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Research paper

Course of hearing loss and occurrence of tinnitus

Ovidiu König [a,1], Roland Schaette [b,c,*,1], Richard Kempter [b,c,d], Manfred Gross [a]

[a] Department of Audiology and Phoniatrics, Charité, Medical Faculty of Berlin, Fabeckstr. 62, 14195 Berlin, Germany
[b] Institute for Theoretical Biology, Humboldt-Universität zu Berlin, Invalidenstr. 43, 10115 Berlin, Germany
[c] Bernstein Center for Computational Neuroscience Berlin, Invalidenstr. 43, 10115 Berlin, Germany
[d] Neuroscience Research Center, Charité, Medical Faculty of Berlin, Schumannstr. 20/21, 10117 Berlin, Germany

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Abstract

Chronic tinnitus is often accompanied by a hearing impairment, but it is still unknown whether hearing loss can actually cause tinnitus. The association between the pitch of the tinnitus sensation and the audiogram edge in patients with high-frequency hearing loss suggests a functional relation, but a large fraction of patients with hearing loss does not present symptoms of tinnitus. We therefore, investigated how the occurrence of tinnitus is related to the shape of the audiogram. We analyzed a sample where all patients had noise-induced hearing loss, containing 30 patients without tinnitus, 24 patients with tone-like tinnitus, and 17 patients with noise-like tinnitus. All patients had moderate to severe high-frequency hearing loss, and only minor to moderate hearing loss at low frequencies. We found that tinnitus patients had less overall hearing loss than patients without tinnitus. Moreover, the maximum steepness of the audiogram was higher in patients with tinnitus (-52.9 ± 1.9 dB/octave) compared to patients without tinnitus (-43.1 ± 2.4 dB/octave). Differences in overall hearing loss and maximum steepness between tone-like and noise-like tinnitus were not significant. For tone-like tinnitus, there was a clear association between the tinnitus pitch and the edge of the audiogram, with tinnitus pitch being on average 1.48 ± 0.12 octaves above the audiogram edge frequency, and 0.81 ± 0.1 octaves above the frequency with the steepest slope. Our results suggest that the occurrence of tinnitus is promoted by a steep audiogram slope. A steep slope leads to abrupt discontinuities in the activity along the tonotopic axis of the auditory system, which could be misinterpreted as sound.

Keywords: Tinnitus; Noise-induced hearing loss; Audiometric difference; Audiogram steepness; Audiogram edge; Tinnitus pitch

1. Introduction

Hearing loss is a risk factor for tinnitus (Chung et al., 1984; Sindhusake et al., 2003, 2004), and even tinnitus patients with normal audiograms might have restricted cochlear damage (Shiomi et al., 1997; Weisz et al., 2005) or hearing loss at frequencies above 8 kHz, which is not detected by normal clinical audiometry (Roberts et al., 2006). The tinnitus sensation and the frequency range of hearing loss are related: when subjects match their tinnitus pitch to a pure tone, most of the matches are at frequencies at which hearing is impaired (Henry et al., 1999); when subjects are asked to judge the contribution of comparison tones to their tinnitus sensation, the resulting tinnitus spectra span wide frequency ranges that correspond to the frequencies where hearing loss is present (Noreña et al., 2002). However, not all patients with hearing loss develop tinnitus, as demonstrated by the higher prevalence of hearing loss compared to tinnitus (Lockwood et al., 2002). It is therefore unclear, which factors of hearing loss contribute to the occurrence of tinnitus.

Tinnitus is believed to arise from alterations in the spontaneous activity of neurons in the auditory system (see, e.g., Eggermont, 2003). In animals, hearing loss through

* Corresponding author. Address: Institute for Theoretical Biology, Humboldt-Universität zu Berlin, Invalidenstr. 43, 10115 Berlin, Germany. Tel.: +49 3020938926.
E-mail address: r.schaette@biologie.hu-berlin.de (R. Schaette).
[1] Both authors contributed equally.

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cochlear damage reduces the spontaneous firing rate in the affected auditory nerve fibers (Liberman and Dodds, 1984). This reduction can cause discontinuities in the profile of spontaneous activity along the tonotopic axis in the auditory pathway. Modeling studies suggest that such discontinuities could be exaggerated by lateral inhibition (Gerken, 1996) and homeostatic changes (Schaette and Kempter, 2006), leading to activity patterns in the models that are consistent with tone-like tinnitus.

