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Residual inhibition functions in relation to tinnitus spectra and auditory threshold shift

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Abstract

Conclusions: Psychoacoustic functions relating the depth and duration of tinnitus suppression (‘residual inhibition’) to the center frequency of band-passed noise masking sounds appear to span the region of hearing loss, as do psychoacoustic measurements of the tinnitus spectrum. The results (1) suggest that cortical map reorganization induced by hearing loss is not the principal source of the tinnitus sensation and (2) provide a necessary baseline for optimizing residual inhibition in individual cases. Objective: To measure residual inhibition functions and tinnitus spectra using sounds spanning the region of hearing loss. Materials and methods: Three subject-driven, computer-based tools were developed and applied to measure psychoacoustic properties of tinnitus and residual inhibition in 32 subjects with chronic tonal, ringing, or hissing tinnitus. Residual inhibition functions were measured with band-passed noise sounds varying in center frequency up to 12.0 kHz. Results: The depth and duration of residual inhibition increased with the center frequency of the band-passed noise stimuli. Near-elimination of tinnitus for up to 45 s was reported by 8/24 (33%) subjects at center frequencies above 3 kHz (these cases distributed across tinnitus types). Tinnitus spectra covered the region of hearing loss with no preponderance of frequencies near the audiometric edge of normal hearing.

Keywords: Tinnitus, residual inhibition, tinnitus pitch matching, neural basis of sound

Introduction

Animal studies have shown that hearing impairment induced by noise exposure leads to a reorganization of the tonotopic map in primary auditory cortex, such that sound frequencies near the edge of the region of hearing impairment come to be over-represented at the expense of sound frequencies in the affected region [1–5]. Cortical reorganization has been linked directly with human tinnitus, which is also usually associated with hearing loss. According to this hypothesis, neurons at the edge of the region of hearing loss come to express the tuning preferences of their unaffected neighbors, thereby enhancing neural activity in this frequency region which is perceived as the tinnitus sensation [6]. Alternatively, map reorganization and tinnitus may be parallel outcomes of changes in dynamic neural activity that occur throughout the deafferented auditory cortex after hearing injury [7]. According to this view, cortical maps are altered when neurons which have lost their principal thalamocortical input respond to input from their unaffected neighbors via horizontal connections in the neocortical laminae, or to input from unaffected neighboring thalamocortical projections. Tinnitus, on the other hand, is a consequence not of map reorganization, but of spontaneous synchronous activity that forms among neurons in the deafferented region and is perceived in accordance with the location of the constituent neurons in the cortical place map. Increased synchronous activity in the affected region has been demonstrated in animal models of hearing loss [8,9] and is believed to reflect loss of surround inhibition following diminished input from thalamocortical pathways.

Psychoacoustic measurements are relevant to the question of the relation of cortical map reorganization to the mechanism of tinnitus [7,10–13]. Models that link tinnitus with cortical map reorganization predict that psychoacoustic assessments of tinnitus
will localize the tinnitus sensation to frequencies at
or near the edge of the audiometric threshold shift
[6]. Models that link tinnitus with spontaneous
synchronous activity in the deafferented frequency
region, on the other hand, predict that the tinnitus
spectrum spans the region of hearing loss in accor-
dance with the depth of loss expressed in the
audiogram, with no necessary preponderance of
dge frequencies [7]. Norena et al. [14] assessed
the tinnitus spectrum in a sample of 10 subjects
using pure tones covering a range of frequencies
including the region of hearing loss. Although two
subjects reported tinnitus spectra peaking near the
region of the audiometric edge, the majority of cases
gave spectra spanning the region of hearing loss. The
latter results are more consistent with the idea that
tinnitus reflects altered neural activity in the region
of hearing loss and not map reorganization which
reflects tuning shifts to the audiometric edge.

