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Tinnitus Treatment with Customized Sounds

Jaime A. Pineda,[1] F. Richard Moore,[2] and Erik Viirre[3]

Departments of [1] Cognitive Science and [2] Music and [3] Division of Head and Neck Surgery, University of California, San Diego, and School of Medicine, La Jolla, California, USA

Abstract: Recent studies have indicated that the pathophysiological basis for tinnitus may be abnormal activity in the auditory areas of the brain rather than aberrant activity in the periphery. Tinnitus-related activity leads to changes in tonotopic representation in auditory cortex. However, such reorganization can be reversed through training-induced changes in the response pattern of cortical neurons. We address this problem by using customized sounds that reproduce the subjective experience to reduce overactive auditory circuits. The results of two preliminary studies indicate that customized sound therapy (CST*) aimed at this central dysfunction reduces tinnitus quickly and safely. Participants described immediate relief, showed changes on the Tinnitus Handicap Questionnaire, and reported changes in hearing threshold within 3 weeks. We also saw changes in the intensity dependence of the auditory N100 in tinnitus patients, supporting the idea that tinnitus reflects a reorganization of tonotopic maps in the auditory cortex. The main correlate of this reorganization was the enhanced contrast between responses to the perceived tinnitus pitch and tones approximately one octave lower. After 3 weeks of CST, the intensity dependence to the tinnitus pitch decreased, making these responses more similar to those from normal subjects responding to tones in the same frequency.

Key Words: customized sound therapy; electroencephalography; intensity dependence; N100; THQ

Tinnitus is the sensation of hearing a sound when no external auditory stimulus is present [1]. Almost all individuals have this experience for brief, unobtrusive periods. However, tinnitus sensations can be constant, loud, and annoying to the point that the sufferer is emotionally affected by this sensation. Chronic sound sensations of tinnitus affect approximately 17% of the general US population [1–3], or approximately 44 million people, and approximately 33% of the elderly [4]. Of this group, estimates project that some 10–12 million individuals will experience tinnitus problems sufficiently serious to seek professional help [5,6]. Approximately 20% suffer to a degree that their quality of life and productivity are impaired [7]. This translates to between 2% and 3% of the population whose lives are adversely affected by tinnitus [8,9]. Estimates anticipate that the number of serious tinnitus cases will increase significantly over the next few years.

A variety of tinnitus treatments have been tried, but hearing aids, maskers, drugs, and surgical interventions thus far have not been shown to be very effective [10, 11]. The US Food and Drug Administration (FDA) has not approved any drugs for treatment of tinnitus, though some studies have focused on medications, including benzodiazepines [12] and antidepressants [13]. Many of the drug treatments that are presently in use for tinnitus are aimed at either the cochlea (e.g., using intratympanic injections of gentamicin, dexamethasone, or lidocaine) or the central nervous system using systemic delivery [14]. In one study, tinnitus subjects with depression treated with nortriptyline had decreased depression levels, functional disability, and tinnitus loudness [15,16].

In general, antidepressants appear to work best for those who are depressed or anxious, who have more severe tinnitus, or who are treated for a longer time with

* CST is a trademark product of Tinnitus Otosound Products, LLC.

Reprint requests: Erik Viirre, MD, PhD, Department of Surgery, School of Medicine, 9500 Gilman Drive No. 0970, University of California, San Diego, La Jolla, CA 92093. Phone: 858-657-8590; E-mail: eviirre@otosound.com

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an adequate dose of medication [13]. Though studies of newer medications are ongoing, the use of current drugs involves a substantial incidence of side effects that individuals wish to avoid or often find intolerable. Finally, psychotherapy for tinnitus does help some, but it is aimed at mitigating the psychological effects of the problem rather than the sound itself. In summary, none of these approaches is effective for the majority of individuals.

Recent studies have suggested that the pathophysiological basis for chronic tinnitus is neural activity in the brain rather than aberrant activity in the peripheral auditory system [17–22]. Functional imaging techniques have demonstrated a relationship between the intensity of tinnitus and the degree of reorganization of the primary auditory cortex. Weiler et al. [23] showed that significant electroencephalography (EEG) spectral changes occur in alpha and theta frequencies in tinnitus patients, particularly over frontal regions of the brain. Shulman and Goldstein [24] interpreted these as changes in the congruence or dyssynchrony in cortical regions in the auditory and frontal cortices. Similarly, magnetoencephalography (MEG) studies [25] have reported increased gamma-band activity in a resting condition in individuals with tinnitus. Studies in experimental animals and humans have suggested that tinnitus is associated with a synchronized hyperactivity in the auditory cortex and proposed that the underlying pathophysiological mechanism is thalamocortical dysrhythmia. Hence, decreased auditory stimulation results in decreased firing rate and decreased lateral inhibition. Consequently, the surrounding brain area becomes hyperactive [26].