Such concepts suggest that the development of tinnitus depends on the course of the audiogram, in that some audiogram shapes are more likely to lead to tinnitus than others. To investigate this hypothesis, we analyzed a sample of patients that all had noise-induced hearing loss from chronic noise exposure in the workplace. This choice of subjects eliminates possible confounding factors that could arise from mixed etiologies of hearing loss. Moreover, none of the patients used a hearing aid at the time of examination.

2. Methods

We performed a retrospective study on data from compensation claimants that had been sent to our clinic for evaluation work-related noise-induced hearing loss from 1993 to 2003. The sample consisted of 71 adults (mean age 56 years; range 38–69 years; all males). The subjects were in good general health and reported an unremarkable history of otological diseases or exposure to ototoxic drugs.

All patients had moderate to severe noise-induced hearing loss caused by chronic noise exposure in the workplace. There were 30 subjects without tinnitus, 24 subjects with tone-like tinnitus, and 17 subjects with noise-like tinnitus. The three groups did not differ significantly in age (no tinnitus: 56.6 ± 1.1 years; tone-like tinnitus 55.0 ± 1.4 years; noise-like tinnitus 56.3 ± 1.6 years). For subjects with tinnitus, the mean reported duration of hearing loss was 10.2 ± 1.24 years, and for subjects without tinnitus 11.67 ± 1.86 years (difference not significant, $p = 0.50$, t-test). All tinnitus subjects had experienced their tinnitus for more than one year, with a mean reported duration of 8.83 ± 1.33 years. The duration of tinnitus experience was not significantly different from the duration of hearing loss ($p = 0.47$, t-test). We note that the duration of hearing loss and tinnitus could not always be reliably determined, as noise-induced hearing loss is slowly progressing, and tinnitus often develops from occasional episodes to a permanent sensation.

All tinnitus patients had chronic bilateral tinnitus, i.e., tinnitus was a permanent sensation, was perceived in both ears with similar pitch, and had persisted for at least one year. We chose to exclude patients with unilateral tinnitus to eliminate possible confounding factors that could arise from assigning the two ears of a single patient to two different groups in the analysis. Moreover, unilateral tinnitus might be different from bilateral tinnitus, as it is often associated with a difference in hearing level between the ears (Chung et al., 1984; Ochi et al., 2003). We also excluded patients using a hearing aid, as hearing aids can reduce tinnitus (Surr et al., 1999; Folmer and Carroll, 2006) and are used in tinnitus therapy (Jastreboff and Jastreboff, 2000).

2.1. Audiological examination

A total of 142 ears (71 right, 71 left) were used in further analysis. Inclusion criteria were (1) no significant air-bone gap at seven test frequencies (0.25, 0.5, 1, 2, 4, 6 and 8 kHz); (2) normal middle ear status with type A tympanograms and a well-defined compliance maximum not less than −100 daPa; (3) normal otoscopic findings; and (4) not using a hearing aid. Pure-tone audiometry was performed with a clinical audiometer calibrated to accepted standards (American National Standards Institute. Specifications for audiometers, S3.6. New York; American National Standards Institute, 1969). Tympanometric measurements were obtained with a middle-ear analyzer calibrated daily according to the manufacturer's instructions.

2.2. Tinnitus matching

For patients with tone-like tinnitus, the tinnitus frequency was determined with two different psychophysical procedures in the ear ipsilateral to the tinnitus: an adaptive method (bracketing) and the method of adjustment. Each procedure involved equating the pitch of a pure tone (0.125, 0.25, 0.5, 0.75, 1, 2, 3, 4, 6 and 8 kHz) to the most prominent tinnitus pitch. There was no statistically significant difference for the means and standard deviations among the different methods for the group data. Because some patients were unreliable in their pitch matching, we repeated the match up to seven times.

2.3. Characterization of the shape of the audiogram

To obtain a measure of the overall amount of hearing loss of a patient we used the area under the audiogram curve. Therefore, the audiogram frequencies were converted to a logarithmic scale, and the resulting audiogram was interpolated linearly between the measured points. Then we calculated the integral from 0.125 to 8 kHz to obtain the area under the audiogram curve.

Audiogram slopes were computed as follows: for each adjacent two frequencies in an audiogram, the difference in dB hearing level was calculated and then divided by the frequency difference measured in octaves. This procedure yields the steepness in dB/octave. The steepness value was then assigned to the geometric mean of the two frequencies to construct derivative audiograms.

