# The functional neuroanatomy of tinnitus

## Evidence for limbic system links and neural plasticity

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**Article abstract**—We used PET to map brain regions responding to changes in tinnitus loudness in four patients who could alter tinnitus loudness by performing voluntary oral facial movements (OFMs). Cerebral blood flow was measured in four patients and six controls at rest, during the OFM, and during stimulation with pure tones. OFM-induced loudness changes affected the auditory cortex contralateral to the ear in which tinnitus was perceived, whereas unilateral cochlear stimulation caused bilateral effects, suggesting a retrocochlear origin for their tinnitus. Patients, compared with controls, showed evidence for more widespread activation by the tones and aberrant links between the limbic and auditory systems. These abnormal patterns provide evidence for cortical plasticity that may account for tinnitus and associated symptoms. Although audiologic symptoms and examinations of these patients were typical, the unusual ability to modulate tinnitus loudness with an OFM suggests some caution may be warranted in generalizing these findings.

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Tinnitus, the perception of sound in the absence of an external acoustical stimulus, is usually associated with sensorineural hearing loss (SNHL). Both conditions are common problems that increase significantly in prevalence with age.[1,2] By the seventh decade, more than 10% of all adults report episodes of severe tinnitus, and more than 35% have moderate to severe hearing loss. Most tinnitus patients make a successful adaptation to the presence of these phantom sounds. For those who fail to adapt, tinnitus may become a source of significant disability. Studies attempting to link the psychoacoustical characteristics of tinnitus, such as loudness and pitch, to its severity have produced inconsistent results. Meikle et al.[3] reported a poor correlation between the perceived severity of tinnitus and its emotional impact, whereas Stouffer and Tyler[4] found a significant correlation between annoyance and loudness.

Although the psychophysical characteristics of tinnitus have been described in some detail, the neural loci and mechanisms that cause tinnitus and its attendant disabilities are poorly understood because of the paucity of suitable techniques for assessing the abnormal neural activation patterns in humans.[5] However, recent advances in PET imaging techniques have made it possible to identify the brain regions responsible for the production of transient, subjective sensations, such as phantom limb pain or hallucinations[6,7] in small numbers of subjects with a low probability of producing false-positive results.[8]

In the present study, we measured cerebral blood flow (CBF) using PET in four patients with cochlear hearing loss who had severe tinnitus localized to one ear. Significantly, all four patients possessed the unusual ability to exert substantial voluntary control over the loudness of their tinnitus by performing an oral facial movement (OFM). We hypothesized that the changes in the loudness of the tinnitus in our patients would be associated with parallel changes in CBF in affected brain regions and that these changes could be mapped by measuring CBF with PET.[9] Because cochlear damage in animals causes significant functional reorganization of the auditory system, due to invasion of deafferented cortical regions by neural activity from unaffected portions of the cochlea,[10-12] we also hypothesized that externally generated sounds would produce an abnormal pattern of cerebral activation in our patients. We tested this hypothesis by mapping the neural response to unilateral stimuli of 500 Hz and 2,000 Hz. These frequencies were chosen because (1) they were in a range where the tinnitus patients would be expected to have normal hearing and (2) their cortical representation was expected to be larger than normal because of their cochlear hearing loss. Preliminary reports of these studies have appeared in abstract form.[13,14]

**Methods.** *Subjects.* Six subjects with normal hearing (one man and five women, aged 22 to 27), free of tinnitus and neurologic disease, served as controls. The four pa-

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tients were recruited by word of mouth through a local tinnitus support group. The two men and two women (aged 47 to 53) had severe tinnitus, cochlear hearing loss, and the ability to significantly alter the loudness of their tinnitus by performing an OFM. All procedures were approved by the Human Subjects Committee, and written informed consent was obtained from all subjects.

