Auditory cortical activation and plasticity after cochlear implantation measured by PET using fluorodeoxyglucose

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Summary

The purpose of this study was to evaluate possible relationships between duration of cochlear implant use and results of positron emission tomography (PET) measurements in the temporal lobes performed while subjects listened to speech stimuli. Other aspects investigated were whether implantation side impacts significantly on cortical representations of functions related to understanding speech (ipsi- or contralateral to the implanted side) and whether any correlation exists between cortical activation and speech therapy results. Objective cortical responses to acoustic stimulation were measured, using PET, in nine cochlear implant patients (age range: 15 to 50 years). All the patients suffered from bilateral deafness, were right-handed, and had no additional neurological deficits. They underwent PET imaging three times: immediately after the first fitting of the speech processor (activation of the cochlear implant), and one and two years later.
A tendency towards increasing levels of activation in areas of the primary and secondary auditory cortex on the left side of the brain was observed. There was no clear effect of the side of implantation (left or right) on the degree of cortical activation in the temporal lobe. However, the PET results showed a correlation between degree of cortical activation and speech therapy results.

KEY WORDS: central nervous system, cochlear implant, neural plasticity, positron emission tomography

Introduction

F-18-fluorodeoxyglucose (FDG) is widely known as a marker used in positron emission tomography (PET) studies of the central nervous system (Ito et al., 1990; Kang et al., 2004; Green et al., 2005; Lee et al., 2005). FDG, being a glucose analog, is used to measure glucose metabolism in tissues. High concentrations of FDG taken up in the brain, reflecting intensive cell metabolism, are a reflection of active functional processes (Alavi et al., 1981; Grafton, 2000; Jacquemot et al., 2003). FDG has quite a long half-life of 111 minutes, which means that a patient can be tested only once during a given experimental condition when using this marker. Another radioisotope used to study the metabolic activity of the brain is water labelled with radioactive oxygen ($H_2{}^{15}O$). Its half-life is 2 minutes and it has been used in many international facilities (Herscovitch et al., 1983; Raichle et al., 1983; Truy et al., 1995). At the time of our study, $H_2{}^{15}O$ could not be used in Poland, and we therefore had to design a test using FDG. However, by selecting appropriate tasks, according to the assumptions of the experiment (tasks previously adopted in pilot studies on healthy people), we were able to obtain a clear picture on PET scans of the metabolic activity in the investigated areas of the temporal lobes. The purpose of this study was to evaluate possible relationships between the duration of cochlear implant use and the results of PET measurements in the temporal lobes performed while subjects listened to speech stimuli. We also investigated whether the implantation side (left or right) had a significant impact on the cortical representation of the functions related to understanding of speech (ipsi- or contralateral to the implanted side) and whether there was any correlation between cortical activation and speech therapy results.

Materials and methods

Nine cochlear implant patients (6 females and 3 males; mean age = 24.04 years; min = 15 years; max = 50 years) were included in this study. PET scans were performed in all the subjects and they all underwent speech therapy. They were all Polish and presented various degrees of proficiency in verbal communication in the Polish language. The patients were right-handed and all suffered from bilateral deafness (5 had prelingual and 4 post-lingual deafness), without additional neurological deficits. Five of them were implanted in the right ear and four in the left

ear. The Nucleus Freedom (Cochlear, Macquarie Park, Australia) implant was used in seven subjects and the Digisonic MXM (Neurelec, Vallauris, France) in two.

To study brain activity, through PET measurements of brain glucose metabolism, a Biograph 6 (Siemens) PET scanner and intravenous FDG were used (Ito et al., 1990; Johnsrude et al., 2002; Lee et al., 2005).

The patients were presented with a cognitive task, namely to discriminate, on the basis of one or more phonemic features, between paired words (Polish words) having different meanings or the same meaning (e.g. *mieć - miecz, dom - tom*).

