Introduction

In this report, we describe a case of success, with a reduction in tinnitus intensity and distress, in a patient submitted to bilateral high frequency rTMS to the dorsomedial prefrontal cortex (DMPFC).

Subjective tinnitus is characterized by the perception of sound in the ears or head in the absence of a corresponding external stimulus. About 5 to 15% of the adult population perceive these sounds chronically. Approximately 1-2% of the general population report severe tinnitus, associated with impairment of daily life. Despite the great amount of literature concerning tinnitus treatment, there are still no evidence-based established treatments for curing tinnitus or for reducing its loudness [1].

Sham-controlled studies revealed beneficial effects using repetitive transcranial magnetic stimulation (rTMS) in the treatment of tinnitus. However, its results currently demonstrate only moderate improvement and high inter-individual variability, indicating the need to optimize strategies, targeting different areas related to tinnitus [2-3]. The evidence that the subcallosal area, which contains medial prefrontal (dorsal and ventral), orbitofrontal and anterior cingulate areas, is important in tinnitus pathophysiology, make this area potential target for tinnitus treatment with rTMS [4-5].

Given the scientific background, we experimented a new rTMS protocol with promising results as described in the following case.

Case Presentation

Patient provided written informed consent. The study was approved by ethics committee (protocol CAEE 48853015.6.0000.5263). A 51 year-old caucasian male, engineer, presenting continuous, bilateral, symmetric tinnitus for 4 years, already treated with pharmacological interventions and tinnitus retraining therapy with no reduction in tinnitus intensity or annoyance. The tinnitus worsened with stress and in silent environment. The patient had no dizziness, hearing loss or fulness in the ears. He had good health, didn't use

any medication regularly and had no complaints of pain in the head or neck. Otolaryngological clinical exam was normal and so were audiometric and laboratory tests.

The Mini International Neuropsychiatric Interview (MINI) v 5.0 revealed no concomitant psychiatric disorders. The symptom was measured using the Tinnitus Handicap Inventory (THI) and visual analog scale (VAS), tinnitus pitch matching (PM), loudness matching (LM) and minimal masking level (MML) at baseline, 2 weeks, 1 and 4 months after treatment.

The rTMS protocol consisted of 10 Hz stimulation at 120% of the resting motor threshold of the extensor hallucis longus. Each session of 10 Hz stimulation applied 3000 pulses to each hemisphere non-simultaneous (6000 pulses total), a duty cycle of 5 seconds on and 10 seconds off, for a total stimulation time of 30 minutes, 5 times a week, consecutively, for 4 weeks, over bilateral DMPFC (Fz electrode site in the 10/20 International EEG system, corresponding to the 25% of the nasion-inion distance), using the fluid-cooled figure 8 coil (Neurosoft, Neuro-MS/D device).

Baseline, 2-weeks, 1 and 4-month follow-up THI and VAS scores and tinnitus loudness and MML are presented in Table 1. At baseline the patient had moderate tinnitus, grading 38 in THI and 7 in VAS. After 4 weeks of rTMS, the patient effectively responded to treatment, as indicated by a drop greater than 20 points in the THI, a reduction of VAS to 0, and MML and tinnitus loudness reduction to 1dB, compared to 18 and 15dB, respectively, at baseline. There were no reported side effects after rTMS. At 4 months the patient displayed sustained remission.

Discussion

To our knowledge, this is the first report of the use of rTMS targeting the DMPFC to treat tinnitus. The treatment of tinnitus is notoriously hard and new alternatives are ghastly needed. In our report, the patient presented an important and sustained reduction of his tinnitus after bilateral DMPFC-rTMS. Our findings suggest that rTMS targeting the medial

prefrontal cortex, specifically the DMPFC, may represent a safe and tolerable therapeutic alternative for tinnitus treatment. Evidence shows that tinnitus patients exhibit significantly less gray matter (GM) volume in ventromedial prefrontal cortex (VMPFC) compared to control participants as well as in DMPFC [4]. Studies identified that the GM reductions in the DMPFC correlated proportionally with the percentage of time participants were aware of their tinnitus. Thus, patients with bigger cortical sulci were aware of their tinnitus more often than those with DMPFC gyrification similar to control participants, suggesting that this area may play a role in tinnitus [5]. In a study using voxel-based morphometry, there was evidence of significant volume loss in the subcallosal area (which includes the DMPFC) in tinnitus patients [6]. Thus, the subcallosal area may be considered as a major hub linking limbic-affective systems with thalamo-cortical perceptual system.

The first clinical study with tinnitus patients stimulated in deeper brain areas was published by Vanneste et al. [7] applying double-cone-coil (DCC) rTMS to the medial frontal cortex of 78 patients, showing improvement depending on the frequency of the stimulation. A second study with 73 patients was published reporting differences between single session and repeated sessions of 1Hz DCC TMS prefrontal stimulation (anterior cingulate cortex) for tinnitus treatment. Both single sessions and multiple sessions suppressed tinnitus distress and intensity transiently. Multiple sessions generated a higher suppression effect in more patients when comparing to single session [8].

A randomized, double-blind pilot trial with 40 patients suffering from chronic tinnitus compared mediofrontal stimulation with DCC, (10Hz) combined with left temporo-parietal stimulation with figure-of-eight-coil (1Hz) to left dorsolateral-prefrontal-cortex stimulation with figure-of-eight-coil (10Hz) combined with temporo-parietal stimulation with figure-of-eight-coil (1Hz). The combination of mediofrontal/temporoparietal-rTMS failed to show better outcome when compared to the group dorsolateral prefrontal/temporo-parietal[9].

Conclusion

The impressive result of this case, with important and sustained reduction of tinnitus annoyance and loudness in a previously treated patient, suggests that rTMS of the DMPFC is a promising approach for the treatment of tinnitus and is worth further investigation. Coil placement is simple and can be accurately achieved without MRI guidance. Even though the DMPFC lies 3-4cm deep, the figure of eight coil can stimulate this area when the motor threshold of the extensor hallucis longus is found [10]. Given this report, it can now be said that randomized sham-controlled trials to assess the efficacy of DMPFC-rTMS in tinnitus are important and could drastically improve patient's treatment safely and effectively.

Conflicts of Interest

The authors report no conflicts of interests.

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Table 1: Treatment evolution data

	Baseline	2 weeks post	1 month post	4 months post
THI	38	16	14	14
VAS	6	0	0	1
Loudness	18	1	3	4
MML	15	0	3	4

THI – Tinnitus Handicap Inventory; VAS – Visual Analog Scale; MML – Minimal Masking Level