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Neural changes associated with speech learning in deaf children following cochlear implantation

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Brain plasticity was investigated, which underlies the gaining of auditory sensory and/or auditory language in deaf children with an early onset deafness after cochlear implantation (CI) surgery. This study examined both the glucose metabolism of the brain and the auditory speech learning using ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET) and the Central Institute of Deaf (CID) test, respectively, both before and after the CI surgery. In a within analysis comparing the pre-CI and the post-CI PET results, CI itself resulted in an increase in the glucose metabolism in the medial visual cortex, the bilateral thalamus, and the posterior cingulate. Compared with the normal hearing controls, the brain activity of the deaf children was greater in the medial visual cortex and bilateral occipito-parietal junctions after the CI. The better speech perception ability was associated with increases in activity in the higher visual areas such as middle occipito-temporal junction (hMT/V5) and posterior inferior temporal region (BA 21/37) in the left hemisphere and associated with decreases in activity in the right inferior parieto-dorsal prefrontal region. These findings suggest that the speech learning resulted in a greater demand of the visual and visuospatial processings subserved by the early visual cortex and parietal cortices. However, only those deaf children who successfully learned the auditory language after CI used more visual motion perception for mouth movement in the left hMT/V5 region and less somatosensory function in the right parieto-frontal region.
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Introduction

The artificial cochlear implant in inner ear can restore the auditory sensation even if this sensation was lost for a long time or deprived of from birth due to the pathology in the peripheral auditory organ. Deaf subjects, who lost their auditory function after they had acquired normal auditory language function (postlingual deaf or late onset deaf), recover their hearing ability following a successful cochlear implantation (CI) often to the extent that they can conduct a telephone conversation. In these postlingual deaf subjects following CI, the visual regions as well as the brain regions located within and outside the classical language associated areas are recruited in an experience-dependent manner during auditory language processing (Giraud et al., 2000, 2001a,b). CI provides an excellent model to understand the brain plasticity underlying the regaining of the auditory speech after prolonged deprivation.

Unlike the postlingual deaf, the results of CI are inconsistent in deaf subjects who lost auditory function either before or around the time of the development of normal language. Following CI, some but not all pre/perilingual deaf subjects gain the function of hearing speech although most gain the function of hearing environmental sounds. This suggests that hearing sounds does not automatically guarantee the acquisition of understanding speech in deaf children who have yet to learn auditory language. In these pre/perilingual deaf patients, the chronological age was one of the critical factors that determined success of the auditory language rehabilitation following CI. The younger the deaf patients are at the time of CI, the better the outcome of the CI (Oh et al., 2003). Because of this, CI surgery is more likely to be practiced only on younger deaf children than on older deaf subjects.

Glucose metabolism is decreased in auditory and related cortex in the younger deaf children or in the postlingual deaf subjects. However, the extent of the cortical hypometabolism is smaller in older subjects with early onset deafness. The hypometabolism of the primary and secondary auditory cortex was related with the extent of the later recovery of speech perception following CI (Lee et al., 2001). Restoration of glucose metabolism of auditory cortex made successful post-CI speech learning unlikely to occur if the profound deaf children got older before the CI. This phenomenon was suggested to represent preoperative cross-modal plasticity against auditory speech learning after the CI.

In the understanding of the CI-induced brain plasticity in these early onset deaf children, there exists more than one type of brain plasticity. One is associated with the regaining of the auditory sensory function and the other with the belated learning of the auditory language overcoming possible pre-CI reorganization of

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cortical neural networks. To elucidate this plasticity, the brain activity was examined using ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET) imaging where the "resting-state" regional cerebral glucose metabolism was measured. These young children were too young to be examined with the repeated exposure of a radioactive substance during a $H_2^{15}O$ PET study. The possibility of using fMRI was also excluded due to the metallic components of the cochlear implantation in the head.

Using FDG-PET, this study investigated the functional neuroanatomy underlying (a) (re)gaining of auditory sensation and (b) acquisition of auditory language. In particular, this study was interested in two different but related questions: (a) what happened in the brain activity in the deaf children after the CI compared to before the CI, and (b) which brain regions were associated with the successful achievement in the auditory speech perception/learning following the CI. The pre/perilingual deaf children who underwent artificial cochlear implantation were enrolled in this study.

Methods

Participants

^{18}F-FDG positron emission tomography (PET) was performed for deaf patients as a clinical presurgical evaluation in Seoul National University Hospital. PET results were used for reference during parental consultation about outcome prediction and rehabilitation process in our institute since previous researches from our group indicated a significant relationship between preoperative cerebral metabolic status and CI outcome (Lee et al., 2001; Lee et al., submitted for publication). Sufficient and detailed explanations for the procedure, risk, and purpose/benefit of the FDG-PET study were given to the parents of the child deaf patients with the other presurgical test procedures. Among the 91 pediatric deaf patients whose parents allowed the FDG-PET as a presurgical evaluation, only 8 patients (3 female and 5 male; 3 left CI and 5 right CD) were followed up both with the positron emission tomography (PET) and Central Institute of Deaf (CID) test after CI.

