noise exposure, or ear infections. He was not taking any medications, and he was a non-smoker and non-drinker. The patient was not in acute distress and was cooperative on examination. All vital signs were within normal limits. Otoscopy revealed normal external auditory canals and clear tympanic membranes with normal mobility on pneumatic insufflation. His facial nerve function was grossly normal. His head and neck examination were unremarkable. The patient said that the tinnitus was very bothersome and specifically requested further work-up. She was started on variant 1 at 1 Hz, 110% motor threshold (MT), targeting the Heschl's gyrus contralateral to tinnitus. Each session delivered 1000 pulses over 16 minutes and 40 seconds without any inter-train interval for 5 consecutive days followed by a weekly treatment session for 5 weeks which resulted in a only 50% improvement in the intensity and frequency of her tinnitus. Later we gave her variant 2 at 1 Hz, 110% MT, targeting the auditory cortex contralateral to tinnitus. Each session delivered 1500 pulses over 25 minutes without any inter-train interval weekly for 5 weeks which resulted in about 90 % improvement in the intensity and frequency of her tinnitus.

Case 2

A 22-year-old male graduate student from Ratlam, presented 2 years ago in ENT OPD after getting rejected from army medical examination, where he got to know that he has healed perforation and a tympanosclerotic patch in the right tympanic membrane. He underwent right tympanoplasty in December 2022, with pre-operative pure tone audiometry showing normal bilateral hearing sensitivity. Post-operatively, he developed a persistent, high-pitched ringing sensation in the right ear that worsened during summer, leading to sleep disturbances and difficulties in studying. A follow-up audiometry in May 2023 revealed mild conductive hearing loss in the right ear, while the left ear remained normal. There was no history of vertigo. Despite on noise masking trial for 6 months, there has been no improvement in tinnitus. He was started on variant 1 at 1

Hz, 110% MT, targeting the Heschl's gyrus contralateral to tinnitus. Each session delivered 1000 pulses over 16 minutes and 40 seconds without any inter-train interval for 5 consecutive days followed by a weekly treatment session for 5 weeks which resulted in a 70 to 80% improvement in the intensity and frequency of his tinnitus.

Case 3

A 33 year old medical officer began having acute onset of tinnitus when she started taking isotretinoin for her nodular acne vulgaris from dermatologist since January 2024. Her oral doses of isotretinoin were stopped but local applications are still continued. Her sensorineural tinnitus continued and persisted throughout. She was not able to tolerate the tinnitus which was bilateral, continuous, more perceived on left than right side. Her pure tone audiometry showed 20 decibel hearing deficits on left side. She tried sound distraction techniques and calcium, vitamin D3 and pyridoxine supplementation but there was no response. She was referred for TMS therapy in September 2024. She was started on variant 1 at 1 Hz, 110% MT, targeting the Heschl's gyrus contralateral to tinnitus. Each session delivered 1000 pulses over 16 minutes and 40 seconds without any inter-train interval for 5 consecutive days followed by a weekly treatment session for 5 weeks which resulted in initial only 40 to 50% improvement in the intensity and frequency of her tinnitus. She was later started on variant 2 at 1 Hz, 110% MT, targeting the auditory cortex contralateral to tinnitus. Each session delivered 1500 pulses over 25 minutes without any inter-train interval weekly for another 5 weeks which resulted in 80-90 % improvement in the intensity and frequency of her tinnitus.