*Audiometry.* Standard audiometric measures were obtained from all subjects before PET. Subjects were tested in a double-walled audiometric sound room with a Grason-Stadler audiometer (GSI 16) and TDH-49 headphones. Air-conduction thresholds were measured at 0.25, 0.5, 1, 2, 3, 4, 6, and 8 kHz. Speech reception thresholds were assessed by live voice using the CID W-1 spondaic word list. Word recognition scores were evaluated using a phonetically balanced word list (C.I.D. Auditory Test W-22) on compact disk. Tympanograms and middle ear reflex measurements were made with a Grason-Stadler Middle Ear Analyzer (GSI 33). A Virtual Otoacoustic Emission Test Instrument (Virtual M330) and a Macintosh IIsi computer were used to test for the presence of spontaneous otoacoustic emissions.

Subjects matched the pitch and loudness of their tinnitus in the affected ear to an external tone presented to the contralateral ear. The external tone was generated by an oscillator (Hewlett-Packard 204C) connected in parallel to a frequency counter (Data Precision 5740) and the external input of the audiometer. The audiologist instructed the patient to vary the frequency of the oscillator until the pitch of the external sound matched the pitch of their tinnitus. The patient instructed the audiologist to increase or decrease the level of the tone until it matched the loudness of their tinnitus. When a subject reported a match, the audiologist recorded the frequency and level (dB HL) of the external tone. Three to four pitch and loudness matches were obtained from each patient during the same session to assure reproducibility.

*Positron emission tomography.* Subjects were positioned in an ECAT 951/31R tomograph (CTI, Knoxville, TN). A 15-second bolus of 70 mCi or less of $^{15}$O-water was given IV as a tracer of CBF. Activation procedures began at the beginning of the injection and continued throughout the scan. PET studies were performed (eyes open, insert earphones worn) using one of three scan sequences: (1) for three controls; 500-Hz tones right ear, followed by 2,000-Hz tones right ear, followed by three scans at rest alternating with three scans performed during a jaw clench, the common feature in the patients' OFMs (eight scans total); (2) four patients had the same sequence as in (1) with tone stimuli delivered to the ear in which tinnitus was reported (eight scans total); (3) three additional controls had scans at rest and during tone sequences only (three scans total).

Tone bursts (80 dB sound pressure level [SPL], 500 msec on, 500 msec off) were presented via Etymotic insert earphones (Etymotic, Elk Grove Village, IL) using a Neuroscan Stim system (Neuroscan, Hearndon, VA). These earphones attenuate environmental sound levels by 30 to 40 dB.[15] Thus, in the already low-noise PET environment, the octave band sound levels from the PET camera were estimated to be less than 10 dB in the ear canal at the stimulus frequencies used in this study.

The initial 60 seconds of emission data, timed from the arrival of the $^{15}$O-water in the brain, were used for image reconstruction (random coincidence correction, measured attenuation, Hann filter, cutoff frequency 0.4 cycles per pixel) and analysis.

*PET data analysis.* Images were converted to the Analyze format (Biodynamics Research Unit, Rochester, MN) thresholded and edited on a slice-by-slice basis, using visual inspection, to remove extracerebral activity (such as scalp, great vessels, muscles, and sinuses) and analyzed by statistical parametric mapping (SPM) using SPM 1995.[16,17] This eliminates between-scan movement, realigns images into the Talairach stereotaxic framework,[18] smooths data with a 15-mm gaussian kernel, and eliminates between-subject global variations in activity by an analysis of covariance. The final products, SPM {Z} images, are the result of the conversion of pixel-specific *t* values to Z scores and show significant between-state changes, specified by SPM contrasts. The SPM {Z} images are the result of "stacking" the individual planes of data generated by the program and projecting the most significant pixel in the three-dimensional set onto sagittal, coronal, and transaxial planes according to the Talairach system. The anterior-posteriore commissural plane and coronal planes through the anterior (AC) and posterior commissures (PC) are shown as heavy solid lines, with smaller divisions in the Talairach system shown as broken lines. Threshold Z scores ($Z = 2.33$, omnibus $p = 0.01$) are shown in red with progressively higher Z scores shown by color changes from red through yellow to white.