For these eight deaf patients, the PET scan and Korean version CID test were taken twice, once before (average age = 5.7 years) the CI and once after (average age = 8.24 years) the CI. The time of the follow-up PET study was on an average 1.2 years after the CI surgery and an average 2.5 years since the pre-CI PET scan. Four of them were congenitally deaf (prelingual) and the other four were perilingual deaf who had lost their hearing/speech function around the time of language acquisition. The CID test scores of these deaf children were all 0 before the CI, and the average CID score was 42 ± 38 (range from 0 to 96) around the time of the post-CI PET scan. The detailed profiles of the patients were listed in Table 1. Prelingual deaf and perilingual deaf were not separately analyzed not only due to insufficient number of patients in this study but also due to reported statistical insignificance in the age of deaf onset as a variable affecting CI outcome (Miyamoto et al., 1994; O'Donoghue et al., 2000). One patient with autism was also included in this study in spite of a possibility of difficulty in developing communication skill even after CI.

FDG PET scans were acquired from 20 right-handed adults as the normal hearing control group (mean age = 25.2 ranged from 19 to 42 years old; 15 male and 5 female; average education = 15.4 years; self-reported right-handed).

^{18}F-FDG positron emission tomography scans

The ^{18}F-FDG positron emission tomography (PET) scans were performed using an ECAT EXACT 47 PET scanner (Siemens-CTI, Knoxville, USA). The intrinsic resolution was 5.2 mm FWHM (full width at half maximum) and the images were simultaneously collected from 47 contiguous planes (thickness of 3.4 mm) with a 16.2-cm longitudinal field of view. Before FDG administration, transmission scanning was performed using three Ge-68 rod sources for the attenuation correction. Forty minutes after injecting the 370 MBq ^{18}F-FDG, the static emission scans were acquired for 20 min in the resting state under the normal environmental noise of the scanner room without an ear plug. The transaxial images were reconstructed using a filtered back-projection algorithm with a Shepp–Logan filter at a cut-off frequency of 0.3 cycles/pixel as a 128 × 128 × 47 matrices of size 2.1 × 2.1 × 3.4 mm.

Analysis of PET scans

Within group comparison

Using SPM99, the PET images were spatially normalized with a standard SPM template brain and spatially smoothed (16 mm

Table 1
Details of the patients profile

Pt. no.	Deaf type	Sex	Deaf onset	CI age (years)	PET scan age		Duration after CI (year)[a]	CID scores[b]		CI side	Number of channels
					Pre-CI	Post-CI		Pre-CI	Post-CI		
1	pre	M	congenital	13.2	11.2	15.3	2.1	0	7	L	22
2	pre	M	congenital	7.4	6.3	8.5	1.1	0	67	R	22
3	pre	F	congenital	9.8	8.3	11.3	1.5	0	0	L	22
4	pre	M	congenital[c]	7.3	6.0	8.7	1.3	0	33	R	24
5	peri	F	1 year, 10 months	3.7	2.1	5.4	1.7	0	83	L	22
6	peri	M	2 years, 10 months	4.0	3.1	4.8	0.9	0	96	R	24
7	peri	M	11 months	4.5	3.6	5.3	0.9	0	0	R	24
8	peri	F	2 years, 3 months	6.1	5.7	6.6	0.5	0	50	R	24
Average				7.0	5.8	8.2	1.2	0	42		

[a] At the time of Post-CI PET since the CI.
[b] Maximum score = 100.
[c] Autistic.

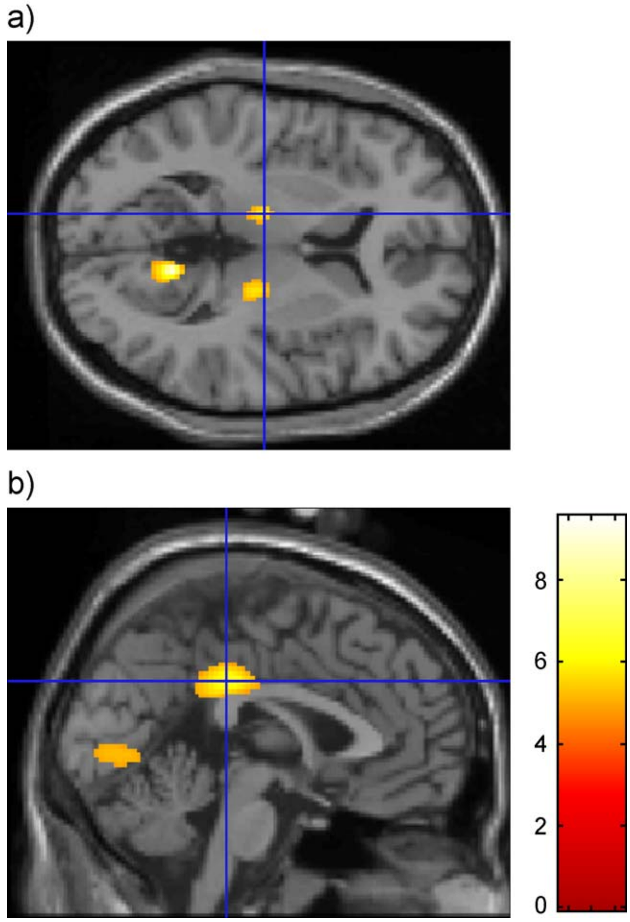

Fig. 1. The glucose metabolism increased after CI (post-CI) relative to that before (pre-CI) in several brain regions including the bilateral ventral posteromedial thalamic regions (a), the medial visual area, and the posterior cingulate gyrus (b) in the deaf children.

