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Cochlear implant efficiency in pre- and postlingually deaf subjects

A study with $H_2{}^{15}O$ and PET

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Summary

We used ^{15}O-labelled water in a PET study to test the efficiency of cochlear implants (CIs) in transmitting auditory information to the brain in 10 profoundly deaf subjects. Five were postlingually deaf, and five were prelingually deaf. All the subjects were right-handed. White noise and verbal stimuli, delivered through the CIs, were used for cortical activation. Similar tasks were performed by six right-handed hearing subjects as a control group. In the postlingually deaf subjects, verbal stimulation activated the transverse temporal gyri (primary auditory cortices) mainly on the side contralateral to the CI. The left posterior superior temporal gyrus (Wernicke's area), and the left inferior frontal gyrus (Broca's area) were also activated irrespective of stimulated side. The location of these activated foci was the same as that of the control group. White noise stimulation led to an increase of regional cerebral blood flow (rCBF) only in the primary auditory cortices of the postlingually deaf subjects, only on the side contralateral to the CI, and the intensity of activation was less than that obtained with verbal stimulation. In the prelingually deaf subjects, Wernicke's area and Broca's area were significantly activated by verbal stimulation, whereas there was no activation in the primary auditory cortices. White noise did not activate the primary auditory cortex in the prelingually subjects. These findings suggest that cortical representation of language is not dependent on early auditory experience, while processing in the primary auditory cortices is experience-dependent. The postlingually deaf subjects had a greater increase of rCBF in the Broca's and Wernicke's areas and better sentence comprehension than the prelingually deaf subjects, which suggests a parallel relation between rCBF increase and the ability to recognize spoken language. $H_2{}^{15}O$-PET with auditory stimulation is an effective means of objectively quantifying the response of auditory and association cortices after CIs in deaf subjects.

Keywords: cochlear implant; PET; activation study; auditory cortex; language cortex

Abbreviations: AC–PC = anterior commissure–posterior commissure; CI = cochlear implant; rCBF = regional cerebral blood flow

Introduction

Artificial electrical stimulation of the cochlear nerve by implanted electrodes (CIs) has been successfully applied to profoundly deaf subjects. This device makes it possible to change auditory input into electronic signals by means of a microphone and a portable speech processor, and to stimulate the cochlear nerve directly. However, even with recent improvements of the technique and the stimulating electrodes, the effectiveness of cochlear stimulation is difficult to assess, and indications for this treatment are still debatable (Balkany, 1983; McIntire *et al.*, 1985; Robin, 1985). PET with ^{15}O-labelled water has been used to measure changes of rCBF in the auditory cortex of deaf subjects with CIs (Herzog *et al.*, 1991). PET activation studies are usually performed in normal volunteers to investigate the response of the brain to various stimuli. Clinically, PET activation studies have been used to determine the method of treatment (Leblanc *et al.*, 1990,

1992) or to evaluate the efficiency of the treatment by measuring the changes of rCBF quantitatively (Herzog *et al.*, 1991). PET activation studies have objectively demonstrated a relationship between the lesions and activated regions of the brain, and differences between subjects in diseased and healthy states (Rumsey *et al.*, 1992, 1994). In the present study, both noise and verbal stimuli were given through the electrodes of the CIs to activate the primary auditory and language cortices. Co-registration of the PET images with MRIs provided the precise location of the auditory and language cortices. A resting condition in which the CIs were switched off, provided a baseline condition free of auditory input to the profoundly deaf subjects. Six right-handed hearing subjects were also studied as a control group to determine the normal pattern of activation.

We also studied differences in the efficiency of CIs in subjects with postlingual and prelingual deafness. Postlingual deafness is the loss of acoustic senses suddenly by accident or gradually by progression to deafness after acquisition of the first language. Prelingual deafness is congenital profound hearing loss or loss of hearing sensation before acquisition of the native language. In this study, we questioned whether the prolonged absence of sound stimulation or auditory perception of language before CI surgery in prelingually deaf subjects made any difference in the response of auditory and language cortices compared with postlingually deaf subjects, and whether the auditory and language cortices remained in the normal site or shifted contralaterally in prelingually, compared with postlingually, deaf subjects. In an activation study with profoundly deaf subjects conducted by Herzog *et al.* (1991), the differences between postlingually and prelingually deaf patients were inconclusive.

Subjects and methods

Subjects

We studied 10 profoundly deaf subjects (eight male and two female), aged 10–62 years (mean 33.7 years). Five were postlingually deaf and five were prelingually deaf. All of them were right-handed. All the postlingually deaf subjects were native Japanese who spoke Japanese as their first language. All the prelingually deaf subjects had acquired Japanese by lip-reading or Japanese sign language as their first language. In each group, the CI systems were implanted on the left side in three subjects and on the right side in two subjects. The subjects' clinical characteristics and educational history are shown in Table 1.

