Evaluation of tinnitus perception vs. tinnitus-evoked negative reactions in human and animal studies

Pawel J. Jastreboff

Dept. of Otolaryngology, Emory University School of Medicine, Atlanta, Georgia, USA

INTRODUCTION

Tinnitus, an auditory phantom perception, occurs in 17% of the population. It is bothersome for about 8%, and severe to debilitating in about 1% of general population. Tinnitus is an important source of disability. Notably, 49% of American soldiers involved in explosions develop tinnitus, while only 25% develop hearing loss. The Veterans Administration spent 1.1 billion dollars for compensation for tinnitus in 2009 alone, and it is expected that this amount will rise to 2.4 billion by 2014.

The fact that so far there is no objective method for detecting the presence of tinnitus in humans and moreover for detecting bothersome tinnitus in humans has significant consequences. It is difficult to verify the presence of tinnitus. Even if somebody has tinnitus, there is no possibility of objective confirmation whether tinnitus is bothersome or if the subject just perceives it without having negative reactions.

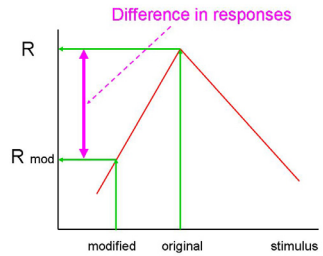
There is a large need for better understanding mechanisms of tinnitus, for development of mechanism-based treatments and for establishing objective methods of evaluation the presence of tinnitus and its severity. The work is hindered by the fact that studies performed so far had a significant limitation - they did not distinguish between the brain areas involved in the perception of tinnitus versus the areas involved in tinnitus-evoked negative reactions, which are responsible for tinnitus being a problem.

This poster proposes a method for determining physiological reactions linked to tinnitus severity in humans or animals in the objective manner. After proper validation the method could potentially be used to determine whether a person or an animal suffer because of tinnitus or just experience it. The results of fMRI study performed on tinnitus and control subjects presented below support the proposed approach and delineate the brain areas involved in tinnitus-evoked reactions, while separating them from areas involved in tinnitus perception.

METHOD

The following reasoning was used to identify physiological reactions linked to tinnitus severity. First, when a subject is exposed to a sound which is as close as possible to her/his tinnitus signal this sound should cause the activation of brain centers involved in both tinnitus perception as well as in tinnitus-evoked negative reactions. However, if the subject is exposed to a synthetic tinnitus sound with similar energy content but modified (e.g., shifted in frequency), it still should activate centers related to the perception of this sound, but it should cause a reduced activation (due to generalization principle) of the brain centers involved in negative reactions to tinnitus. By subtracting activity of the second condition from the first one it should be possible to delineate the brain centers involved in negative reactions evoked by tinnitus.

Fig 1. Dependence of the strength of reaction on the similarity to original stimulus



Unfortunately, this approach alone is not sufficient as the results may reflect just the difference in reactions to two different sound stimuli. Therefore, the second component of the method utilizes the prediction that more severe tinnitus should evoke stronger negative reaction.

While using the approach with correlating brain activation with tinnitus severity is suggestive, alone it does not prove that these areas are involved in tinnitus-evoked negative reactions because it is possible to argue that the increased importance of tinnitus may produce a stronger perceptual representation.

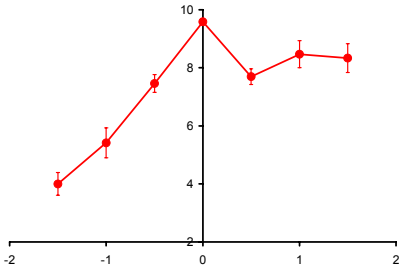
However, combining both approaches and correlating the observed differences in responses to the original and modified tinnitus sound with tinnitus severity provides a strong indication that the delineated structures are indeed related to tinnitus-evoked problems.

Third component of the method is the requirement that observed changes in activation and their correlation with tinnitus severity should neither depend on the psychoacoustical characterization of tinnitus nor on functional properties of subjects' auditory system (e.g., audiogram, sound tolerance).

fMRI RESULTS

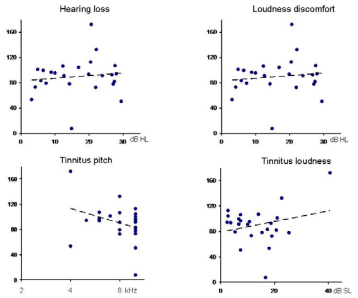
In fMRI study the imaging was performed while tinnitus subjects were exposed to the reconstructed sound of their individual tinnitus and to the same sound but with spectrum shifted by 1.5 octave. The fMRI differences were correlated with tinnitus severity and a variety of audiological and psychological measures. The details of methodology and results are presented in the oral presentation, Tue, Now 15, 2011 at 11:00. (What brain centers are linked to tinnitus-induced distress? - An f-MRI study. W. Delb(1), D. Wiebelt (1), C Lux- Wellenhof (1), PJ Jastreboff (2); (1) Department of Phoniatrics and Audiology, Medical Faculty Mannheim, Heidelberg University, Germany; (2) Department of Otolaryngology, Emory University School of Medicine, Atlanta, USA)

Fig 2. Dependence of the similarity of reconstructed tinnitus sound on the extent of spectrum shift



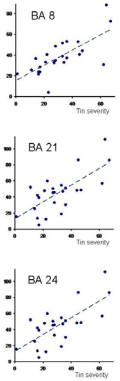
Note that the decrease of similarity follows the generalization principle and the shift of the spectrum of reconstructed tinnitus sound used in fMRI evaluation by 1.5 octave resulted in highly significant reduction of the similarity from 9.58 ± 0.102 (on zero to 10 scale) to 4.00 ± 0.390 ($p<0.00001$).

Fig 3. Lack of correlation of presented in Fig 4 differences in activations with hearing loss, loudness discomfort levels, tinnitus pitch and tinnitus loudness matches



Correlation of the difference in activation in Brodmann's area 21 with average Hearing loss ($r=0.216$, NS), Loudness discomfort ($r=0.077$, NS), Tinnitus pitch ($r=0.147$, NS) and Tinnitus loudness match ($r=0.309$, NS). Note lack of correlation of the activation with main hearing properties of subjects and psychoacoustic of tinnitus. Results for Brodmann area 8 and 24 (the anterior cingulate cortex) show lack of correlations for listed variables, with the exception of borderline significance ($p<0.05$) for loudness match for area 8.

Fig 4. Correlations of the differences in activation in Brodmann area 8, 21 and 24 by reconstructed vs. shifted tinnitus sound with tinnitus severity



Tinnitus severity was measured by Tinnitus Questionnaire (TQ). There is highly significant correlation for all areas with $r=0.720$ $p<0.0001$, $r=0.714$ $p<0.0001$ and $r=0.687$ $p<0.001$ for Brodmann's area 8, 21 and 24, respectively.

CONCLUSIONS

- Presented results support described methodology of delineating the brain areas involved in tinnitus distress using fMRI measurements.
- Importantly, this approach could be utilized for any physiological measure (e.g., electrical or magnetic brain activity or any type of imaging technique), and may yield an objective method for assessing tinnitus severity in human or animals.
- Further studies, particularly assessing potential changes observed during and after successful tinnitus therapy would be of both theoretical and clinical importance, and should help in establishing an objective method for assessing tinnitus severity.