Brain Stimulation 14 (2021) 1467–1469

Contents lists available at ScienceDirect

Brain Stimulation

journal homepage: http://www.journals.elsevier.com/brain-stimulation

Successful suppression of musical hallucinations with low-frequency rTMS of the left temporo-parietal junction: A case report

Keywords:
Musical hallucinations
rTMS
Temporo-parietal junction

A B S T R A C T

Background: Inhibitory low frequency repetitive transcranial magnetic stimulation (rTMS) of the temporo-parietal area has been applied to treat both auditory verbal hallucinations as well as tinnitus.

Objective: We hypothesized that 1 Hz rTMS to the left temporoparietal junction (TPJ) may be beneficial in alleviating musical hallucinations (MH), another condition with auditory experiences in the absence of an external source.

Methods: Here we describe a patient with almost insufferable life-long MH with comorbid depression, who received inhibitory rTMS to the left TPJ as well as the right dorsolateral prefrontal cortex (DLPFC).

Results: The intrusiveness and frequency of her MH as well as her depressive symptoms alleviated quickly and substantially, and once-a-week maintenance therapy with rTMS seemed to preserve this amelioration. Future studies will hopefully reveal whether this is a viable treatment approach for other patients suffering from MH with or without comorbid depression.

© 2021 Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

Musical hallucinations (MH) have previously been described mainly in sensorineural hearing loss. Occasionally MH are associated with psychiatric or neurological disorders [1–3]. MH may occur with no underlying morbidity [3]. Usually, musical hallucinations can be phenomenologically distinguished from involuntary musical imagery (INMI), or “earworms”. MH are experienced as music heard either inside or outside of the subject's head, while INMI refers to involuntary and/or compulsive *imagery* of music [3]. In patients with psychotic disorders, MH are less common than auditory verbal hallucinations (AVH) [3].

Functional brain imaging of patients with schizophrenia and tinnitus has demonstrated increased activity in temporo-parietal areas [4,5]. Inhibitory low frequency repetitive transcranial magnetic stimulation (rTMS) of the temporo-parietal area has been used to treat both AVH as well as tinnitus [6,7]. Most common stimulation targets have been the left temporo-parietal junction (TPJ) for AVH and the left auditory cortex for tinnitus [6,7].

Cosentino et al. reported a case with complex auditory hallucinations caused by traumatic brain injury of the right temporal pole [1]. Another case report of a patient with MH with no brain pathology demonstrated hypermetabolism of the superior temporal gyri, anterior cingulate, left orbital frontal, and medial temporal cortices in PET imaging [8].

2. Material and methods/case report

A 61-year-old woman was admitted from her psychiatric outpatient clinic to the therapeutic neuromodulation unit of Turku University Hospital at the departments of Clinical Neurophysiology and Psychiatry, for assessment and treatment of life-long MH. She had previously been treated for recurrent major depressive disorder (MDD) that had started at the age of 30, and anxiety, using various antidepressants and benzodiazepines, and psychotherapy, with some amelioration of the symptoms.

Seven years before rTMS-treatment the patient had been treated for pneumonia using corticosteroids, and she suffered a two-month psychosis. After the psychotic episode, she had started to experience her MH as more continuous and disturbing than before. She described the hallucinations as songs from the 60's and 70's that repeated and looped like an LP record skipping. The hallucinations were persistent and intrusive, disrupting her daily life. Before rTMS treatment, hallucinations were daily, approximately 70% of the time she was awake. She perceived MH as loud as a normal conversation.

Before treatment the patient's BDI score was 26 and Montgomery-Åsberg Rating Scale (MÅDRS) score was 29, both indicating moderate depression. Her Beck Anxiety Inventory (BAI) score was 17, falling in the range of mild to moderate anxiety (Fig. 1D).

https://doi.org/10.1016/j.brs.2021.09.011
1935-861X/© 2021 Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