All the subjects had CI surgery with a multi-channel CI system (Cochlear Implant Mini system 22, Cochlear Ltd, Melbourne, Australia) 12 days to 7 years before the PET study, and conventional X-ray films confirmed that the electrode was in the base turn of the cochlea. In the CI system, a microphone is used to pick up sound signals and convert them into electronic signals which are conveyed to a speech processor, where formants of sound are extracted (Tong *et al.*, 1982). The output of the speech processor is delivered to the electrode array, where selected electrodes stimulate residual auditory neurons. The CI surgery was confirmed to be equally successful in all deaf subjects by checking the sensation of sound in all 22 channels of the electrode.

A control group of six hearing men (aged 24–36 years; mean 29.2 years) were studied in the same way as the deaf subjects. All were right-handed and native Japanese.

The protocol was approved by the Ethical Committee of Kyoto University Faculty of Medicine, and all subjects gave their written informed consent for the study.

PET

PET scanning was performed with a PCT-3600W (Hitachi Medical Co., Tokyo, Japan) PET imaging device (Sadato *et al.*, 1993; Shibasaki *et al.*, 1993). This system permits the simultaneous acquisition of 15 transverse slices with inter-slice spacing of 7 mm. Images were reconstructed to a full width at half maximum of 9 mm in the transaxial direction and 6.5 mm in the axial direction. Field of view and pixel size of the reconstructed images were 256 mm and 2 mm, respectively. Transmission scans were obtained with a standard plate source of ^{68}Ge/^{68}Ga for attenuation correction of the emission images. The tissue activity concentration in the PET images was cross-calibrated against a scintillation counter using a cylindrical phantom filled with an ^{18}F-solution. Each subject's head was immobilized with an individually customized headholder constructed of a fast-hardening foam mold (Kearfott *et al.*, 1983). The room was dimly lit, and the subjects kept their eyes open.

For the measurement of rCBF, ~1110 MBq (30 mCi) of ^{15}O-labelled water in 6 ml saline was injected into the cubital vein over 15 s with an automatic injector, and static data acquisition began at the onset of the injection and lasted for 120 s.

Sound stimuli

The deaf subjects confirmed that they perceived sound when the CI was switched on. The hearing subjects were fitted with a single earphone on one side (the right side in three and the left side in the other three) and the ear on the other side was plugged so that the sound stimulated only one ear. PET scans were performed during three conditions: no sound stimulation (resting condition), white noise stimulation and word stimulation (Naito *et al.*, 1995). In the resting condition, the speech processor of the CI system was switched off. The noise condition was the direct stimulation of the speech processor connected to a tape recorder in line, with the electronic signal consisting of white noise recorded on audiotape. The volume of the noise signal was a level that the subjects perceived distinctly but did not find too abrasive. This level was in the range of 60–70 dB, which is considered to be of sufficient volume for stimulation of the primary

Table 1 *Patient information*

Patient no.	Age/sex	Age at onset of deafness (years)	Cause of deafness	Side of CI	Period of CI usage before PET	Highest educational achievement	Speech recognition	
							Vowel (%)	Speech tracking score (no. of words)*
Postlingual								
1	55/F	54	Unknown	Left	12 days	High school	76	11
2	10/M	9	Head injury	Right	1 month	Primary school	92	14.8
3	45/M	41	Head injury	Right	3 years	College	100	25.6
4	52/M	46	Chronic otitis media	Left	1 month	High school	48	6
5	62/M	53	Temporal bone fracture	Left	7 years	High school	76	13.4
Prelingual								
6	42/M	<1	Aminoglycoside toxicity	Right	3.8 years	High school†	44	0
7	30/F	1	Meningitis	Left	7 weeks	High school†	36	ND
8	18/M	<1	Unknown	Right	1 month	High school†	36	ND
9	11/M	<1	Unknown	Left	22 months	Primary school†	60	2.3
10	12/M	<1	Meningitis	Left	3 years	Primary school†	44	6

ND = no data. *Normal score, ~40 words; †school for the deaf.

auditory cortex (Elberling *et al.*, 1981). The volumes of noise and word stimuli were fixed for each subject. During word stimulation, subjects heard simple sentences from the CI system and then repeated them silently. The sentence list was made by the Audiological Society of Japan, and the same set of sentences was used for all subjects. These sentences were presented to all subjects by the same examiner through a microphone at the rate of 40 words per minute, and the electronic signals stimulated the CI directly. The examiner hid his mouth from the subjects so that they could not lip-read. The tasks were started 30 s before the administration of $H_2{}^{15}O$ and continued until the end of the scan. Testing at each condition was repeated twice. The between-scan interval was 10 min.

Test of hearing ability

On the day after the PET studies, the auditory–verbal ability of all the deaf subjects was examined by a vowel recognition test without lip-reading, and by a speech tracking test in eight out of 10 subjects. Vowel recognition ability was assessed by the accuracy of the spoken vowel. The speech tracking test involved counting the number of words the subjects correctly recognized when they heard sentences without the help of the examiner's mouth movement. Speech recognition ability was assessed by the number of words correctly repeated during 1 min (speech tracking score).