The analytical threshold for the SPM analysis was set at $Z = 2.33$, which corresponds to an omnibus $p \leq 0.01$. All Z maxima selected for tabulation or discussion, or both, met that criterion and, in addition, were located in brain regions associated with sensory-motor control systems, the auditory system, or the limbic system. Although not all Z maxima meeting the criterion are tabulated or discussed, the figures depict all sites where $Z \geq 2.33$, even if the spatial extent is as small as a single voxel. Larger contiguous areas may contain multiple Z maxima; only some of these are included in the tabulations and discussions.

**Results.** *Subjects.* Tinnitus patients had mild to severe, high-frequency (greater than 2,000-Hz) cochlear hearing loss ranging from 30 to 70 dB, normal middle ear function, no evidence of central auditory abnormalities, and no spontaneous otoacoustic emissions. The patients reported continuous high-pitched ringing in one ear (one in the left, three in the right). Tinnitus pitch matches occurred at frequencies near the peak of the hearing loss and at sound levels 5 to 10 dB above the threshold of hearing. OFM produced a significant increase in tinnitus loudness in two patients (one right and one left ear localization) and a decrease in loudness in the other two (both right ear localization). Normal controls all had hearing levels of 25 dB or better from 250 through 8,000 Hz and normal tympanograms, middle ear reflexes, speech reception thresholds, and speech discrimination scores.

*Response to OFM.* Normal controls. CBF measurements from normal controls were used to define the cortical regions normally activated by the OFM. Analysis of the CBF data using the SPM contrast, normal (OFM − rest), yielded an SPM {Z} image with the expected, strong foci of increased CBF in bilateral sensory-motor cortex and the supplementary motor area. Talairach x, y, and z coordinates (mm) and Z scores corresponding to the left and right