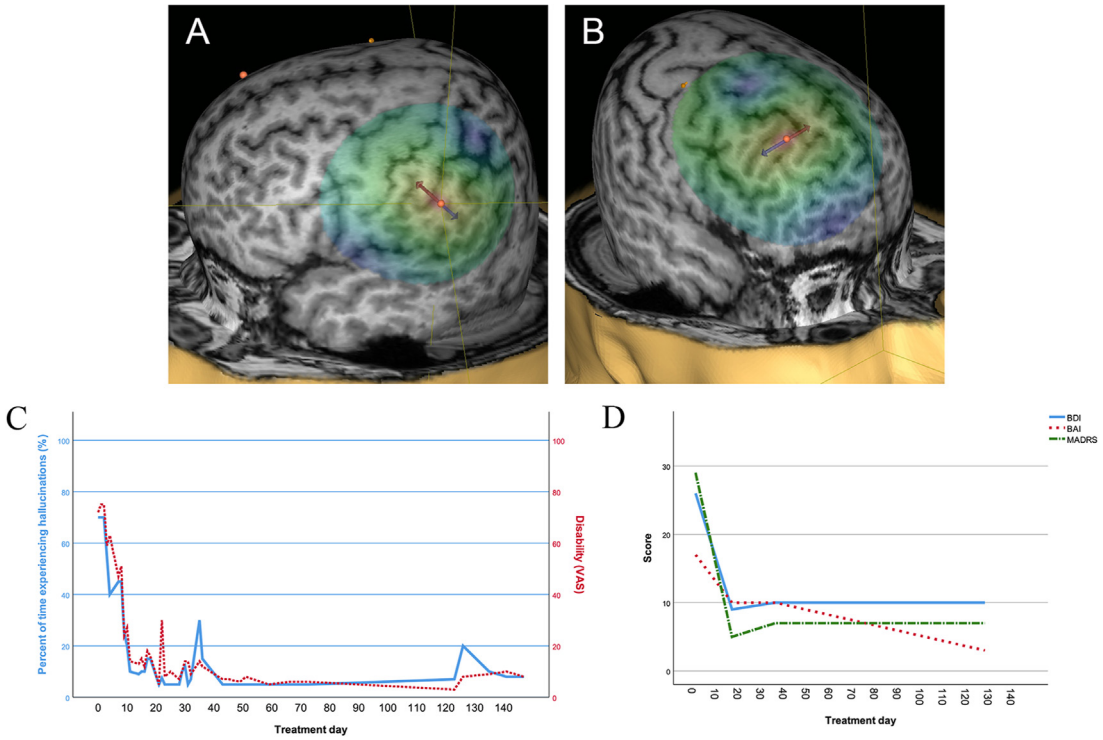

Fig. 1. Two stimulation targets for therapeutic rTMS.
(1A) Stimulation target 1: left temporo-parietal junction, low-frequency stimulation at 1 Hz (1400 pulses/session)
(1B) Stimulation target 2: right dorsolateral prefrontal cortex, low-frequency stimulation at 1 Hz, 700 pulses/session
(1C) Patient reported percentage of time per day experiencing musical hallucinations (y-axis, blue line) from the baseline at the beginning of the treatment to final follow up at 21 weeks. Patient-reported disability due to the musical hallucinations measured on the visual analogue scale (VAS) (y-axis, red dotted line) from start of treatment to final follow-up at 21 weeks.
(1D) BDI, BAI and MADRS scores over time.

The patient's 3T head MRI was normal. rTMS was delivered using a biphasic figure-of-eight coil and eXimia NBS Navigation System (eXimia TMS system, Nexstim Ltd., Helsinki, Finland). The patient received rTMS to the left TPJ (700 pulses and a 10 min break with following 700 pulses, 1Hz, 95% of resting motor threshold), to treat her MH. To treat depression and anxiety we included the right DLPFC (700 pulses, 1Hz, 95% of resting motor threshold) with a low number of pulses because we expected an additive effect with multilocus stimulation and, in addition, that the psychiatric symptoms would ameliorate after disappearance of MH. DLPFC was located as described by Mylius et al. [9] and the TPJ was located as the midpoint of a line connecting EEG electrode locations T3 and P3 (Fig. 1AB).

The patient tolerated the rTMS with no adverse effects. Treatment began with an intensive period of 25 daily treatment sessions spread over five weeks. Sessions were gradually decreased to once a week. After five sessions the patient experienced a marked decrease in the frequency, length, and intrusiveness of the MH. The experienced loudness of the hallucinations diminished from as loud as a conversation to the level of typical background music in department stores. The total daily time experiencing the MH (TDT-MH) declined from 70% to 25% of time awake (- 64%). The patient's visual analogue scale (VAS) score on a mm-scale from 0 (no distress) to 100 (most disabling symptoms), denoting disability and distress attributable to the MH, declined from 72 to 24 mm (- 67%). After the five-week intensive treatment period, the TDT-MH was 15% (a 79% decline) and the disturbance VAS score was 12 mm (an 83% decline) (Fig. 1C).

A final follow-up appointment was after 21 weeks of treatment and the TDT-MH had declined by 89% (from 70% to 8% of time awake). The disturbance VAS score had declined from 72 to 18 mm (- 75%). Also, the patient's BDI scores dropped from 26 to 5 points (- 81%) and MÅDRS scores from 29 to 5 (- 83%); BAI scores from 17 to 10 (- 41%), from baseline to the 21-week follow-up appointment (Fig. 1D). The patient was content with the outcome and continued in once-a-week maintenance therapy. Treatment is ongoing so there is no data on persistence of the effect after discontinuing rTMS.

3. Discussion

To our knowledge, this is the first case report on using rTMS to successfully treat MH in a patient with no known pathology.