Hearing thresholds of the CIs were measured in nine out of 10 subjects (all postlingual and four prelingual) on the second day after the PET studies. The results were averaged in each group and statistically compared by the Student's *t* test.

Registration of PET and MRI

Four deaf subjects (three postlingual and one prelingual) and six hearing subjects had MRI scans which were obtained with a 1.5-Tesla Signa Imager (GE Medical Systems, Milwaukee, Wisc., USA) with a standard head coil covering the whole brain, and using a T_1-weighted sequence. Slices were 3 mm thick without a slice gap. All the images in each patient were interpolated and reconstructed to a voxel size of $2\times2\times2$ mm.

The MRI and PET data sets were first rotated axially and coronally to fit the midsagittal plane, and PET data were co-registered with MRI data by tracing the inner structure and brain contour of the midsagittal and parasagittal section (±10 mm) of the reconstructed MRI individually (Shibasaki *et al.*, 1993). The original 15-slice PET data set was also interpolated to an isotropic volume through a linear interpolation, giving the same voxel size of the MRI. After the co-registration, MRI and PET data sets were transferred on the stereotaxic grids of Talairach's atlas (Friston *et al.*, 1989; Shibasaki *et al.*, 1993; Senda *et al.*, 1994).

The other six deaf subjects did not have MRIs because their CIs had already been implanted. The PET data sets of these subjects were rotated parallel to the anterior commissure–posterior commissure (AC–PC) plane (Friston *et al.*, 1989; Minoshima *et al.*, 1993), and resliced as described above (voxel size of $2\times2\times2$ mm).

Data and statistical analysis

Functional images of rCBF were calculated from the $H_2{}^{15}O$ PET data in each subject by using a standard arterial input function (Sadato *et al.*, 1993). Six rCBF images of each subject were globally normalized to correct fluctuations of the global CBF among successive scans (Fox *et al.*, 1984, 1989). Two images of each of the three conditions were averaged after normalization. Subtracted images were obtained for the word condition minus the resting condition and the noise condition minus the resting condition. The subtracted images were superimposed on the individual MRI data set after rotation and interpolation, by the method described above, and visually inspected at all available slice levels in the axial and coronal planes.

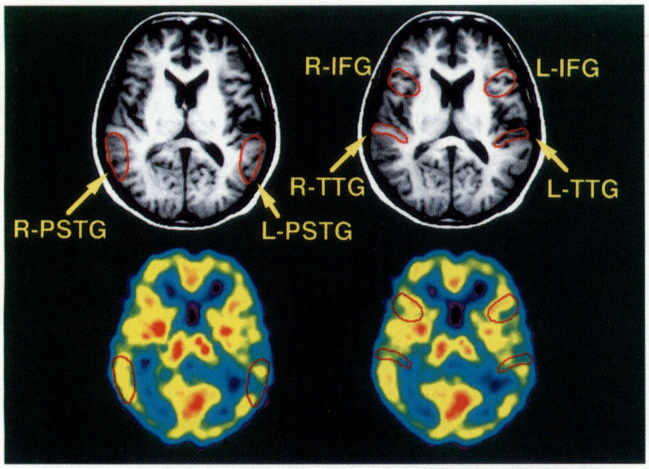

Fig. 1 Regions of interest were placed with reference to the corresponding MRI after the co-registration of PET and MRI. The slice levels were 8 and 12 mm above the AC–PC plane. The same regions of interest were transferred to the PET image. In the patients without MRIs, regions of interest were placed on the PET images with reference to the atlas of Talairach and Tournoux (1988). R and L = right and left; IFG = inferior frontal gyrus; TTG = transverse temporal gyrus; PSTG = posterior superior temporal gyrus.

Regions of interest were placed on the bilateral transverse temporal gyri (primary auditory cortex, Brodmann's area 41), the posterior superior temporal gyri (Brodmann's area 42 and 22) and the inferior frontal gyri (Brodmann's area 44 and 45) with reference to individual MRIs (Fig. 1). In the subjects for whom no MRI was available, regions of interest were placed with reference to Talairach's atlas (Talairach and Tournoux, 1988). First, transformation of PET images on the stereotaxic coordinated grids was done according to the direct PET-based landmark method by Friston *et al.* (1989). Each region of interest was placed on a slice that was considered to be the centre of each area (z = +8 to 12 mm from the AC–PC plane). The centres of regions of interest were $x = \pm 45$ mm, $y = -25$ mm for the transverse temporal gyri, $x = \pm 50$ mm, $y = -40$ mm for the posterior superior temporal gyri, and $x = \pm 48$ mm, $y = +5$ mm for the inferior frontal gyri. The same regions of interest were transferred to measure rCBF on averaged images in each condition individually.

