Auditory cortical activation in severe-to-profound hearing-impaired patients monitored by SPET

Studio dell'attivazione della corteccia uditiva in pazienti con ipoacusia grave-profonda mediante SPET

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Parole chiave
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Summary

Single photon emission tomography was used to map blood flow increase in temporal and parietal cortex after auditory stimulation in 25 subjects: 10 normal-hearing, 10 severe-profound hearing-impaired and 5 totally deaf. After a 500 Hz pure tone stimulation, a marked perfusion increase was observed, particularly at the level of the contralateral auditory temporal cortex. Blood flow increase in temporal and parietal cortical areas of normal subjects was significantly higher than that observed in severe-to-profound hearing-impaired patients. In all cases, following 500 Hz pure tone acoustic stimulation, the most lateral sagittal slice tomograms (48.75 and 56.25 mm) showed the highest blood flow increase. Statistically significant differences were also observed between normal subjects and hearing-impaired patients in the 48.75 mm sagittal tomogram. In 2 hearing-impaired patients, the single photon emission tomography pattern showed activation of the intermediate sagittal tomogram, suggesting a possible new tonotopic cortical arrangement. No significant activation was present in totally deaf patients. In conclusion, Single Photon Emission Tomography appears to be a useful tool in the evaluation of auditory cortical activation and cortical plasticity, in severe-to-profound hearing-impaired patients. Moreover, it could be a useful test for the study of auditory central pathways.

Riassunto

In questo studio è stata utilizzata la Single Photon Emission Tomography (SPET) per rilevare, dopo stimolazione acustica, gli incrementi del flusso ematico nella corteccia temporale e parietale di 25 soggetti (10 normoacusici, 10 con deficit uditivo grave-profondo e 5 completamente sordi). Dopo stimolazione con un tono puro a frequenza 500 Hz, sono stati osservati un marcato aumento della perfusione ematica ed una attivazione prevalente della corteccia temporale uditiva controlaterale al lato stimolato. Gli incrementi del flusso sanguigno nelle aree corticali temporali e parietali sono apparsi significativamente più elevati nei soggetti normali rispetto a quelli con ipoacusia grave-profonda. Per i tagli sagittali, in tutti i casi dopo stimolazione acustica, i tomogrammi più laterali (48,75 e 56,25 mm) hanno mostrato il maggiore incremento di flusso ematico. In due pazienti ipoacusici, le immagini SPET mostrano anche un'attivazione dei tomogrammi intermedi suggerendo un probabile riarrangiamento tonotopico corticale. Nei soggetti sordi-profondi non è stata riscontrata nessuna attivazione corticale significativa. In conclusione, la SPET sembra in grado di valutare l'attivazione della corteccia uditiva anche in pazienti con ipoacusia grave-profonda, evidenziando inoltre la plasticità corticale e dimostrandosi un test di grandi potenzialità, a costi accettabili, per lo studio della funzione uditiva.

Introduction

In severely hearing-impaired subjects, definition of the threshold of low frequencies and assessment of central auditory function are difficult to achieve with the auditory tests (Auditory Brainstem Responses, Middle Latency Response, Late Latency Responses, Magnetic field recordings) currently available. In fact, ABR, still the only reliable objective diagnostic tool, cannot be elicited by low frequency stimuli in profoundly hearing-impaired subjects while the clinical relevance of MLR, LLR and Magnetic field recordings has not yet been well defined as these procedures are influenced by recordings. Information concerning low frequencies currently plays a major role in therapeutic planning, on account of the technological and surgical improvements (cochlear implants, implanting hearing aids, etc.).

Positron emission tomography (PET) [1-3] and functional magnetic resonance (fMR) [2 4 5] have already been used to investigate cortical auditory function.

PET has been proposed to identify the brain areas related to auditory perception [1 2]. Recently, Kawase et al. studied regional cerebral blood flow in normal volunteers during speech sounds in auditory-visual perception [3]. Nevertheless, the widespread use of

PET is limited by elevated costs, the complication of the technique and the need of a linear accelerator.