These theories suggest that overactive feedback loops in the brainstem-thalamus-auditory cortex may be the underlying mechanism of this problem. Indeed, research from our own laboratory [27] has shown that the brain activity of tinnitus sufferers in response to sounds similar to their tinnitus is different from the response to other sounds or from the brain response to sounds of people without tinnitus. This suggests that aberrant activity exists in the sound-processing circuits for sounds that the tinnitus sufferer hears. We have hypothesized that mechanisms of lateral inhibition in the auditory areas of the brain act to confine the activity, driving the tinnitus sound perception to regions representing specific frequencies in the central auditory cortex and increasing the contrast between tinnitus-related activity in these regions and spontaneous activity in adjacent regions. This leads to increased tinnitus perception and to what most tinnitus sufferers hear—a tone or group of tones, as opposed to cacophonous noise containing all frequencies.

Furthermore, the perception of tinnitus has been observed to be enhanced when the person perceiving the subjective noise "attends" to it and associates it with unpleasant emotions [28]. In this scenario, the person experiencing tinnitus is annoyed by the sound, thereby activating the limbic system. A feedback mechanism under control of the limbic system is assumed to give rise to an increased generation of tinnitus-related activity [29,30]. The increased perception can then lead to increased annoyance, completing a positive feedback cycle that will render tinnitus persistent and annoying. In short, individuals experiencing tinnitus unintentionally condition themselves to aggravate tinnitus through negative reinforcement. Shulman [31] demonstrated the changes in cortical and limbic regions in tinnitus subjects as compared to controls and hypothesized a final common pathway for tinnitus.

This model for the etiology of tinnitus suggests that, though tinnitus may be triggered by events in the periphery, the mechanisms that cause tinnitus to be a persistent and annoying condition are in the brain [32,33]. Positron emission tomography, functional magnetic resonance imaging (fMRI), and EEG/MEG studies have shown that tinnitus-related activity in the auditory cortex gives rise to changed cortical representations of the tinnitus pitch [26,34] and enhanced contrast between responses to tones at the tinnitus pitch and tones of lower frequencies [27]. These studies support the idea that tinnitus-related neuronal activity is confined to certain isofrequency regions of the auditory cortex. Moreover, it has been shown that the changes in the size of the tonotopic map in the auditory cortex can be induced by training [35]. Taken together, these findings suggest that the observed tinnitus-related changes in the organization of the auditory cortex are the result of the involuntary learning process described earlier. Because training-induced changes in the response pattern of cortical neurons can be reversed by habituation, we hypothesize that habituation will ameliorate tinnitus.

Indeed, tinnitus retraining therapy (TRT), introduced by Jastreboff et al. [28,36], makes use of such a habituation mechanism. However, TRT uses white or broadband noise (i.e., noise containing all frequencies) as the habituating stimulus. The rationale behind the use of white noise is to generate a decreased signal-to-noise ratio between the tinnitus-related neuronal activity and random background activity in the auditory system. This background activity is achieved by introducing a quasi-random, stimulus-related signal in all of the parallel, tonotopic channels of the auditory system. TRT is available currently, but it is expensive, time-consuming, of long duration, and only incompletely effective. More precise methods of habituation have been suggested by computational models of tinnitus [37–41]; for a review, see Husain, [42,43]. These models explain how a decreased auditory input resulting from a peripheral hearing deficit can give rise to a specific tinnitus pitch. When the tinnitus sound itself is used as a habituation stimulus,

Langner's model predicts that the tinnitus should disappear. This model also assumes that the limbic system is a necessary component for stabilizing the tinnitus perception. On the basis of these models, we propose to use a frequency-specific or "custom-made" sound similar to an individual's tinnitus for habituation purposes. We conjecture that using a customized sound and mimicking the tinnitus as closely as possible should be highly efficient in reducing the perception of tinnitus.