The calculated data were compared for regional differences with the factors of conditions (resting, word and noise) and subjects of each group in each hemisphere by repeated measures ANOVA with a Greenhouse–Geisser correction (Geisser and Greenhouse, 1958) because of the repeated measurements in each subject. For comparison among three subject groups (normal, post- and prelingually deaf subjects) in each condition, we employed a one-way ANOVA because the comparisons were between groups. The baseline rCBF data were compared with the factors of subject groups (control, post- and prelingually deaf), and hemisphere by a one-way ANOVA with *post hoc* Scheffé's *F* test. The three subject groups (control group, post- and prelingually deaf subjects) were compared for differences in rCBF changes in each condition using a one-way ANOVA with *post hoc* Scheffé's *F* test. Statistical significance was defined as $P < 0.05$.

Results

Co-registration of PET and MRI

Co-registration of PET and MRI images in a postlingually deaf subject is shown in Fig. 2. Subtracted images obtained for the word condition minus the resting condition, and the noise condition minus the resting condition were superimposed on the axial MRI. Areas of increased rCBF were clearly visible in the transverse temporal gyrus (Heschl's gyrus; primary auditory cortex), the left posterior superior temporal gyrus (Wernicke's area), and the left inferior frontal gyrus (Broca's area). The primary auditory cortices were activated mainly on the side contralateral to the CI. Wernicke's and Broca's areas were consistently activated in the left hemisphere.

Resting condition

Table 2 summarizes the rCBF of the hearing and deaf subjects in each condition. In the resting condition, no laterality of rCBF was observed in the primary auditory cortices, the posterior superior temporal gyri, or the inferior frontal gyri. Compared with the control group or the prelingually deaf subjects, the postlingually deaf subjects showed a lower baseline (resting) rCBF in the primary auditory cortex on the side contralateral to the CI, and the difference was significant in three groups [one-way ANOVA, $F(2,13) = 6.13$, $P < 0.05$]. After the *post hoc* Scheffé's *F* test, significance was observed in post- versus prelingually deaf subjects, and in postlingually deaf subjects versus control group ($P < 0.05$). The other areas demonstrated no significant differences in baseline among the subject groups.

Task conditions vervus resting condition

Primary auditory cortices

In the hearing subjects, verbal stimulation caused significant increases of rCBF in the primary auditory cortex contralateral to the stimulated side [repeated measures ANOVA, $F(1,5) = 8.64$, $P < 0.05$]. There were no significant increases of rCBF in the noise condition.

In the postlingually deaf group, significant increases of rCBF occurred in the bilateral primary auditory cortices during verbal stimulation [repeated measures ANOVA: ipsilateral, $F(1,4) = 12.29$, $P < 0.05$; contralateral, $F(1,4) = 56.31$, $P < 0.0005$]. Noise stimulation activated the primary auditory cortex only on the side contralateral to the CI [repeated measures ANOVA, $F(1,4) = 12.11$, $P < 0.05$]. Cortical activation by verbal stimulation was greater than that caused by white noise [repeated measures ANOVA:

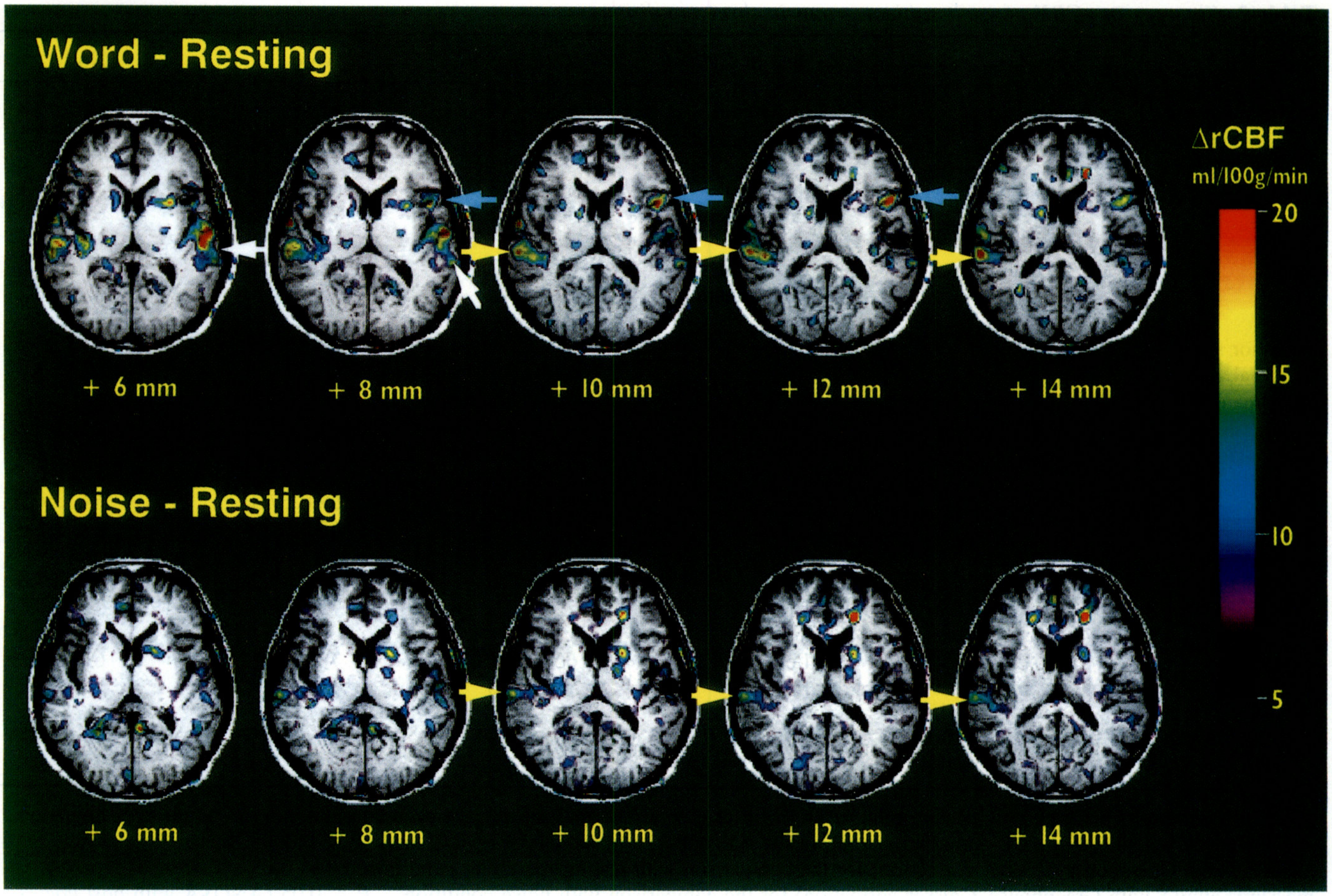

Fig. 2 Subtracted PET images of Subject 1 superimposed on her MRI in axial sections. She is postlingually deaf and had CI surgery on the left side. Co-registration of PET and MRI clearly shows the activated foci in the primary auditory cortex contralateral to the CI side (yellow arrows), Wernicke's area (white arrows), and Broca's area (blue arrows) in the left cerebral hemisphere during verbal stimulation (top). During noise stimulation, only the primary auditory cortex was intensely activated (bottom). The scale is the value of rCBF change after global normalization. The number at each slice level is the distance (in millimetres) from the AC–PC plane.

ipsilateral, $F(1,4) = 10.37$, $P < 0.05$; contralateral, $F(1,4) = 16.20$, $P < 0.01$].

In the prelingually deaf subjects, the contralateral primary auditory cortex was only weakly activated by verbal stimulation, which did not reach the statistical significance threshold. White noise did not activate the primary auditory cortices, and the differences in rCBF changes between the word and noise conditions were not significant.

Language association cortices

During verbal stimulation, the left superior temporal gyrus (Wernicke's area) showed a significant increase of rCBF in all three groups [repeated measures ANOVA: control, $F(1,5) = 9.97$, $P < 0.05$; postlingual, $F(1,4) = 11.97$, $P < 0.05$; prelingual, $F(1,4) = 8.05$, $P < 0.05$] compared with the resting condition, whereas no significant activation was seen in the right superior temporal gyrus. No significant rCBF increases occurred in either area of either group during noise stimulation. Verbal stimulation, compared with white noise, caused a significantly greater increase of rCBF in Wernicke's area in postlingually deaf group [repeated measures ANOVA, $F(1,4) = 8.09$, $P < 0.05$].

The left inferior frontal gyrus (Broca's area) showed significant increases of rCBF during verbal stimulation in all three groups [repeated measures ANOVA: control, $F(1,5) = 8.22$, $P < 0.05$; postlingual, $F(1,4) = 13.47$, $P < 0.05$; prelingual, $F(1,4) = 9.92$, $P < 0.05$], whereas no significant activation was seen in the right inferior frontal gyrus. No significant rCBF increases occurred in either area of either group with noise stimulation. In the postlingually deaf subjects, Broca's area also showed a significantly greater rCBF increase during verbal stimulation than during noise stimulation [repeated measures ANOVA, $F(1,4) = 8.07$, $P < 0.05$].

Increment of rCBF: comparison among three groups

Table 3 shows the increment of rCBF during white noise and verbal stimulation compared with the resting condition.