The patients performed the task in the supine position with the elimination of visual stimuli: their eyes were closed and they wore blindfolds. They also wore headphones for the actual speech task. The patients first underwent a trial speech listening task, during which they used a potentiometer on the headphones in order to select a comfortable individual sound intensity. The actual speech listening task took about 40 minutes and immediately after it the patients underwent the PET scans, remaining in the supine position and with their eyes still closed. The PET data acquisition lasted for about 20 minutes. The subjects underwent three PET imaging trials: immediately after first fitting of the speech processor (activation of the cochlear implant) and one and two years later.

Using Syngo 2006 data analysis software (Siemens, Munich, Germany), the standardized uptake value (SUV) was calculated, from the PET images, for 71 specific brain areas. Instead of quantifying regional brain glucose metabolism in specific temporal areas and analyzing their mutual correlations, regional glucose metabolism was estimated by referring regional tissue concentration of FDG in analyzed areas to the mean whole brain concentration (SUV_{mean} = average value for the whole brain). The SUV_{mean} was calculated considering the average SUV for each of the 71 cortical areas analyzed. The individual mean SUV values for the right and left sides were also calculated; these values corresponded to the average SUV in the right and left hemispheres respectively, and they were calculated without taking into account the asymmetrical structures (the areas considered numbered 63 after subtraction of the asymmetrical ones). The level of activation of the symmetrical areas was then compared between the hemispheres.

The results were described using the arithmetic and statistical algorithms for a single condition (the first PET trial), with respect to subsequent PET trials. A mathematical calculation of the difference in SUVs between the left and right side of the brain was done giving, as a result, a percentage value that was subjected to further analysis. Thereafter, the percentage differences between the left and right side (L-R%) were calculated for the analyzed areas. A positive L-R% result indicated a preponderance of activation on the left side, while a negative value indicated the right side to be more active. In accordance with the left-sided model of the brain for right-handed subjects, it was assumed that the predominant areas activated during the speech perception in the patients participating in this study would be on the left side of the brain. This aspect was also evaluated.

The next stage of the data analysis consisted of comparison of the cortical activity underlying the L-R% differences in the temporal areas specific to speech functionality in the three PET trials: 1st vs 2nd ; 2nd vs 3rd; and 1st vs 3rd. To examine the correlation between PET and speech therapy results, the 2nd PET trial result was compared with the difference between the 2nd and 1st PET trials for monosyllabic words, polysyllabic words and sentences. Similarly, the result of the 3rd PET trial was compared with the difference between the 3rd and 1st PET trials. The analysis was performed for the following areas of the brain: Heschl temporal gyrus, superior temporal gyrus and angular gyrus. We also evaluated, in all three PET trials, whether activation of the analyzed brain areas depended on the side of cochlear implantation.

The Mann-Whitney U test for independent variables and the Wilcoxon test for dependent variables were used for statistical analysis; p-values <0.05 were considered statistically significant.

The Ethics Committee Review Board at the Medical University of Warsaw approved the project.

Results

The PET results are summarized in table 1, which shows the L-R% values recorded in the three trials, in each patient, for the following brain areas: angular gyrus, Heschl temporal gyrus, middle and superior temporal gyri. The empty fields in the table indicate the lack of data for the 2nd PET trial in patient #1 and for the 3rd trial in patient #8. The patients in question failed to attend for these scheduled PET trials, which therefore were not performed. Higher levels of regional tissue concentration of FDG in subsequent trials (presented as L-R%) were clearly notable in the left-sided structures in majority of patients (Fig. 1, Table I), which means that the left side of the brain is preferentially activated by listening to speech stimuli. However, the data analysis showed that the difference was statistically significant in only two of the analyzed cortical areas: the Heschl temporal gyrus (a statistically significant difference between the 1st and 2nd trials, $p=0.035$) and the superior temporal gyrus (a statistically significant difference between the 2nd and 3rd trials, $p=0.018$). In the other brain areas tested (the angular and middle temporal gyri), no statistically significant difference in L-R% was shown between subsequent trials ($p>0.05$).