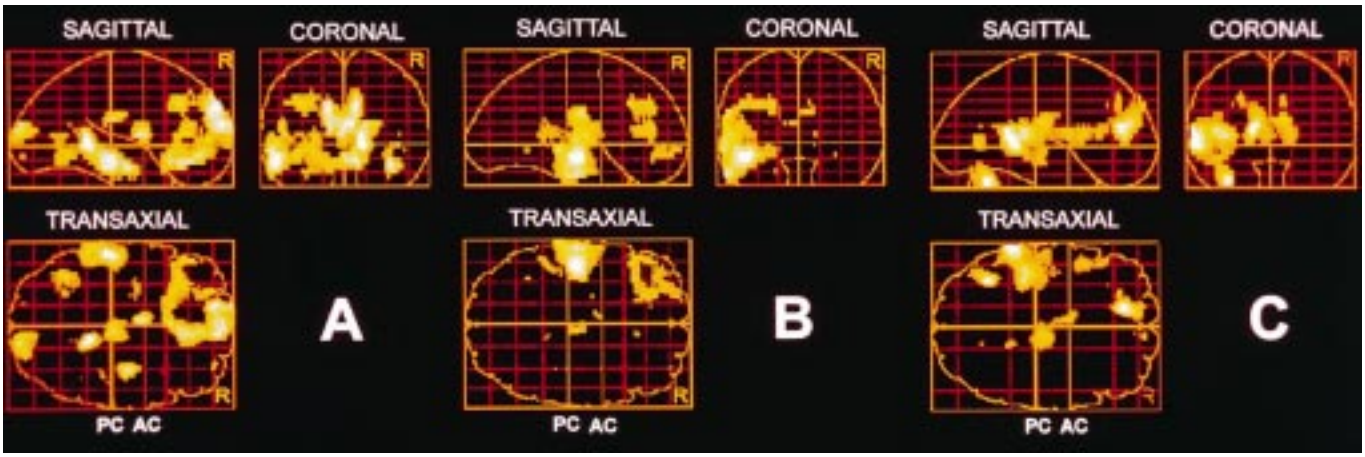


*Figure 1. Cerebral activation sites in tinnitus patients. Anatomic data and Talairach coordinates of maximal Z scores are presented in table 1. Part A shows loci in the temporal lobe and other sites where CBF fell significantly, relative to the resting state, in two patients (both localized sound to R ear) whose tinnitus loudness decreased during an OFM: SPM contrast = patient (OFM − rest), Z range 2.33 to 3.84. Part B subtracts the expected effects of the OFM in controls from the effects in the patients with the SPM contrast = [patient (rest − OFM) − control (rest − OFM)]. A focus that is predominately in the left temporal lobe remains: Z range 2.33 to 3.90. Part C shows brain regions where CBF changed significantly in the three patients with right ear tinnitus during the OFM: SPM contrast = OFM loudness decrease (rest − OFM) + OFM loudness increase (OFM − rest), Z range 2.33 to 4.14. Note increase in Z-score maximum in the superior temporal gyrus relative to part B (at −58, −44, 8, Z = 4.14) with extension medially and inferiorly to the hippocampus.*

sensory-motor cortex and supplementary motor area were, respectively, −52, 0, and 8 where Z = 6.17; 58, 0, and 24 where Z = 5.29; and 0, −6, and 44 where Z = 4.84.

Patients with OFM-induced increases in tinnitus loudness. In the two patients who reported an increase in the loudness of their tinnitus (one right ear, one left ear) during the OFM, the expected increases in CBF in sensory-motor cortical regions were found, as in the controls. In addition, there were also CBF increases that exceeded the omnibus $p = 0.01$ threshold in the primary auditory cortex (left superior temporal gyrus, Brodmann's area 41) and a region between the medial geniculate nuclei: SPM contrast = patient (OFM − rest) (table 1).

To separate the changes in CBF that were due to the increase in tinnitus loudness from those due exclusively to the OFM, we subtracted the OFM-induced increases in CBF measured in normal control subjects (see table 1) from those found in patients: SPM contrast = [patients (OFM − rest) − control (OFM − rest)] (see table 1). A posterior thalamic region, containing the left medial geniculate nucleus, remained activated in this analysis that shows the brain regions where there is an increase in neural activity that is due exclusively to the increases in tinnitus loudness.

Patients with OFM-induced decreases in tinnitus loudness. Two patients reported a significant decrease in the loudness of their tinnitus during the OFM. Both localized their tinnitus to the right ear. In these two patients, the OFM caused a significant reduction in CBF in the posterior and mid-portion of the left middle temporal gyrus relative to their own resting state: SPM contrast = (rest − OFM) (figure 1A and table 1). To further distinguish the changes in CBF due to the decrease in tinnitus loudness from changes in CBF due to the OFM itself, we performed an additional analysis: SPM contrast = [patients (rest − OFM) − control (rest − OFM)](see figure 1B and table 1). This analysis revealed a prominent region of reduced CBF in the left temporal lobe (Brodmann's areas 21 and 41) and the left hippocampus. Thus, the reduction in the loudness of tinnitus in the right ear was associated with a unilateral reduction of CBF in contralateral (left) temporal lobe.

Patients with OFM-induced changes in right ear tinnitus. Three patients localized their tinnitus to the right ear. One reported a loudness increase, whereas the other two reported a loudness decrease during the OFM. To take advantage of these opposing perceptual effects and to maximize the statistical power of our study, we performed an analysis of the data from all three patients with right ear tinnitus to identify the common regions of the brain affected by a change in tinnitus loudness during the OFM: SPM contrast = [loudness decrease (rest − OFM) + loudness increase (OFM − rest)] (see figure 1C and table 1). This analysis revealed a prominent *unilateral* site of activation in the temporal lobe contralateral to the ear in which they reported their tinnitus (Brodmann's areas 21 and 41). This region contains 813 pixels with 10 local maxima and extends medially and inferiorly to the hippocampus. Additional activation was observed in the right thalamus, including the medial geniculate as well as other neural sites shown in the figure.

