Otology

Role of auditory brain function assessment by SPECT in cochlear implant side selection

Studio della funzione uditiva corticale mediante SPECT per la scelta di lato negli impianti cocleari

W. DI NARDO[1], S. GIANNANTONIO[1], D. DI GIUDA[2], E. DE CORSO[1], L. SCHINAIA[1], G. PALUDETTI[1]

[1] Institute of Otorhinolaryngology, [2] Institute of Nuclear Medicine, Catholic University of the Sacred Heart, Rome, Italy

SUMMARY

Pre-surgery evaluation, indications for cochlear implantation and expectations in terms of post-operative functional results remain challenging topics in pre-lingually deaf adults. Our study has the purpose of determining the benefits of Single Photon Emission Tomography (SPECT) assessment in pre-surgical evaluation of pre-lingually deaf adults who are candidates for cochlear implantation. In 7 pre-lingually profoundly deaf patients, brain SPECT was performed at baseline conditions and in bilateral simultaneous multi-frequency acoustic stimulation. Six sagittal tomograms of both temporal cortices were used for semi-quantitative analysis in each patient. Percentage increases in cortical perfusion resulting from auditory stimulation were calculated. The results showed an inter-hemispherical asymmetry of the activation extension and intensity in the stimulated temporal areas. Consistent with the obtained brain activation data, patients were implanted preferring the side that showed higher activation after acoustic stimulus. Considering the increment in auditory perception performances, it was possible to point out a relationship between cortical brain activity shown by SPECT and hearing performances, and, even more significant, a correlation between post-operative functional performances and the activation of the most medial part of the sagittal temporal tomograms, corresponding to medium-high frequencies. In light of these findings, we believe that brain SPECT could be considered in the evaluation of deaf patients candidate for cochlear implantation, and that it plays a major role in functional assessment of the auditory cortex of pre-lingually deaf subjects, even if further studies are necessary to conclusively establish its utility. Further developments of this technique are possible by using trans-tympanic electrical stimulation of the cochlear promontory, which could give the opportunity to study completely deaf patients, whose evaluation is objectively difficult with current audiological methods.

KEY WORDS: Brain SPECT • Cochlear implant • Auditory cortex activation • Pre-lingually deaf

RIASSUNTO

La valutazione preoperatoria, le indicazioni all'impianto cocleare e le aspettative in termini di risultati funzionali post-operatorie rappresentano ancora problematiche di difficile soluzione nei pazienti adulti sordi pre-linguali. Lo scopo di questo lavoro è quello di verificare l'utilità della SPECT nella valutazione pre-operatoria di un gruppo di pazienti preverbali adulti candidati all'impianto cocleare. Sette sordi profondi preverbali sono stati sottoposti a SPECT cerebrale previa iniezione di 740 MBq di 99mTc-HMPAO in condizioni basali e di stimolazione acustica multi-frequenziale bilaterale e simultanea, con acquisizione di 6 tomogrammi sagittali per ambedue le cortecce temporali di ciascun paziente. I dati ottenuti hanno evidenziato una asimmetria interemisferica dell'estensione e dell'intensità di attivazione delle aree temporali stimolate. Un solo paziente ha mostrato una scarsa attivazione corticale dopo stimolazione acustica, che si è dimostrata del tutto coerente con i dati della valutazione clinica del soggetto, gravemente deficitario dal punto di vista uditivo e linguistico, mettendo in seri dubbi l'opportunità di eseguire l'impianto cocleare. Coerentemente con i dati di attivazione cerebrale ottenuti, gli altri pazienti sono stati impiantati prediligendo il lato che si attivava maggiormente in risposta allo stimolo acustico. Valutando il guadagno nelle prestazioni di percezione uditiva, si è potuto apprezzare una correlazione tra attività corticale dimostrata dalla SPECT e performance uditive, e tra performance funzionali post-operatorie ed attivazione dei tomogrammi temporali sagittali più mediali, corrispondenti alle medie-alte frequenze. Alla luce di queste considerazioni, noi riteniamo che la SPECT possa essere considerata nella valutazione dei pazienti ipoacusici candidati all'impianto cocleare, e che rivesta un ruolo di primaria importanza nella valutazione funzionale della corteccia uditiva dei pazienti preverbali, pur essendo necessari ulteriori studi per definirne l'effettiva utilità. Ulteriori sviluppi di questa tecnica si potranno avere con l'utilizzo della stimolazione elettrica trans-timpanica del promontorio, che potrebbe offrire così la possibilità di studiare anche i soggetti completamente sordi, la cui valutazione è difficoltosa con le metodiche audiologiche attuali.