Table 2 *Changes in rCBF of each subject group in three conditions*

Brain area	Deafness	Side of CI*	Resting	Word	Noise
Primary auditory (Brodmann area 41)	Hearing	Ipsilateral	63.4±7.3	67.5±8.5	64.7±7.8
		Contralateral	64.0±5.8**	74.8±4.8†	65.7±3.5
	Postlingual	Ipsilateral	55.1±8.8	63.0±8.4†,§	55.8±8.1
		Contralateral	54.3±6.2**	71.1±8.0‡,¶	62.1±12.9†
	Prelingual	Ipsilateral	61.0±6.2	65.1±4.6	62.2±4.8
		Contralateral	66.1±5.2**	73.8±6.0	67.9±8.2
Posterior superior temporal gyrus (Brodmann area 42, 22)	Hearing	Left	61.5±6.1	69.2±8.3†	63.7±5.7
		Right	67.5±3.7	69.1±4.2	67.5±3.5
	Postlingual	Left	52.3±7.2	63.4±7.7†,§	56.4±7.3
		Right	58.6±4.1	64.2±4.5	59.9±4.2
	Prelingual	Left	62.1±6.4	68.0±7.3†	64.1±6.7
		Right	62.5±3.3	65.3±1.9	63.7±5.0
Inferior frontal gyrus (Brodmann area 44, 45)	Hearing	Left	66.1±7.0	75.9±9.2†	68.9±7.8
		Right	72.5±8.2	73.2±6.5	72.5±8.7
	Postlingual	Left	66.6±9.4	78.0±14.2†,§	69.2±10.6
		Right	70.6±6.0	71.7±7.7	72.0±8.7
	Prelingual	Left	68.5±6.8	73.5±8.3†	70.2±10.1
		Right	71.6±7.0	72.3±7.0	70.7±9.8

Values, expressed as mean±SD rCBF (ml min^{-1} 100 g^{-1}, after globally normalization), for each condition are based on five subjects. *Ipsilateral means side of the CI; and contralateral means side opposite to the CI; $^{\dagger}P < 0.05$ and $^{\ddagger}P < 0.0005$ (repeated measures ANOVA with Greenhouse–Geisser correction) for the comparison with resting (baseline) condition; $^{\S}P < 0.05$ and $^{\P}P0.01$ (repeated measures anovA with Greenhouse–Geisser correction) for the comparison with noise condition; $^{**}P < 0.05$ (ANOVA with *post hoc* Scheffé's F test) for the comparison of resting (baseline) rCBF between hearing subjects and postlingual deafness, or between pre- and postlingual deafness.

Table 3 *Differences in rCBF changes in each subject group*

Brain area and condition	Side of CI*	Hearing subjects	Postlingual deafness	Prelingual deafness	Post- versus pre-†	
					S-value‡	P
Primary auditory						
Word—resting	Ipsilateral	4.12±7.25	7.84±2.36	4.08±5.41	9.70	n.s.
	Contralateral	10.74±2.32	16.78±3.88§	7.69±6.02	7.37	0.016
Noise—resting	Ipsilateral	1.35±6.20	0.64±1.02	1.19±3.14	7.43	n.s.
	Contralateral	1.67±3.94	7.78±7.13	1.83±5.61	9.76	n.s.
Superior temporal gyrus						
Word—resting	Left	7.70±5.60	11.04±1.39	5.81±1.14	4.94	0.040
Inferior frontal gyrus						
Word—resting	Left	9.74±3.33	11.42±6.76	4.97±4.17	6.37	n.s.

Values, expressed as mean±SD of changes in rCBF (ml min^{-1} 100 g^{-1}), for each group are based on five subjects. *Ipsilateral means side of the CI; contralateral means side opposite to the CI. †Statistic values are for the comparison between post- and prelingually deaf subjects (ANOVA with *post hoc* Scheffé's F test).$^{\ddagger}S$-value means critical difference obtained from *post hoc* Scheffé's F test ($P < 0.05$); $^{\S}P < 0.01$ (ANOVA) for the comparison with the ipsilateral side.

In the primary auditory cortices, the postlingually deaf group showed a greater increase of rCBF on the side contralateral to the CI than on the ipsilateral side, and a significant increase of rCBF during verbal stimulation [ANOVA, $F(1,8) = 19.41$, $P < 0.01$]. The control group showed a tendency towards greater activation in the contralateral side than in the ipsilateral side during verbal stimulation, although it did not reach the statistical significance threshold. The prelingually deaf group did not show laterality of rCBF changes in the primary auditory cortices during either sound stimulation. Compared with prelingually deaf subjects, subjects with postlingual deafness had a significantly greater increase in rCBF in the contralateral primary auditory cortex during verbal stimulation ($P < 0.05$, *post hoc* Scheffé's F test).

In the language association cortices, only the left superior temporal gyrus (Wernicke's area) showed a significant difference in the increment of rCBF between post- and prelingually deaf groups ($P < 0.05$, *post hoc* Scheffé's F test). The control group showed no significant differences compared with either deaf group in either Wernicke's or Broca's area.

Language comprehension

The comprehension of spoken sentences in the verbal stimulation condition was better in the postlingually deaf subjects than in the prelingually deaf subjects, as confirmed by the subjects after the PET study, but the accuracy could not be quantified. The accuracy of the vowel recognition test without lip-reading was 78.4±19.9% in postlingual and 41.8±12.8% in prelingual subjects (Table 1); the difference in scores between the groups was significant ($P < 0.01$, Student's t test). The speech tracking scores are listed in Table 1. Average hearing thresholds with the CIs were 50.7±5.1 dB in the postlingually deaf group and 50.0 ± 9.4 dB in the prelingually deaf group; the differences were not significant.