On the other hand, fMR has been used to assess auditory cortex activation evoked by different pure tone stimuli [4 5]. In these studies, functional images of auditory cortex activation were obtained at the level of Heschl's gyrus, middle temporal gyrus, superior temporal gyrus, and *planum temporale* [5]. Moreover, the existence has been revealed of a frequency specific organization in the medio-lateral, fronto-occipital and cranio-caudal extension in both hemispheres of the auditory cortex. In fact, the activated areas for the high tone were identified more frontally and medially orientated than the low stimulated areas [4]. Finally, fMR is a non-invasive and non-radioactive method but studies are limited by the presence of noise produced by echo planar imaging, elevated costs, the complicated technique and the time-consuming performance. In addition, fMR is not suitable to study cochlear-implanted patients.

Single Photon Emission Tomography (SPET) is used to evaluate activation of the auditory cortex and regional blood flow modifications after acoustic stimulation [6-12]. In a previous investigation, we studied the relationship, using multifrequency stimulus, between auditory cortex perception and the frequency of acoustic stimuli, in normal subjects. We demonstrated the tonotopic distribution of acoustic stimuli in the auditory cortex, using SPET, and hypothesized that brain SPET may be useful to obtain reliable semi-quantitative information on low frequencies.

In the present investigation, auditory cortex activation has been assessed, using SPET, in a group of severe-to-profound hearing-impaired patients, The results obtained in these subjects have been compared with those from totally deaf and normally-hearing subjects.

Materials and methods

A total of 25 subjects were enrolled in the study:

- 10 normally-hearing subjects (5 male, 5 female, age range 28-55 years);
- 10 patients (5 male, 5 female, age range 32-53 years) presenting post-lingual, progressive, bilateral, severe-to-profound sensorineural hearing-loss, with auditory residuals in the low frequency domain. In these patients, deafness had appeared 5-15 years earlier. All patients underwent fitting hearing aid, as soon as possible, none of whom presented a sound deprivation effect;
- 5 totally deaf patients (3 male, 2 female, age range 21-57 years).

Clinical and neuroradiological investigations ruled out neurological diseases, in all cases.

After informed consent had been given, all subjects underwent SPET by means of a four-head cerebral tomograph *CER.TO 96* (Selo, Italy) [14]. The subjects were resting, blindfolded, with an indwelling needle mounted in an arm vein, 10 min prior to injection, in a dimly lit room, as noiseless as possible. After the injection of 333 MBq ^{99m}Technetium (Tc)-Hexa-Methyl-Propylene-Amine-Oxime (HMPAO), the head of the patient was settled into a flexible headrest and then carefully introduced into the gantry. The exact position of the canthomeatal line was recorded using two adjustable light-guides, mounted on the gantry at an angle of 90°. A 15' examination was performed. A total 9.5' stimulation was delivered, from 2' before until 7.5' after a second injection of 666 MBq ^{99m}Tc-HMPAO without moving the patient. All subjects were stimulated with a 500 Hz pure tone, delivered through a TDH 49 headphone, at two different levels: 40 dBHL for normally-hearing subjects and 115 dBHL (the highest available intensity) for severe-to-profound hearing-impaired and totally deaf patients. The better hearing ear was stimulated in the pathologic group (5 right and 5 left ears) while in the normal control group, 5 right and 5 left ears were stimulated.

At the end of the stimulation, a further 25' study was carried out. Reconstructed transversal, coronal, and sagittal slices were oriented according to the three spatial planes, using an appropriate software programme, which also permitted the realignment of the sagittal sections to the canthomeatal line, on the basis of the data recorded by the light-guides. The pre-stimulation study was then subtracted from the post-stimulation acquisition. To this end, the frames of the post(Po)- and pre(Pe)-stimulation acquisitions were scanned sequentially and in parallel, with the pixels at the same positions in the two studies. The following subtraction was then performed:

$$CpPo - CpPe = CpSu$$

Cp = content of the pixel
Su = subtracted study

Cerebral auditory areas were defined on the basis of a stereotaxis atlas [15]. The detailed limits of temporal and parietal acoustic areas were considered in the atlas and then visually reported on SPET slices by the same reader. In the pre-stimulation and subtraction frames, temporal uptakes were calculated by two circular Regions of Interest (ROI) drawn symmetrically on three consecutive coronal slices (nominal slice thickness 7.5 mm). Parietal uptakes were measured, for the same slices, with two symmetrical irregular ROIs, the maximal sizes of which did not exceed those of the circular ROI. Using a 70% isocontourn, a whole-brain ROI (W) was drawn on summed pre-stimulation and subtraction slices. The total counts of all selected ROI, temporal (T), parietal (P) and whole-brain (W), in the pre-stimulation and subtraction frames were divided by the respective number of pixels. The counts per pixel of temporal ROI were added T up P together, separately, in the pre-stimulation and subtraction slices. The same procedure was performed for parietal ROI. Mean temporal (T) and parietal (P) values were calculated and then divided by W in pre-stimulation and subtraction images, namely**.**

