PET Evidence of Neuroplasticity in Adult Auditory Cortex of Postlingual Deafness

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Controversy regarding functional reorganization in the adult brain remains. To investigate whether neuroplasticity is present in adults with postlingual deafness, we examined the pattern of cerebral glucose metabolism on ^{18}F-FDG brain PET images of postlingually deaf patients by comparing the auditory cortical activation pattern with those of age- and sex-matched healthy control subjects. We also correlated the cerebral glucose metabolism in deaf patients with the duration of deafness using statistical parametric mapping. **Methods:** In the resting state (eye closed, ears unoccluded in a dark and quiet environment), ^{18}F-FDG brain PET scans were performed on 9 postlingually deaf patients and 9 age- and sex-matched healthy volunteers. Significant increases and decreases of regional cerebral metabolism in the patient group were estimated by comparing their PET images with those of the healthy volunteers using *t* statistics at every voxel. To reveal regions in which metabolism was significantly correlated with the duration of deafness, the general linear model with the duration of deafness as a covariate was tested at each voxel. **Results:** When we compared ^{18}F-FDG brain PET images of postlingually deaf patients with those of age- and sex-matched healthy control subjects by performing a *t* test at every voxel, the glucose metabolism of deaf patients was significantly ($P < 0.001$) lower than that of the control subjects in both anterior cingulate gyri (Brodmann area 24 [BA24]) and superior temporal cortices (BA41, BA42) and in the right parahippocampal gyrus. No area showed a significant increase of metabolism in deaf patients with the same threshold. When we correlated glucose metabolism of deaf patients with the duration of deafness after total deprivation of hearing capability using a general linear model with the duration of deafness as a covariate at every voxel, metabolism in both anterior cingulate gyri (BA24) and superior temporal cortices (BA41, BA42) showed a significant ($P < 0.005$) positive correlation with the duration of deafness. **Conclusion:** This study suggests that plasticity is present in adult brains of postlingually deaf patients. In the mature brain, auditory deprivation decreased neuronal activity transiently in primary auditory and auditory-related cortices, and, over time, functional reorganization likely takes place in the auditory cortex. Plasticity was prominent in superior temporal and anterior cingulate gyri in the sensory-deprived mature brain and militated against postimplantation improvement in patients with cochlear implants.

Key Words: hearing disorders; glucose metabolism; cochlear implants; brain mapping; PET

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The development of modern noninvasive brain imaging techniques, such as PET and functional MRI (fMRI), the increasing prevalence of cochlear implantation, and new, effective rehabilitation methods for profound or total hearing loss (*1*) have led to increasing interest in human functional reorganization in auditory-related cortex in individuals with prelingual deafness (*2–7*). In brain activation studies of prelingual deafness using $H_2{}^{15}O$ PET (*5,6*) or fMRI (*4*), the auditory cortex was found to be activated by sign language presented visually. These findings demonstrate the capacity of the auditory cortex for cross-modal reorganization after auditory deprivation of the human brain. Investigations of cerebral glucose metabolism in deaf patients using ^{18}F-FDG PET have provided other functional evidence of neuroplasticity (*2,3,7*). Cerebral glucose metabolism in the primary auditory and related cortices in individuals with prelingual deafness was shown to decrease in younger patients, but to increase as they aged, and, in fact, recovered fully or even exceeded normal level of activation. The recovery of metabolism in older individuals was explained by plastic changes in the auditory neuronal circuitry due to the expansion of the afferent neural network by other sensory systems. That expansion was possible because of the lack of functional specialization of the auditory cortex in younger individuals and its resultant vulnerability to other forms of sensory stimulation. That plasticity was demonstrated to prevent the recovery of the designated hearing function of auditory neural substrates after cochlear implantation and rehabilitation in prelingually deaf patients (*7*).

Controversy regarding functional reorganization in adults still remains (*8*). Few systematic imaging investigations have been performed that address neuroplasticity in postlingually deaf patients, who lost their hearing capability

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after language acquisition. Nevertheless, outcome studies of cochlear implantation in postlingually deaf patients suggest the possible existence of the plasticity in the auditory cortex resembling prelingual deafness. For instance, patients with a longer duration of profound deafness tend to show a worse prognosis after cochlear implantation (*9,10*).