Audiogram edges were detected in a two-step process. First we determined the frequency range where hearing levels had not dropped more than 20 dB below the best hearing level observed in the audiogram. In this range, we looked for a maximum of the second derivative of the audiogram (computed from the derivative audiogram using the method described above) to identify the audio-

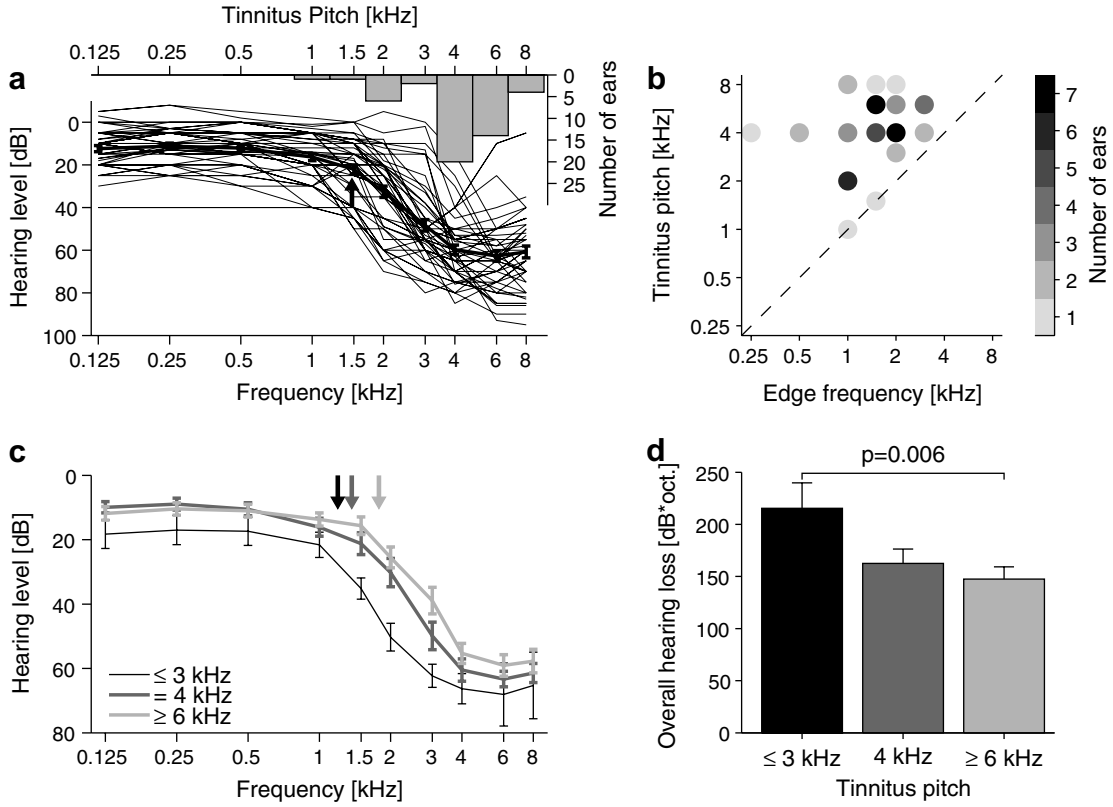

Fig. 1. Association between tinnitus pitch, audiogram edge, and overall amount of hearing loss. (a) Audiograms (thin lines) of 24 patients with tone-like tinnitus, mean audiogram (thick line), and distribution of tinnitus pitch (bars). Tinnitus pitch is located predominantly at frequencies above the mean audiogram edge (arrow) where hearing is impaired. (b) Tinnitus pitch vs. audiogram edge frequency. The gray level of each point denotes the number of ears with the corresponding combination of edge frequency and tinnitus pitch. (c,d) Mean audiograms (lines in c) and audiogram edges (arrows in c) and overall amount of hearing loss (d) of patients grouped by tinnitus pitch ($\leqslant 3$ kHz, 4 kHz, $\geqslant 6$ kHz). The groups with a tinnitus pitch of $\leqslant 3$ kHz (black) and $\geqslant 6$ kHz (light gray) significantly differed in their overall amount of hearing loss. Error bars denote ± 1 s.e.m.

gram edge. If no edge could be identified in that way, the highest frequency that still met the 20 dB hearing level criterion was said to be the audiogram edge. To compute the mean audiogram edge across individuals, edge frequencies were first converted to a logarithmic scale, and then averaged.

2.4. Significance tests

Unpaired two-sample t-tests were used to determine whether differences were significant. We used a significance level of $\alpha = 0.05$. Whenever more than one test was carried out on a data set, a Bonferroni correction was applied to adjust the significance level ($\alpha = 0.05/n$ for n tests).