Table II shows the results of the correlation analysis between the PET results obtained in the three trials and the speech therapy results (recognition of monosyllabic words, polysyllabic words and sentences). In the 2nd trial, after one year of cochlear implant use, a significant correlation was found for the Heschl, angular and superior temporal gyri. In the 3rd trial, performed two years after cochlear implantation, the correlation analysis showed no statistical significance.

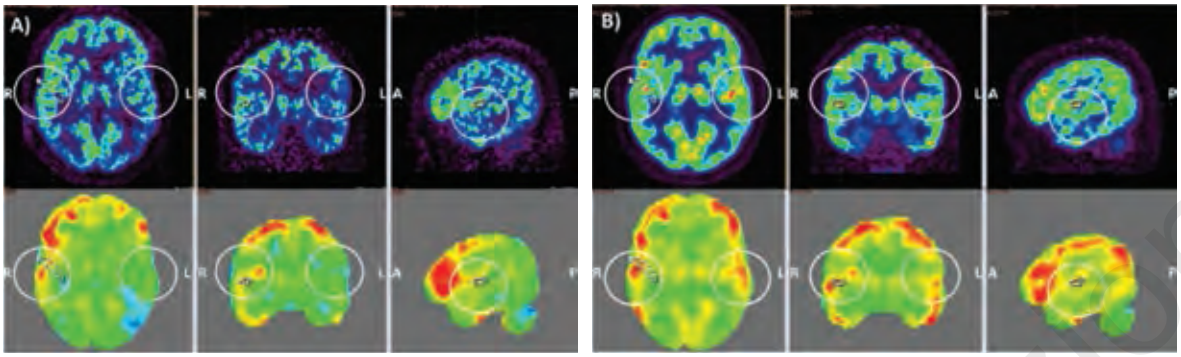

Figure 1 - Auditory cortical activation and plasticity after cochlear implantation measured by PET using fluorodeoxyglucose.
PET scans of the brain showing Heschl temporal gyri at the time of cochlear implant activation (panel A) and after 2 years of cochlear implant use (panel B) in one example case (patient #4). The main changes in cortical activation after cochlear implantation are observed mainly in the temporal areas, as presented here in the Heschl temporal gyri (marked with white circles for easier identification). The increase in regional tissue concentration of FDG in subsequent trials was clearly notable in the left-sided structures, which means that the left side of the auditory cortex was preferentially activated by listening to speech stimuli.

Table I - Values of percentage differences in SUV between the left and right side (L-R%) in three subsequent PET trials recorded in all the patients individually.

Area of the brain examined	Trial	Patient results: L-R% Prelingual deafness (pts 1-5)					Postlingual deafness (pts 6-9)			
		#1	#2	#3	#4	#5	#6	#7	#8	#9
Angular gyrus	1st	0.029	-0.168	0.077	-0.106	0.014	-0.044	0.091	0.037	0.054
	2nd		0.021	0.072	-0.017	0.018	0.052	0.083	0.023	0.077
	3rd	0.021	-0.026	0.098	0.011	0.023	0.037	0.068		0.112
Heschl gyrus	1st	-0.052	-0.168	0.057	0.011	-0.056	-0.054	0.036	-0.119	-0.058
	2nd		0.012	0.054	0.026	-0.041	0.042	0.058	-0.129	-0.032
	3rd	0.021	0.059	0.101	0.053	-0.013	-0.025	0.076		-0.056
Middle temporal gyrus	1st	-0.017	-0.296	0.077	-0.103	-0.021	-0.126	0.056	0.071	0.018
	2nd		-0.043	0.081	0.036	-0.031	0.098	-0.069	0.024	0.034
	3rd	-0.009	-0.026	0.092	0.019	-0.001	0.045	0.014		0.026
Superior temporal gyrus	1st	-0.002	-0.131	0.042	-0.05	-0.027	-0.112	-0.034	0.087	0.027
	2nd		0.076	0.057	-0.084	-0.021	0.039	0.014	0.037	0.032
	3rd	0.02	0.079	0.072	0.068	-0.013	0.071	0.018		0.039

Table II - Correlation between PET results in three trials and speech therapy results (recognition of monosyllabic words, polysyllabic words and sentences) in three cortical areas.