In this paper we describe computer-based tools
designed to evaluate tinnitus spectra using narrow-
band noise stimuli with center frequencies covering
the audiogram. Audiograms were measured up to
20 kHz where warranted. In addition, we extended
the analysis to ‘residual inhibition’ (RI, a temporary
suppression of tinnitus by masking sounds which
outlasts the duration of the masker) [12]. Eggermont
and Roberts [7] suggested that RI occurs when
masking sounds presented at supra-threshold levels
inject inhibition into the deafferented region of the
tonotopic map, briefly segregating the synchronous
activity underlying the tinnitus sensation. If so, RI
functions relating the depth and duration of RI to
masking sounds of different center frequencies
should show optimal tinnitus suppression covering
the range of hearing loss in the audiogram, provided
that the masking sounds can be heard. In this
preliminary report application of tools for measuring
tinnitus spectra and RI functions to a baseline
sample of 32 tinnitus cases is described.

Materials and methods

Subjects

Thirty-two adults (mean age 55.8 ± 18.0 years, range
33–74 years; 19 male) were recruited from the ENT
clinic at McMaster University Medical Center or by
advertisements in the local newspaper. Subjects
reported chronic stable tinnitus persisting for an
average of 10.6 ± 7.4 years (range 0.4–30.1 years)
and gave a mean loudness rating for their tinnitus of
42.0 ± 17.9 (range 10–80), which corresponds to the
midpoint between ‘moderate’ to ‘strong’ on a
logarithmic Borg CR100 psychophysical scale
known to relate subjective loudness to sound pres-
sure level as a power function in normal hearing
subjects [15]. Subjects signed a consent form and
were reimbursed for their parking fees but not
otherwise remunerated. All study procedures were
approved by the McMaster University Office of
Research Ethics.

Apparatus and procedure

Assessment tools were three adaptive, subject-directed
computerized procedures (Familiarization Pro-
gram, Tinnitus Tester, and RI Tester, see below) pro-
grammed in Visual Basic. All sounds were pre-
pared in Matlab and delivered by a sound card
(Creative Audigy 2) through a programmable at-
tenuator (Tucker-Davis PA5) using Sennheisser
HDA-200 headphones. Behavioral responses were
recorded by a Powermate USB Multimedia control-
ler (Griffin Technologies), which allowed subjects to
turn and then depress a bidirectional dial to record
their decisions.

In their first visit to the laboratory subjects were
interviewed to obtain information about their tinni-
tus and completed the Tinnitus Handicap Inventory.
Audiograms were measured to 20 kHz using a GSI-
61 audiometer. Subjects completed the Familiariza-
tion Program and then the Tinnitus Tester, which
assessed psychoacoustic properties of tinnitus. The
session lasted about 2 h. In a second visit 1 week
later RI functions were measured by the RI Tester.

Familiarization Program. This program introduced
subjects to the graphical user interface used for all
procedures. By proceeding stepwise through a brief
series of tasks, subjects learned how the computer
program responded to their input from the dial by
changing the sounds they heard and the images seen
on the screen. The tasks also familiarized subjects
with the concepts of loudness and pitch, which
changed on separate trials as subjects manipulated
dial settings. The Familiarization Program required
about 15 minutes for completion.