All data analysis was carried out using MATLAB 7 (The MathWorks Inc., Natick, Massachusetts).

3. Results

To reveal features of audiograms that promote the occurrence of tinnitus we analyzed data from 71 patients with noise-induced hearing loss. Thirty patients had no tinnitus, 24 patients had tone-like tinnitus, and 17 patients had noise-like tinnitus. When patients with tone-like tinnitus were asked to match pure tones (0.125, 0.25, 0.5, 0.75, 1, 2, 3, 4, 6, or 8 kHz) to the dominant pitch of their tinnitus sensation, tinnitus pitch was generally matched to frequencies above the audiogram edge (see Section 2) where hearing is impaired (Fig. 1a and b). On average, tinnitus pitch was 1.48 ± 0.12 octaves above the audiogram edge, and there was a weak but significant correlation between edge frequency and tinnitus pitch ($r = 0.30$, $p = 0.04$).

To further examine the relation between tinnitus pitch and hearing loss, we grouped the patients by tinnitus pitch ($\leqslant 3$ kHz, 4 kHz, $\geqslant 6$ kHz) and calculated the mean audiogram as well as the mean audiogram edge frequency for each group. We also determined the overall amount of hearing loss as quantified by the area under the audiogram curve for each ear (see Section 2), and then computed the mean overall hearing loss for each group. As can be seen in Fig. 1c and d, patients with a tinnitus pitch $\leqslant 3$ kHz had the worst hearing and the lowest audiogram edge frequency, whereas those with a pitch $\geqslant 6$ kHz had the best hearing and the highest audiogram edge frequency, and the 4 kHz group was intermediate. Significant differences were observed between the groups "$\leqslant 3$ kHz" and "$\geqslant 6$ kHz' for the average edge frequency ($p = 0.005$, t-test) and the overall amount of hearing loss ($p = 0.006$, t-test), whereas differences

between the groups "$\leqslant 3$ kHz" and "4 kHz", as well as between the groups "4 kHz" and "$\geqslant 6$ kHz" failed to achieve significance.

The observed relation between tinnitus pitch and the amount and frequency-range of hearing loss suggested that the occurrence of tinnitus could depend on the severity of hearing impairment. We therefore, compared the overall amount of hearing loss of subjects with and without tinnitus. Surprisingly, we found that hearing-impaired patients with tinnitus (tone-like and noise-like) on average had less hearing loss than those without tinnitus (Fig. 2a), and the difference was highly significant ($p = 6 \times 10^{-4}$, t-test). The difference within the tinnitus group (tone-like tinnitus vs. noise-like tinnitus), on the other hand, was not significant ($p = 0.26$, t-test, Fig. 2b). Similarly, we found that tinnitus patients and subjects without tinnitus differed in the location of the mean audiogram edge. Patients with tinnitus had an average edge frequency of 1.31 kHz $\pm$ 0.09 octaves, whereas patients without tinnitus had a mean edge frequency of 0.82 kHz $\pm$ 0.12 octaves. This difference was highly significant, too ($p = 7 \times 10^{-6}$, t-test). When the tinnitus-group was subdivided into tone-like and noise-like tinnitus, we obtained a mean edge of 1.47 kHz $\pm$ 0.1 octaves for tone-like tinnitus, and 1.11 $\pm$ 0.12 octaves for noise-like tinnitus. The difference between the two groups just failed to achieve significance ($p = 0.03$, t-test) because of the Bonferroni correction.

The mean audiograms in Fig. 2c show that, on average, subjects with and without tinnitus had similar hearing levels at the lowest and the highest frequencies, whereas the course of the audiograms at intermediate frequencies was different. To quantify the course of the audiograms at intermediate frequencies we determined the maximum steepness for each audiogram (see Section 2). This analysis revealed that tinnitus patients tended to have steeper audiogram slopes than subjects without tinnitus. Subjects without tinnitus had a mean maximum steepness of -43.1 ± 2.4 dB/octave, whereas patients with tinnitus had a mean maximum steepness of -52.9 ± 1.9 dB/octave (Fig. 2d). The difference in mean maximum steepness between patients with and without tinnitus was significant ($p = 0.002$, t-test). After subdividing the tinnitus group, we obtained a mean maximum steepness of -53.4 ± 2.5 dB/octave for tone-like tinnitus, and -52.2 ± 3.1 dB/octave for noise-like tinnitus (Fig. 2e). This difference was not significant ($p = 0.91$, t-test). For tone-like tinnitus, the tinnitus pitch was on average 0.81 $\pm$ 0.1 octaves above the frequency of the steepest slope of the audiogram. Moreover, there was a significant correlation between tinnitus pitch and the frequency of the steepest slope of the audiogram ($r = 0.33$, $p = 0.022$).