	Correlation test results – statistical significance (p values) Monosyllabic words		Polysyllabic words		Sentences	
Examined cortical areas	Difference between 2nd and 1st trials	Difference between 3nd and 1st trials	Difference between 2nd and 1st trials	Difference between 3nd and 1st trials	Difference between 2nd and 1st trials	Difference between 3nd and 1st trials
Angular gyrus	0.012*	0.050	0.012*	0.401	0.012*	0.161
Heschl gyrus	0.012*	0.093	0.012*	0.161	0.012*	0.123
Superior temporal gyrus	0.012*	0.093	0.012*	0.401	0.012*	0.161

* = statistically significant results

Only in the angular gyrus did cortical activation seem to correlate with an improvement in identification of monosyllabic words, but statistical analysis showed this correlation to be on the borderline of statistical significance (p=0.05).

Discussion

The first years of life constitute the critical period for speech and language development, in which the development of auditory and verbal functions at cere-

bral level is most intensive (Sharma et al., 2002, 2005). The plasticity of auditory and verbal functions decreases with age (Fryauf-Bertschy et al., 1997), therefore implantation in prelingually deafened adults is a controversial issue (Green et al., 2005). Worldwide literature (Fitzpatrick et al., 2004; Green et al., 2005; Kos et al., 2009) and clinical practice have shown that cochlear implantation in prelingually deafened adult patients does not improve speech intelligibility, or affect articulation or language skills. However, in such cases it brings about notable change in hearing and broadens the range of frequencies perceived, and patients are mostly satisfied with the benefits of cochlear implantation. This is confirmed by the findings of other authors (Shpak et al., 2009) and is also consistent with what we have observed in our own clinical practice.

The patients involved in this study were asked to distinguish, on a phonetic and a semantic level, between pairs of words. Taking into account the fact that after the first fitting of the speech processor (activation of the cochlear implant) it is rare or almost impossible for patients to be able to discriminate minor phonetic differences in words (Fu et al., 2002; Walravens et al., 2006), it becomes obvious that in our study in the 1st PET trial only the detection of sound at cortical level could be evaluated.

In our study, the majority of patients with either post- or prelingual deafness presented a similar cortical activation tendency to that observed in healthy subjects as described in the literature (Neville and Bavelier, 1998; Brett et al., 2002; Johnsrude et al., 2002; Tzourio-Mazoyer et al., 2007), i.e., activation mainly of left-sided temporal regions and frontal areas of the brain.

Not all the patients presented, in the temporal cortex, the expected pattern of higher SUVs contralaterally to implanted ear. In the first trial, in five cases, the verbal stimuli predominantly activated the auditory cortex contralateral to the implant, which is in agreement with the findings of other authors (Herzog et al., 1991; Giraud et al., 2000). However, in four patients it was the ipsilateral side that showed higher regional tissue concentrations of FDG. In our study, regional glucose metabolism was estimated by referring regional tissue concentration of FDG in analyzed areas to the mean whole brain concentration (SUV_{mean} = average value for the whole brain). For small areas such as the Heschl temporal gyri, it cannot be excluded that results are due to computational inaccuracies. Another explanation for the above phenomenon might be that the four patients in question had developed a pattern of brain functionality that resulted in the contralateral ear to the implanted one being dominant for years before the surgery. This contralateral ear presented better hearing but the patients did not want to implant the better ear. All the pros and cons regarding choice of ear for implantation were discussed with the patients before the surgery. Those four patients ultimately decided to implant the worse hearing ear. This may have led to a situation whereby the area of the cortex previously stimulated by the better hearing ear continued to respond more actively to a signal "input" from the cochlear implant even though it came from the ipsilaterally implanted ear. The same explanation might apply to cortical activation in the superior and middle temporal gyri and the angular gyrus, where the preponderance of the activation was not always consistent with the expected pattern, i.e. contralateral to the side of implantation, and did not depend on the auditory perception levels, including levels of perception of speech. The results of our study showed a tendency, over time, towards increasing levels of activation in the predominant hemisphere (the left one) which correlated positively with increasing levels of auditory perception and with speech therapy results.