FWHM), once it was converted to Analyze format. The CI-induced changes were examined by directly comparing the post-CI PET with the pre-CI PET of the individual deaf patients using a paired t test. A cluster composing of contiguous 10 voxels, which exceeded a threshold of uncorrected $P < 0.001$ ($T = 4.79$), was considered significant.

Between-group comparison

Two between-group analyses were performed with a fixed effect model, one between the pre-CI PET and the normal hearing controls and the other between the post-CI PET and the same normal hearing control group using SPM99. Since the extent of the hypometabolism was too extensive to report here in detail given the scope of this paper (part of results reported elsewhere, Lee et al., 2001), mainly the hypermetabolism of the deaf children compared with the normal controls are reported in this study. Threshold of the corrected $P < 0.05$ was applied to detect any significant group differences.

Correlation analysis

Each patient's image was spatially normalized in a two stage process. In the first stage, each PET image was normalized into the standard SPM (SPM99) PET template from Montreal Neurological Institute (MNI) brain. Then, we computed an average image across all the normalized images. In the second stage, each once-normalized image was again normalized for the second time to the average normalized image computed from the first 16 normalized images (a study specific template). This two-stage normalization process was performed as a way to improve the consistency in the registration among the images because our PET images were from children whereas the SPM99 PET template image was from adults. Following the two-stage normalization, all the images were normalized by global counts using proportional scaling and spatially smoothed with 16 mm FWHM, with which the mean count of the FDG uptake in whole gray matter in each PET image would be 50. Each pair of PET images of individual patients, that is, a pre-CI

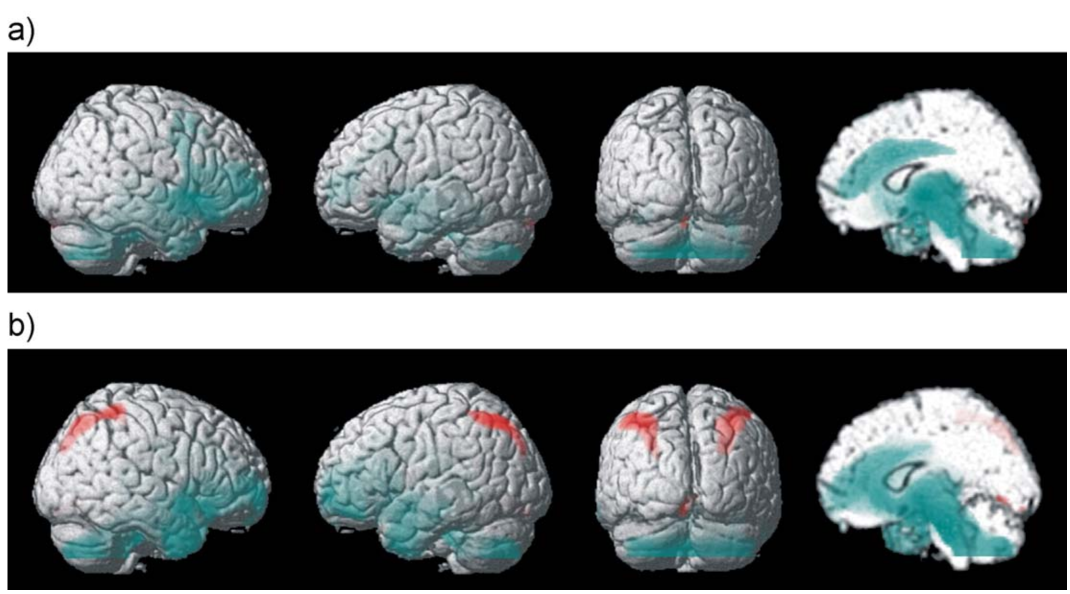

Fig. 2. Brain regions showing significantly (corrected $P < 0.05$) different brain activity in the profound deaf children ($n = 8$) compared to the normal hearing adults control (NC) group ($n = 20$). Rendered brain showed hypermetabolic (shown in red) and hypometabolic (shown in the blue) regions in the deaf children (a) before CI surgery (pre-CI PET) and (b) after CI surgery (post-CI PET) relative to the NC group.

Table 2
Brain regions showing the changes in the glucose metabolism following cochlear implantation

	L/R	Brain area	Brodmann area	MNI coordinate			T value[a]	Cluster size[b]
				x	y	z		
Increase	M	Lingual gyrus	18/19	12	−56	4	9.51	631
	M	Cuneus	17	−10	−94	−6	5.45	(included)
	M	Posterior cingulate	31/23	0	−32	32	6.89	550
	L	Ventral posteromedial thalamus		−14	−16	6	6.45	67
	R	Ventral posteromedial thalamus		22	−20	4	6.21	98
Decrease	M	Rectus/orbitofrontal gyrus	11	10	22	−14	7.45	224
	R	Orbitofrontal gyrus	11	−6	20	−16	5.85	13

[a] Local maxima of clusters. Each cluster was composed of more than 10 significant voxels ($P < 0.001$ uncorrected, $T = 4.79$).
[b] Number of voxels. Voxel size is 2 × 2 × 2 mm. L: left; R: right; M: medial.