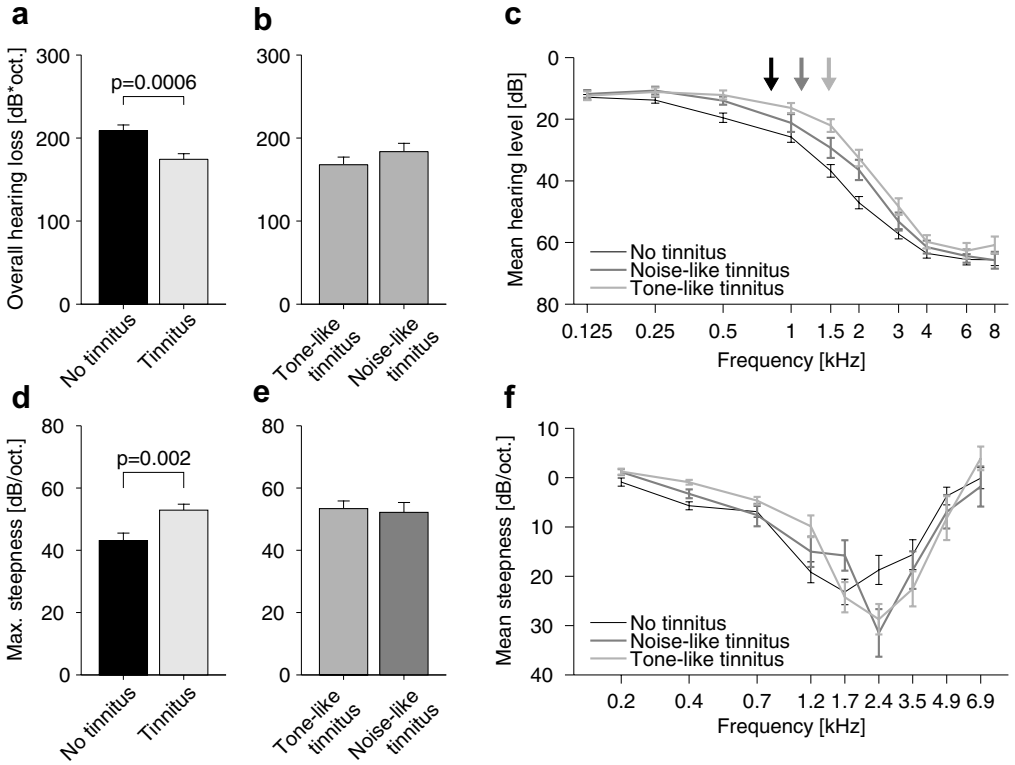

Fig. 2. Audiometric differences between hearing-impaired patients with and without tinnitus. (a) Patients without tinnitus ($n = 30$) had significantly more overall hearing loss than patients with tinnitus ($n = 41$). (b) The mean overall hearing loss in patients with tone-like tinnitus ($n = 24$) and noise-like tinnitus ($n = 17$) was not significantly different. (c) Mean audiograms (lines) and audiogram edge frequencies (arrows) of patients without tinnitus (black), with noise-like tinnitus (dark gray), and with tone-like tinnitus (light gray). (d) Audiograms of patients with tinnitus had a significantly higher mean maximum steepness than those of patients without tinnitus. (e) The mean maximum steepness of the audiograms of patients with tone-like and noise-like tinnitus was not significantly different. (f) Mean derivative audiograms; color assignments as in (c). Error bars denote ± 1 s.e.m.

4. Discussion

In this study, we analyzed a sample of patients with moderate to severe noise-induced hearing loss due to chronic noise-exposure in the workplace. We found that patients with and without tinnitus significantly differed in the course of their audiograms. On average, the patients with tinnitus had less hearing loss, steeper maximum slopes of their audiograms, and the edges of their audiograms were located at higher frequencies compared to the patients without tinnitus (Fig. 2). We did not find significant differences in these parameters between tone-like and noise-like tinnitus.