The level of speech intelligibility cannot be determined unambiguously using PET with FDG due to the fact that the areas responsible for understanding speech are not fixed entities that respond, in the same way, to "general" verbal stimuli (Mummery et al., 1996; Neville et al., 1998; Brutt et al., 2002; Ojemann et al., 2002; Tzourio-Mazoyer et al., 2007). Numerous processes during speech perception, such as the analysis of phonetic, semantic, memory, associative, visual, tactile, and emotional inputs, etc., involve a certain degree of dispersion of central nervous system activation. This precludes, in the course of long-term cognitive tasks, unambiguous conclusions about the level of understanding, or not understanding, of speech.

Our study showed that in post-lingually deafened patients, who have developed normal speech perception mechanisms and who previously used spoken language for communication, cochlear implantation improved the quality of hearing. It also allowed understanding of speech, based on a peripheral hearing prosthesis. Our results of cochlear implantation in deafened adults are in agreement with those of other authors (Dawson et al., 1992; Hiraumi et al., 2007; Lazard et al., 2010).

In our study, the main changes in cortical activation in adult patients after cochlear implantation occurred in the temporal areas – the primary (Heschl temporal gyrus) and secondary auditory cortex (superior temporal gyrus). The decrease in the difference in activation level between the left and right side (L-R%), in favor of the left, was notable, even in the cases in which the level of activation remained higher on the right side even when the left ear was the one implanted. Further evaluation, in a larger number of implanted pre- and post-lingually deafened patients, is needed to explain the mechanisms of the shift in the hemispheric activation induced by auditory experience solely in one ear (in the case of unilateral cochlear implantation) and differences in this phenomenon between right and left cochlear implantation.