PAROLE CHIAVE: *SPECT cerebrale • Impianto cocleare • Attivazione corteccia cerebrale • Ipoacusia preverbale*

Introduction

Cochlear implants (CIs) have radically changed the clinical history of subjects with severe-to-profound hearing loss, allowing a complete recovery of auditory function in most cases. The clinical benefit and cost/effectiveness of unilateral CIs in post-lingually deaf patients is undisputed, both in children [1 2] and adults [3-5]. Nonetheless, pre-surgical evaluation, indications for cochlear implantation and expectations in terms of post-operative functional results are still challenging topics in pre-lingually deaf adults. Parameters such as duration of auditory deprivation, rehabilitation and pre-implant audiological assessment often cannot provide sufficient evidence to establish potential recovery in these subjects. This is confirmed by the extreme variability of the results in post-operative hearing performances of pre-lingually deaf recipients. In current pre-surgical evaluation, there is lack of auditory cortical brain function assessment due to the absence of proper investigations. Functional brain imaging, such as Single Photon Emission Computed Tomography (SPECT), may become a useful tool to overcome this deficiency, exploring in a completely non-invasive and reliable manner the behaviour of the auditory cortex. SPECT has already been used in the assessment of auditory cortex activation and changes in regional cerebral blood flow after acoustic stimulation [6-9]. However, there are limited studies in the literature regarding evaluation of auditory function in severe-to-profound hearing impaired CI candidates.

Materials and methods

The procedure was reviewed and approved by the Local Review Board at Catholic University of the Sacred Heart and was conducted according to principles expressed in the Declaration of Helsinki. We enrolled 7 right-handed CI candidates (4 women, 3 men), aged from 10 to 25 years (mean age of 17.4 years). Each patient or caregiver signed a written informed consent after receiving exhaustive explanations concerning the procedure and its general risks. The entire group was affected by pre-lingually bilateral severe-to-profound hearing loss (Fig. 1). Each patient, although having acquired oral communication, showed inadequate benefit from conventional hearing aids at the time of testing (≤ 50% sentences recognition score at 70 dB-HL with hearing aids in free field). Clinical and neuroradiological investigations ruled out neurological disease in all cases. Each patient was studied with a baseline brain SPECT as well as a second on, performed after bilateral simultaneous multi-frequency acoustic stimulation. Subjects were resting, blindfolded, with an indwelling needle mounted in an arm vein, 10 min prior to injection, in a dimly lit room that was as noiseless as possible. Images were acquired using a CER.TO 96 (SE.LO, Italy) cerebral tomograph, made up of a gamma-camera system with 4 detectors. The baseline SPECT was carried out after intravenous administration of 333 MBq of ^{99m}Technetium-Hexa-Methyl-Propylene-Amine-Oxime (^{99m}Tc-HMPAO), and image acquisition lasted 15 min. The exact position of the canthomeatal line was recorded using two adjustable light-guide, mounted on the gantry. SPECT with activation consisted of exposure to a bilateral and simultaneous acoustic stimulus, consisting of pure pulsed multi-frequency tones (250 Hz, 500 Hz, 1000 Hz, 2000 Hz and 4000 Hz), presented through headphones at the highest available intensity (125 dB-HL), with a progressive change in the frequency every 15 sec. After the first 2 min of acoustic stimulation, 666 MBq of intravenous ^{99m}Tc-HMPAO were administered, keeping the acoustic stimulus for an additional 5 min. At the end of the stimulation, a further 25 sec study was carried out. Reconstructed transaxial, coronal and sagittal slices were oriented according to the three spatial planes, using an appropriate software programme, which also allowed realignment of the sagittal section 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, using the following subtraction algorithm:

$$Pc_{post} - Pc_{pre} = Pc_{sub}$$

where Pc_{post} stands for pixel content of the acquisition after stimulation; Pc_{pre} stands for pixel content of the baseline scan and Pc_{sub} stands for pixel content of the subtraction study. Temporal uptake of the injected radiopharmaceutical was calculated by selection of symmetrical Region Of Interest (ROI), drawn on 6 consecutive sagittal tomograms, starting from 18.75 mm and ending up to 56.25 mm laterally to the median line in the two hemispheres (18.75 mm, 26.25 mm, 33.75