PET image and a post-CI PET image, was adjusted within the pair with grand mean scaling. Following this preprocessing, a difference image for each patient was composed by subtracting the pre-CI PET image from the post-CI PET image.

The difference images from each deaf patient were subjected to a second-level analysis where a correlation was computed in a voxel-wise manner using SPM99. The correlation was computed between the individual difference images and the individual differential CID scores. The relationship between the changes in the CID scores (ΔCID) and the changes in the glucose metabolism (ΔFDG uptake) between the two PET scans of each patient was assessed with a random effect model where the subject variable was used as a random factor. Here the ΔFDG uptake and the ΔCID were defined as follows: the ΔFDG uptake = post-CI FDG uptake (from post-CI FDG-PET) − pre-CI FDG uptake (from pre-CI FDG-PET); ΔCID = post-CI CID score − pre-CI CID score. Since all the deaf children scored zero before CI surgery (pre-CI CID score), ΔCID was actually the score of the post-CI CID.

All the regions consisting of 10 contiguous voxels that exceeded a rather lenient threshold of an uncorrected $P < 0.01$ ($T = 3.14$) are reported here as significant in this analysis. A less stringent threshold was used since this analysis was a second-level analysis with a limited number of subjects ($n = 8$). The local maxima of a significant cluster were reported as the coordinates of the MNI template against which the first stage of the spatial normalization was performed using SPM99. Both a positive and a negative correlation were reported. The statistical parametric map, that is, SPM {t} from the voxel-based t statistics, was rendered on the average template brain provided in SPM99. An uncorrected $P < 0.05$ threshold was used for display purpose. The Talairach and Tournoux Atlas (1988) was used to localize the significant clusters and Dimitrova et al. (2002) was referred to for cerebellar localization.

Results

Behavioral measure

The CID test reflects both the ability to repeat aurally what the patients heard as well as the ability to perceive the speech sounds. The average CID score of the eight deaf CI patients after CI was 42 (standard deviation = 38; ranged from 0 to 96; maximum 100). The younger the children were at the time of CI surgery, the higher the CID scores were achieved. However, the correlation between the age of the implantation and the CID score did not reach statistical significance ($P > 0.1$, $R^2 = 0.265$). This study did not identify any statistical differences between the sex, the side of the CI, or the type of device used (or number of device channel).

PET results

Comparison between the pre-CI PET and the post-CI PET of the deaf children

FDG uptake was increased in the medial visual regions including the lingual gyrus extended to the medial posterior region of the cuneus following the CI. Additional increases were also found in the bilateral ventral posteromedial thalamic regions (Fig. 1a) and the posterior cingulate region (BA 31/23) (Fig. 1b) in the post-CI PET compared to the pre-CI PET. FDG uptake was decreased in the rectus gyrus and orbitofrontal gyrus bilaterally in the post-CI

Table 3
Brain regions showing a greater glucose metabolism before or after the CI in deaf children than in normal hearing adults

L/R	Brain area	BA	Before CI > NC					After CI > NC				
			MNI coordinates			T*	Cluster[a]	MNI coordinates			T*	Cluster[a]
			x	y	z			x	y	z		
M	Lingual G.	17/18	0	−92	−22	6.37	61	−2	−88	−14	5.60	133
								−2	−76	−8	5.50	
								6	−72	−4	5.43	
R	Superior parietal G.	7	46	−52	62	5.40	23	30	−72	50	7.17	1213
								38	−44	60	6.22	
L	Superior parietal G.							−32	−68	52	7.08	1090

[a] Cluster size: number of voxels. Voxel size is 2 × 2 × 2 mm. G: gyrus; M: medial; L: left; R: right.
* T value: local maxima of clusters. The height threshold corrected $P < 0.05$, $T = 5.26$ was applied.

Table 4
Brain regions showing correlations between the changes in the glucose metabolism and the CID scores after cochlear implantation

	L/R	Brain area	Brodmann area	MNI coordinate			P value*	Cluster size[a]
				x	y	z		
Positive	L	middle occipito-temporal junction	37	−42	−70	4	<0.003	95
	L	inferior posterior temporal region	21/37	−66	−44	−18	<0.006	39
	L	cerebellar deep nucleus		−10	−52	−34	<0.007	19
Negative	R	inferior parietal/dorsolateral prefrontal cortex	40/9/44	54	−30	30	<0.001	3240
	R	fusiform gyrus	18	40	−94	−28	<0.003	163
	R	middle occipital gyrus	37/19	66	−72	−12	<0.006	91

* Local maxima of clusters. Each cluster was composed of more than 10 significant voxels ($P < 0.01$, uncorrected, $T = 3.14$).
[a] Number of contiguous significant voxels. Voxel size is 2 × 2 × 2 mm. L: left; R: right.

PET compared to the pre-CI PET. The MNI coordinates of the local maxima in the significant clusters are reported in the Table 2.

