When asked which treatment they preferred all patients found both treatments similar. Two patients suffered skin erythema and chemosis in frontal anodal electrodes zone during active-tDCS, one patient after one session, and the other after 3 sessions. Both patients withdrew from the trial for this reason. This adverse effect resolved after 48 h.

In this preliminary study in patients with ET, inhibitory tDCS of the cerebellum did not produce any acute or long lasting benefits using the described stimulation paradigm.

Two studies have shown positive antitremoric effects using rTMS on the cerebellum [2,3]. In one of the studies, the clinical effect persisted for three weeks after rTMS sessions [3]. One possible explanation for the negative results of our study, is that the electrical field strength in tDCS, although applying bilateral stimulation, is too low to create neuromodulatory effects.

Besides the small number of patients included due to the exploratory nature of the study, two further limitations of the study should be pointed out. The first of these is the intrinsic difficulty in assessing tremor in clinical trials, especially for accelerometric assessments which may have a great intra-subject variability. Nevertheless, this was minimized due to our crossover controlled design, and the use of a self-reported disability scale. Secondly, it is not clear whether it is possible to stimulate the human cerebellum through the intact scalp using tDCS. We collected no direct evidence to ensure that we had stimulated the cerebellum. Placement of the stimulating electrodes in accordance with previous studies [4] led us to suppose that cerebellar hemispheres were actively stimulated. We did not compare cerebellar stimulation with stimulation of other brain regions. However, the central pathways involved in the pathophysiology of tremor are incompletely known and cortical regions might be implicated. Thus, to preserve the singular stimulation of cerebellar areas we used the same stimulation location to make the sham stimulation.

In conclusion, we failed to find an effect of tDCS of the cerebellum in ET in this small and preliminary study.

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Deep Transcranial Magnetic Stimulation in a Woman With Chronic Tinnitus: Clinical and fMRI Findings. Seeking Relief From a Symptom and Finding Vivid Memories by Serendipity

Tinnitus is an auditory sensation that is not due to an external acoustic stimulus, occurring in approximately 10–15% of the adult population [1]. Although the pathophysiology of tinnitus is still barely understood, it has been assumed that chronic symptoms are due to an altered pattern of neuronal activity. Functional neuroimaging studies have suggested altered neuronal activity in both auditory and non-auditory pathways [2].

There is no current treatment for tinnitus that has shown efficacy unequivocally. Several studies evaluated the effect of rTMS on tinnitus using both high (>1 Hz) and low (<1 Hz) frequency protocols, showing contrasting results [3]. However, the standard rTMS coils used in these studies were able to stimulate to a depth of 1–2 cm from the scalp, thus failing to directly stimulate deeper cortical structures that may be involved in tinnitus physiopathology [3]. The relatively new H-coil allows researchers and clinicians to stimulate deeper brain structures (deep TMS). The efficacy and safety of deep TMS in patients with various neuropsychiatric disorders has already been assessed in several studies, and the device is now cleared by the US FDA for treating depression [4].

The potential therapeutic value of this technique in treating tinnitus has not been explored to date. We here report the effect of deep TMS treatment on clinical assessment measures and fMRI activation patterns in a woman with chronic tinnitus.

A 58-years-old Caucasian woman with unilateral, left sided, chronic tinnitus came to our attention in January 2013. She could trace back the onset about 15 years earlier, after suffering mechanical trauma. She described the sound as a continuous noise, with increasing intensity. The patient underwent several pharmacological treatments (glutathione sodium salt 600 mg/day, clonazepam up to 2 mg/day, acamprosate up to 333 mg six times/day) without substantial benefit. She voluntarily discontinued medications about one month before visiting our service. Before starting deep TMS she provided written informed consent for the collection of her data for research, participation in the study, and subsequent publication.

Table 1
Regions of interest.