Tinnitus Tester. This computerized procedure as-
essed the quality of the tinnitus sensation (ear,
loudness, bandwidth, and frequency spectrum to
limit of the subjects’ audiogram) and gave a brief test
for RI. The following steps were completed in the
order indicated. (1) Localize your tinnitus sensation.
Subjects used the dial to select one of three options:
left ear, right ear, or both ears. (2) Adjustment of
sound intensity. Subjects used the dial to adjust the
loudness of a 0.5 kHz pure tone to a comfortable
level. This level was used in steps (3) and (4) to
present sound clips for tinnitus assessment. (3)
Bandwidth of tinnitus. Subjects indicated whether
their tinnitus was ‘tonal’, ‘ringing’, or ‘hissing’. Three sound clips were presented to illustrate these choices, consisting of a 5 kHz pure tone (‘tonal’ tinnitus) and two Gaussian band-pass noise maskers with a center frequency (CF) of 5 kHz differing in bandwidth. The two bandwidths were approximately ±5% of CF at −20 dB (called BPN5 herein) and the other ±15% of CF at −20 dB (called BPN15 herein; these two bandwidths illustrated ‘ringing’ and ‘hissing’ tinnitus, respectively). Subjects used the dial to sample the sounds and indicate their choice. (4) Temporal properties. Subjects indicated whether their tinnitus was steady or pulsing. Sound clips controlled by the dial illustrated their two choices. (5) Tinnitus loudness rating. Subjects rated the perceived loudness of their tinnitus using the dial to select a position on a Borg CR100 scale with the following quasi-logarithmic anchors: 0, ‘extremely weak’; 30, ‘moderate’; 50, ‘strong’; 70, ‘very strong’; and 100, ‘extremely strong’ [15]. (6) Tinnitus loudness matching. Subjects were presented with sound clips with center frequencies ranging from 0.5 to 12.0 kHz. Bandwidth was determined by the selection made in step 3 (pure tone, BPN5, or BPN15). Subjects adjusted the loudness of each sound (presented twice in a random order) to match the loudness of their tinnitus, up to a maximum sound pressure level (SPL) of 95 dB. (7) Tinnitus likeness ratings. Subjects rated the pitch of each of the sounds presented in step (6) for similarity to the pitch of their tinnitus using a Borg CR100 scale (0 = not at all, 30 = not very similar, 50 = somewhat similar, 70 = very similar, 100 = identical). Each sound was rated three times in a random order. A profile of the tinnitus spectrum was thus generated. (8) Sound threshold at 1.0 kHz. Subjects increased the loudness of a 1.0 kHz tone until it was just audible; 65 dB was added to this level. Subjects then matched the loudness of each of three maskers to this stimulus. Two masking stimuli were PBN15 noise maskers with center frequencies of 0.5 and 5.0 kHz. The third masking stimulus was a custom masker generated by the computer program according to the spectrum of the tinnitus measured in step (7). (9) Brief RI test. The three masking stimuli of step 8 were tested for RI. On trials of 90 s duration subjects listened to their tinnitus for 30 s followed by a masker for 30 s and then 30 s of silence. During the silence subjects adjusted the dial to indicate whether their tinnitus had increased (+5 maximum), decreased (−5 meant tinnitus was eliminated), or had not changed (0). Ratings were given separately for each ear, if bilateral tinnitus was indicated in step 1. After their tinnitus had returned, subjects pressed the dial to initiate the next trial. Each masking stimulus was tested three times by this procedure in a mixed order. The Tinnitus Tester required about 1 h for completion.

Residual Inhibition Tester. The RI tester measured ‘RI functions’, which related the magnitude and duration of RI to a standardized set of 11 BPN15 maskers differing in CF and a 12th stimulus which was white noise (WN). The stepwise progression of the RI Tester was as follows. (1) Threshold at 1.0 kHz. Using the dial, subjects completed a staircase procedure measuring the threshold of a 1.0 kHz pure tone. (2) Loudness matching. Subjects adjusted the loudness of each of 12 masking stimuli to match the loudness of a 1 kHz tone presented at 65 dB SPL, up to a limit of 95 dB SPL. The CFs of the PBN15 maskers were 0.5, 1.0, 2.0, 3.0, 4.0, 5.0, 6.0, 7.0, 8.0, 10.0, and 12.0 kHz. Stimuli were presented once in a random order. (3) RI Function. Subjects listened to each of the 12 masking stimuli (11 PBN15 stimuli and 1 WN stimulus) 3 times on discrete trials given in a random order. On each trial subjects listened to their tinnitus for 30 s followed by a masker for 30 s; an RI rating was then given using the same procedure as step 9 in the Tinnitus Tester. After the rating was given, subjects depressed the dial to indicate when their tinnitus had returned to normal (thus giving a measure of RI duration). Following the dial press or 45 s (whichever came first), the next trial commenced. The RI test required about 1 h for completion.

Data analysis

Mean audiograms, tinnitus spectra (the likeness ratings from step 7 of the Tinnitus Tester), and RI functions (RI depth and duration, from step 3 of the RI tester) are reported for groups of subjects reporting tonal, ringing, and hissing tinnitus. RI functions reported by subjects with bilateral tinnitus were similar for the two ears and were therefore collapsed over ears. Between-subject variability was depicted by overlaying individual tinnitus spectra and RI functions within each group. These descriptive analyses were supplemented by nonparametric statistical tests (Friedman analyses of variance by ranks or sign tests) as described herein.