Comparison with normal hearing control adults

Before the CI surgery, only limited regions in the posterior medial lingual cortex (BA 18) and in the right superior parietal region were hypermetabolic in the brain of the deaf children compared to the normal hearing adult control group (Fig. 2a, Table 3). After the CI, the extensive hypermetabolic regions were found both in the left and right occipito-parietal regions as well as in the posterior medial region of the lingual gyrus (Fig. 2b), although the age differences between deaf and normal subjects were reduced by the time of the post-CI PET scan.

As expected, the FDG uptake in the extensive brain regions including the thalamus, brain stem, cingulate gyrus, and inferior prefrontal regions were significantly lower than in the normal

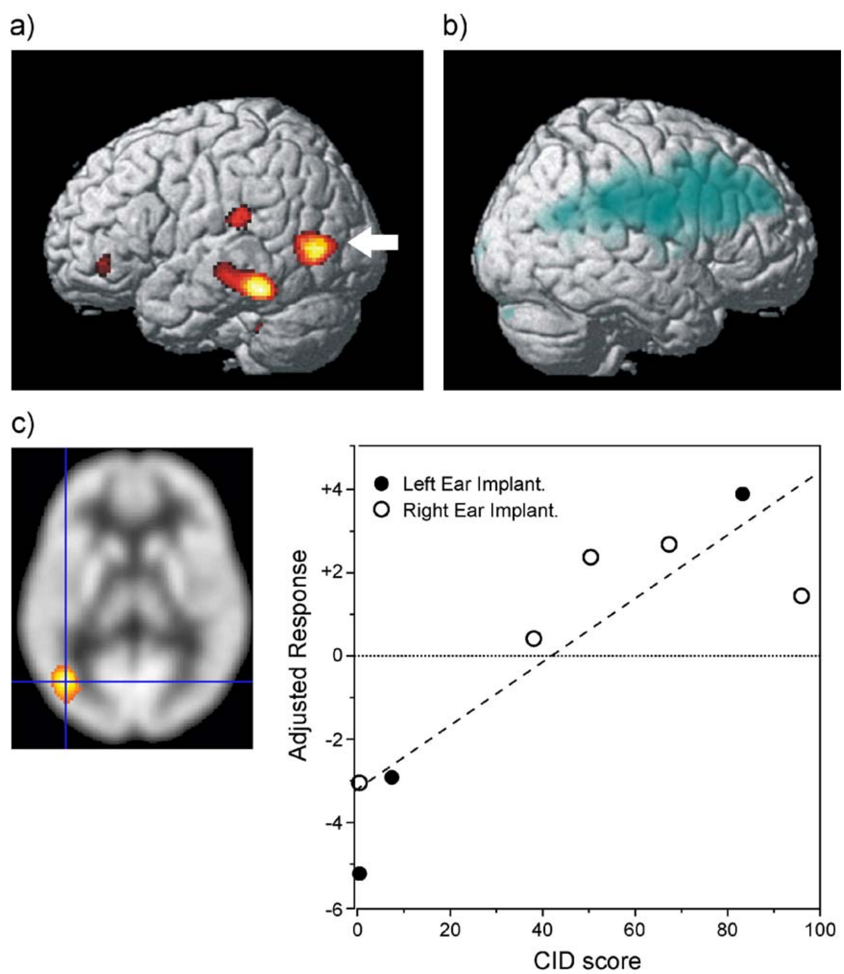

Fig. 3. (a) Brain regions with a positive correlation between the increases in the FDG uptake and the increase in the auditory speech perception ability after CI. The white arrow indicates the left occipito-temporal junction. (b) The brain regions with a negative correlation between the FDG uptake changes and the CID score. (c) The correlation between the auditory perception ability measure by the CID score and the relative increase in the FDG uptake from the pre-CI relative to the post-CI at the left occipito-temporal junction. Each patient's data was indicated according to the side of the CI ear (left ear = filled; right ear = empty).

adults (Fig. 2). These hypometabolic regions could reflect both the age difference between the deaf and normal groups and the deaf-specific decrease in brain activity according to our previous findings on the developmental changes in brain FDG uptake (Kang et al., 2003). Though we did not report the hypometabolic regions of the deaf children in detail in this paper, the extent of the brain regions showing group differences were shown on the rendered brain in comparison to the normal adults in Fig. 2. The hypometabolic regions of the deaf children compared to the normal controls are shown in blue and the hypermetabolic regions are shown in red.

Covariate analysis with the CID score increase

The changes in the FDG uptake following the CI were compared with the level of speech perception ability to localize the brain regions where the FDG uptake increase was positively correlated with the improvement in speech perception. The CID score after CI was positively correlated with the increasing glucose metabolism in the brain regions such as the junction of the middle occipital and posterior temporal regions (BA 37), the inferior temporal region (BA 21), the deep nucleus of the cerebellum ($P < 0.01$ uncorrected). The inferior ventrolateral prefrontal region (BA 47), and the primary cortical region in the superior temporal gyrus also showed a trend ($P < 0.05$ uncorrected). Those regions were all found in the left hemisphere, and the MNI coordinates of the local maxima of a significant cluster are listed in Table 4. In particular, the linear relationship between the CID score and the changes in the regional glucose metabolism at the left middle occipito-temporal junction ($x, y, z = -42\ -70\ 4$) (Fig. 3a) is depicted in Fig. 3c. In this graph, each patient data point is shown in terms of relationship between the CID score (shown in X axis) at the time of the post-CI and the adjusted ΔFDG score (shown in Y axis).