*Stimulation of right ear with 500-Hz and 2,000-Hz tones.* Although the analysis of the patients with right ear tinnitus showed an effect confined to the left temporal lobe, pure tone stimuli delivered to the right ear of the patients and controls produced *bilateral* activation of the transverse temporal gyri and adjacent portions of the superior temporal gyri: SPM contrast = (2,000 Hz − rest). The results of unilateral stimulation of the controls are presented in figure 2A and table 2. The results of unilateral stimulation of the patients are presented in figure 2B and table 2. In the patients, but not in the controls, activation was seen unexpectedly in the left hippocampus: SPM contrast = patient (2,000 Hz − rest) (see figure 2B and table 2). To compare activation sites in patients and con-

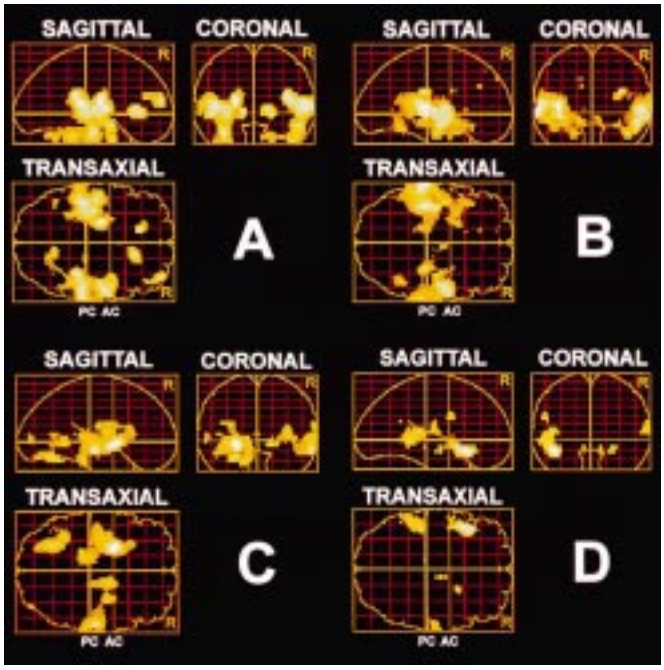


*Figure 2. Cerebral activation by 2,000-Hz tones. Anatomic loci and Z scores at sites of maximal effects are presented in table 2. Part A shows loci where 2,000-Hz tones activated the brains of six normal subjects: SPM contrast = control (2,000 Hz − rest), Z range 2.33 to 3.88. Part B shows the results of the same analysis conducted in the three patients with right ear tinnitus: SPM contrast = patient (2,000 Hz − rest), Z range 2.33 to 4.33. Note increase in Z-score maximum compared with normal subjects (A) and activation of limbic areas (hippocampus). Part C shows the effect of 2,000-Hz tones in patients relative to control: SPM contrast = 2,000 Hz (patient − control), Z range 2.33 to 3.91. Patients have extensive activation of left hippocampal and lenticular nuclear sites compared with that of controls. Part D shows sites of 2,000-Hz tone activation in patients relative to control subjects with removal of effects of resting state: SPM contrast = [patient (2,000 Hz − rest) – control (2,000 Hz − rest)], Z range 2.33 to 3.79. Cortical areas where 2,000-Hz stimuli produced excess activation in patients, relative to control subjects, are shown. Absent hippocampal activation implies limbic activation in tinnitus patients is present in the resting state.*

trols more directly, we subtracted the activation sites in normal subjects from those in patients during 2,000-Hz stimulation: SPM contrast = 2,000 Hz (patient − control) (see figure 2C and table 2). This image shows excessive activity in the left hippocampal area and the lenticular nuclei in the patients. To determine whether this excess activity was attributable to external auditory stimuli or, alternatively, the result of intrinsic neural activity present at rest, we removed the effects of the subject-specific resting state activity: SPM contrast = [patient (2,000 Hz − rest) − control (2,000 Hz − rest)](see figure 2D and table 2). Evidence for excess activation in the brains of the patients remained in primary auditory cortex and anterior portions of the left temporal lobe and insula, but not in the hippocampal and lenticular nuclei.

