Tinnitus-related cortical regions evaluated by fMRI

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Introduction. Chronic subjective tinnitus is defined as an individual sound sensation in the absence of a real physical sound stimulus. It is estimated that approximated every ninth person in the western hemisphere has tinnitus [1]. Approximately 1% of individuals experience their tinnitus so annoying that they search for medical attention with various treatments [2,3] which is of important socio-economical impact. Imaging studies with positron emission tomography (PET) and functional magnetic resonance (fMRI) have identified various active brain areas in patients with chronic subjective tinnitus, however it is not known which areas are relevant for generating tinnitus.

Methods. Six patients with chronic subjective tinnitus and six age-matched healthy, normal hearing volunteers were scanned with fMRI using a block design. Tones at 2940, 3000 and 3060 Hz were presented as 50 ms beeps at a rate of 5 per second over a sound proven headphone above MR noise level. These three frequencies and silence were presented blockwise pseudorandomized. Attention of the subjects was attracted to the tones by asking for button press if a change in frequency could be realized. On a Siemens Magnetom Vision MR scanner at 1.5 T we acquired 37 slices covering the whole brain using a single-shot EPI sequence with Cartesian readout at TE/TA/FA 66/4000 ms / 90° and a bandwidth of 2080 Hz/pixel.
Data preprocessing and analysis was performed with SPM 99. Contrasts of different tones minus silence were evaluated at a significance threshold level of $p < 0.05$ corrected for multiple comparisons (Fig. 1,2). Furthermore, the contrast all tones minus silence was calculated and threshold at $p < 0.001$ corrected (Fig. 3).

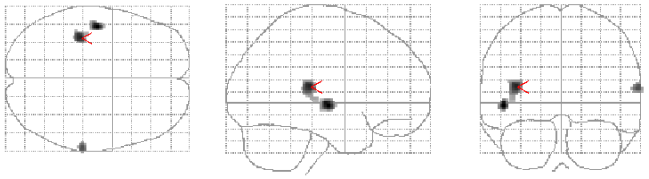

Fig. 1 34 year old normal hearing subject right handed with no tinnitus. 3000 Hz minus silence, threshold $p < 0.05$ corrected for multiple comparisons. Only primary auditory areas are visible.

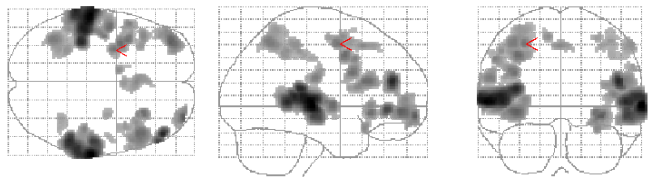

Fig. 2 53 year old female with chronic subjective unilateral tinnitus at 1.5 kHz. 3000 Hz minus silence, $p < 0.05$ corrected for multiple comparisons. Not only primary auditory areas, among others also prefrontal activation near Broca's area.

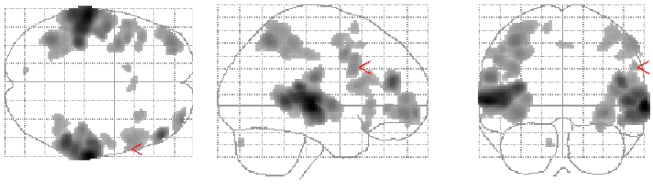

Fig. 3 Same Patient as fig. 2, all frequencies (2940, 3000 and 3060 Hz) minus silence, threshold $p < 0.001$ corrected for multiple comparisons. Activation outside primary auditory areas even at this high significane threshold level.

Results. Activation in primary auditory areas was found in all subjects. In controls, these were the only areas detected at $p < 0.05$ corrected for multipüle comparisons (Fig.1). Areas of variable locations were identified at lower significance levels. Four of the 6 patients showed active regions areas in prefrontal cortex near Broca's area at significance levels of $p < 0.05$ corrected (Fig. 2), the other two patients showed similar located areas at $p < 0.001$ uncorrected. Even at this low threshold level, similar areas were not detected in healthy controls. In the contrast all tones minus silence at $p < 0.001$ corrected, the same four patients showed activation neighbouring Broca's area (Fig. 3) while the other two failed to show activation outside primary auditory areas at this significance level.

Discussion. The administered beeps clearly induce activation of the primary auditory cortex in patients with chronic subjective tinnitus and controls. In patients additional activity was found near Broca's area which were not present in our volunteers. Because the location of activity varied between patients, a group analysis failed to depict significant activation. In 4 of 6 patients, however, contrasting all three frequencies together against silence showed highly significant activations outside primary auditory area, namely prefrontal region near broca's area. All patients were investigated also by presenting beeps at their tinnitus frequencies ± 2%. This activated only primary auditory areas. Therefore, we explain the exceptional activation at 3 kHz ± 2% in one patient as masking effect, because the administered frequencies were identical to this patient's tinnitus. Another patient who was not included in the study because of broad-band tinnitus, but was investigated with our paradigm, also failed to show significant prefrontal activation.
Summarized tonal stimulation of patients with chronic subjective tinnitus fMRI demonstrated similar active areas in the prefrontal cortex and associated auditory cortex compared to imaging studies with tinnitus patients without stimulation[4,5]. The prefrontal and limbal activation explain the annoying character of tinnitus and the success of psychotherapeutic approaches [2] which probably decrease activities in these areas.

References

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