Results

Hearing function and properties of tinnitus

All subjects showed some degree of hearing loss (thresholds >25 dB HL) at frequencies ≤16 kHz. In 13/32 cases (40.6%) hearing thresholds were normal in both ears to 4 kHz and in 8/32 cases (25.0%) to 8 kHz. Hence 25% of our sample showed normal
hearing in both ears up to 8 kHz but varying degrees of impairment at higher frequencies.

Using sound clips in the Tinnitus Tester as examples, 43.8% (14/32) of subjects described their tinnitus as ‘tonal’, 34.4% (11/32) as ‘ringing’, and 21.9% (7/32) as ‘hissing’. Thirty subjects reported a stable tinnitus and the remaining two cases a steady pulsating tinnitus. Twenty-four subjects reported bilateral tinnitus and eight subjects unilateral tinnitus (six right ear). All forms of tinnitus (tonal, ringing, and hissing) were represented within the bilateral and unilateral groups. We present results from the 24 subjects reporting bilateral tinnitus herein, which conveys the overall picture while simplifying the graphical presentation.

Relation of tinnitus spectra and RI functions to hearing loss

The mean audiogram, tinnitus spectrum (likeness ratings), and RI functions (depth and duration) are presented for all bilateral cases in Figure 1, broken down according to whether tinnitus was described as tonal, ringing, or hissing. The edge of normal hearing (threshold >25 dB) is demarcated by a broken line in the audiograms (panel A) and projected onto the tinnitus spectra in panel B and the RI function for depth in panel C. Mean likeness ratings increased with CF in each subgroup (overall Friedman $\chi^2 = 63.0, p < 0.000$), reaching asymptote and spanning the region of hearing loss with no apparent diminution except at the highest frequency tested (12 kHz, which some subjects with tonal or ringing tinnitus could not hear). When the subgroups were considered separately, the effect of CF on likeness ratings was significant for hissing ($p < 0.0027$) and tonal ($p < 0.0001$) subjects but not within the ringing subgroup considered alone. RI functions for depth and duration (presented in panels C and D, respectively) resembled the tinnitus spectra, with RI depth and duration increasing at higher CFs within the hissing and tonal groups but showing a shallow trend in ringing tinnitus. When the tinnitus groups were considered as a whole the

Figure 1. Averaged data are presented separately for subjects reporting tonal, ringing, or hissing tinnitus. (A) Audiogram. The region of hearing loss is identified by a broken line and projected into panels B and C. (B) Tinnitus spectrum determined from likeness ratings (left ordinate) and intensity of the sound stimuli used in the likeness rating procedure (intensity adjusted by each subject to match the loudness of their tinnitus, right ordinate). The horizontal broken line at a likeness rating of 40 corresponds to the region where subjects reported that the center frequency of the sounds was beginning to resemble their tinnitus. (C) RI depth (left ordinate) and intensity of the stimuli used to measure the RI function (right ordinate). Subjects adjusted the intensity of each stimulus to equal that of a 1.0 kHz tone at 65 dB SPL. The broken horizontal line denotes no reported change in the tinnitus sensation (−5, tinnitus gone). (D) RI duration. In panels C and D, the data points to the left are for the WN stimulus.
The effect of CF was significant for RI depth ($\chi^2 = 23.3, p < 0.0096$) as well as for RI duration ($\chi^2 = 26.2, p < 0.004$). When the groups were considered separately, the effect of CF was significant only for RI depth in hissing tinnitus ($p < 0.022$). Mean RI depth reached a rating of $-2.7$ (54%) at 8 kHz within the hissing group where masker bandwidth most closely matched the subject’s tinnitus. At this frequency RI duration was approximately 20 s in these subjects. Overall, 17/24 (70.8%) of subjects reported at least some degree of RI between 8 kHz and 12 kHz. RI depth averaged $-1.46$ (29%) at 8 kHz when averaged over all subjects.