The aim of this study is to investigate whether neuroplasticity is present in adults with postlingual deafness. The underlying assumption is that glucose metabolism within the auditory cortex of postlingually deaf patients should increase according to the duration of deafness if reorganization due to plasticity took place. To address this issue, we examined the pattern of cerebral glucose metabolism on ^{18}F-FDG brain PET images of postlingually deaf patients by comparing the auditory cortical activation pattern with those of age- and sex-matched healthy control subjects. We also correlated the cerebral glucose metabolism in deaf patients with the duration of deafness using statistical parametric mapping (SPM) (*11–14*).

MATERIALS AND METHODS

Subjects

Seventeen postlingually deaf patients underwent PET scans at Seoul National University Hospital between March 1995 and August 2000. Eight of the 17 patients who had lost their hearing capability before the age of 20 were excluded so that the findings of this study are not confounded by the onset age of deafness. Nine patients (3 men, 6 women; mean age, 44.5 ± 9.5 y) were finally selected. Nine age- and sex-matched healthy volunteers (3 men, 6 women; mean age, 43.4 ± 13.6 y) served as control subjects. Exclusion criteria for the control subjects included a history of any neurological, psychiatric, or significant medical illnesses or a past history of substance abuse. All patients and control subjects were right-handed. The duration of deafness in patients ranged from 0.2 to 23 y (mean duration, 8.3 ± 8.2 y). The clinical features of the patients are listed in Table 1. PET scans were performed for the deaf patient as a clinical presurgical evaluation. Sufficient and detailed explanations for the procedure, risk, and purpose or benefit of the ^{18}F-FDG PET study as an evaluation method for prediction of postsurgical outcome were given to the patients by clinicians, whereas the other presurgical test procedures were explained.

TABLE 1
Clinical Features of Deaf Patients

No. of patients	Sex	Age (y)	Duration of deafness (y)	CID score (%)
1	M	58	0.2	—
2	F	30	0.7	—
3	F	34	0.8	100
4	F	39	1.4	58
5	F	53	6.0	74
6	M	53	10.0	82
7	M	44	13.0	40
8	F	42	20.0	34
9	F	56	23.0	—

CID = Central Institute of Deaf.

PET Scans

^{18}F-FDG brain PET scans were performed on the patients and healthy volunteers using an ECAT EXACT 47 PET scanner (Siemens-CTI), with an intrinsic resolution of 5.2-mm full width at half maximum (FWHM). Images were simultaneously collected of 47 contiguous planes with a thickness of 3.4 mm, to give a 16.2-cm longitudinal field of view. Before ^{18}F-FDG administration, transmission scanning was performed using 3 ^{68}Ge rod sources for attenuation correction. Static emission scans began 30 min after the injection of 370 MBq ^{18}F-FDG and continued for 30 min in the resting state (eye closed, ears unoccluded in a dark and quiet environment). Transaxial images were reconstructed using a filtered backprojection algorithm with a Shepp–Logan filter at a cutoff frequency of 0.3 cycle/pixel as 128 × 128 × 47 matrices of size 2.1 × 2.1 × 3.4 mm.

Speech Perception Test

Six of the 9 patients received cochlear implantation after the PET scan, and speech perception performance testing was then performed using the Korean version of the Central Institute of Deaf (CID) tests. During the test, each subject was instructed to listen to and then repeat 20 commonly sentences without visual cues. The sentences consisted of 3 simple Korean words. The CID score is defined as the ratio of correct response to total trials, and a higher CID score means a better prognosis for cochlear implantation. The best CID scores after sufficient periods of patient education are shown in Table 1.

Image Analysis

Imaging data were analyzed using the SPM 99 (Wellcome Department of Cognitive Neurology, Institute of Neurology, University College of London) program implemented in the Matlab (Mathworks Inc.) software environment (*11–14*).

