Cortical Networks Subserving the Perception of Tinnitus—a PET Study

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INTRODUCTION

Many disorders of the auditory system are associated with tinnitus (1, 2). Several theories about the basic patho-mechanisms have been proposed, partly supported by circumstantial evidence from different experimental studies (e.g. 3, 4). Although the accurate localization of the source of the tinnitus related neuronal activity and the underlying patho-mechanisms are still controversial, most models of tinnitus generation claim that the perception and further processing of the tinnitus signal happens in the cerebral cortex (5). Recently, PET, fMRI and SPECT have been used in the attempt to identify objective correlates for this tinnitus-specific central activity (6–10). Although conflicting, these results point to involvement of particular networks subserving perception and analysis of acoustic signals, processing of emotional responses and memory.

The aim of the present study was to test the hypothesis of central involvement in tinnitus perception by means of positron-emission tomography (PET). PET-images were obtained in subjects with severe tinnitus during their habitual tinnitus experience and during suppression of this sensation by lidocaine and masking sound. It was expected that specific regional abnormalities of neuronal function would be revealed by the brainmap subtraction method.

MATERIALS AND METHODS

Subjects

Eight right-handed healthy volunteers (3 females, 5 males, aged 26–56 years, mean age 39 years) with severe monosymptomatic, chronic uni- or bilateral tinnitus were included in the study (2 left, 2 right, 4 bilateral). The range of the duration of the tinnitus was between 1 and 8 years, mean 3 years. Complete oto-neurological and audiological evaluations revealed no abnormal findings. Pitch match showed exclusively high-frequency noise and/or pure-tone type tinnitus with loudness matches between 5 and 15 dB SL.

Data acquisition and analysis

PET-imaging with $\text{H}_2\text{O}$ as tracer was performed with the ECAT Exact HR47 tomograph (Siemens/CTI) in 3D mode. Six emission scans were initiated at 60,000 true cts after bolus injection of 500 Mbq $\text{H}_2\text{O}$ in single 40 s frames. The presentation of the auditory stimuli was initiated 10 s prior to injection. PET images were reconstructed after correction for attenuation and scatter in a resolution of 18-mm FWHM (Hann-filter). MR brain images were obtained and co-registered to the PET-images and the Talairach coordinate system (11). t-statistic maps were created after a pixel-by-pixel subtraction of PET-volumes using DOT (two-tailed t-statistic, pooled SD of all intracranial voxels) (12).

Tinnitus suppression

Tinnitus was suppressed by narrow band noise of 1/3 octave corresponding to the minimum-masking-level of each subject (Scan 2, 3: $[\text{TIN(M)} - ]$), and by an i.v. bolus injection of 1.5 mg/(kg body weight) lidocaine over a period of 5 min (Scan 5, 6: $[\text{TIN(L)} - ]$). During Scan 1 and 4($=[\text{TIN} + ]$) subjects had their
habitual tinnitus sensation. Scans with tinnitus sensation \([\text{TIN}+]\) were contrasted to scans without tinnitus sensation \([\text{TIN} (\text{M}) -]\) and \([\text{TIN} (\text{L}) -]\).

RESULTS

The subtraction of conditions with suppressed tinnitus (masking or lidocaine) from conditions with habitual tinnitus revealed a number of consistent sites of activation. Several sites in prefrontal regions (superior and middle frontal gyri) and associative auditory regions (middle temporal gyrus) were activated in the right hemisphere, whereas a part of the limbic system (amygdaloid body) was activated in the left hemisphere (Table I, Fig. 1). Activations in the posterior part of the right hemisphere (superior parietal lobule), in an anterior midline structure (anterior cingulate), and in the left temporal lobe (superior temporal gyrus) were obtained only in single subtractions. Despite the use of different methods to suppress tinnitus (acoustically vs pharmacologically), we found consistent sites of activation in auditory processing areas.

Table I. Results of the subtractions of conditions with suppressed tinnitus from baseline conditions in all subjects. Talairach coordinates in mm: \(x = \) lateral to midline, right (+)/left (−); \(y = \) anterior (+)/posterior (−) of anterior commissure; \(z = \) above (+)/below (−) the intercommissure plane. \(BA:\) Brodmann area. \(R:\) right, \(L:\) left

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<th>Localization</th>
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<td>R superior frontal gyrus (GFs)</td>
<td>15 55 −6</td>
<td>10 3.4</td>
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<td>8 44 −7</td>
<td>10 4</td>
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<td>R middle frontal gyrus (GFm)</td>
<td>23 27 42</td>
<td>8 3.7</td>
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<td>30 32 22</td>
<td>9 4</td>
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<td>R middle temporal gyrus (GTm)</td>
<td>60 −19 −12</td>
<td>21 3.9</td>
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<td>59 −7 −25</td>
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<td>L superior temporal gyrus (GTS)</td>
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<td>−52 −33 6</td>
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<td>−20 −10 −15</td>
<td>22 3</td>
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<td>L amygdaloid body (NA)</td>
<td>−13 −11</td>
<td>−3.2</td>
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<td>−20 −10 −15</td>
<td>22 3</td>
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<td>R anterior cingulate gyrus (AC)</td>
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<td>32 3.5</td>
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<td>−66 42 7</td>
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<td>R superior parietal lobule (LPS)</td>
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Fig. 1. Brain maps of activation associated with the perception of tinnitus. Activated peaks marked with white arrows. Dotted lines indicate position of the intersectional plane between axial and coronal images. Co-ordinates (z [axial] and y [coronal]) according to Talairach (12). GFs: superior frontal gyrus; GFm: middle frontal gyrus; GTm: middle temporal gyrus; NA: amygdaloid body; AC: anterior cingulate; LPS: superior parietal lobule.
and in brain areas subserving higher cognitive functions.

DISCUSSION

All tinnitus, whether generated peripherally or centrally in the auditory pathways, is hypothesized to engage specific functional systems in the cerebral cortex (5). Results of consistent activation of different brain sites, as revealed in the present study, support this hypothesis and suggest that disabling tinnitus is associated with activity in different functionally linked cortical and subcortical areas. Activation of sites in the temporal lobes, the right prefrontal lobe, the anterior cingulate, the amygdaloid body, and the parietal region showed conspicuous spatial consistency with results from recent functional brain imaging studies which have uncovered some of the central mechanisms of the processing of auditory signals, emotion, memory and attention (e.g. 13–15). We therefore claim that these mental operations also subserve the perception of tinnitus.

Gathering the result from former functional brain imaging studies on tinnitus perception and our sites of activation, we find growing support for the initial hypothesis of involvement of specific systems subserving the processing of auditory signals, emotion, and attention in tinnitogenesis (6–10). Annoying tinnitus has failed to become habituated and by that causes permanent activation of brain regions normally subserving the processing of external auditory stimuli and different other cognitive functions. Alternatively, tinnitus may in some cases be generated internally without any pathology in the periphery of the auditory system.

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