Tw = T/W
Pw = P/W

Finally, the following ratios were calculated separately, contralaterally and ipsilaterally to the acoustic stimulus:

RTw = (TwS-TwB)x100/TwB
RPw = (PwS-PwB)x100/PwB
B = pre-stimulation study
S = subtraction study

These were regarded as percentage increase of cortical perfusion resulting from auditory stimulation. A circular ROI was then drawn on the temporal acoustic cortex of six consecutive sagittal slices (E, F, G, H, I, L) from 18.75 mm (E) to 56.25 mm (L) laterally to the midline, on the side contralateral to the stimulus. The counts per pixel of pre-stimulation and subtraction ROI were divided by W and the percentage increases in cortical perfusion were calculated with the same ratios as in coronal slices.
Student's paired and unpaired t tests were used in the statistical analyses with significance set at $p < 0.05$.

Results

Hearing threshold and stimulated ear of severe-to-profound hearing-impaired patients are reported in Table I.
Results were defined in terms of blood flow increase in coronal and sagittal tomograms.
SPET data obtained in normal subjects and affected patients are reported in Tables II and III.
Cortical activation in all deaf patients was always < 0.02%, both in temporal and parietal homolateral and contralateral cortex. The same results were obtained in sagittal tomograms of the contralateral temporal region.
In normal subjects, mean coronal values of perfusion increase (%), in the temporal and parietal cortex following stimulation, were, respectively, 19.76 (± 8.29) and 7.97 in the contralateral side, (± 3.1) 4.24 (± 1.9) and 1.42 (± 0.89) in the homolateral side; while in patients affected by severe-profound hearing loss, mean values were: 8.63 (± 5.6) and 4.07 (± 2.6) in the contralateral side, 1.62 (± 2.2) and 0.43 (± 0.7) in the homolateral side.
In normal subjects. mean values of perfusion increase in contralateral temporal cortex following stimulation, identified in sagittal tomograms at different levels (18.75 mm, 26.25 mm, 33.75 mm, 41.25 mm, 48.75 mm) were, respectively: -1.15 (± 1.6), -0.85 (± 1.4), -0.23 (± 0.7), 0.41 (± 3), 13.34 (± 6.9) and 10.93 (± 8.6); while in patients affected by severe-profound hearing loss were, respectively: -0.74 (± 0.9), -1.21 (± 2.7), -0.55 (± 1.6), -0.71 (± 2.9), 7.68 (± 3.7) and 12.44 (± 7.2).
Coronal SPET images are shown in Figure 1.

Table I. Hearing threshold (dB HL) of stimulated ear in severe-to-profound hearing-impaired patients.

Patient	Side	125 Hz	250 Hz	500 Hz	1000 Hz	2000 Hz	4000 Hz	8000 Hz
1	Right	80	95	100	100	105	NR	NR
2	Right	NR	95	110	120	NR	NR	NR
3	Left	NR	85	75	90	115	NR	NR
4	Left	NR	NR	105	100	95	90	80
5	Left	60	65	70	75	70	100	NR
6	Right	50	70	70	100	110	110	NR
7	Left	70	90	95	105	110	NR	NR
8	Right	70	70	90	100	105	100	105
9	Right	60	85	90	95	80	85	90
10	Right	65	90	95	95	100	105	NR
Mean		*65*	*82.77*	*90*	*98*	*98.88*	*98.33*	*91.66*
SD		*9.5*	*11.4*	*14.1*	*11.3*	*14.9*	*9.3*	*12.5*

NR = no response.

Table II. Stimulated ear and perfusion increments (%) in temporal and parietal cortex: mean coronal values following 500 Hz stimulation.

A) Normal subjects.