DISCUSSION

Tinnitus can originate anywhere along the audiologic pathway but its role of cortical control is interesting from both scientific and therapeutic points. The neural substrates of tinnitus in humans have demonstrated neuronal hyperexcitability objectively represented in the central auditory system and overactivation of left temporal gyrus (Heschl's gyrus) through its diverse pathophysiology and of the functional interplay between sensory, cognitive and affective systems.⁶ Local field potential providing input to intra-cortical neural excitability at these two regions during tinnitus experience signals represent the sum of local synaptic voltages and this corresponds to the low-pass filtered range less than 200 Hz. The evidence shows that thalamocortical dysrhythmia due to enhanced theta and gamma activity could be responsible for tinnitus.⁷

A new and innovative promising approach for the treatment of tinnitus is rTMS as this directly affects tinnitus-related brain activity. High-frequency rTMS increases cortical excitability, while low-frequency rTMS is considered to inhibit the neural activity in stimulated

regions. The hyperexcitability in the auditory cortex can be reduced using low-frequency rTMS. Clinical efficacy and safety of rTMS in the treatment of chronic tinnitus have been examined in 29 randomized controlled trials involving 1228 chronic tinnitus patients.⁸ They were compared with sham-rTMS, rTMS exhibited significant improvements in the tinnitus handicap inventory scores at 1 week (mean difference [MD]: -7.92, 95% confidence interval [CI]: -14.18, -1.66), 1 month (MD: -8.52, 95% CI: -12.49, -4.55), and 6 months (MD: -6.53, 95% CI: -11.406, -1.66) post intervention showing that rTMS can effectively ameliorate chronic tinnitus. Of all included studies, 93.10% stimulated the auditory cortex as a predominant stimulation site, wherein 77.78% stimulated the left auditory cortex, regardless of which ear was affected. There is strong evidence that the left primary auditory cortex is a potential target for the 1-Hz-rTMS treatment of tinnitus in pilot studies.⁹

To the best of our knowledge, this is the first reported case of the application of low frequency rTMS over two different brain target regions in a patient with tinnitus from India. Our all 3 patients exhibited significant clinical improvements after 10 treatment sessions without any noticeable side effects. EEG activity differs significantly between tinnitus and healthy patients.

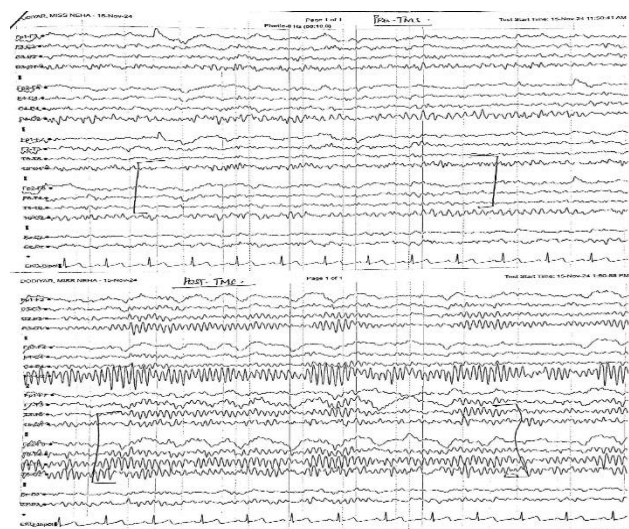


Figure 1: The comparative pre-TMS and post-TMS change for reduction in frequencies and electrophysiological activation at right temporal cortical regions.

Indeed, evidence suggest that strong reductions in tinnitus loudness were associated with increases in alpha power in the stimulated auditory cortex.¹⁰ However, our case report should be interpreted with caution because of the lack of a placebo control; the heterogeneity among the current treatment protocols of rTMS on tinnitus and limited numbers of patients.

CONCLUSION

TMS is one of the safest and effective approach for treating chronic debilitating tinnitus as seen from our clinical interventions in 3 cases. Further studies and clinical trials are necessary to validate the effectiveness of rTMS in broader populations, but these early results provide hope for better treatments options for those suffering from chronic tinnitus. The use of rTMS could potentially fill a critical gap in tinnitus management, offering a non-invasive alternative to current therapies.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

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Cite this article as: Khairkar P, Rathore VS, Sharma A, Khivsara A, Raghuvanshi Y, Khairkar R. One Hz low frequency repetitive transcranial magnetic stimulation to Heschl's gyrus and auditory cortex in patients of tinnitus: a case series and review of literature. *Int J Otorhinolaryngol Head Neck Surg* 2025;11:249-51.