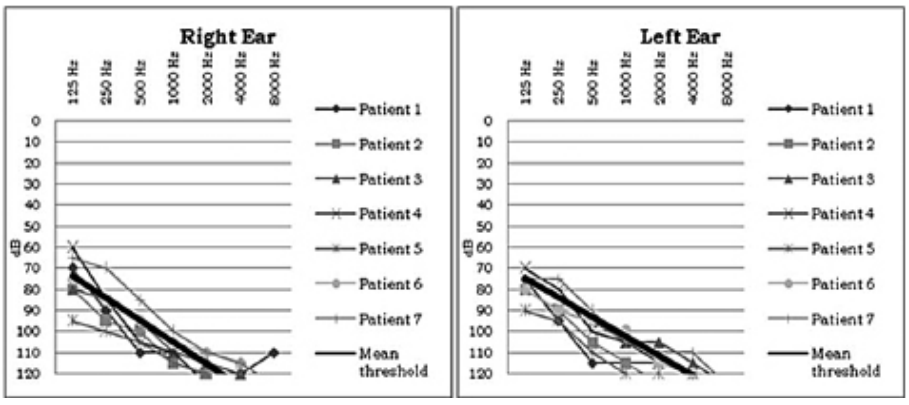


Fig. 1. Pure tone threshold for all 7 patients. The black line shows the mean value in dB-HL per ear.

Table I. Values of increment in cerebral blood flow following acoustic stimulation from the nearest to the farthest sagittal slices from the median line, for both sides in each patient.

	mm from the median line	18.75	26.25	33.75	41.25	48.75	56.25
Patient 1	Right cortex	4.17	4.17	11.36	20.00	30.89	11.90
	Left cortex	5.20	6.29	15.23	21.12	29.13	14.12
Patient 2	Right cortex	11.13	6.90	10.50	12.24	24.20	9.11
	Left cortex	9.23	9.23	6.50	8.23	17.11	6.22
Patient 3	Right cortex	14.20	8.50	11.60	8.60	23.70	10.40
	Left cortex	7.90	6.80	10.40	10.50	14.60	9.40
Patient 4	Right cortex	14.50	12.23	6.60	12.60	11.20	11.70
	Left cortex	17.20	16.30	5.40	18.50	17.80	21.40
Patient 5	Right cortex	0.00	0.00	0.00	3.57	2.83	6.05
	Left cortex	0.00	0.00	2.18	1.34	1.79	5.54
Patient 6	Right cortex	15.53	18.25	10.20	8.67	12.88	13.00
	Left cortex	18.21	20.18	12.34	16.68	20.88	25.71
Patient 7	Right cortex	13.89	14.28	12.87	13.14	11.79	16.32
	Left cortex	12.75	15.62	12.55	19.23	21.59	25.89