Given this theoretical background, we have approached the problem of tinnitus treatment by using customized sound—more specifically, a replica of the subjective tinnitus experience—to reduce the overactive sound-processing circuits. This report outlines our preliminary results with treating individual with tinnitus. We describe two studies: an initial pilot study (study 1) and one with a more formalized protocol (study 2). Customized sound therapy (CST) involves an initial session with a sound specialist, during which a "customized" sound is created for each individual and closely mimics the subjective tinnitus. This is followed by a period of several weeks to months during which the individual listens to the customized sound for several hours every day while going about normal daily activities. The patient wears a sound player carrying the sound that is played back to the individual. This external sound appears to calm the internal overactive circuits and is *not* associated with annoyance and anxiety. Unlike the process for TRT, we do not use directive counseling in the context of CST. Directive counseling would tend to draw the individual's attention to the tinnitus, whereas habituation is designed to draw attention away from the tinnitus. In this regard, combining directive counseling and CST would be counterproductive.

METHODS AND PARTICIPANTS

Study 1

We recruited a total of 11 tinnitus patients (mean age, 46.8 ± 11.7 yr) and 16 control subjects (mean age, 39.1 ± 10.7 yr) for a pilot study to examine the effects of CST during a short-term habituation process. Subjects participated in this first experiment at different times, varying between 1 and 24 months. All patients were fitted with a customized sound mimicking their subjective tinnitus. Tinnitus patients and control subjects underwent at minimum 1 hour of CST training. Tinnitus patients used their own customized sound as the habituation stimulus. Control subjects used a narrow noise band centered on 4 kHz as the habituation stimulus. Responses to both were recorded before and after habituation. Six of the subjects had hearing tests. We recorded responses to pure-tone sounds at and below the tinnitus frequency before and after the 1-hour habituation treatment.

Study 2

After completion of pilot study 1, we implemented a more formalized and longer-duration protocol. Eight subjects underwent an initial clinical evaluation. We first required tinnitus subjects to complete the Tinnitus Handicap Questionnaire (THQ) [44], and subsequently we audiometrically evaluated all subjects and recorded their EEGs. We conducted the initial evaluation, audiological assessment, and EEG on the same day. On a separate day, subjects' tinnitus sound experiences were characterized and recorded on an MP3 sound player. We then asked tinnitus subjects to listen to the customized sound. Subjects underwent 3 weeks of CST therapy for 6–8 hours every day. Tinnitus subjects used their own customized sound as the habituation stimulus. All tinnitus individuals had a pitch of nearly 4 kHz. They maintained log entries of the duration of each listening session. Halfway through the training period, we scheduled a second session to characterize the tinnitus sound to ensure that the stimulus still matched the subjects' tinnitus perception. After 3 weeks, all subjects underwent a second EEG and audiological assessment and a final clinical evaluation. Tinnitus subjects were required to complete the THQ a second time.

We selected subjects between the ages of 20 and 60 years if they exhibited "primary tinnitus" as defined by Dr. Craig Formby and Dr. Susan Gold, MS, CCC-A, of the University of Maryland Medical Center, Tinnitus and Hyperacusis Clinic. Primary-tinnitus subjects are those presenting to the otology clinic with a main complaint of tinnitus, regardless of type and degree of hearing sensitivity. Severe and profound hearing loss excluded a subject from the study. Furthermore, subjects' tinnitus had to be present all the time with constant sound quality. Subjects were initially interviewed at the Otolaryngology Clinic to ensure that they met all exclusionary criteria. (Those criteria are for mild tinnitus as opposed to tinnitus of the severe disabling type.) Of eight subjects who started the 3-week CST treatment, five completed the protocol. Two subjects dropped out after reporting strange sounds from their MP3 player that seemed to make their tinnitus worse. In one case, the cause of the disturbing sounds was a defective MP3 player; in the other case, the disturbing sounds were caused by an artifact in the conversion of the digitized sound from the WAV to the MP3 file format. In one case, data were excluded because the subject did not wear the MP3 player for the requisite time and was not present for the follow-up examination owing to scheduling conflicts.

ASSESSMENTS

Tinnitus Handicap Questionnaire

Subjects in both studies completed the THQ on the first day of participation. The THQ consists of 27 statements relating to the impact of tinnitus on an individual's life. It contains three subscales relating to mental health, hearing, and attitude toward tinnitus [44]. Subjects respond by rating each statement on a 0–100 scale. A 100 means total agreement, whereas a 0 means total disagreement.