There were also brain regions in which the CI-induced decrease of glucose metabolism was correlated with the greater level of speech perception. These brain areas were all in the right hemisphere including the right inferior parietal region (BA 41) extended to the dorsolateral prefrontal regions (BA 9, 44), the right posterior occipital region such as the fusiform gyrus, and the right middle occipital region (BA 37). These brain regions with a negative correlation were shown on the rendered brain in Fig. 3b.

Discussion

This study investigated what happened in the brain in the pre/perilingual deaf children when the auditory experience began after CI. Unlike other studies, this study compared the brain activity observed before CI with that after CI in the early onset deaf subjects. Firstly, the differences between the pre-CI PET and the post-CI PET were examined regardless the degree of the auditory speech learning after the CI. Caution was exercised in interpreting the results to distinguish the CI-induced brain changes from the developmental changes referring to our previous study upon the age-associated FDG changes in a large cohort of pre-operative deaf children (Kang et al., 2003). Secondly, the differences between the deaf children and the normal hearing subjects were examined using the pre-CI PET and the post-CI PET. Lastly, the changes in the brain activity were investigated more specific to children with a better speech perception following the CI. A significant positive correlation was investigated between the changes in the glucose metabolism (ΔFDG uptake) and the changes in the speech perception ability following CI (ΔCID). In the evaluation of speech perception, the deaf patients were asked to repeat words that they heard without seeing the speaker's lip movement.

Individual variation in the rehabilitation results of speech learning was great (0–96 in CID score) even though all the children experienced auditory sensation following the CI surgery. How their language acquisition in post-CI deaf children differed from the normal hearing children was questioned. In the normal hearing children, both the auditory and visual sensations were available from the very beginning of the language acquisition. If profound deaf children had developed their own speech perception before surgery based only on uncompromised sensory functions such as vision, the course of the auditory language acquisition of these deaf children following the CI must be very different from that of normal developing children.

The post-CI children might need to *match* the new auditory sensation with the preexisting facility of language/communication. They need to learn to use both the visual and auditory speech cue though their CI-derived auditory sensation is far from the normal audiological qualities. This matching requires extensive de novo *learning* in these children. This is the largest difference between speech learning of post-CI pre/perilingual deaf children and speech learning of the post-CI postlingual deaf subjects. The post-CI postlingual deaf subjects already had their template for speech sounds and had mastered the spoken language before their loss of hearing. In that CID is measuring not only the speech hearing, but also the ability to repeat the words they hear without seeing the lip movement, the children with high CID scores must have been able to generate intelligible speech sounds by learning to use not-so-perfect auditory sounds. This learning requires more than just mimicking the sounds. However, unlike the lip reading without sound in profound deaf, the post-CI children must have heavily used the lip movement cues, which synchronize with newly coming auditory sensation. To learn how to use lip movement cues in synchrony with the speech sounds, there must be brain plasticity after CI surgery.

In a series of recent neuroimaging studies (Giraud et al., 2000, 2001a), the integration of audio-visual inputs in the auditory speech perception was crucial for the successful speech perception in post-CI deaf subjects. In our study, the gaining of auditory sensation resulted in a greater demand of the visual and visuospatial processings, subserved by the early visual cortex and parietal cortices. This finding agrees with the findings of Giraud et al. (2000, 2001a) despite the differences in the imaging modality (FDG-PET vs. the $H_2^{15}O$-PET study) or the deaf patient group (pre/perilingual deaf children vs. postlingual deaf adults).

CI-induced changes in brain activity and aging effects

An increased activity following the CI was found in the bilateral ventral posteromedial thalamic regions as well as in the posterior cingulate and the medial visual region. According to our previous finding (Kang et al., 2003), the thalamic nuclei were the regions showing linear increases in the FDG uptake during the development of deaf children. The increase of activity in these particular thalamic regions in the post-CI scan might be the result of aging/maturation between the two PET scans (separated by average 2.45 ± 1.03 year). However, it is interesting to note that only the specific restricted regions of the thalamus showed the post-CI increases in FDG uptake. Under the given resolution of PET, these bilateral regions would be a junction of the ventral posterior medial (VPM) and the ventral posterior lateral (VPL) thalamic regions. The VPM thalamic region is known to be involved with the somatosensory relay from the head while the VPL involves the other body parts. The clinical literature suggests that lesions in the junction of the VPM and VPL thalamic regions could cause a syndrome of sensory disturbances in the corner of mouth and the palm of the hand, which is known as cheiro-oral syndrome (Shintani et al., 2000). It is possible that the CI could have enhanced the somatosensory processing from the mouth region due to an increase in aural–oral communication in these children.

