Ultrasound activates the auditory cortex of profoundly deaf subjects

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Using three-dimensional PET, the cortical areas activated by bone-conducted ultrasound were measured from five profoundly deaf subjects and compared with the cortical areas of normal-hearing subjects activated by stimuli through bone-conducted ultrasonic, air-conducted, bone-conducted, and vibro-tactile hearing aids. All of the hearing aids, including the ultrasonic hearing aid, consistently activated the medial portion of the primary auditory cortex of the normal volunteers. The same cortical area was also significantly activated in the profoundly deaf subjects although the percentage increase in regional cerebral blood flow (rCBF) was smaller than in normal subjects. These results suggest that extra-cochlear routes convey information to the primary auditory cortex and can therefore produce detectable sound sensation even in the profoundly deaf subjects, who reported a sensation themselves. NeuroReport 12:583-586 © 2001 Lippincott Williams & Wilkins.

Key words: Auditory cortex; PET; Profoundly deaf; Ultrasound hearing

INTRODUCTION

Recent studies [1,2] have suggested the use of ultrasonic hearing aids to help the profoundly deaf detect environmental sounds or even spoken words. However, since Gavreau reported that bone-conducted ultrasound is audible [3] there has been controversy over the mechanisms responsible for ultrasound hearing. Amongst several hypotheses proposed to account for ultrasonic hearing, one predicts that certain bio-mechanical demodulations transform ultrasound into low frequency audible sounds [4], and others hypothesize a contribution by cochlear hair cells [5-7] or vestibular hair cells [1,8].

It is important, therefore, to elucidate the ultrasonic hearing mechanism not only to provide conclusive evidence relevant to the above-mentioned debate, but also to determine the possible usefulness of ultrasonic hearing aids. We therefore measured the cortical areas activated by ultrasound stimulation using three-dimensional PET to investigate this phenomenon further.

MATERIALS AND METHODS

Subjects: We studied nine normal volunteers, all men, aged 22-49 years (mean 30.6 years), who were all right-handed according to the Edinburgh inventory [9]. They had no history of hearing deficits. The protocol was approved by the Institutional Review Board, and all subjects gave their written informed consent for the study.

A small plastic catheter was placed in the cubital vein of each subject's left arm for injection of the radioisotope. The subjects lay in a supine position with their eyes closed and patched and their heads immobilized with an elastic band and sponge cushions. Each subject had 10 consecutive PET scans with a 10 min interval between scans. A complete session consisted of two rest scans and eight scans with hearing conditions through four different types of hearing aid: bone-conducted ultrasonic (U), vibro-tactile (V), air-conducted sonic (A), and bone-conducted sonic (B) hearing aids.

To determine the cortical representation of the ultrasonic effect in the deaf subjects, five profoundly deaf subjects, two men and three women aged 52-66 years (mean 57.8 years), were included in the PET study. Patient information is summarized in Table 1. Since no age-related difference in ultrasonic hearing was found in our previous study [2], age matching was not considered. They underwent 10 consecutive PET scans; five under hearing conditions with an ultrasound hearing device and five rest scans. Other settings were identical to the normal control group.

Stimulus presentation: Tone bursts of 1 kHz with a length of 100 ms, including linear 10 ms rising and falling ramps, were presented through the hearing aids. The inter-burst interval was set at 600 ms. For the ultrasonic hearing aid a 40 kHz sinusoid, amplitude-modulated by the 1 kHz tone
bursts, was presented on the right sternocladial mastoid muscle using a ultrasound vibrator (MA40E75, Murata Co., Kanazawa, Ishikawa, Japan). For the vibro-tactile hearing aid the tone bursts were presented as the most clearly perceiving tactile sensation level using a tactile hearing aid (TACTAID 7, Audiological Engineering Corp. Somerville, MA, USA). Among the seven vibrators of TACTAID 7, only one vibrator giving the highest sensitivity for the tone bursts was attached 2 cm below the ultrasound vibrator. For the air-conducted sonic hearing aid the tone bursts were presented through ear-insertion type stereo headphones (EarTone, EARCabet Safy Corp., Indianapolis, USA) at the most clearly perceiving (MCP) level determined for each subject, which was a sensation level of 60 dB on average. For the bone-conducted sonic hearing aid a bone conduction stimulator (Audiometer AA67, Rion Co., Kokubunji, Tokyo, Japan) was attached at the forehead and the bursts were presented at the MCP level.

The subjects’ task was to detect the stimuli presented via the above-mentioned four hearing aids (U, V, A, B). The background noise level was 58 dB (A).

**PET scans:** The PET scans were performed using a General Electric Advance tomograph (GE, Milwaukee, WI, USA) with the interslice septa retracted. The physical characteristics of this scanner have been described in detail elsewhere [10,11]. This scanner acquires 35 slices with an interslice spacing of 4.25 mm. In the 3D mode, the scanner acquires oblique slices with a maximum cross-coincidence of +11 rings. A 10 min transmission scan using two rotating Ge-68/Ga-68 sources was performed for attenuation correction. CBF images were obtained by summing the activity during the 60 s following the first detection of an increase in cerebral radioactivity after the i.v. bolus injection of 10 mCi $^{15}$O-labeled water [12]. The images were reconstructed with the Kinahan–Rogers reconstruction algorithm [13]. Hanning filters were used, giving transaxial and axial resolutions of 6 and 10 mm (full-width at half-maximum; FWHM), respectively. The field of view and pixel size of the reconstructed images were 256 mm and 2 mm, respectively. No arterial blood sampling was performed, and thus the images collected were those of tissue activity. Tissue activity recorded by this method is nearly linearly related to rCBF [14,15].