Prior to statistical analysis, all images were spatially normalized into the Montreal Neurological Institute (MNI) (McGill University) standard template to remove the intersubject anatomic variability (*13,15*). The Affine transformation was performed to determine the 12 optimal parameters used to register the brain on the template. Subtle differences between the transformed image and the template were removed using the nonlinear registration method in which the weighted sum of the predefined smooth basis functions is used in discrete cosine transformation. Spatially normalized images were smoothed by convolution with an isotropic gaussian kernel with 16-mm FWHM. The aim of smoothing was to increase the signal-to-noise ratio and to account for variations in the subtle anatomic structures. The effects of global metabolism were removed by normalizing the count of each voxel with respect to the total count of the cortical area (proportional scaling in SPM).

Significant increases and decreases of regional cerebral metabolism in the patient group were estimated by comparing their PET images with those of the healthy volunteers using *t* statistics at every voxel (9 patients vs. 9 control subjects). Voxels with a *P* value of <0.001 (uncorrected for multiple comparisons) were considered to carry significant difference. To simplify interpretation, the *t* values were transformed to the standard gaussian distribution (*z* score).

To reveal regions in which metabolism was significantly correlated with the duration of deafness, the general linear model with the duration of deafness as a covariate was tested at each voxel,

and voxels with P values of <0.005 (uncorrected) were considered to significant.

RESULTS

Group Comparison

When we compared ^{18}F-FDG brain PET images of postlingually deaf patients with those of age- and sex-matched healthy control subjects by performing a t test at every voxel, after removing the intersubject anatomic variability of brain and the effects of global glucose metabolism, the glucose metabolism of deaf patients was significantly ($P < 0.001$) lower than that of the control subjects in both anterior cingulate gyri (Brodmann area 24 [BA24]) and superior temporal cortices (BA41, BA42) and in the right parahippocampal gyrus (Fig. 1). Brain areas with significantly decreased metabolism, Brodmann area, their location in the MNI standard space, and maximum z value within the volume (cluster) are shown in Table 2. No area showed a significant increase of metabolism in deaf patients with the same threshold.

Correlation Analysis

When we correlated glucose metabolism of deaf patients with the duration of deafness after total deprivation of hearing capability using a general linear model with the duration of deafness as a covariate at every voxel, metabolism in both anterior cingulate gyri (BA24) and superior temporal cortices (BA41, BA42) showed a significant ($P < 0.005$) positive correlation with the duration of deafness (Table 3). Brain areas with a significant positive correlation are shown in Figure 2, in which the threshold of $P < 0.01$ was used rather than $P < 0.005$ for significance. On the other hand, the metabolism in the visual association area of the right occipital cortex ($[x, y, z] = [44, -72, -10]$, $z = 2.78$) showed a significant ($P < 0.005$) negative correlation with the duration of deafness.

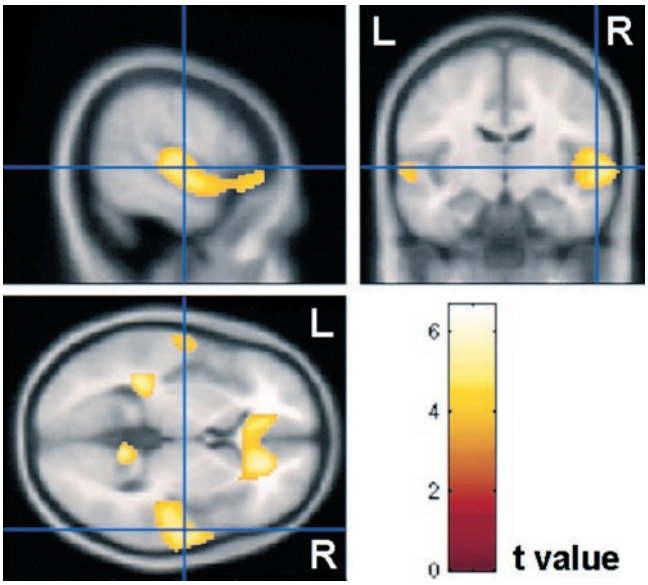

FIGURE 1. Brain areas with significantly decreased glucose metabolism in postlingually deaf patient ($P < 0.001$, uncorrected). Metabolism was decreased in both anterior cingulate gyri and superior temporal cortices and in right parahippocampal gyrus.