This study also found a brain region, which showed a reduction in glucose metabolism following the CI, namely the bilateral (more strongly in the right side) rectus gyrus/orbitofrontal region in the frontal lobe. However, because this region overlapped with the region that showed a significant reduction in the FDG-PET uptake as the deaf children grew older without CI surgery (Kang et al., 2003), the FDG uptake decrease in these regions at the time of post-CI PET relative to the pre-CI PET appeared to be an artifact of the aging effect.

Increased activity in medial visual regions after CI compared with pre-CI

The most significant increase in FDG uptake following the CI was observed in the medial visual regions (lingual gyrus and cuneus). Before the CI compared to normal hearing adults, hypermetabolism of the medial early visual region was also found in the deaf children, but with greater extent after the CI. The recruitment of the early visual region during speech comprehension was well documented in the rehabilitated postlingual deaf patients following the CI (Giraud and Truy, 2002, Giraud et al., 2001). Despite the difference between the imaging modalities ($H_2^{15}O$ PET and FDG-PET) and between activation ($H_2^{15}O$ PET) and baseline (FDG-PET) studies, this early visual region increased the activity after the CI.

However, this increased brain activity was observed in the post-CI deaf children regardless of their individual differences in auditory speech hearing ability. This study did not find any evidence that the brain activity in this early visual area was correlated with the patient's auditory speech hearing ability. The increased activity in the visual region could be explained as showing an increased cross-modal plasticity or an increased demand for a visual cue parallel with the increasing new but not-so-perfect auditory sensation from the artificial cochlea.

Increased hypermetabolism in parietal cortex of the deaf children after CI relative to the normal hearing controls

Any group difference observed after the CI compared with normal controls, which became greater in comparison to the group differences observed before the CI, might indicate the brain plasticity associated with the use of CI. The hearing experience would reduce the difference between the deaf children and the normal hearing controls. However, using the artificial cochlear device might require further brain regions than the normal hearing people, showing increased brain activity following CI. Because of this, this study aimed to investigate the CI-associated changes in hypermetabolism rather than hypometabolism.

This study found an extensive increase in brain activity in not only the early visual region but also in the bilateral parietal region. The activity of the occipito-parietal region was greatly enhanced bilaterally in the deaf children after CI compared to the normal hearing adults. With further examination with a lenient threshold (uncorrected $P < 0.001$, ext = 10), it was noticed that these regions had been slightly hyperactive even before the CI. The hypermetabolism found in these areas before the CI existed particularly in the right superior parietal region. Whatever the functions of these regions were, the demand for these functions could have increased after CI. Since the regions including the superior parietal regions were related to the visuospatial attention ("where pathway"), it seemed that the demand for visuospatial attention in the environmental space might have increased after the CI due to the lately available auditory information from the environmental space.

Better speech perception and increased activity in left middle occipito-temporal junction (BA 37) and posterior inferior temporal region (BA 21/37)

Those CI-induced brain changes discussed above were independent of the extent to which the post-CI deaf children could hear and repeat the words after the CI. The brain regions that were associated with the performance of the auditory speech perception test were different from the CI-induced brain changes regardless of speech hearing ability.

The post-CI enhancement in the glucose metabolism in the left middle occipito-temporal junction was correlated most ($P <$ 0.003, T = 4.60) with the higher CID scores. Note that the regional glucose metabolism increase was a relative term, that is, the greater glucose metabolism in the post-CI scan "relative to" the pre-CI PET scan. For those who succeeded well in learning how to perceive auditory speech, the left middle occipito-temporal junction (BA 37/19) was actively recruited along with the left inferior temporal region (BA 21/37), but these areas were relatively inactive before the CI surgery. Those with relatively small amount of enhancement or with a reduction in the glucose metabolism in these areas after CI surgery failed to learn auditory speech.

Considering that the quality of sound delivered from the implanted artificial cochlea device is not as perfect as sound heard by a normal hearing person, the increased activity in these higher visual regions for motion processing might indicate a greater demand of visual processing. The post-CI children who learned successfully to hear speech might have utilized the visual cues to enhance the auditory perception of speech. Left middle occipito-temporal junction (BA 37) was within the well-known human MT/V5 area, which was associated with visual motion processing in humans (Dupont et al., 2003; Zeki et al., 1991) or tactile motion processing (Bundo et al., 2000; Hagen et al., 2002; Watson et al., 1993). In post-CI deaf children, any visual motion areas associated with the auditory speech perception might represent watching the mouth/facial cue movement of the speakers.

Recently, a neuroimaging study showed that hMT/V5 or BA 37 regions [left ($x, y, z = -46\ -69\ 4$) or right BA 37 ($x, y, z = 46\ -61\ 4$)] were also involved in watching the mouth movement (gurning) relative to the fixation or relative to speech (lip) reading (Campbell et al., 2001). In pre/perilingual deaf children with CI, watching mouth movement might be very important for speech learning because they need to pay more attention to the mouth movement to enhance their imperfect auditory sensation. Unlike normal hearing children, in post-CI deaf children, the integration of auditory speech and visually presented objects (cross-modal integration) will be critical.