Discussion

Activation methods and analysis

The use of activation PET to study task-related changes in rCBF is well established in normal volunteers (Roland, 1993). In the present study, profoundly deaf subjects with CIs were investigated by activation PET during auditory stimulation. Although co-registration of PET and MRI demonstrated some activated foci in addition to primary auditory cortex and language cortices, we studied only three regions of interest. Cortical language localization has been investigated with intraoperative stimulation mapping (Ojemann *et al.*, 1988, 1989; Ojemann, 1991; Haglund *et al.*, 1994) and activation PET studies in normal volunteers (Petersen *et al.*, 1988; Wise *et al.*, 1991; Howard *et al.*, 1992; Zatorre *et al.*, 1992). The choice of location of regions of interest in our study is consistent with these studies for language association cortices in the left hemisphere. The statistical parametric mapping method (Friston *et al.*, 1990, 1991) might demonstrate areas of significantly increased rCBF in brain regions other than auditory association cortices, but variation in the side of CI placement would have diminished the intensity of activation in the primary auditory cortex when intersubject analysis was performed. Hence, the statistical analysis was performed on changes of rCBF measured in limited regions of interest. A larger number of patients in each group (postlingual, left CI; postlingual, right CI; prelingual, left CI; prelingual, right CI) might enable us to analyse the data with statistical parametric mapping in the future. However, the intrasubject comparison of rCBF changes between the resting condition and sound stimulation is a simple and useful method for assessing the efficiency of individual CIs (Naito *et al.*, 1995).

Resting condition

In the primary auditory cortex contralateral to the CI, baseline rCBF was significantly lower in the postlingually deaf group than in the prelingually deaf group and the control group. The higher baseline in the control group might be explained by the difference of the resting condition compared with that of the postlingually deaf group. The noise level in the PET scanning room was ~50 dB. The hearing subjects might have been stimulated by the surrounding noise despite their earplug, whereas the deaf subjects could hear no noise when their CIs were switched off (Naito *et al.*, 1995).

The higher rCBF in the primary auditory cortices in the prelingually deaf group than in the postlingual group might be explained by absence of exposure to auditory stimuli. Wanet-Defalque *et al.* (1988) reported higher glucose metabolism in the visual cortex of blind subjects than in normal subjects. They explained that some immature connections, normally disappearing as a result of visual experience, could persist in subjects with early visual deprivation, and could contribute to the higher level of ^{18}FDG uptake reflecting neuronal activity. Because the rCBF is known to be paralleled by the regional metabolic rate of glucose, the finding of a higher rCBF in the primary auditory cortex in the prelingually deaf patients is consistent with their explanation, as our prelingually deaf patients received very little, if any, auditory stimulation until the CI surgery.

Task conditions versus resting condition

Primary auditory cortex

Our results for the hearing subjects indicated that our method of using verbal stimulation could activate the primary auditory sensory area contralateral to the side of stimulation and the language association cortices in the left hemisphere. This is consistent with the previous PET studies of language activation in hearing subjects (Petersen *et al.*, 1988; Wise *et al.*, 1991; Howard *et al.*, 1992; Zatorre *et al.*, 1992). In the noise condition, however, very little activation was observed, even in the primary auditory cortices. Noise stimulation did not induce sensory activation, suggesting that abrasive sound stimulation might reorganize neuronal signals at a precortical level in normal subjects. The results of hearing subjects were not consistent with those of postlingually deaf subjects, whose contralateral primary auditory cortices were significantly activated by noise. Differences of rCBF in the resting condition, discussed previously, or the difference of stimulating apparatus between hearing subjects and deaf groups might be one reason for the weak activation in the hearing subjects. Another explanation is the different character of the noise. Zatorre *et al.* (1992) used intermittent noise bursts rather than a continuous signal for noise stimulation and reported the increase of rCBF in the primary auditory cortices. Intermittent noise bursts might provide greater neuronal excitation in the primary auditory cortices than continuous noise stimulation, as continuous sensory stimuli often fail to provide much neuronal excitation. Fox and Raichle (1984) showed that flash photic stimulation caused linear increase of rCBF in the primary visual cortex up to 7.8 Hz, declined with frequency increases beyond 7.8 Hz up to 60 Hz. They concluded that stimulus rate is a significant determinant of rCBF response in the visual cortex.

As for the deaf subjects, stimulation of the cochlear nerve through the CI electrode is thought to be sufficient for cortical activation since we observed a >10% increase of rCBF in the primary auditory cortex with both verbal and noise stimulation in the postlingually deaf subjects and the intensity of stimulation was similar for all the subjects. In the postlingually deaf group, verbal stimulation caused a significant increase of rCBF in the contralateral primary auditory cortex, as was also shown in the hearing subjects. This result suggests that almost normal neuronal function of the primary auditory cortex remains after hearing loss in the postlingually deaf subjects.