Although our control subjects were younger than our tinnitus patients, it is highly unlikely that this age difference is a confounding factor. First, the data from all but one of our SPM contrast controls for potential CBF differences in the resting state by virtue of the fact that they are either within-group comparisons or they account explicitly for potential differences in the resting-state CBF (see contrast specifications in tables and figure legends). Second, the only between-group contrast that did not control for differences in the resting state (see figure 2C and table 2, 2,000 Hz [patient − control]) shows an increase in the older tinnitus patients compared with the controls. Because previous studies show that aging causes a decrease in CBF, not an increase, as observed in our study,[19] it is unlikely that our results are due to the effect of aging.

**Discussion.** The neural origins and mechanisms underlying tinnitus are largely unknown. The strong association between SNHL, cochlear injury, and tinnitus led to early speculations that tinnitus was due to abnormal discharges by the cochlea.[20] A more recent review refines this hypothesis and suggests three possible cochlear mechanisms for the production of tinnitus.[21] Other data, based on auditory event-related potential measurements,[22] clinical data noting the development of tinnitus after surgical transection of the auditory nerve, persistence of tinnitus after transection of the auditory nerve, or ablation of the cochlea, imply that tinnitus has a central origin.[23-26] Our data suggest that the tinnitus experienced by our patients arises in the central auditory system and not the cochlea. The data that support this contention are as follows. External tone bursts presented to just *one cochlea* produced *bilateral* activation of auditory cortical regions in controls and patients with tinnitus (see figure 2, A and B). This finding is consistent with the rich network of decussating pathways that occur proximal to the cochlea and cochlear nuclei.[27] However, when our patients altered the loudness of their tinnitus with an OFM, we observed *unilateral* and *not bilateral* changes in CBF (see table 1 and figure 1). This suggests that a more central part of the auditory pathway, and not the cochlea, is the site of the spontaneous neural activity responsible for this symptom.

It is of interest to note that the activation sites in our patients with right ear tinnitus were confined to the hemisphere opposite to the ear in which our patients reported their sounds (Note: only one patient reported left ear tinnitus, a sample too small for independent analysis). Thus, the perceptual localization of tinnitus to one ear appears to be linked to activity in the opposite cerebral hemisphere.

As in any initial study of a newly described and apparently unusual phenomenon (among 1,000 respondents to the most recent American Tinnitus Association survey, only 0.2% appear to exhibit the phenomenon [G. Reich, personal communication]), some cautionary statements are appropriate. Because our subjects were chosen because of their ability to alter tinnitus loudness by performing an OFM, there may be some unique pathophysiologic aspect of

***Table 1*** *Talairach coordinates of regional maxima after OFMs*

| Subject type, SPM contrast, anatomic site (Brodmann's area) | x | y | z | Z score |
|---|---|---|---|---|
| Loudness increased, patients (OFM − rest) | | | | |
| L transverse temporal gyrus (BA 41) | −22 | −36 | 12 | 3.05 |
| Loudness increased, patient (OFM − rest) − control (OFM − rest) | | | | |
| Posterior thalamus, between medial geniculates | −12 | −36 | 8 | 3.45 |
| Loudness decreased, patient (rest − OFM) | | | | |
| L middle temporal gyrus, midportion (BA 21) | −52 | −30 | −12 | 3.70 |
| L middle temporal gyrus, posterior (BA 21) | −54 | −44 | 0 | 3.17 |
| Loudness decreased, patient (rest − OFM) − control (rest − OFM) | | | | |
| L middle temporal gyrus (BA 21) | −42 | −18 | −8 | 3.90 |
| Mesial portion, L transverse temporal gyrus (BA 41) | −54 | −12 | 8 | 3.19 |
| L hippocampus | −20 | −8 | −20 | 2.49 |
| Right ear tinnitus, loudness decrease (rest − OFM) + loudness increase (OFM − rest) | | | | |
| L middle temporal gyrus (BA 21) | −58 | −44 | 8 | 4.14 |
| L transverse temporal gyrus (BA 41) | −42 | −34 | 12 | 3.64 |
| L hippocampus | −40 | −22 | −8 | 2.87 |
| R posterior thalamus (includes medial geniculate) | 12 | −24 | 8 | 2.89 |