Pure-Tone Audiometry Procedure

In study 2, prior to recording of the EEG and event-related potentials (ERP), subjects had bilateral audiograms using adult routine clinical procedures with appropriate level of contralateral masking as needed. We obtained pure-tone air and bone conduction hearing sensitivity thresholds for the standard audiometric frequencies of 250 Hz to 8 kHz in a double-walled sound suite meeting current American National Standards Institute standards for threshold air conduction and bone conduction testing. We used a Macio MA-41 portable audiometer (Maico Diagnostics, Eden Prairie MN) with a current calibration sticker for the pure-tone testing. The audiometer has standard Telephonic THD-39 earphones with MX-41-AR ear cushions (Audiometrics, Oceanside CA) and a standard Radioear B-71 bone vibrator (Radioear Corp., New Eagle PA). Behavioral loudness discomfort levels (LDLs) were also recorded at each frequency in both ears using pulsed pure tones with a 200-msec duration and 50% duty cycle. We instructed each subject to push the signal button when an increasing continuous pulsed pure tone reached a subjective loudness level that represented initial annoyance. The LDL was repeated at each standard test frequency to determine whether the initial level was stable or adjusted upward. The most intense LDL was recorded between the two trials.

Study 2 subjects underwent an otoscopic examination, tympanogram, and ipsilateral acoustic reflex screening. We obtained middle-ear measures using a currently calibrated, portable Grason-Stadler GS-17 acoustic immitance Middle Ear Analyzer (Grason Stadler Inc., Madison WI). Standard clinical procedures using clean probe tips were used for all middle-ear measures. We obtained initial baseline auditory brainstem response and auditory middle latency responses for each subject using a currently calibrated and certified electrically safe Biologic Brain Atlas (Advanced Biologic Corp., Toronto, Quebec, Canada) evoked potential machine with ER-3 insert earphones. Auditory brainstem response and auditory middle-latency response two-channel recordings followed clinical recording and analysis parameters outlined in Ferraro's *Laboratory Exercises in Auditory Evoked Potentials* [45]. The evoked potential recording protocols sequentially programmed into the Brain Atlas were the same for each subject. Total testing time for the entire audiological assessment was approximately 50–60 minutes.

CREATING THE CUSTOMIZED SOUND

The perceptual experience of tinnitus was characterized in both studies using a successive approximation technique. We asked individual subjects to verbally describe the "sounds" they experienced. In response to the subjects' statements, sounds were synthesized using high-precision, general-purpose sound synthesis software. The tinnitus sound is synthesized according to the description provided by the subjects using the program "pcmusic" [46]. In an iterative process, the resulting sound was played back to the subjects, who responded with suggested adjustments, such as altering the pitch, number of components, balance, or quality of the synthetic sound. In response to these suggestions, we modified the sound description file and repeated the process until the subjects reported that the synthesized sound matched their subjective tinnitus experience well. This sound was used to produce two audio files. One contained a pulsed version of the subjects' tinnitus sound (250-msec pulse duration, 50% duty cycle), and the other was a 180-sec-long continuous sound. We then downloaded the digitized sound into a small portable digital sound playback device (MPEG-player). The time needed for this successive approximation procedure varied, depending on the subjects' ability to describe their subjective experience of tinnitus and on their ability to characterize differences between the tinnitus they experience and the sounds being synthesized by the computer. For most subjects, it required approximately two or three 2-hour sessions. Before beginning CST, we required subjects to confirm that the habituation sound matched their tinnitus during two or more sessions separated by at least a week. Adjustments to the stimulus were needed for some subjects after CST had progressed a few weeks. It seemed clear that this was owing to changes in the characteristics of the tinnitus itself rather than a mismatch in the initial sounds. The frequency content of a typical "customized" stimulus is shown in Figure 1.