**Anatomical MRI:** For anatomical reference, a high-resolution, whole-brain MRI for each subject, except for one deaf subject who had a cochlear implant, was obtained separately, using a standard 1.5 T MRI system (Horizon; GE, Milwaukee, WI, USA). A regular head coil and a conventional T1-weighted, spoiled-Grass volume sequence with a flip angle of 30°, echo time 5 ms, repetition time 33 ms, and field of view 24 cm, were used. A total of 124 transaxial images were obtained. Matrix size was $256 \times 256$, slice thickness was 1.5 mm, and pixel size was $0.937 \times 0.937$ mm.

**Data analysis:** The data were analyzed with statistical parametric mapping (SPM96: from the Wellcome Department of Cognitive Neurology, London, UK) implemented in Matlab (Mathworks Inc., Sherborn MA, USA) [16–18]. The scans from each subject were realigned using the first image as a reference. Following realignment, all images were transformed into a standard stereotaxic space [19] and filtered with a Gaussian kernel of 20 mm FWHM along the x, y, and z axes. After the appropriate design matrix was specified, the condition, subject, and co-variate effects were estimated according to a general linear model at each and every voxel. The design matrix included global activity as a confounding covariate, and this analysis can therefore be regarded as an ANCOVA [16]. To test hypotheses about regionally specific condition effects, these estimates were compared using linear contrasts. The resulting set of voxel values for each contrast constituted a statistical parametric map of the statistic SPM(t). The SPM(t) were transformed to the unit normal distribution (SPM(z)). A significance of $p < 0.05$, with correction for multiple comparisons at voxel level, was used as the statistical threshold [17,18].

To identify the cortical areas commonly activated by ultrasound, vibration, airway sound and bone sound in the normal control group, a conjunction analysis was performed [20]. With this approach, several hypotheses were tested, and it was asked whether all the activations in a series of task pairs were jointly significant. We compared four different task pairs of hearing-aid condition/rest to identify the areas activated by hearing irrespective of type of device.

To identify the cortical areas related to the detection of ultrasound in the deaf group, the results from the normal control group was utilized as a priori hypotheses as to which regions in the deaf subjects would show an increase in the rCBF during the hearing condition with the ultrasonic device compared to the rest condition. As voxel-level significance has a strong influence on the regional specificity of the activation, the foci activated irrespective of hearing aids with voxel-level significance ($p < 0.05$, with correction for multiple comparisons over the entire brain) in the conjunction analysis were used as an anatomically constraining hypothesis for the deaf group. As the basis of the statistical inference from any activations that were at the full width at the half-maximum (FWHM) of the pre-specified location in SPM(z), we used the $p$ value of the voxel-level with a Bonferroni correction for the number of prespecified locations. The FWHM of SPM(z), which indicates the extent of the autocorrelation in the data, or the dependency of one voxel’s $Z$ value on its neighbors, was estimated in the variance of the first derivatives of SPM(z) over three directions.

**RESULTS**

Four different types of stimuli (U,V,A and B) activated the medial area of the left transverse temporal convolutions (Brodman’s area 41) of the normal controls (Fig. 1). An area which was consistently activated irrespective of hear-
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Fig. 1. The activated cortical areas by bone-conducted ultrasonic (upper left), vibro-tactile (upper right), air-conducted sonic (lower left), and bone-conducted sonic stimuli (lower right).

Fig. 2. The cortical area consistently activated by four types of stimuli for the normal controls. This area was also significantly activated by the ultrasound for the profoundly deaf.

Fig. 3. rCBF at the commonly activated area whose Talairach's coordinates were −32, −32, 22. R: rest condition; U: bone-conducted ultrasonic stimuli; V: vibro-tactile stimuli; A: air-conducted sonic stimuli; B: bone-conducted sonic stimuli. Z = 4.29, p = 0.000 (0.022 corrected).

ing aid was found in the medial portion of the left transverse temporal convolutions (Fig. 2, Fig. 3), whose Talairach's coordinates were x = −32, y = −32, z = 22. For the profoundly deaf, this area was also significantly activated by the ultrasonic stimulation, although the mean increase in rCBF was significantly less than those of normal controls as shown in Fig. 3.

DISCUSSION
The four different types of stimuli activated a small common area whose Talairach's coordinates were −32, −32, 22. This suggests that there are routes transmitting four different stimuli into a small common region in the auditory cortex, where is also activated in the profoundly deaf by ultrasonic stimuli. This region is responsible for the sound sensation induced by the ultrasonic stimuli for both subject groups, suggesting that ultrasound may be useful for transmitting sound information to the auditory cortex.

Since the profoundly deaf subjects who participated in the study had no sound sensitivity below 20kHz, the contribution of the cochlear hair cells was not possible and the detection of audible low frequency sounds generated by bio-mechanical demodulation was also impossible for the profoundly deaf. These possibilities, however, can not be ruled out for normal-hearing subjects.

Interestingly, vestibular stimulation has been reported to contralaterally activate a wide area, including the temporoparietal junction [21,22] and the posterior insula [22]. Furthermore, several previous studies have suggested that the vestibular bundle on the eighth nerve, particularly that from the saccular nerve, responds to acoustic stimuli [23–25]. Even after complete destruction of cochlear hair cells, but with preservation of vestibular hair cells in the guinea pig, acoustically evoked responses could be recorded from the round window up to the auditory cortex [23]. Our subjects perceived the bone-conducted ultrasound but not the air-conducted ultrasound. It is therefore possible to speculate that some of the vestibular hair cells detected the bone-conducted ultrasound and transmitted this information to the auditory cortex to generate a sound representation.

CONCLUSION
Bone-conducted ultrasound consistently activated the medial portion of the primary auditory cortex of the profoundly deaf subjects. This result suggests that extracochlear routes contribute to convey ultrasonic information to the primary auditory cortex.

REFERENCES

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