OFM = oral facial movement; SPM = statistical parametric mapping.

their problem, in addition to having the OFM-loudness control phenomenon, that separates them from other patients with tinnitus. However, all the other clinical manifestations of tinnitus in our patients, such as character (i.e., continuous ringing), loudness, localization to one ear, variation of loudness over time, and a pitch that corresponds to the frequencies affected by SNHL, are characteristic of the majority of patients with tinnitus.[4,28,29] This suggests that these patients have typical tinnitus plus the OFM-control phenomenon and that generalization of our results to a larger population may be appropriate. Further studies should help resolve this issue. We are also aware of constraints on statistical methods that are inherent in small samples. This issue has been addressed by Andreasen et al.[8] in a study of the effect of sample size in PET. They state that "as sample size decreases, false negatives begin to appear, with some loss of pattern and peak detection; there is no corresponding increase in false positives." Their study included samples with as few as six sets of data. Our smallest groupings were two to three subjects, with three repetitions of the condition yielding six to nine sets of data. Thus, we believe that the risk is low that our small sample size has lead to a rejection of the null hypothesis when it is true, i.e., we are unlikely to have made an incorrect identification of a site of neural activation. SPM methodology has been used in single-subject studies by Silbersweig et al.,[7] providing additional support for the validity of the methods we used. Finally, we have no direct, independent method to verify the contention made by our patients that they have changed the loudness of their tinnitus. However, our experimental results showing OFM-induced CBF changes in auditory centers in patients but not controls are consistent with the loudness changes reported by the patients. This same general strategy has been used to study hallucinations, another phantom sensation for which there are no valid external measures.[7] We have relied on the patient's own descriptions of the effects of the OFM in designing our study and performing the data analyses.

The brain regions activated by external sounds were more extensive in our tinnitus patients with cochlear hearing loss than those in normal subjects. This is shown most clearly by the data in figure 2D, which show the additional sites activated by 2,000-Hz stimuli in the patients that were not activated in normal controls. This expanded area of activation in patients with cochlear hearing loss and tinnitus is consistent with observations in animals that demonstrate dramatic reorganization of the auditory cortex after damage to high-frequency portions of the cochlea.[30] Immediately after the production of the cochlear lesion, neural activity in the deafferented high-frequency portion of the cortex is reduced. After several months of recovery, this region becomes responsive to lower frequencies that lie along the border of the high-frequency hearing loss. As a result, frequencies associated with normal hearing, adjacent to the region of loss, cause more widespread cortical activation than normal. Our results (see figure 2D) show that a similar phenomenon occurs in humans. We are unable to determine whether these plastic changes are the result of cochlear hearing loss, tinnitus, or a combination of these factors. Future studies of patients with high-frequency hearing loss, without tinnitus, are required to make this determination.