EEG Procedures

We recorded auditory evoked potentials in both studies. Data were recorded from 15 electrode sites mounted on an elastic cap and located over a variety of scalp sites (F3, Fz, F4, C3, Cz, C4, P3, Pz, P4, T3, T4, T5, T6, O1, and O2 according to the modified International 10–20 System). We recorded eye-movement artifact, partic-

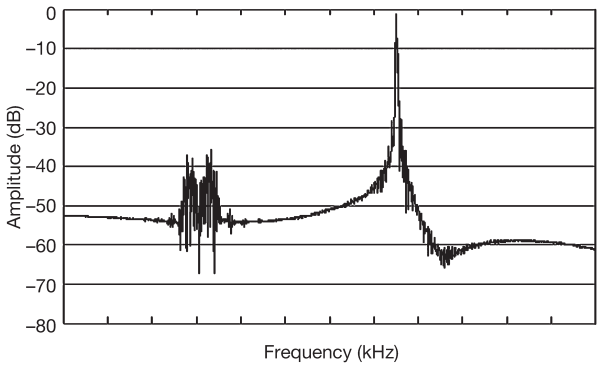

Figure 1. Spectrogram of a typical tinnitus habituation stimulus, showing two closely spaced narrow-band noises centered at 2,800 Hz and 3,225 Hz and a very-narrow-band noise centered at 7,417 Hz that is almost 40 dB stronger than the first two.

ularly blinks, from vertical and/or horizontal electrooculogram electrodes. All electrode sites were referred to linked mastoids. Within each series, 80 stimuli of different intensities, for a total of 400 stimuli, were presented in random order and at intervals varying randomly between 1 and 3 seconds. The EEG was amplified by 10,000 and band-pass filtered between 0.01 and 100 Hz at 3 dB down. We recorded and digitized analog signals at a sampling rate of 250 Hz. For stimulus presentation and data acquisition and analysis, the ADAPT scientific software [47] was used.

Auditory Stimulation

Auditory stimulation in both studies consisted of sine waves generated by a function generator (Goldstar FG2002C; LG Precision, Seoul, South Korea). The intensity and duration of each stimulus were set by a specially designed programmable logarithmic amplifier that is controlled in real time by a stimulus presentation and data collection program running in ADAPT. Auditory stimuli of five different intensities were presented through insert earphones (Eartone 3A transducers with Earl link foam eartips; Cabot Safety Co, Indianapolis IN).

Stimulus Protocol

Tinnitus subjects underwent either 1 hour (study 1) or 3 weeks (study 2) of habituation. During study 2, they were required to wear their MPEG player and listen to the customized habituation sound for 6–8 hours daily as they went about their normal activities. The intensity of the habituation sound was set by the individual so that the tinnitus perception was slightly louder than the habituation sound. Experience from study 1 indicated that subjects had difficulty in distinguishing the continuous habituation sound from their tinnitus. Hence, to help individuals compare the loudness of their tinnitus to that of the habituation sound, we instructed them to use the pulsed version of their customized sound. This facilitated the determination of the requisite intensity, at which point they could switch over to the continuous sound for the habituation itself. We required subjects to document the time during which the sound player was used and the intensity settings.

RESULTS

Hearing Tests

Audiograms were taken from 7 of the tinnitus subjects and 13 of the control subjects in study 1. One of the tinnitus subjects had mild hearing loss, and three had moderate hearing loss on the right ear, whereas five had mild hearing loss, and none had moderate hearing loss on the left ear at their tinnitus frequency. The hearing tests in study 2 (Table 1) showed mostly normal hearing in both tinnitus and control subjects at 1 kHz and 2 kHz. At 4 kHz, four of eight tinnitus subjects had mild or moderate hearing loss in their right ear, and five of eight subjects had mild hearing loss in their left ear. Conversely, only 2 of 12 control subjects had mild or moderate hearing loss in their left ear, and only 1 of 12 control subjects had moderate hearing loss in the right ear.

Tinnitus Handicap Questionnaire

The average score on the THQ dropped from 48.9 to 44.7 after 3 weeks of CST. A paired *t*-test showed this to be only marginally significant ($p = .12$).

Tinnitus Perceptions

Most subjects indicated changes in their tinnitus perceptions very soon after beginning CST, in one case even after trying out the habituation sound for only a few

Table 1. Hearing Loss in the Tinnitus and Control Groups

Hearing Loss	Right			Left		
	1 kHz	2 kHz	4kHz	1 kHz	2 kHz	4 kHz
Tinnitus						
WNL	7	6	4	8	7	3
Mild	1	1	1	0	1	5
Mod	0	1	3	0	0	0
Control						
WNL	12	12	10	12	12	11
Mild	0	0	1	0	0	1
Mod	0	0	1	0	0	0

WNL = within normal limits.