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References

1. Alavi A, Reivich M, Greenberg J, et al (1981). Mapping of functional activity in brain with 18F-fluoro-deoxyglucose. Semin Nucl Med 11: 24-31.
2. Brett M, Johnsrude IS, Owen AM (2002). The problem of functional localization in the human brain. Nature Review Neuroscience 3: 243-249.
3. Dawson PW, Blamey PJ, Rowland LC, et al (1992). Cochlear implants in children, adolescents, and prelinguistically deafened adults: speech perception. J Speech Hear Res 35: 401-417.
4. Fitzpatrick E, Séguin C, Schramm D (2004). Cochlear implantation in adolescents and adults with prelinguistic deafness: outcomes and candidacy issues. International Congress Series 1273: 269-272.
5. Fryauf-Bertschy H, Tyler RS, Kelsay DM, et al (1997). Cochlear implant use by prelingually deafened children: the influences of age at implant and length of device use. J Speech Lang Hear Res 40: 183-199.
6. Fu QJ, Shannon RV, Galvin JJ 3rd (2002). Perceptual learning following changes in the frequency-to-electrode assignment with the Nucleus-22 cochlear implant. J Acoust Soc Am 112: 1664-1674.
7. Giraud AL, Truy E, Frackowiak RS, et al (2000). Differential recruitment of the speech processing system in healthy subjects and rehabilitated cochlear implant patients. Brain 123: 1391-1402.
8. Grafton ST (2000). PET: activation of cerebral blood flow and glucose metabolism. Adv Neurol 83: 87-103.
9. Green KM, Julyan PJ, Hastings DL, et al (2005). Auditory cortical activation and speech perception in cochlear implant users: effects of implant experience and duration of deafness. Hear Res 205: 184-192.
10. Herscovitch P, Markham J, Raichle ME (1983). Brain blood flow measured with intravenous H2(15)O. I. Theory and error analysis. J Nucl Med 24: 782-789.
11. Herzog H, Lampreht A, Kühn A, et al (1991). Cortical activation in profoundly deaf patients during cochlear implant stimulation demonstrated by H2(15)O PET. J Comput Assist Tomogr 15: 369-375.
12. Hiraumi H, Tsuji J, Kanemaru S, et al (2007). Cochlear implants in post-lingually deafened patients. Acta Otolaryngol Suppl (557): 17-21.
13. Ito Y, Sakakibara J, Honjo I, et al (1990). Positron emission tomographic study of auditory sensation in a patient with cochlear implant. Arch Otolaryngol Head Neck Surg 116: 1437-1439.
14. Jacquemot C, Pallier C, LeBihan D, et al (2003). Phonological grammar shapes the auditory cortex: a functional magnetic resonance imaging study. J Neurosci 23: 9541-9546.
15. Johnsrude IS, Giraud AL, Frackowiak RS (2002). Functional imaging of the auditory system: the use of positron emission tomography. Audiol Neurootol 7: 251-276.
16. Kang E, Lee DS, Kang H, et al (2004). Neural changes associated with speech learning in deaf children following cochlear implantation. Neuroimage 22: 1173-1181.
17. Kos MI, Deriaz M, Guyot JP, et al (2009). What can be expected from a late cochlear implantation? Int J Pediatr Otorhinolaryngol 73: 189-193.
18. Lazard DS, Bordure P, Lina-Granade G, et al (2010). Speech perception performance for 100 post-lingually deaf adults fitted with Neurelec cochlear implants: comparison between Digisonic® Convex and Digisonic® SP devices after a 1-year follow-up. Acta Otolaryngol 30: 1267-1273.
19. Lee HJ, Kang E, Oh SH, et al (2005). Preoperative differences of cerebral metabolism relate to the outcome of cochlear implants in congenitally deaf children. Hear Res 203: 2-9.
20. Mummery CJ, Patterson K, Hodges JR, et al (1996). Generating 'tiger' as an animal name or a word beginning with T: differences in brain activation. Proc Biol Sci 263: 989-995.
21. Neville HJ, Bavelier D (1998). Neural organization and plasticity of language. Curr Opin Neurobiol 8: 254-258.
22. Ojemann GA, Schoenfield-McNeill J, Corina DP (2002). Anatomic subdivisions in human temporal cortical neuronal activity related to recent verbal memory. Nat Neurosci 5: 64-71.
23. Raichle ME, Martin WR, Herscovitch P, et al (1983). Brain blood flow measured with intravenous H2(15)O. II. Implementation and validation. J Nucl Med 24: 790-798.
24. Sharma A, Dorman MF, Kral A (2005). The influence of a sensitive period on central auditory development in children with unilateral and bilateral cochlear implants. Hear Res 203: 134-143.
25. Sharma A, Dorman MF, Spahr AJ (2002). A sensitive period for the development of the central auditory system in children with cochlear implants: implications for age of implantation. Ear Hear 23: 532-539.
26. Shpak T, Koren L, Tzach N, et al (2009). Perception of speech by prelingual pre-adolescent and adolescent cochlear implant users. Int J Audiol 48: 775-783.
27. Truy E, Deiber MP, Cinotti L, et al (1995). Auditory cortex activity changes in long term sensorineural deprivation during crude cochlear electrical stimulation: evaluation by positron emission tomography. Hear Res 86: 34-42.
28. Tzourio-Mazoyer N, Hervé PY, Mazoyer B (2007). Neuroanatomy: tool for functional localization, key to brain organization. Neuroimage 37: 1059-1060.
29. Walravens E, Mawman D, O'Driscoll M (2006). Changes in psychophysical parameters during the first month of programming the nucleus contour and contour advance cochlear implants. Cochlear Implants Int 7: 15-32.