TABLE 2
Brain Areas with Significantly Decreased Metabolism in Deaf Patients (Threshold: $P = 0.001$, Uncorrected)

Brain area	Brodmann area	Coordinates (x, y, z)	z value
Left hemisphere			
Anterior cingulate	24	−10, 34, 14	4.20
Superior temporal	41, 42	−60, −10, −2	3.48
Right hemisphere			
Anterior cingulate	24	18, 38, 8	4.54
PHG		10, −50, 4	4.16
Superior temporal	41, 42	62, −6, −4	3.98

PHG = parahippocampal gyrus.

DISCUSSION

Cerebral glucose metabolism of postlingually deaf patients decreased in the anterior cingulate gyri and the superior temporal cortices of both hemispheres and in the right parahippocampal gyrus. Metabolism in both anterior cingulate gyri and superior temporal cortices correlated positively with the duration of deafness. Decreased metabolism but gradual recovery according to the duration of deafness in the auditory cortex of the superior temporal regions and anterior cingulate gyri suggests that plastic changes in the brain occur in individuals with postlingual deafness.

The prognostic relevance of cross-modal plasticity, which was shown in prelingual deafness (*7*), can also be inferred from our results in adult brains. There was a tendency toward a poorer prognosis after cochlear implantation (lower CID score in Table 1) as the duration of deafness increased (correlation coefficient = 0.73; $P = 0.09$). This result not only agrees with those of previous outcome studies of cochlear implantation in postlingual deafness but also indirectly relates the prognosis after cochlear implantation with the metabolism in auditory-related cortices. In adult

TABLE 3
Brain Areas Showing Positive Correlation Between Metabolism and Duration of Deafness (Threshold: $P = 0.005$, Uncorrected)

Brain area	Brodmann area	Coordinates (x, y, z)	z value
Left hemisphere			
Anterior cingulate	24	−12, 32, 14	4.12
Superior temporal	41, 42	−44, −26, 8	2.69
Right hemisphere			
Anterior cingulate	24	14, 30, 12	4.43
Superior temporal	41, 42	62, −6, −4	2.85

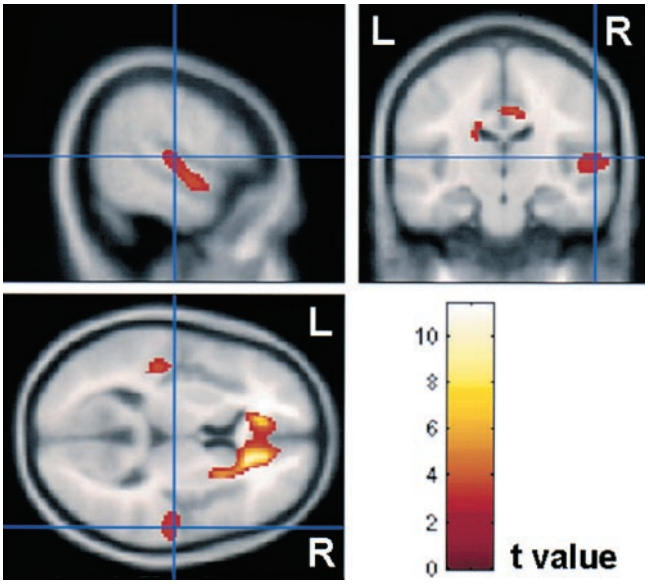

FIGURE 2. Brain areas show positive correlations between metabolism and duration of deafness ($P < 0.01$, uncorrected). They were significantly correlated in both anterior cingulate gyri and superior temporal cortices.

postlingually deaf patients, reorganization of those areas after an extended period without sound or language input may have caused metabolic recovery and prevented the deaf patients from acquiring speech perception skills after the sound restoration by cochlear implantation.

In our preliminary study (*16*), the relationship between the level of cerebral glucose metabolism and neuroplasticity was examined by evaluating the changes that occurred in glucose metabolism before and after cochlear implantation in postlingually deaf patients. Glucose metabolism in the auditory cortex of the hemisphere contralateral to the implantation recovered to normal levels and speech perception performance was good after cochlear implantation only in those patients who showed a hypometabolic area in the auditory cortex before cochlear implantation. On the contrary, a patient showing normal glucose metabolism in the auditory cortex before cochlear implantation showed no change of glucose metabolism and no improvement in speech perception performance after cochlear implantation.