The mechanism of action of TPJ stimulation remains elusive, but we presume that it may be similar to that of therapeutic rTMS for AVH [6]. The TPJ integrates input from the thalamus and the limbic system with that from the visual, auditory, and somatosensory systems.

Because the patient received treatment to both the left TPJ as well as the right DLPFC, we cannot rule out that the ameliorating effects came from the stimulation of the DLPFC, relieving her psychiatric symptoms. We think it is unlikely that the positive treatment effect came from the DLPFC stimulation alone, as the pulse amount (700 p) was rather low. MH are often mood congruent in patients with psychiatric disorders [2], which was not the case in our patient. We thus conclude that each of the two cortical targets

for rTMS probably influenced separate portions of the symptom profile, maybe with additive effects prolonging the efficacy of treatment, as has been shown for therapeutic rTMS in tinnitus patients, using a target combination of the left auditory cortex (low-frequency rTMS) and the left DLPFC (high-frequency rTMS) [10].

Financial disclosures

Janne Nordberg- Reports no disclosures.
Tero Taiminen- Reports no disclosures.
Lauri Virtanen- Reports no disclosures.
Satu K. Jääskeläinen- Reports no disclosures.
Noora M. Scheinin- Reports no disclosures.

Declaration of competing interest

All authors declare no conflicts of interest.

References

[1] Cosentino G, Giglia G, Palermo A, Panetta ML, Lo Baido R, Brighina F, et al. A case of post-traumatic complex auditory hallucinosis treated with rTMS. Neurocase 2010;16:267–72. https://doi.org/10.1080/13554790903456191.
[2] Golden EC, Josephs KA. Minds on replay: musical hallucinations and their relationship to neurological disease. Brain 2015;138:3793–802. https://doi.org/10.1093/brain/awv286.
[3] Moseley P, Alderson-Day B, Kumar S, Fernyhough C. Musical hallucinations, musical imagery, and earworms: a new phenomenological survey. Conscious Cognit 2018;65:83–94. https://doi.org/10.1016/j.concog.2018.07.009.
[4] Silbersweig DA, Stern E, Frith C, Cahill C, Holmes A, Grootoonk S, et al. A functional neuroanatomy of hallucinations in schizophrenia. Nature 1995;378:176–9. https://doi.org/10.1038/378176a0.
[5] Lockwood AH, Salvi RJ, Burkard RF, Galantowicz PJ, Coad M Lou, Wack DS. Neuroanatomy of tinnitus. Scand Audiol Suppl 1999;28:47–52.
[6] Hoffman RE, Boutros NN, Berman RM, Roessler E, Belger A, Krystal JH, Charney DS. Transcranial magnetic stimulation of left temporoparietal cortex in three patients reporting hallucinated "voices". Biol Psychiatr 1999;46:130–2. https://doi.org/10.1016/S0006-3223(98)00358-8.
[7] Lefaucheur JP, Aleman A, Baeken C, Benninger DH, Brunelin J, Di Lazzaro V, et al. Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS): an update (2014–2018). Clin Neurophysiol 2020;131:474–528. https://doi.org/10.1016/j.clinph.2019.11.002.
[8] Cavaliere C, Longarzo M, Orsini M, Aiello M, Grossi D. Fronto-temporal circuits in musical hallucinations: a PET-MR case study. Front Hum Neurosci 2018;12. https://doi.org/10.3389/fnhum.2018.00385.
[9] Mylius V, Ayache SS, Ahdab R, Farhat WH, Zouari HG, Belke M, et al. Definition of DLPFC and M1 according to anatomical landmarks for navigated brain stimulation: inter-rater reliability, accuracy, and influence of gender and age. Neuroimage 2013;78:224–32. https://doi.org/10.1016/j.neuroimage.2013.03.061.
[10] Kleinjung T, Eichhammer P, Landgrebe M, Sand P, Hajak G, Steffens T, et al. Combined temporal and prefrontal transcranial magnetic stimulation for tinnitus treatment: a pilot study. Otolaryngol Head Neck Surg 2008;138:497–501. https://doi.org/10.1016/j.otohns.2007.12.022.

Janne Nordberg*
Department of Clinical Neurophysiology, University of Turku and Turku University Hospital, Turku, Finland

Tero Taiminen, Lauri Virtanen
Department of Psychiatry, University of Turku and Turku University Hospital, Turku, Finland

Satu K. Jääskeläinen
Department of Clinical Neurophysiology, University of Turku and Turku University Hospital, Turku, Finland

Noora M. Scheinin
Department of Psychiatry, University of Turku and Turku University Hospital, Turku, Finland

* Corresponding author. Department of Clinical Neurophysiology Turku University Hospital, Kiinamyllynkatu 4-8, 20520, Turku, Finland.
E-mail addresses: janne.nordberg@tyks.fi, jannor@utu.fi (J. Nordberg).

7 September 2021
Available online 28 September 2021