Activation of the primary auditory cortex by verbal stimulation was significantly greater than that caused by white noise stimulation in the postlingually deaf group, which indicates that neuronal signals from the CI system induced by the sound of speech provide more intense activation than those induced by noise. This difference could also be explained by the difference in attention required to perform the tasks. Our verbal condition required sentence comprehension and silent repeating, which requires much more attention than the noise condition. Attention to sensory modality is known to increase the cortical rCBF. Meyer *et al.* (1991) showed that the increment of rCBF in the primary somatosensory cortex during vibrotactile stimulation was greater when the subjects attended to the stimulus, compared with when they were simultaneously engaged in a distraction task. Our result is not consistent with the report of Herzog *et al.* (1991), in which the primary auditory area showed only minor differences of activation between white noise and sequential words stimulation. Although direct comparison between our task and that of Herzog *et al.* (1991) is not possible with regard to attention, difference in attention could be one possible explanation.

In the prelingually deaf group, the contralateral primary auditory cortex was only weakly activated during verbal stimulation. The higher baseline rCBF in prelingual deafness than in postlingual deafness might account for the smaller increase in rCBF as discussed previously. Considering different behaviour of the primary auditory cortex in the pre- and postlingually deaf groups, we suggest that processing in the primary auditory cortices is experience dependent.

Language association cortices

A significant increase of rCBF was observed in Wernicke's and Broca's areas during verbal stimulation in each group. The activation in Broca's area is another difference between our findings and those of Herzog *et al.* (1991). They attributed the absence of activation in Broca's area to the subjects' silence during the investigation. In the present study, the subjects also remained silent, but repeated the given sentences silently. This task condition is considered to lead to the activation of Broca's area (Wise *et al.*, 1991), although the task performances could not be measured during the PET studies.

The activated areas were, even in prelingually deaf subjects, the same in their location and intensity as in the hearing subjects, indicating that no shift of auditory associated language cortices had occurred after the prolonged absence of sound. Further, language dominance existed in the left hemisphere regardless of the side of the CI, or the kind of deafness. These results suggest that the dominant hemisphere for language might be determined not only by acquiring auditory language skills but also by other factors such as lip-reading or sign language, or might be congenitally determined.

Neville *et al.* (1994) reported that hearing subjects born to deaf parents demonstrated asymmetric activation of the left inferior frontal gyrus, the inferior frontal sulcus, the precentral sulcus and the superior temporal sulcus when reading English sentences, and that congenitally deaf subjects showed asymmetric activation of the inferior frontal gyrus, inferior frontal sulcus and precentral sulcus in a functional MRI study. They also reported that compared with hearing subjects, deaf subjects reading English sentences had less consistent activation of the left superior temporal sulcus, and viewing American sign language resulted in less laterality in the superior temporal sulcus and precentral sulcus. Neville *et al.* (1995) also reported that additional areas activated by American sign language but not by English sentences in deaf subjects included the left dorsal parietal cortex, the right superior temporal sulcus and the right posterior lateral sulcus. Their results with reading and sign language stimulation are not necessarily consistent with our results obtained with verbal stimulation because their stimulation was visual, and our auditory stimulus was considered to stimulate the superior temporal sulcus more intensely. Further, their finding that visual verbal stimulation could activate the superior temporal sulcus and inferior frontal gyrus in the left hemisphere of hearing subjects appeared to justify activation of these areas for evaluating verbal ability of deaf subjects. Because our deaf subjects had no organic lesions in those areas, it is unlikely that reorganization of language cortices occurred because of space-occupying lesions (Haglund *et al.*, 1994). In summary, we suggest that language laterality is not dependent on early auditory experience.

Increment of rCBF and language comprehension

Although the hearing thresholds of subjects with CIs were not significantly different in the two deaf groups, the prelingually deaf subjects showed less activation than the postlingually deaf subjects in the primary auditory and auditory associated language cortices with the same stimulation, which is consistent with the report of Neville *et al.* (1994) who suggested that the auditory associated brain activity might be diminished by the longer period of hearing loss in the prelingually deaf subjects. Another possible cause of reduced activation in the prelingually deaf group was the time of deafness onset. Absence of auditory verbal stimulation during acquisition of language skills might have suppressed the neuronal activities of auditory associated language cortices.

The difference in the intensity of activation in language cortices between post- and prelingually deaf subjects may be attributed to the recognition of hearing language, because in our study the comprehension of given sentences was better in postlingually deaf subjects than in prelingually deaf subjects. The accuracy of the vowel recognition test was significantly better in the postlingually than in the prelingually deaf group, and the speech tracking scores indicated better comprehension of spoken words in the postlingually deaf group. The comprehension of spoken language was not necessarily related to the time after CI surgery (Table 1), and recovery in hearing language was better in the postlingually deaf group. These results suggest that the intensity of activation in the auditory associated language cortices with verbal stimulation is consistent with the ability for heard language recognition, and the activation PET study can provide objective information on the cortical response to CI stimulation of the auditory nerve. The co-registration of PET and MRI with region of interest placement is a feasible method for the clinical assessment of individual CI efficiency.

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