Panel B of Figure 1 also reports the sound pressure levels that subjects matched to the loudness of their tinnitus in step 6 of the Tinnitus Tester, and panel C the sound pressure levels that equalized the perceived loudness of the maskers in step 2 of the RI Tester (right ordinates in both cases). Because our subjects had high frequency hearing loss, the sound pressure levels chosen by the subjects tended to be higher for sounds of high CF. This effect was more pronounced for the tinnitus loudness matches (panel B, particularly for tonal and ringing tinnitus) than for the masker level adjustments (panel C), because the bandwidth of the sounds that subjects matched to the loudness of their tinnitus in panel B differed between groups in order to approximate the bandwidth of their tinnitus. The sounds used to measure the RI functions in panel C (and D) were BPN15 sounds in all groups, which may have permitted some off-frequency listening. SPL differed among the masking sounds used for the RI test ($\chi^2 = 84.9, p < 0.0001$), being lowest at 1.0 kHz and highest at 5.0 kHz, and relatively stable above 5.0 kHz, where some auditory recruitment may have occurred. RI duration correlated weakly with masker SPL within subjects (mean $r = 0.154, p = 0.047$) but RI depth did not (mean $r = -0.091, p = 0.323$).

Figure 2 shows tinnitus spectra (panel A) and RI functions (panels B and C) overlaid for individual subjects, separately for the tonal, ringing, and hissing groups. Although considerable individual variability was evident in the tinnitus spectra within each group (panel A), overall 21 of 24 bilateral cases showed likeness ratings reaching asymptotes for stimuli with CFs covering the region of hearing loss. These 21/24 subjects ($p < 0.002$, sign test) gave maximum likeness ratings at CFs above 4.0 kHz, followed in most cases by a decrease at 12.0 kHz (a stimulus that was not well matched for loudness to the other stimuli owing to hearing impairment). The three subjects that gave decreased likeness ratings for CFs above 4.0 kHz had hearing thresholds $\geq 60$ dB.
above 2.0 or 3.0 kHz where the perceived loudness of the stimuli may also have been a problem. RI functions for depth and duration (panels B and C, respectively) were also variable between subjects in each tinnitus group. Although most subjects reporting RI indicated modest suppression, near-elimination of tinnitus (a scale rating $\geq -4.0$) was reported by 8/24 (33%) subjects at CFs $>3.0$ kHz for up to 45 s, with no apparent relation of such cases to tinnitus type. For two of these subjects sounds with lower CF were also effective. RI depth and duration produced by the WN masker is shown to the left of RI functions for each subject in Figure 2, and also in Figure 1 for the averaged data. WN was generally as effective at inducing RI as BPN15 sounds in each group. However, for two subjects in the hissing group RI duration was markedly greater for BPN15 maskers with CFs $>4.0$ kHz than for WN. Inspection of RI functions for depth shows that BPN15 maskers with CFs below 4.0 kHz made tinnitus worse in ringing and particularly in tonal tinnitus (5/19 subjects in these groups combined), but not for hissing tinnitus. However, the depth and duration of RI induced by BPN15 sounds of the highest CF did not differ among the tinnitus types.

It will be recalled that 25% of our total sample of 32 tinnitus cases showed normal audiograms at or below 8.0 kHz but hearing loss at higher frequencies. The tinnitus spectra and RI functions for these subjects were similar to subjects with hearing loss below 4.0 kHz, with both groups showing the deepest and most persistent RI to BPN15 maskers with CFs $>4.0$ kHz. Compared with the clinically impaired hearing group, subjects with clinically ‘normal’ hearing tended to experience a worsening of tinnitus when the CF of the maskers was $<4.0$ kHz.