minutes in the laboratory. Generally, they thought that *their tinnitus was much more bearable when the habituation sound was present* and that the tinnitus was less bothersome at other times. For CST to be effective, the stimulus has to be audible but must not be so loud as to mask the tinnitus itself. Therefore, the intensity settings that tinnitus subjects used on their noise generator gave an estimate of the loudness of the tinnitus. Though most subjects did not keep a detailed log of the volume settings on their MP3 players, clearly the volume setting required for the habituation sound to be just audible over the subject's internal tinnitus perception decreased over time, in one case so much that the subject exhausted the available intensity settings and the stimulus had to be resynthesized at a lower intensity. Paradoxically, none of the subjects reported a decrease in subjective tinnitus loudness.

In four of the five subjects who completed the 3 weeks of CST, hearing threshold at the frequency closest to the subject's tinnitus pitch improved by 10 dB or more (Fig. 2). However, in one case, a 10-dB improvement in one ear was offset by a 10-dB decrement in the other ear. Some subjects reported changes in the sound quality of their tinnitus, so that their habituation sound was no longer a match for their tinnitus perception. When a new habituation sound mimicking the changed tinnitus perception was synthesized, the subjects reported the CST to be as effective as before. At least two subjects continued treatment for a total of 23 months.

The EEG recording procedure required the determination of hearing thresholds prior to each session. This provided records of the tinnitus subjects' hearing thresholds at their tinnitus frequency. These hearing thresholds were determined using nonstandard equipment and methods. Nonetheless, they were carried out under defined conditions so that changes in the measurements reflected changes in hearing threshold. The first threshold measured was set to 0 dB normalized hearing level (nHL), and all other measurements were plotted with reference to it. After 1 hour of habituation, the hearing threshold at the tinnitus frequency was lowered by as much as 15 dB nHL. Over several weeks of habituation training, we observed hearing thresholds at the tinnitus frequency to decrease by as much as 25 dB nHL.

Electrophysiology

In study 1, we assessed the short-term effects of habituation on the electrophysiology by recording the N100 component from tinnitus and control subjects before and after 1 hour of CST. For the tinnitus patients, the habituation sound was the one used in habituation training, and the stimuli used for recording the N100 component were 1,000-Hz tones and the tinnitus frequency tones. For control subjects, the stimuli used for recording the N100 component were 1,000-Hz and 4,000-Hz tones. Their habituation stimulus was a narrow noise band centered around 4,000 Hz. As shown in Figure 3, tinnitus patients tended to show a greater N100 intensity-dependence (i.e., slightly higher slopes) on their tinnitus tones than on the control 1,000-Hz tone, both before and after habituation. In contrast, control subjects showed the reverse relationship. This supports the hypothesis that an EEG/ERP index of tinnitus is likely but shows little effect of short-term habituation on this index.