	Anatomical location	Side	MNI coordinates			Z	K cluster
			x	y	z		
T0	Superior temporal gyrus (BA42)	Right	68	−30	8	6.78	3017
	Fusiform gyrus (BA 18)		26	−78	−14	5.00	1722
	Precuneus		24	−52	54	3.59	41
	Cuneus		12	−80	28	4.05	111
	Cingulum (BA 23)		6	−28	30	3.62	68
	Cingulum (BA 24)		6	12	32	3.59	35
	Middle frontal gyrus		36	10	38	3.58	47
	Inferior frontal gyrus		44	36	−6	4.30	308
	Cerebellum		26	−54	50	4.52	69
	Superior temporal gyrus (BA 41)	Left	−64	−22	14	6.03	4838
	Fusiform gyrus (BA 18)		−22	−74	−8	4.51	842
	Precuneus		−10	−52	64	4.24	589
	Cingulum		−18	−22	44	3.94	41
	Cingulum		−4	−2	38	3.73	94
	Superior frontal gyrus		−26	54	8	3.73	122
	Middle frontal gyrus		−38	2	52	3.47	34
	Postcentral gyrus		−24	−30	66	3.61	43
	Precentral gyrus		−36	28	36	3.73	45
T2	Superior temporal gyrus	Right	68	−26	8	4.30	95
	Superior temporal gyrus	Left	−62	−24	10	5.46	408
T3	Superior temporal gyrus	Right	64	−32	8	5.53	774
	Superior temporal gyrus	Left	−62	−24	10	5.02	366

The patient received 20 min of H1-coil deep TMS to the left temporoparietal cortex at a 18 Hz frequency at 110% motor threshold for 10 working days (five days a week). The resting motor threshold was obtained by stimulation to the left motor cortex, and defined as the minimum stimulator output intensity that causes a motor response (that is, twitching of the contralateral abductor policis brevis muscle in the hand). The coil was then moved 4.5 cm posteriorly and 6.5 cm laterally toward the left shoulder of the patient, according to Rosenberg et al. protocol [6]. She was clinically assessed through the Tinnitus Handicap Inventory (THI) at baseline (T0), after one week of deep TMS treatment ($N = 5$ sessions, T1), after two weeks of deep TMS treatment ($N = 10$ sessions, T2), and at the 2-week follow-up after the last deep TMS session (T3). The patient underwent fMRI evaluations at T0, T2, and T3.

The THI is a self-rated 25-item questionnaire, with each item rated 4, 2 or 0 according to whether the response is Yes, Sometimes, or No, respectively. According to the scores obtained, the tinnitus may be classified as "very mild" (0–16), "mild" (18–36), "moderate" (38–56), "severe" (58–76), and "catastrophic" (78–100) [5]. fMRI scanning was performed on a 1.5-T MR scanner (Siemens Magnetom Sonata). Conventional T1-weighted images were acquired for anatomical reference. Functional images were acquired using single-shot spin-echo echo planar imaging (TR/TE = 3500/50 ms, matrix = 64 × 64, FOV = 192 × 192 mm^2, resolution = 3 × 3 × 3 mm^3; 36 axial slices). Sound-evoked BOLD response was elicited at the above timepoints by making the patient listen to classical music in four ON-OFF cycles, according to a block design paradigm, through a headphone attenuating scanner-generated sounds. The SPM5 (http://www.fil.ion.ucl.ac.uk/spm) package was used for data processing and statistical analysis. More details on fMRI and deep TMS procedures are given in the "Supplementary Materials" section.

Through the deep TMS treatment course, THI scores showed a slight, but constant decrease (T0: 80; T1: 74; T2: 72; T3: 64), showing a drop of the clinical severity of tinnitus from "catastrophic" to "severe." The patient reported the tinnitus to disappear during the deep TMS session proper, but to reappear after about 2–3 min, although to a lesser intensity. Musical stimulation produced temporal cortex activation in each of the three experimental sessions (Table 1). At T0, cortical activation spread all over the brain, and its level (extension and percentage signal change) was higher in the left hemisphere (the side of tinnitus perception) compared to the right (V_{L0} + 29%, ΔS_{L0} + 22%). At T2, activation decreased compared to T0 in the auditory cortex both at left (V_{L2} − 92%, ΔS_{L2} − 38%) and at right (V_{R2} − 97%, ΔS_{R2} − 19%). At T3, cortical activation was smaller in left hemisphere with respect to right (V_{L3} − 27%, ΔS_{L3} − 22%). After one week of treatment the patient started reporting pleasant memories about her childhood; memories were so vivid that in the following deep TMS sessions she continuously brought us photographs of her childhood to make us part of her reminiscences. This behavior persisted during the second week of deep TMS treatment and decreased progressively after the end of the sessions.