		Contralateral		Homolateral	
Subject	**Side**	**Temporal**	**Parietal**	**Temporal**	**Parietal**
1 NH	Left	26.6	8.8	6	1.2
2 NH	Left	26	9.2	3.92	2.08
3 NH	Right	5.42	2.48	0.31	0.04
4 NH	Left	23.42	11.12	6.32	2.12
5 NH	Left	22.2	7.4	3.5	0.8
6 NH	Left	23.24	12.14	6.54	2.23
7 NH	Right	7.2	5.3	3.2	1.2
8 NH	Right	26.1	10.2	4.9	2.2
9 NH	Left	12.2	4.02	2.42	0.34
10 NH	Right	25.22	9.07	5.3	2.08
Mean		19.76	7.97	4.24	1.42
SD		8.2	3.1	1.9	0.8

B) Severe-to-profound hearing-impaired patients.

		Contralateral		Homolateral	
Patient	**Side**	**Temporal**	**Parietal**	**Temporal**	**Parietal**
1	Right	12.2	4.6	0.6	0.5
2	Right	9	3.7	3.03	0.6
3	Left	6.3	3.03	0.7	0.3
4	Left	2	1.2	0.7	
5	Left	4.89	2.86	0	0
6	Right	9	7.5	0.2	0
7	Left	6.5	1.7	1.25	0.07
8	Right	4.3	2.1	0.5	0.1
9	Right	22.43	9.5	7.43	2.22
10	Right	9.73	4.53	1.83	0.12
Mean		8.63	4.07	1.62	0.43
SD		5.6	2.6	2.2	0.7

Coronal-temporal slices contralateral to the stimulated ear, showed the greatest increases in blood flow when compared to all other areas in severe-to-profound hearing-impaired patients as well as in normal subjects (Tables II, IV). Mean blood flow increase in temporal and parietal cortical areas of normal subjects was significantly higher than that of severe-to-profound hearing-impaired patients (Tables II, IV).

The most lateral sagittal tomograms showed the highest blood flow increase after 500 Hz pure tone stimulation, in all cases (Tables III, IV). In severe-to-profound hearing-impaired patients, the highest activation appeared in the 56.25 mm tomogram while in normal cases in the 48.75 mm tomogram (Tables III, IV).

Two of the severe-to-profound hearing-impaired patients showed activation in the intermediate contralateral temporal areas (#10 33.75 mm and 26.25 mm; (#7 33.75 mm and 41.25 mm), while these areas were activated (#8 41.25 mm) only in one patient in the control group.

Student's t test results showed statistically significant differences for 48.75 mm sagittal slice.

Table III. Stimulated ear and perfusion increments (%) in contralateral temporal cortex following 500 Hz stimulation (sagittal tomogram study).

A) Normal subjects.

Subject	Side	18.75 mm	26.25 mm	33.75 mm	41.25 mm	48.75 mm	56.25 mm
1 NH	Left	-4.76	-2.63	-2.38	-2.32	4.08	11.63
2 NH	Left	0	0	0	0	20	32
3 NH	Right	0	0	0	0	16.28	2.08
4 NH	Left	0	0	0	0	14.63	6.89
5 NH	Left	0	0	0	0	14.08	4.08
6 NH	Left	0	0	0	0	14.63	6.98
7 NH	Right	-1.78	0	0	0	6.12	8.51
8 NH	Right	0	0	0	8.69	7.6	16.33
9 NH	Left	-2.6	-3.5	0	0	27.13	15
10 NH	Right	-2.38	-2.44	0	-2.22	8.89	5.88
Mean		-1.15	-0.85	-0.23	0.41	13.34	10.93
SD		1.6	1.4	0.7	3	6.9	8.6

B) Severe-to-profound hearing-impaired patients.

Patient	Side	18.75 mm	26.25 mm	33.75 mm	41.25 mm	48.75 mm	56.25 mm
1	Right	0	0	0	-2.04	10	24.44
2	Right	0	-1.96	-3.92	0	7.84	17.95
3	Left	-2.44	-2.56	0	-3.57	7.84	20.59
4	Left	0	-2.22	-2.22	-2.22	2.13	2.04
5	Left	0	0	0	0	7.14	9.52
6	Right	-1.69	-3.77	-1.96	0	15.38	7.02
7	Left	-1.75	-2	0.84	5.8	7.84	3.39
8	Right	0	0	0	0	4.08	12.19
9	Right	0	-4.76	0	-5.13	4.08	13.04
10	Right	-1.58	5.17	1.67	0	10.53	14.28
Mean		-0.74	-1.21	-0.55	-0.71	7.68	12.44
SD		0.9	2.7	1.6	2.9	3.7	7.2

Discussion

The present and previous personal results are similar to those observed in the auditory cortex of normal humans and animals following electrophysiologic [15 16] biomagnetic [17-21] and PET [1-3] investigations, i.e., a stronger activation of the most lateral temporal region of the contralateral temporal auditory cortex after 500 Hz acoustic stimulation, while multi-frequencial stimuli activated a larger cortical surface [12].