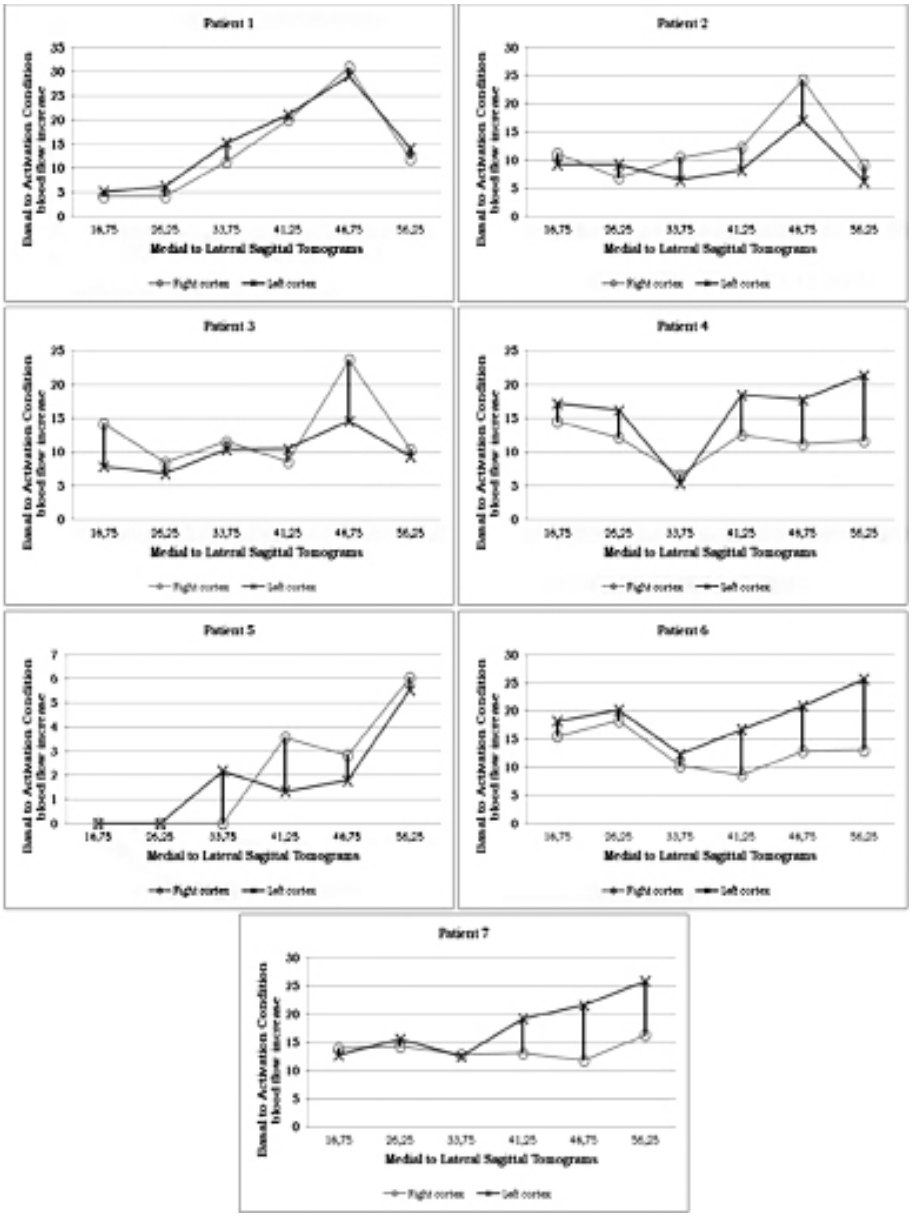
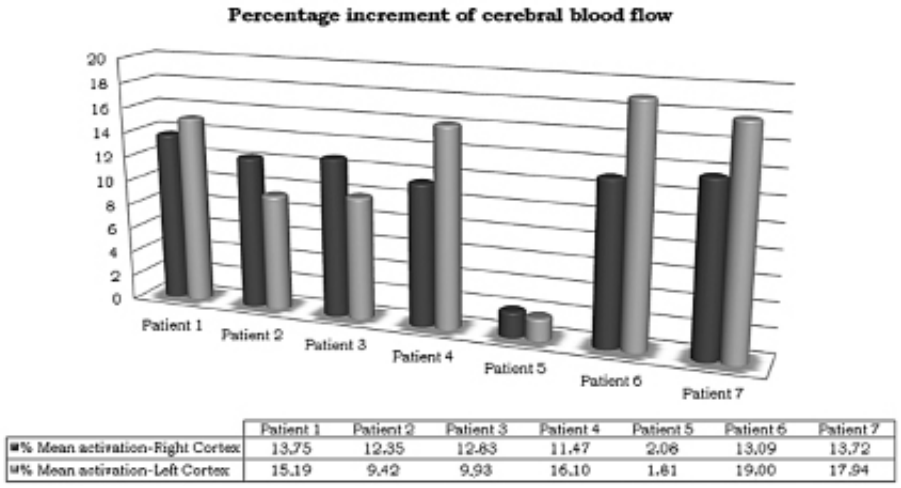


Fig. 2. Increase in cerebral blood flow following acoustic stimulation from the nearest to the farthest sagittal slices from the median line, for both sides in all patients.

mm, 41.25 mm, 48.75 mm and 56.25 mm from the median line). Using a 70% isocontour, a whole-brain ROI was drawn on summed pre-stimulation and subtraction slices. The mean counts per pixel of pre-stimulation and subtraction temporal ROI were divided by those of the whole-brain ROI. Percentage increases in cortical perfusion resulting from auditory stimulation were calculated, as previously reported [10].

Results

SPECT results were defined in terms of blood flow changes in the examined patient's left and right temporal auditory brain cortex sagittal tomograms, starting from the baseline condition and ending in a condition of increased regional blood flow because of the higher neuronal metabolic activity from multi-frequency acoustic stimulation. Table I and Figure 2 show the percentage increase in blood flow for each patient. Overall, inter-hemispherical asymmetry of the activation extension and intensity of the stimulated temporal areas can be noticed. Figure 3 shows, for each patient, the average increase of blood flow in the 6 sagittal tomograms for both sides, with the relative asymmetry in the right-left activations. Blood flow in the patients increased after si-



	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
% Mean activation-Right Cortex	13.75	12.35	12.83	11.47	2.08	13.09	13.72
% