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Hearing safety from single- and double-pulse transcranial magnetic stimulation in children and young adults

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Abstract

Introduction—Concerns regarding hearing safety have limited the number of studies using transcranial magnetic stimulation (TMS) in children and young adults. The objective of this study was to examine the safety of TMS with regards to hearing in a group of 16 children and young adults (17.3 ±4.9 years) with and without brain injury.

Methods—Pure-tone hearing thresholds and distortion-product otoacoustic emissions were measured before and after exposure to single- and paired-pulse TMS (1–2 sessions of 149–446 TMS pulses at a median of 49%–100% maximum stimulator output over a 2.2 hour period).

Results—No mean change in hearing outcomes was noted. In addition, no clinically significant change in hearing threshold was observed in any participant, and participants did not experience a subjective change in hearing following TMS exposure.

Conclusions—Single- and double-pulse TMS administered within the parameters used in this study, which included hearing protection, can be used in children and young adults without impacting hearing. This study provides further evidence for hearing safety after TMS exposure in children and young adults.

Keywords

Hearing; transcranial magnetic stimulation; pure-tone threshold; distortion-product otoacoustic emissions; safety

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Conflict of Interest Statement:

None of the authors have potential conflicts of interest to be disclosed.

Transcranial magnetic stimulation (TMS) is a non-invasive method of neurostimulation and neuromodulation that has been studied extensively in the last 30 years (1). Although most TMS research has been conducted in adults, work in the last decade suggests the potential for TMS in studying neural excitability and pathways in children and adolescents (2, 3). Applications of TMS in pediatrics have been primarily diagnostic, focusing on developmental neurophysiology (4–6), and neurophysiological abnormalities resulting from brain injury (7, 8). Therapeutic applications of TMS have been explored with some success in adults with stroke (9), psychiatric disorders (10), and epilepsy (11). However, the utility of TMS for therapy in children and adolescents has not been studied as carefully. Despite the prospective benefits of pediatric therapies due to developmental neuroplasticity, the lack of TMS research in children is due, in part, to concerns over safety (12).

TMS coils emit a brief acoustic artifact, ranging from 100 – 120 dB peak Sound Pressure Level (pSPL), during pulse generation, and a small proportion of adults have experienced transient changes in hearing immediately after exposure (3, 13–15). To address this issue, two committees assessing the safety of TMS in clinical practice and research recommended the use of hearing protection (i.e., earplugs) during TMS stimulation (12, 16). Rossi et al. indicated that a primary concern specific to TMS safety in children was the potential for noise induced hearing loss. Due to the smaller size of the external auditory canal, children have a higher resonance frequency and increased sound pressure level at the tympanic membrane than in adults (17), which may increase their susceptibility to acoustic injury.

In a TMS study with a typical diagnostic testing time and TMS exposure (a median of 19 TMS pulses at a median stimulation intensity of 68% maximum stimulator output), Collado-Corona and colleagues reported no significant change in pure tone thresholds in a group of 18 children without hearing protection (18). In another study designed to inform investigators and Institutional Review Boards on the safety of TMS use in children, the theoretical risk to hearing was analyzed and described to be minimal based on comparing the level of noise from a TMS pulse, its frequency, and exposure time to standards set by the National Institute for Occupational Safety and Health (3). To further support the use of TMS in young participants, we examined safety from acoustic injury after TMS exposure in a group of children and young adults. TMS was conducted for the purposes of a pathophysiological investigation of cortical excitability in individuals with childhood-onset motor disabilities, not relevant for the current analysis. We exposed participants to a longer TMS session with more stimuli than previously reported (18). Participants used hearing protection as advised (12, 16), allowing assessment of the effects of standard TMS protocols on hearing. We hypothesized a priori that there would be no change in hearing as measured by behavioral and physiologic responses after exposure to TMS.

Methods

Participants

Sixteen children and young adults (17.3 +/− 4.9 years, range 9 – 24 years, 10 female) participated in this study (Table 1). Nine participants were healthy volunteers (HV group), and 7 participants had brain injury due to perinatal stroke or trauma in the first year of life

(BI group). Participants were included if they had good general health and could understand and comply with instructions. Individuals in the BI group were chosen on the basis of the diagnosis of dystonia (by K.E.A) in one wrist (left wrist for BI1 – BI6, right wrist for BI7) that began before 13 years of age. Dystonia was identified using the Hypertonia Assessment Tool (19). Participants did not undergo TMS if they had a history of seizures in the previous 2 years, used anti-seizure medicine, had pre-existing hearing loss, or had devices implanted within or near the head that could not be safely removed. Due to the use of anti-seizure medicine, 2 individuals in the BI group (Subjects 4 and 5) were not exposed to TMS. Consequently, these 2 BI subjects underwent hearing testing at baseline only.

This was a sub-study in a larger parent study including biomechanical assessments (20), sensory testing (21), electroencephalographic testing (22), magnetic resonance imaging (MRI), and posturography to learn more about the consequences of childhood brain injury. The study protocol was approved by the NIH Institutional Review Board and conducted in accordance with the ethical principles of the Helsinki Declaration. All participants over 18 years of age and parents/guardians of minor participants gave written informed consent prior to the start of the study. All participants under 18 years of age gave written assent.

Study design

The effect of TMS noise exposure on hearing was tested using a pretest-posttest design (Figure 1). All 16 participants first had a baseline hearing evaluation in which outcomes were measured twice, in Test 1 and Test 2 (“Baseline”). The 14 individuals eligible for TMS then underwent Session 1 of TMS testing (“TMS noise exposure”). Subjects returned on another day for Session 2 of TMS testing (“TMS noise exposure”), and within 30 minutes of this last TMS session, a follow-up hearing evaluation was conducted in 13 subjects (“Follow-up”). In one HV (Subject 8), the follow-up hearing evaluation was completed 6 days after the second TMS session because the participant had a headache immediately following TMS and chose not to continue testing for the remainder of the day. This participant’s Follow-up hearing data were not included in the Baseline vs. Follow-up analysis. The time between the Baseline and Follow-up hearing test for each participant is included in Table 1 (M: 12.7, SD: ± 9.5 days). Between hearing evaluations, participants were not exposed to any significant noise, per self-report. MRI scans in accordance with the parent study were not performed between the two hearing evaluations to avoid confounding effects of the MRI scanner noise on hearing.

Hearing evaluations

Hearing tests were conducted in sound suites meeting American National Standards Institute (ANSI) criteria (23) using a Grason-Stadler (Eden Prairie, MN, USA) diagnostic audiometer (GSI-61). Pure-tone thresholds for air conduction (500–8000 Hz) were established using ER3A insert earphones (Etymotic Research, Inc. Elk Grove Village, IL, USA). Middle ear function was measured using an acoustic immittance unit (GSI Tymp Star, GSI-33). Distortion product otoacoustic emissions (DPOAEs) were evaluated using an Otodynamics (Hatfield, Hertfordshire, UK) Echoport Otoacoustic Emission System supported by ILO V6 Clinical OAE software. DPOAEs were evaluated in one-quarter octave decrements from 7996-842 Hz, using a frequency (f) ratio of $f_2/f_1 = 1.2$, with levels (L_1 and L_2) set at 65 dB

SPL and 55 dB SPL, respectively. DPOAEs are low-level sounds emanating from the outer hair cells in the healthy cochlea following stimulation of the ear with paired tonal stimuli. Reduction in DPOAEs may be associated with clinical or even subclinical changes in cochlear function following noise exposure (24).

The baseline hearing assessment finished approximately 30 minutes before the first TMS session. Following otoscopic inspection, 226 Hz tympanometry and acoustic reflex threshold testing for contralaterally (500, 1000 and 2000 Hz) and ipsilaterally (1000 Hz) presented stimuli were conducted. Conventional audiometric techniques were used for behavioral audiometric assessment, and included determination of speech recognition thresholds and pure-tone thresholds for each ear. Following the initial determination of pure-tone thresholds, the earphones were removed, the patient was given a short break, the earphones were reinserted, and a second pure-tone audiogram was established. Additionally, DPOAEs were recorded twice with removal and replacement of the ear probe between measures.

Following otoscopic inspection and tympanometry, air-conducted pure-tone thresholds were established a single time for each ear at 500–8000 Hz. DPOAEs were recorded in the same manner as at baseline, with repeated measurement following removal and replacement of the ear probe. All participants were queried regarding subjective change in hearing, aural fullness, and tinnitus following the final TMS session.

TMS sessions

There were two TMS sessions, each focused on one hemisphere of the brain. TMS targeted the primary motor cortex, and EMG was recorded from the contralateral first dorsal interosseous muscle. The targeted brain region was marked on a fitted skull cap. Bilateral hearing protection was provided by formable earplugs (noise reduction rating = 29 dB, McKeon Products, Inc., Warren, MI, USA). TMS was administered through a figure-of-eight coil (Magstim Co., Whitland, Dyfed, UK, Magstim 200^2 monophasic stimulator, maximum field strength of 2.2 Tesla, inner-loop coil diameter of 70mm). The number of TMS pulses given and the median stimulation intensity varied between TMS sessions and participants (Table 1) based on each participant's toleration. In general, the TMS sessions included single-pulse (hot spot mapping, motor threshold, ipsilateral motor evoked potential, contralateral silent period, and ipsilateral silent period measurements) and paired-pulse (short intra-cortical inhibition) TMS protocols that are commonly performed to characterize features of the corticospinal system (16). Total testing time ranged from two to three hours, with a mean time of 2.2 ± 0.3 hours. Participants took breaks as necessary to maintain alertness during testing.

Acoustic artifact of TMS

In a previous study of acoustic noise from TMS, different stimulators were shown to exhibit different noise profiles (25), which could vary with the exact coil position used (26), so we quantified the acoustic artifact of a TMS pulse using the same stimulator model we used in our study. The noise spectrum and peak noise of a single TMS pulse at 100% maximum stimulator output (MSO) was determined using a figure-of-eight coil. All sound measures were conducted in a double-walled sound treated booth. The noise spectrum of the TMS

pulse was measured by acoustical engineers from Scantek, Inc. (Columbia, MD, USA) using a Norsonic N-840 real-time analyzer via a Norsonic N-116 precision sound level meter, a Norsonic N-1201 preamplifier and a Norsonic N-224 A/C output adaptor (Lierskogen, Norway). The peak SPL of the TMS pulse was recorded via an IEC 711 ear simulator type RA0045 (G.R.A.S. Sound & Vibration A/S, Skovlytoften, Denmark) mounted on the right side of a Knowles Electronics Manikin for Acoustic Research (KEMAR, Knowles Electronics, Itasca, IL). Microphone power and 200V polarization were supplied by a Sound Connect amplifier (Listen, Inc., Boston, MA, USA) via a Brüel & Kjaer 2669 preamplifier and UA0123 flexible adapter (Brüel & Kjaer, Skodsborgvej, Denmark). Peak SPL was measured by a Larson Davis 800B sound level meter (PCB Piezotronics, Inc., Depew, NY, USA).

During measurements, the TMS coil was positioned tangent to the surface of the KEMAR above the right primary motor cortex area (C4 according to the International 10–20 system) with the handle of the figure-of-eight coil pointing towards the inion. The coil was within one-half cm of the surface of the KEMAR and approximately 10 cm from the one-half inch random incidence microphone.

Outcome measures

The two quantitative outcome measures in this study were pure-tone thresholds (octave frequencies from 500–8000 Hz and interoctave frequencies 3000 and 6000 Hz) in dB HL and DPOAE (at each quarter octave band of stimulation from 1001–6726 Hz) in dB SPL. Levels of the DPOAE signal and background noise were both measured. Using a method modeled after Reavis and colleagues (27), emissions were classified as valid and present, valid and absent, and invalid. When the signal to noise ratio was greater than or equal to +6 dB, and the emission amplitude exceeded −20 dB SPL, the emission was considered valid and present. When the signal to noise ratio was lower than +6 dB and the noise levels were lower than our 95th percentile reference range for noise at each frequency, the emission was considered valid and absent. When the signal to noise ratio was lower than +6 dB and the noise levels exceeded our 95th percentile reference range, the data at that frequency were considered invalid, and were treated as missing data. DPOAE levels were measured in dB SPL, and subsequently converted to μPascals (μPa) for the purpose of post hoc data calculations and analysis. Absent responses were assigned a value of 0 μPa. DPOAE levels from the two baseline and two final assessments were compared. DPOAEs at 842 Hz and 7996 Hz were not included in this analysis due to interference from physiologic noise in the low frequencies, and difficulty achieving L_1 and L_2 targets necessary to obtain emissions at 7996 Hz.

Clinical analysis of outcome measures

Audiometric threshold stability was evaluated for each ear using two pure-tone based evaluation criteria that examined change from baseline. The first was a binary (yes/no) determination based on the American Speech Language Hearing Association (ASHA) definition of significant change in hearing, initially designed to monitor for ototoxic changes. This defines a significant decline in hearing as a 10 dB decrease at any two consecutive frequencies, a 20 dB decrease at any single frequency, or loss of response at 3

consecutive test frequencies where a response was previously present (28). Additionally, the National Cancer Institute's adverse event scale, Common Terminology for Clinical Adverse Events (CTCAE v4.02), was used to grade changes in pure-tone thresholds (29). This system assigns grades ranging from Grade 1 (greater than 20 dB decline in hearing at any one frequency) to Grade 4 (indication for cochlear implant). Responses to follow-up questions regarding subjective change in hearing, aural fullness, and tinnitus following the TMS session(s) were recorded as "yes" or "no."

Statistical analysis of outcome measures

Linear mixed models were used to examine pure-tone thresholds and DPOAE level in two separate analyses. The first analysis (Baseline Test 1 vs. Test 2) addressed the stability of repeated pure-tone threshold and DPOAE measurements made consecutively within one day. This was done to establish the expected within-day measurement variability as a reference point to later assess changes between the pre-TMS and post-TMS measurements. In this analysis, only the baseline hearing evaluation was examined and data from both subject groups (HV and BI) were combined. Data from both ears were also combined due to a lack of difference in outcomes between ears. Main factors in the model included the trial number (Baseline Test 1, Baseline Test 2), and the frequency tested. The interaction between main factors was included in the model.

The second analysis (Baseline vs. Follow-up) assessed any changes in pure-tone threshold and DPOAE levels due to TMS exposure by comparing the baseline to the follow-up hearing evaluation. If multiple measurements were made during a single hearing assessment, data from both measurements were averaged in the model. Main factors in the model included the day (Baseline, Follow-up), the group (HV, BI), and the frequency tested. All interactions between main factors were included in the model. A significant interaction between day and frequency would indicate that changes in outcomes between baseline and follow-up varied for different frequencies tested. This interaction was of particular interest because of the well-known high frequency-notch associated with noise induced hearing loss (30).

In both analyses, subject age was included as a covariate to investigate the effect of age on hearing changes due to TMS. In the comparison of measurements at Baseline and Follow-up, the number of TMS pulses applied on the same side of the tested ear was also included as a covariate to understand whether changes in hearing vary with TMS exposure. An intraclass correlation covariance structure was used in both analyses in order to take into account correlations among multiple measurements per subject. Analyses were implemented in SAS (SAS institute Inc., Cary, NC) using PROC Mixed (31) to conduct linear mixed models. All statistical tests were conducted with a significance level of 0.05. Bonferroni correction for multiple comparisons was applied when necessary.

Results

Acoustic artifact of TMS

The spectral output of a figure-of-eight coil used to evaluate TMS artifact was bimodal with the primary peak occurring near 5000 Hz and a peak C-weighted output of approximately

100 dB SPL. The second spectral peak occurred slightly lower than 2000 Hz, with a peak C-weighted output of 95 dB SPL. The peak C-weighted output of the figure-of-eight coil at the test position (C4) with the handle of the TMS coil held tangent to the surface of the KEMAR towards the inion measured from the right ear was 127.6 dB SPL. The peak C-weighted output received by the left (contralateral) ear to stimulation did not exceed 115.0 dB SPL.

Clinical effects of TMS exposure on hearing

Table 2 presents the change in pure-tone threshold from Baseline Test 1 to Follow-up for each participant in both subject groups, for each ear, and at each frequency measured. In the table, zero indicates no change, negative values represent better hearing sensitivity at Baseline than Follow-up, and positive values represent better hearing sensitivity at Follow-up than Baseline. Despite minor changes, none of the participants in either group had a clinically significant change in hearing using the ASHA criteria for hearing change and none had a gradable change in hearing using the National Cancer Institute's CTCAE v4.02 (no participants had a CTCAE grade of 1, 2, 3, or 4). All of the participants in both groups denied subjective change in hearing and tinnitus following TMS. All of the BI patients and eight HV denied aural fullness, and one HV reported aural fullness after the second TMS session.

Test-retest stability of outcome measures (Baseline Test 1 vs. Test 2)

Figure 2 shows the correspondence between repeated pure-tone threshold (a) and DPOAE (b) measurements, and the variation of both measurements at different frequencies. There was no significant interaction between trial number and frequency tested ($p > 0.05$) on the pure-tone threshold measurement, nor was there an effect of trial number ($p > 0.05$), or age ($p > 0.05$). Similarly, there was no significant interaction effect of trial number and frequency ($p > 0.05$), and no main effect of trial number ($p > 0.05$) or age ($p > 0.05$) on DPOAE measurements. A significant effect of frequency was noted in both models (pure-tone threshold: $F(6,88) = 3.14$, $p = 0.0078$; DPOAE: $F(11,165) = 12.51$, $p < 0.0001$) and can be appreciated graphically in Figure 2. However, this variation across frequencies is expected and is not relevant to the test-retest stability of the outcome measures.

Effect of TMS exposure on outcome measures (Baseline vs. Follow-up)

Figure 3a shows the comparison of pure-tone thresholds between the Baseline and Follow-up hearing evaluations. There was a three-way interaction between testing day, group, and frequency on pure-tone thresholds ($F(12,60) = 2.57$, $p = 0.008$), so data from the HV and BI groups were analyzed separately. In both subject groups, there were no significant interactions between day and frequency (HV: $p > 0.05$, BI: $p > 0.05$), and no effect of day (HV: $p > 0.05$, BI: $p > 0.05$), age (HV: $p > 0.05$, BI: $p > 0.05$), or number of TMS pulses (HV: $p > 0.05$, BI: $p > 0.05$) on the pure-tone thresholds. Figure 3b shows the comparison of DPOAE level between the Baseline and Follow-up evaluations. Due to a three-way interaction between testing day, group, and frequency on the DPOAE level measurements ($F(22,110) = 2.47$, $p = 0.001$), two linear mixed models were used to study the HV group and BI group separately. There were no interactions between day and frequency (HV: $p > 0.05$, BI: $p > 0.05$), and no effects of day (HV: $p > 0.05$, BI: $p > 0.05$), age (HV: $p > 0.05$,

BI: $p > 0.05$), or number of TMS pulses ($p > 0.05$ for HV and BI) on DPOAE levels in either subject group.

Discussion

No changes in hearing were found after exposure to TMS in behavioral or physiologic assessments in a group of children and young adults with and without brain injury. Hearing loss that occurs immediately following noise exposure may recover, and as such is considered a temporary threshold shift. We did not observe temporary hearing loss within 30 minutes of the last TMS session in 13 participants available for immediate follow-up testing. We are unable to rule out temporary shifts in hearing after the initial TMS session because we did not measure hearing immediately afterward; however, no subjective symptoms of hearing loss were reported following either exposure.

These results provide the TMS community with empirical evidence to support the auditory safety of single- and paired-pulse TMS over the primary motor cortex in children and young adults that includes use of hearing protection and conforms to the dosing in this study (1–2 sessions of 149–446 TMS pulses at a median of 49%–100% MSO over a 2.2 hour period with a maximum peak C-weighted noise of 127.6 dB SPL). In addition, there is no age-related effect in hearing outcomes among TMS participants in the age range of 9 – 24 years, nor is there an effect of the number of TMS pulses administered near the ear tested.

Our analysis of the test-retest stability of the pure-tone thresholds and DPOAE levels indicated no significant difference between tests on the same day. These results are consistent with published findings on the test-retest reliability of audiometric thresholds (32) and DPOAEs (33). Similarly, the effect of frequency on DPOAE is well known (34). The differences across frequency for pure tone thresholds in both subject groups are smaller than the step size of 5-dB used for threshold determination and are not clinically meaningful.

Limitations to interpretation of these results are that we cannot generalize hearing safety to children less than 9 years of age, in whom the ear canal has not reached its full adult size (35), in conditions where hearing protection is not worn, for TMS paradigms resulting in greater exposure, for variations in TMS coil placement, and in populations more vulnerable to noise induced hearing loss.

In conclusion, we have shown no measurable changes in hearing in a small group of children and young adults after exposure to single- and paired-pulse TMS while wearing hearing protection. Future studies are necessary to describe hearing outcomes in children below the age of 9 years and also in response to different stimulation protocols, including repetitive TMS.

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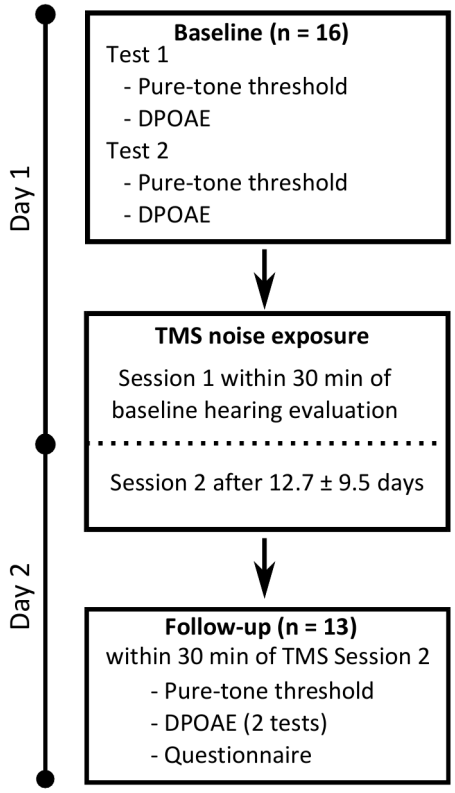

Figure 1.
Study design depicting audiometry and TMS exposure for day 1 and day 2.

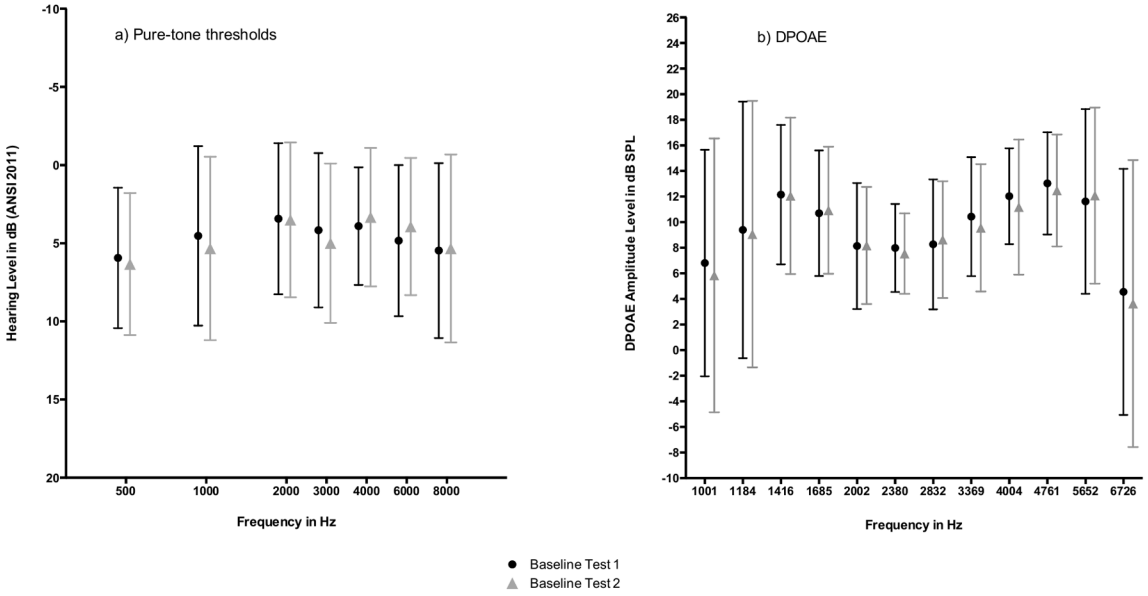

Figure 2.

Stability of repeated pure-tone threshold (a) and DPOAE (b) levels in the Baseline hearing evaluation. Data from both ears and from both groups (HV and BI) are combined. Vertical bars represent ±1 SD from the mean. Pure-tone thresholds are shown as a standard audiogram with a logarithmic abscissa (frequency axis) and a reversed ordinate (hearing level axis). The mean and standard deviation of DPOAE measurements were computed in μPa prior to converting to dB SPL.

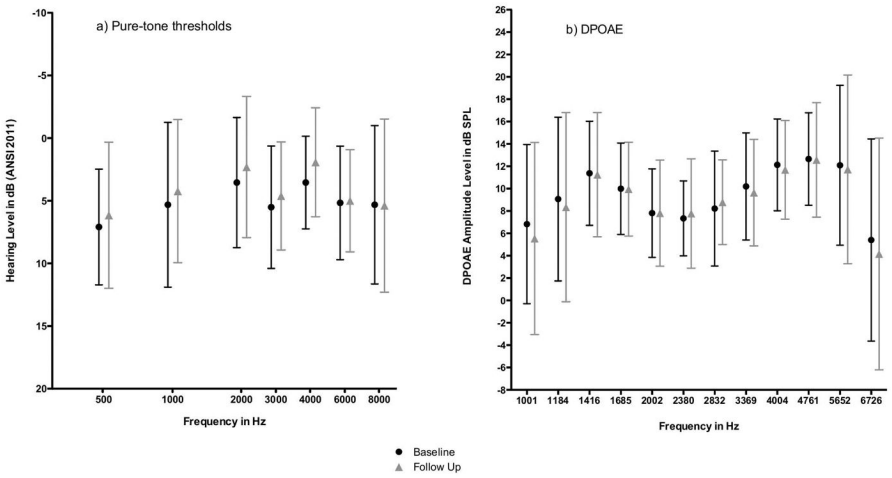

Figure 3.

Effect of TMS noise exposure on pure-tone threshold (a) and DPOAE level (b). Baseline data represent the average of Baseline Test 1 and Test 2. Follow-up DPOAE levels represent the average of two tests from the Follow-up evaluation. Data from both ears and from both groups (HV and BI) are combined. Vertical bars represent ±1 SD from the mean. Pure-tone thresholds are shown as a standard audiogram with a logarithmic abscissa (frequency axis) and a reversed ordinate (hearing level axis). The mean and standard deviation of DPOAE measurements were computed in μPa prior to converting to dB SPL.

Table 1

Subject demographics, number of transcranial magnetic stimulation (TMS) pulses, median TMS intensity, and time between baseline and follow-up hearing evaluations. TMS exposure occurred over two sessions, one targeting the right primary motor cortex (M1) and another targeting the left M1.

Group	Subject No.	Age (yrs)	Sex	R M1: No. TMS pulses/Intensity (% MSO)[e]	L M1: No. TMS pulses/Intensity (% MSO)[e]	Baseline –follow-up gap (days)
HV	1	9.4	F	237 / 100	394 / 60	6
HV	2	10.9	M	0 / -	446 / 69	14
HV	3	13.9	M	149 / 80	346 / 70	4
HV	4	14.4	F	316 / 100	333 / 72	7
HV	5	16.7	F	381 / 60	285 / 59	5
HV	6	16.8	F	350 / 66	297 / 59	9
HV	7	19	F	300 / 62	291 / 71	1
HV	8	23.5	F	330 / 49	280 / 62	20
HV	9	23.9	F	289 / 72	260 / 65	15
BI	1[a]	11.2	F	153 / 60	0 / -	7
BI	2[a]	13.6	M	355 / 66	0 / -	27
BI	3[a]	16.8	F	326 / 70	366 / 60	27
BI	4[a,d]	18.8	F	0 / -	0 / -	-
BI	5[a,d]	19.3	M	0 / -	0 / -	-
BI	6[b]	23.5	M	335 / 57	300 / 60	7
BI	7[c]	24.7	M	199 / 80	246 / 65	29

HV = healthy volunteer; BI = brain injury; F = female; M = male; R = right; L = left;

- = not applicable

[a] Perinatal stroke of left middle cerebral artery

[b] Traumatic brain injury at 10 months of age

[c] Perinatal stroke of basilar artery

[d] No TMS exposure; excluded from baseline vs. follow-up comparison

[e] Median stimulation intensity (% Maximum Stimulator Output)

Table 2

Change in pure-tone threshold from Baseline Test 1 to Follow-up. Zero indicates no change. Negative values indicate better hearing sensitivity at Baseline than Follow-up. Positive changes indicate better hearing sensitivity at Follow-up than Baseline. Small changes in pure-tone thresholds were distributed relatively evenly across frequencies, between ears, across groups, and in the positive and negative directions. None of these small changes qualified clinically as a change of hearing according to the ASHA and CTCAE criteria.

Group	Subject No.	Age (yrs)	Right Ear							Left Ear						
			500 Hz	1000 Hz	2000 Hz	3000 Hz	4000 Hz	6000 Hz	8000 Hz	500 Hz	1000 Hz	2000 Hz	3000 Hz	4000 Hz	6000 Hz	8000 Hz
HV	1	9.4	5	0	0	−5	−5	5	10	−5	0	5	0	0	10	0
HV	2	10.9	−5	−10	0	−5	0	−5	0	0	10	0	−5	0	0	−5
HV	3	13.9	0	0	0	0	5	5	5	0	0	−5	0	0	5	0
HV	4	14.4	−5	−5	−5	0	0	0	0	0	0	0	5	5	5	0
HV	5	16.7	0	0	0	−5	0	−10	0	0	0	−5	5	0	0	−5
HV	6	16.8	5	5	5	0	5	5	10	0	0	0	5	0	0	5
HV	7	19	5	0	10	0	0	5	0	5	0	0	0	5	5	0
HV	9	23.9	5	5	0	0	0	0	0	−5	−5	−5	0	0	−5	5
BI	1	11.2	5	−5	0	5	5	−5	0	0	0	−5	0	−5	0	5
BI	2	13.6	0	0	5	5	0	0	5	−5	−5	5	0	5	−5	−5
BI	3	16.8	−10	−5	0	0	0	0	−5	−10	−5	0	0	0	0	10
BI	6	23.5	0	0	5	0	10	0	−5	0	5	5	0	5	0	−5
BI	7	24.7	0	0	−5	5	0	5	−5	−5	0	0	−5	5	0	−5

HV = healthy volunteer; BI = brain injury