Overall, deep TMS was associated with some modest, but progressive clinical improvement, as assessed through the THI, and with well-defined changes in brain activation pattern, that tended to return toward the initial activation pattern after the end of deep TMS sessions.

A high-frequency deep TMS protocol was chosen because of the high baseline activation of the left temporal cortex showed by fMRI. Such protocols have been successfully adopted by others [7], indicating that the interference of high-frequency stimulation with hyperactive neural circuitries could reduce tinnitus by generating "virtual lesions" in the temporal lobe [8].

fMRI at T0 showed lateralized temporal lobe hyperactivation, as previously reported for organic tinnitus patients [9]. Deep TMS seemed to normalize this temporal lobe activation pattern, leading to a more symmetric activation similar to health. However, this normalization only weakly corresponded to the modest clinical improvement, and is confounded by the open label and repeated exposure confounds.

The present case raises the issue of the validity of the "excitatory rTMS paradigm." In fact, we showed on the fMRI reduced activation of several superficial and deep brain regions after 18 Hz stimulations.

The vivid reminiscences reported by our patient after one week of deep TMS sessions are consistent with a role for the temporal lobe in long-term memory. This effect is uncommon in other studies of temporal lobe stimulation. Nevertheless, it is known since Penfield first obtained it with direct electrical temporal lobe stimulation in epilepsy patients in 1958 [10,11]. The memories were largely parts of the patients' auras, and seizures occurred commonly after the stimulation; however the present case slightly differs from Penfield's reports as the patient did not have a history of epilepsy.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.brs.2014.02.005.

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Subconjunctival Hemorrhage After High Frequency Right-sided Repetitive Transcranial Magnetic Stimulation

Dear Editor:

We present a 45 year old man who experienced a subconjunctival hemorrhage (SCH) after his 8th session of high frequency right-sided repetitive transcranial magnetic stimulation (rTMS). To date, there is no reported association of rTMS with SCH.

Case

The patient is a 45 year old HIV-positive married white male in the US Navy referred for rTMS for treatment of major depressive disorder and posttraumatic stress disorder (PTSD). He has a history of complex regional pain syndrome with chronic right lower extremity pain and deep vein thrombosis.

His medications at the start of his rTMS sessions were citalopram 40 mg daily, bupropion XL 150 mg daily, prazosin 2 mg at bedtime, trazodone 200 mg at bedtime, pregabalin 75 mg twice daily, amlodipine 10 mg daily, tolterodine 4 mg daily, omeprazole 20 mg daily, clomiphene 50 mg daily, elvitegravir 150 mg daily, cobicistat 150 mg daily, emtricitabine 200 mg daily, tenofovir 300 mg daily, warfarin 7.5 mg daily except 10 mg on Monday, Wednesday and Friday, tadalafil 10 mg as needed, oxycodone 5 mg as needed daily, cholecalciferol 400 units daily and calcium carbonate 500 mg twice daily.

Pretreatment Montgomery-Asberg Depression Rating Scale (MADRS) was 20, PTSD Checklist - Military Version (PCL-M) was 77, and Patient Health Questionnaire (PHQ-9) was 16. He began rTMS (with the NeuroStar device) to primarily target PTSD using high frequency (20 Hz) stimulation applied to the right dorsolateral prefrontal cortex. Each treatment consisted of 20 Hz over 2 s with 26 s quiet period, for a total of 1700 pulses delivered over 20 min at 80% of motor threshold (MT). MT was determined by visible twitch of the left abductor pollicis brevis in the "MT Hunt position" as per Neuronetics guidelines and was 1.15 which was higher than the published average (1.0) of the Neuronetics system. Coil was 6 cm anterior to the location where MT was determined, which was 75 mm away from his right eye and 145 mm away from his left eye. Coil angle was +20°. A Neuronetics insert (senstar pad) was used and placed between the coil and the scalp. During his first session he had localized scalp discomfort but found using a stress ball and placing gauze under the magnet helpful.

During his third session, his chair position was changed for comfort and MT was recalculated to 1.06 and coil angle was +15°. He endorsed right eye pain and dryness that was not alleviated by any parameter adjustments. During his 9th session, he reported blood in his left eye after returning home from his 8th session. On exam, there was visible blood in his left subconjunctiva and he was immediately referred to his primary care provider and Ophthalmology. His International Normalized Ratio