**Discussion**

Our findings corroborate the results of Norena et al. [14] in showing that tinnitus spectra extend well into the region of hearing loss without a preponderance of frequencies at or near the edge of the region of auditory threshold shift. The tinnitus spectra described in Figure 1 were assessed with sounds resembling the bandwidth of each subject’s tinnitus (pure tonal, ringing, or hissing tinnitus) and did not differ appreciably as a function of tinnitus type. For tonal and ringing tinnitus a roll-off occurred in the likeness matches at the highest frequency tested (12 kHz), probably because loudness matching of the sounds to tinnitus was less successful at this frequency for these subjects where pure tones or BPN5 sounds were used to assess the tinnitus spectrum. The results suggest that the sensation of tinnitus reflects changes in neural dynamics occurring throughout the region of hearing loss [7] rather than an over-representation of edge frequencies known to occur after noise-induced hearing impairment [6].

RI functions which are described here for the first time point to a similar conclusion. Based on psychoacoustic measurements of tinnitus [10] and studies of animal models of hearing loss [8,9], Eggermont and Roberts [7] suggested that tinnitus occurs when increased synchronous neural activity forms in the region of hearing impairment following a decrease in surround inhibition consequent on hearing injury. Synchronous neural activity may be the basis of the normal perception of sound, but in tinnitus such activity is unconstrained by surround inhibition and thus may spread over more frequencies and occur without acoustic input. This hypothesis implies that presentation of supra-threshold sounds in the affected frequency region should segregate synchronous neural activity by restoring intracortical inhibition, thereby dampening the tinnitus sensation. Our RI functions, which generally paralleled tinnitus spectra and the region of audiometric threshold shift, are consistent with this view. The mean duration of RI at the asymptote of RI depth was about 20 s, which is consistent with earlier reports [12] and implies a physiological time constant for a process the details of which are unknown.

Some features of the RI functions are noteworthy. Although RI depth and duration were significantly greater for BPN15 sounds of higher CF in the averaged data, considerable variability was present between subjects. At the group level RI functions for depth and duration tended to be most pronounced for subjects with hissing tinnitus where the bandwidth of the BPN15 masking sounds most closely resembled the bandwidth of their tinnitus. Nevertheless, subjects reporting RI depth approaching tinnitus elimination for up to 45 s (the maximum duration that we assessed) were seen in all tinnitus groups (8/24 subjects overall). WN maskers were generally as effective at inducing RI as BPN15 maskers, although tinnitus elimination was more commonly reported following BPN15 maskers with high CFs. The effect of high frequency BPN15 sounds on RI duration may have been greater had subjects been permitted to assess their tinnitus for longer than 45 s. BPN15 maskers and WN maskers made tinnitus worse for 5/19 tonal and ringing subjects, but this outcome was not reported by hissing cases. The presence of so much variability among our subjects leads one to ask whether we can identify variables and procedures that may optimize RI for individual cases. The present findings provide a necessary baseline for answering this question.
The sounds used to measure tinnitus spectra and RI functions in the present study were equated for sensation level for each subject by our computer-based tools. Because subjects had high frequency hearing loss, sounds of high CF were generally presented at higher sound pressure levels, particularly when tinnitus spectra were measured for tonal and ringing tinnitus where the bandwidth of the sounds was narrower (pure tones or BPN5 stimuli, respectively) than in hissing cases (BPN15 stimuli). All subjects were presented with BPN15 maskers when RI functions were measured. During RI testing within-subject correlations between SPL and RI variables were weak or non-significant, suggesting that CF influenced the shape of the RI functions. Nevertheless the bandwidth of the frequency response of the basilar membrane at high sound pressure levels is likely to be broad [16]. RI induced by maskers of high CF might profit from enhanced segregation of synchronous neural activity consequent on spectral splatter at these frequencies. Another contributing factor could be that more neurons become refractory at high sound pressure levels.

Eight of our total sample of 32 subjects (25%) would have been judged to have normal hearing by clinical audiometry to 8 kHz. However, all eight of these subjects showed high frequency hearing losses, had tinnitus, and experienced RI at high frequencies. To fully appreciate the meaning of these data, age-matched control subjects without tinnitus need to be assessed audiometrically. Were control subjects without tinnitus to show normal hearing above 12 kHz, the role of high frequency hearing loss in tinnitus would be suggested. This could have implications for the prevention of tinnitus and for the design of hearing devices aimed at reducing tinnitus sensations [7,17].

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References

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