In the severe-to-profound hearing-impaired patients with minimal residual hearing for low frequencies, an analogous significant activation in the contralateral cortical areas, mainly within the most lateral regions of the auditory cortex, was observed. Thus, the distribution pattern of cortical activation seems to be similar to that of normal subjects, but activation levels are significantly lower, due to the different auditory threshold. The reliability of these data is supported by the absence of cortical activation in totally deaf patients. In two cases, a perfusion increase was detected in some intermediate tomograms (Table III/B: #7: 41.25 mm and 33.75 mm tomograms; #10: 26.25 mm and 33.75 mm tomograms). These findings could be explained by an expansion of the residual low frequencies cortical representation to the areas where higher frequencies are normally located, thus suggesting a possible new tonotopic cortical arrangement. However, studies on a larger number of patients need to be carried out in order to achieve a satisfactory explanation of these results and to define the eventual relationship between cortical activation,

Table IV. Summary of results.

A) Perfusion increments (%) in temporal and parietal cortex.

	Contralateral		Homolateral	
Subjects	**Temporal**	**Parietal**	**Temporal**	**Parietal**
Normal	19.76 (± 8.2)	7.97 (± 3.1)	4.24 (± 1.9)	1.42 (± 0.89)
Hearing impaired	8.63 (± 5.6)	4.07 (± 2.6)	1.62 (± 2.2)	0.43 (± 0.7)

B) Mean coronal values following stimulation.

Subjects	**18.75 mm**	**26.25 mm**	**33.75 mm**	**41.25 mm**	**48.75 mm**	**56.25 mm**
Normal	-1.15 (± 1.6)	-0.85 (± 1.4)	-0.23 (± 0.7)	0.41 (± 3)	13.34 (± 6.9)	10.93 (± 8.6)
Hearing impaired	-0.74 (± 0.9)	-1.21 (± 2.7)	-0.55 (± 1.6)	-0.71 (± 2.9)	7.68 (± 3.7)	12.44 (± 7.2)

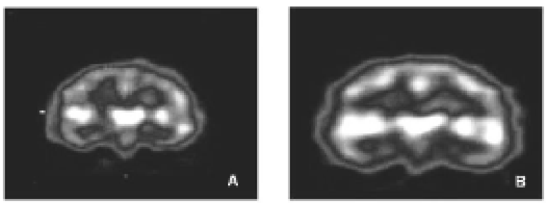

Fig. 1. Severe-to-profound hearing impaired patient. Perfusion increment in most lateral sagittal tomogram after 500 Hz monofrequency stimulus.
A. Pre-stimulation slice.
B. Post-subtraction slice.

auditory threshold and auditory deprivation.
Our data seem to confirm SPET effectiveness in the assessment of central auditory pathway function, even in severe-to-profound hearing-impaired patients. SPET is reasonably inexpensive, easy to perform and fairly widely used. Radiation doses delivered are the same or lower than those used in a traditional X-ray study. In addition, SPET could represent a reliable method for objective information concerning low frequency acoustic residuals, when other available auditory investigations do not yield useful results. In a future perspective, SPET may be taken into account for the selection of cochlear implants, since careful assessment of central auditory pathways and possible information concerning low frequency auditory residuals should be mandatory prior to surgery. Moreover, with this technique it is possible to evaluate cortical activity after speech and multifrequential tonal stimuli, and it could thus be used to predict the success of cochlear and auditory brainstem implant.
In conclusion, this preliminary study represents an important step in the use of SPECT for diagnosis and treatment of deafness, for the selection and follow-up of cochlear implant. In fact, this technique is reasonably inexpensive, easy to perform and fairly widely used. Finally, the radiation doses delivered are the same or lower than those in a traditional X-ray study.

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