Plastic change in the cerebral cortex of the adult brain has been demonstrated in animal studies. Injury-induced reorganization was reported in the somatosensory, visual, and motor cortices of adult animals after restricted peripheral lesions (*17–25*). In the auditory system, experience-dependent alterations in receptive field properties were investigated by partial destruction of the cochlea (*26–28*). The resulting topographic map of sound frequency changed in the contralateral auditory cortex of the lesioned cochlea. The area representing the frequency range damaged by the lesion shrunk and was partly occupied by an expanded representation of adjacent sound frequencies. The frequency organization of the auditory cortex was also modified in animals by training, which involved frequency discrimination tasks, classical conditioning procedures, and Hebbian covariance (*29–31*).

Some recent studies suggest that plastic changes in the human brain also occur after childhood, although the belief that cross-modal reorganization occurs exclusively in the immature human brain has prevailed and controversy regarding this issue remains (*8*,*32*,*33*). Kujala et al. (*32*) compared event-related potentials from the early-blind, late-blind, and sighted adults during sound-discrimination tasks, in which each participant was asked to ignore or count silently the deviant tones (occasional higher frequency tones) among a sequence of standard tones. In both groups of blind individuals, the scalp location of maximal electrical activity in response to the higher frequency deviant tones was significantly posterior (parietal and occipital regions) to that of sighted subjects. This result contradicted the common belief that cross-modal reorganization only occurs during early development. In late-blind patients, functionally relevant cross-modal plasticity was not found by PET and transcranial magnetic stimulation studies by one group (*34*), but another group (*33*) found somatosensory-to-visual cross-modal plasticity but not auditory-to-visual cross-modal plasticity.

Underlying mechanisms that might mediate the plastic change in auditory cortex of adult postlingual deafness observed in this study remain to be elucidated (*17*,*35*). Plastic changes might be mediated by several mechanisms (*36*). The changes can occur in local connectivity within the primary auditory cortex or in subcortical connectivity between auditory cortex and subcortical structures, such as the thalamus or brain stem. These possibilities are unlikely because the loss of auditory sensation occurred late in our adult postlingually deaf patients, and the patients who showed more plasticity showed poorer sensory recovery after cochlear implantation. Other possibilities include corticocortical connectivity between different sensory modalities (*37*,*38*) or corticocortical connectivity between the auditory cortex and multimodal cortices, such as the parietal cortex. Because we observed the plastic changes in postlingually deaf adults, changes in functional connectivity between the sensory region and multimodal cortices seems plausible. We found that the brain activities increased both in bilateral superior temporal gyri (BA41, BA42) and in anterior cingulate gyri (BA24) with increased the duration of deafness, after the initial decreases. It is still difficult to know whether those 2 regions were functionally connected or which functions each area might be recruited for after long-term sensory loss. Further studies to test functional connectivity or cross-sensory modality function are needed.

Ito et al. (*39*) presented a result that is contradictory to that described herein in their early ^{18}F-FDG PET studies on postlingually deaf individuals. They found that the longer the duration of deafness, the lower the cerebral glucose metabolism in auditory cortex. However, the reliability of

this finding may be questioned because the ^{18}F-FDG PET images were visually, rather than quantitatively, interpreted.

We may explain the accompanying hypometabolism in the right parahippocampal gyrus in the following manner: The decreased activity may be due to the anatomic and functional connectivity between the parahippocampal gyrus and the auditory cortex. It may also be possible that reduced language and auditory information may reduce the metabolic activity in this region, which is associated with memory (*40*).

CONCLUSION

This study suggests that plasticity is present in adult brains of postlingually deaf patients. In the mature brain, auditory deprivation decreased neuronal activity transiently in primary auditory and auditory-related cortices, and over time, functional reorganization likely takes place in the auditory cortex over time. Plasticity was prominent in superior temporal and anterior cingulate gyri in the sensory-deprived mature brain and militated against postimplantation improvement in patients with cochlear implants.

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