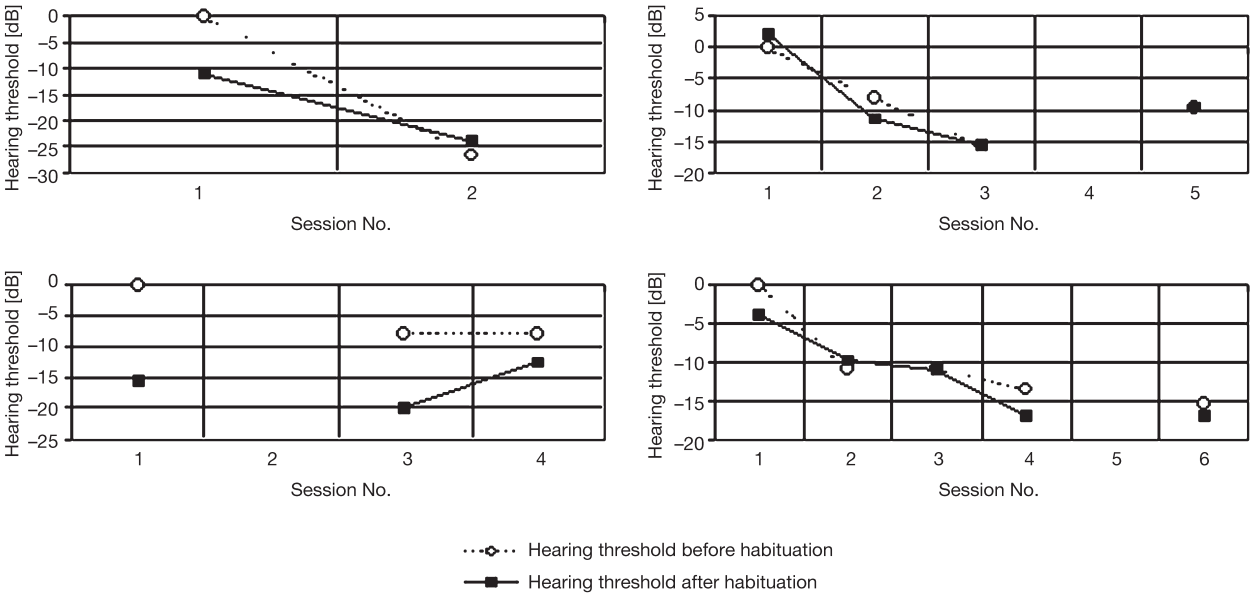

Figure 2. Changes in four tinnitus subjects' hearing levels at the tinnitus frequency during habituation training.

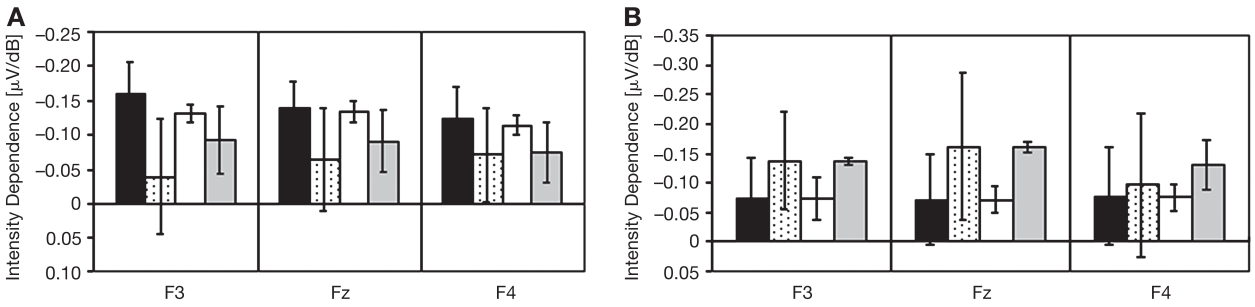

Figure 3. N100 intensity dependence in response to A) tinnitus frequency (4000 Hz) and B) control frequency (1000 Hz). Note that tinnitus subjects showed slightly higher slopes to their tinnitus tones than to the controls' 1,000-Hz tone, both before and after habituation. In contrast, control subjects showed the reverse relationship.

In study 2, comparison of the N100 responses (slope) before and after 3 weeks of CST showed a decrease in the intensity dependence in response to the 4-kHz tinnitus frequency tones (Fig. 4). Furthermore, the intensity dependence of the control 2-kHz tones (approximately one octave below the tinnitus frequency) was also significantly decreased in tinnitus subjects. Both tinnitus and the recruitment due to hearing loss may have influenced the intensity dependence of the N100 response to tinnitus frequency tones. Because CST caused a lowering of the subjects' hearing thresholds at frequencies near their perceived tinnitus pitch, these results reflect an effect of CST, regardless of whether the observed change is caused by a decrease of tinnitus-related neuronal activity or decreased recruitment due to lowered hearing thresholds.

DISCUSSION

Recent studies indicate that an altered afferent input to the auditory pathway may be the initiator of a complex sequence of events resulting in the generation of tinnitus at the central level of the auditory nervous system [17]. The results of our two studies indicate that CST aimed at this central dysfunction can reduce chronic tinnitus quickly and safely. This tinnitus suppression may reflect aspects of "residual inhibition" (RI), though distinct mechanisms may be involved as well. RI is the temporary suppression of tinnitus that occurs after the offset of an appropriate masking stimulus [48,49]. Some participants in this study described immediate relief, effects on the THQ, and changes in hearing threshold within 3 weeks. Observations from one subject indicate that most of the tinnitus relief is gained during the first 4–8 weeks of CST. After this initial period, apparently wearing the sound device regularly is unnecessary, and the experience with this one subject indicates that using the habituation sound occasionally as needed may be sufficient. Also, in contrast to TRT, no directive counseling was required for CST to show effects. The underlying rationale for CST is to draw subjects' attention away from their tinnitus, and reports indicate that though subjects readily perceive their tinnitus and the habituation sound if they choose to, CST helps them to *ignore* their tinnitus. Directive counseling in connection with CST might actually be counterproductive because it might remind subjects of the annoyance associated with untreated tinnitus and thereby draw their attention to their tinnitus rather than away from it. Because it produces effects after only a few weeks of treatment without involving directive counseling or requiring frequent regular visits