The relation in our patient sample between tinnitus pitch and the frequency-range of hearing loss (Fig. 1a and b) is consistent with results in earlier studies: tinnitus pitch is predominantly matched to frequencies above the audiogram edge (Henry et al., 1999), and tinnitus spectra as measured by Noreña et al. (2002) and Roberts et al. (2006) correspond to the frequency-range of hearing loss. A distributed spectrum of the tinnitus percept could also explain why some of our subjects were unreliable in matching the pitch of their tinnitus to pure tones, which has also been observed in other studies (Burns, 1984).

The prevalence of tinnitus has been reported to increase with increasing hearing loss in noise-exposed workers that were routinely screened (Chung et al., 1984), whereas in those claiming compensation for work-related hearing loss, the tinnitus prevalence was approximately constant over a wide range of hearing thresholds (McShane et al., 1988). Moreover, Phoon et al. (1993) found that noise-exposed workers with tinnitus had higher average hearing thresholds than those without tinnitus, whereas we found that subjects without tinnitus had more overall hearing loss than subjects with tinnitus. These discrepancies could be due to a different choice of subjects and a different inclusion criterion for tinnitus. We only analyzed subjects with chronic tinnitus experiencing a permanent tinnitus sensation, whereas other studies also included subjects with occasional episodes of tinnitus. However, the inconsistent results on the relation between tinnitus and hearing loss could also indicate that hearing thresholds alone might be insufficient to predict the occurrence of tinnitus. We therefore also analyzed the shape of the audiogram. To quantify the course of the audiogram, we chose the audiogram steepness, as it is largely independent of the overall amount of hearing loss. We could thus demonstrate that not only the amount of hearing loss, but also the shape of the audiogram might be an important factor for the occurrence of tinnitus. In our sample of patients, tinnitus was connected to audiograms with a steep slope, the maximum steepness of the audiograms of tinnitus subjects was significantly higher compared to subjects without tinnitus.

Psychophysical studies demonstrate that steeply sloping hearing loss is associated with local improvements in frequency discrimination thresholds (McDermott et al., 1998; Thai-Van et al., 2002, 2003), which has been interpreted as a correlate of cortical reorganization. Cortical reorganization is believed to play a role in the development of tinnitus (Rauschecker, 1999; Eggermont and Roberts, 2004). Interestingly, only subjects with a hearing loss slope of more than 50 dB/octave displayed a significant improvement in frequency discrimination (Thai-Van et al., 2002). This value is close to the mean maximum steepness in our tinnitus patients (-52.9 ± 1.9 dB/octave), and greater than the mean maximum steepness of our subjects without tinnitus (-43.1 ± 2.4 dB/octave, Fig. 2d).

Animal studies have found substantial cortical reorganization (Rajan and Irvine, 1998; Komiya and Eggermont, 2000; Seki and Eggermont, 2002; Noreña et al., 2003; Noreña and Eggermont, 2005) and increased spontaneous firing rates of cortical neurons (Seki and Eggermont, 2002; Noreña and Eggermont, 2006) after hearing loss. The earliest stage in the auditory pathway where increases in spontaneous activity after hearing loss have been observed is the dorsal cochlear nucleus (Kaltenbach and McCaslin, 1996). These increases in spontaneous firing rate were correlated to behavioral evidence for tinnitus (Brozoski et al., 2002; Kaltenbach et al., 2004). Increased spontaneous firing rates developed in those parts of the dorsal cochlear nucleus that received input from damaged parts of the cochlea (Kaltenbach et al., 2002). Modeling studies indicate that the shape of the profile of increased spontaneous activity in the auditory brainstem depends on the extent and type of cochlear damage (Schaette and Kempter, 2006). For steep audiogram slopes, induced for example by damage to hair cell stereocilia in the high-frequency range, this model predicts steep, abrupt transitions in the spontaneous firing rate of neurons along a tonotopic axis in the central auditory system. The strongest changes are observed at the transition from good to impaired hearing, with spontaneous firing rates peaking in the region of hearing loss. This peak could be misinterpreted by central auditory structures as a sound-evoked pattern, leading to the perception of a sound. The perceived pitch of this 'model tinnitus' would correspond to frequencies above the audiogram edge.

As a future perspective, studies combining high-resolution audiometry, psychophysical procedures identifying cochlear dead regions (Moore et al., 2000) and precise characterization of the tinnitus percept would be desirable to further elucidate the relation between tinnitus and hearing loss. Detailed audiometric data from patients with and without tinnitus would also provide a suitable basis for theoretical modeling studies on tinnitus development, which could help to understand how hearing loss could lead to tinnitus.

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