However, watching mouth movement in the deaf children may not necessarily be the same as silent speech reading in normal subjects. In neuroimaging studies of normal subjects (Campbell et al., 2001), the left posterior superior temporal sulcus (STS) rather than the hMT/V5 area was responsible for speech reading. In profound deaf subjects, we observed increased activity in hMT/V5 area. Activity of lower level than STS would have been necessary for successful addition of new not-so-perfect auditory information to visual cues. Silent speech reading itself could be a prerequisite skill from which the further development of speech learning may occur. On the other hand, silent speech reading might be a previous communication skill from which the patients have to wean away to increase the efficacy of auditory speech processing.

In addition to the left middle occipito-temporal junction, we observed the same types of metabolic changes in the left posterior ventral inferior temporal region (BA 21/37). This region is considered as one of the higher-level visual processing areas, which is part of the ventral visual pathway ("what pathway"). This cortical region was located slightly lateral to the BA 37 region, which was reported to be a multimodal language region (x, y, z = −40 −38 −16) in the ventral pathway where activation was observed in response to the words relative to a nonword letter string in sighted subjects, late-blind and congenitally blind, despite the different modality used (visual and tactile) (Buchel et al., 1998).

Speech perception should be related with an ability to read words. Recent study demonstrated the left visual word form area (VWFA) in the occipito-temporal junction (Cohen et al., 2003). However, due to the lack of information regarding reading skill development in our patient group, we could not test the relationship between reading skill and speech perception, or reciprocal influences of the two functions before and after the CI. Among the three youngest children of our study, only two (patient 5 and 6 but not patent 7) were those with best outcomes. The age of the post CI PET in those two children was a little below (5.4 and 4.8 years old, respectively) than the age of formal schooling in normal children (6 years old). Therefore, it is unlikely that those with better CI outcome was associated with Korean alphabet learning, which in turn increased the glucose metabolism either in the left occipito-temporal junction or the left posterior inferior temporal region. However, the reading/writing skill is certainly one factor that should be closely examined in future studies.

Development of phonological grammar should be also considered. The development of speech perception can be associated with the phonological grammar with which acoustic sounds were combined to words or phrase. Recent data indicated that phonological grammar involves the left superior temporal and the left anterior supramarginal gyrus (Jacquemot et al., 2003). However, none of those regions were found to show significant correlation with CID score increases after CI in our study.

The early auditory cortex in the left superior temporal region might be also related with the post-CI language development. With the lower threshold (uncorrected $P < 0.05$), we found the region in the primary auditory cortex (BA 41; x, y, z = −36 −28 14) showing a positive correlation. This indicates that auditory processing must have recovered more in good learners but less in the poorer learners. The exact localization was difficult probably due to (1) the low spatial resolution of FDG PET, (2) the two step spatial normalization procedures, and (3) no available MRI anatomy scan in those CI patients. However, this study estimated the localization of a significant cluster in the primary auditory cortex, near the Heschl's sulcus (BA 41). The same difficulty was met in the localization of the cluster in cerebellar deep nucleus. This deep nucleus appeared to be the left dentate nucleus, which was part of learning-related circuit.

No significant positive correlation was found in the right auditory region nor any brain region in the right hemisphere. In the right hemisphere, a rather distinctive negative correlation was found between the magnitude of the FDG uptake changes and the speech perception ability after the CI (see Fig. 3b).

Greater reduction in the right parieto-frontal activity in better speech learners

Poor learners had a rather enhanced glucose metabolism following the CI compared to the pre-CI in the inferior parietal and dorsolateral prefrontal regions in the right hemisphere. The enhanced glucose metabolism in the parieto-prefrontal region in the right hemisphere could have been associated with more visuospatial processing in these poor learners. The deaf children with a poorer outcome after CI might have depended more on the visuospatial function subserved by the right inferior parietal–dorsolateral prefrontal network, while those with a better outcome might have depended less. Cortical metabolism in the right parieto-frontal cortex was reduced more in better speech learners. However, it is premature to state whether these changes were the results or the cause of a poor CI outcome.

Limitation of this study

Since there was no normal pediatric PET template, this study normalized the PET images in two stages to improve the consistent registration between the pre-CI PET and the post-CI images, if necessary. This procedure might have resulted in slight off alignment from the MNI template and its coordinates. Despite the limits imposed by the small sample size, the spatial resolution of PET, and the pediatric brain without normal control problems, this study yielded insights on the nature of the brain plasticity, which was associated with the integration of newly acquired sensory information with linguistic facility in cochlear implantees.

This study did not present a detailed documentation of the type or nature of the language communication of these deaf children before and after CI. However, it is unlikely that they had been skilled lip readers or efficient signers as they were too young at the time of the CI surgery. A future research will be devoted to understand the types of verbal communication (lip reading or sign language) before surgery in relationship to the CI outcome and corresponding brain changes.

Conclusions

Our analysis on differential image data of pre and post-CI PET suggested that the brains of successful learners were different from those of the poor learners. In the successful learners, the left middle occipito-temporal junction was hypometabolic before surgery and became hypermetabolic in correlation with their mastery of speech learning. Since this area was within the brain region viewed as hMT/V5 (BA 37), the motion perception possibly from watching the mouth movement seems important in successful speech learning after the CI. We suggest that the middle occipito-temporal junction (BA 37) is involved in integrating the visual and the auditory speech cues (cross-modal integration) in the rehabilitation of pre/perilingual deaf children after the CI.

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