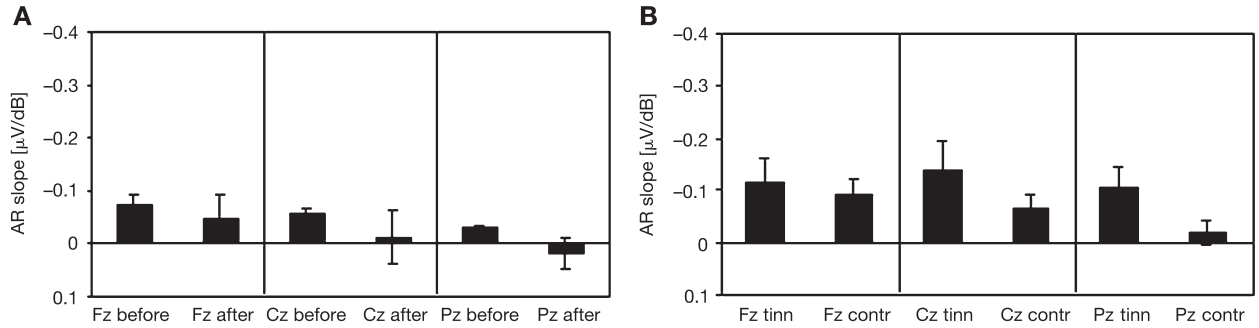

Figure 4. Responses to 4-Hz tinnitus frequency tones A) before versus after customized sound therapy and B) tinnitus versus control.

to health care professionals, CST is expected to provide quick and lasting relief from tinnitus at relatively low cost. Further, though adding a replica of the annoying sound that tinnitus patients experience would appear to be even more annoying, the method of playing the replica at the same volume as the experienced sound minimizes any discomfort. Subjects in this study tolerated the sound well.

The hearing loss observed at the tinnitus frequencies raises the possibility that the stronger intensity dependence observed in the responses of tinnitus subjects to tinnitus frequency tones may have been caused by recruitment (abnormal loudness growth) rather than tinnitus. However, the reduced intensity dependence observed in responses to 2,000-Hz tones, one octave below the tinnitus frequency, is opposite to the effect of recruitment and thus not attributed to it. Rather, we attribute this effect on intensity dependence to lateral inhibition caused by the tinnitus-related activity in auditory cortex.

The observed changed intensity dependence of the auditory N100 response in tinnitus subjects in the present studies and in previously published findings [19,27,50–52] indicate that tinnitus is accompanied by a reorganization of the tonotopic map in the auditory cortex. The main correlate of this reorganization in our studies was the enhanced contrast between responses to tinnitus frequency and tones approximately one octave lower than the perceived tinnitus pitch. After 3 weeks of CST, the intensity dependence of responses to tinnitus frequency tones was decreased, rendering the responses to tinnitus frequency tones more similar to responses from normal subjects to tones in the same frequency range. The main difference between tinnitus sufferers and controls manifested itself in the response to tones one octave below the tinnitus frequency (2 kHz in our studies). The change in the EEG pattern induced by CST manifests in responses to the tinnitus frequency. However, the contrast between responses to tinnitus frequency tones and tones one octave below the tinnitus frequency was not changed after 3 weeks of CST. Therefore, whether longer CST treatments can completely reverse the cortical reorganization associated with tinnitus remains to be seen.

Our studies on the effectiveness of CST were conducted without a placebo treatment and were not blinded. This may be a limitation, because other studies on tinnitus treatments (e.g., Dobie, 1999 [53]) reported strong placebo effects. However, to conceive of a placebo condition that is truly blinded is difficult, because CST subjects have to undergo the sound-matching process to create their own habituation stimulus. Consequently, all study subjects will know whether they are being habituated to a sound mimicking their tinnitus or to a "placebo" sound. However, to assess the efficacy of CST in a crossover trial with comparable therapies might be possible, as that study design would not require a placebo condition and blinding.

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