***Table 2*** *Talairach coordinates of regional maxima for activation sites in response to 2,000-Hz tones, right ear*

| Analysis, SPM contrast, subject number, anatomic site (Brodmann's area) | x | y | z | Z score |
|---|---|---|---|---|
| Normal subjects, control (2,000 Hz − rest) (n = 6) | | | | |
| L thalamus | −22 | −12 | 12 | 3.88 |
| L transverse temporal gyrus (BA 41) | −40 | −28 | 8 | 3.68 |
| L hippocampus | −30 | −32 | 0 | 3.35 |
| R superior temporal gyrus (BA 22) | 32 | −40 | 20 | 3.70 |
| R transverse temporal gyrus (BA 41) | 50 | −30 | 12 | 3.63 |
| Patients with right ear tinnitus, patients (2,000 Hz − rest) (n = 3) | | | | |
| L superior temporal gyrus (BA 22) | −58 | −32 | 8 | 4.33 |
| L transverse temporal gyrus (BA 41) | −38 | −26 | 8 | 4.31 |
| L hippocampus | −34 | −18 | −4 | 4.01 |
| R superior temporal gyrus (BA 22) | 62 | −34 | 8 | 3.66 |
| R transverse temporal gyrus (BA 41) | 52 | −4 | 8 | 3.97 |
| Patients versus controls, 2,000 Hz (patient − control) | | | | |
| L lenticular nucleus | −22 | −2 | −4 | 3.91 |
| L hippocampus | −14 | −34 | −20 | 3.14 |
| | −44 | −20 | −12 | 2.69 |
| R middle temporal gyrus (BA 21) | 56 | −20 | −8 | 3.52 |
| R superior temporal gyrus (BA 22) | 58 | −28 | 0 | 2.92 |
| Patients versus controls, patient (2,000 Hz − rest) − control (2,000 Hz − rest) | | | | |
| L anterior superior temporal gyrus (BA 38) | −40 | 18 | −12 | 3.79 |
| Mesial portion, L transverse temporal gyrus (BA 41) | −44 | −34 | 8 | 3.12 |

SPM = statistical parametric mapping.

The ability of our patients to voluntarily and substantially modulate the loudness of their tinnitus by performing an OFM provides compelling evidence for the development of new neural links between auditory centers and other sensory-motor areas in the CNS. One of our patients reported that she could control her tinnitus loudness by a variety of maneuvers, some of which were purely sensory (e.g., pressure applied to scalp by a second person). A small number of patients who develop tinnitus after the surgical treatment of acoustic neuromas and damage to the auditory nerve are able to modulate the loudness or pitch, or both, of their tinnitus by making voluntary eye movements (gaze-evoked tinnitus).[31-35] This eye-control phenomenon is thought to be the result of anomalous connections between neural systems in the brainstem controlling eye movements and those subserving audition. Because gaze-evoked tinnitus appears a month or more after surgical treatment, it is conceivable that the phenomenon is the result of the formation of aberrant neural connections with auditory portions of the brain. We suspect that analogous changes have occurred in the brains of our patients who can modulate their tinnitus with an OFM.

Although most patients are able to adapt to the presence of their phantom auditory sensations, all four of our patients stated that tinnitus caused severe disruptions in their lives. Because tinnitus loudness and other psychoacoustical characteristics of tinnitus do not always correlate with measures of severity,[3,4] other factors must determine the emotional impact of tinnitus. Hallam et al.[36] have hypothesized that persistent or repeated high levels of arousal, or the attachment of affective significance to the sensation, impedes the development of tolerance to these phantom sounds. Our data suggest that the neural systems mediating tinnitus may be linked to systems controlling emotions *via* the hippocampus, a portion of the limbic system, that is the gateway to centers mediating emotional control and an important component of memory systems.[25,37,38]

We believe that our success in identifying specific neural sites where CBF changes as tinnitus loudness changes may lead to the use of PET to assess the efficacy of new treatments for this disorder. Pre- and post-treatment functional imaging studies may provide the highly desirable, objective, and independent measures of tinnitus. Tinnitus caused by cochlear lesions may be the auditory analog of the phantom limb pain experienced by some amputees. Like the severity of phantom limb pain,[6] the severity and the psychological impact of tinnitus may depend on the nature and extent of plastic transformations within the central auditory system.

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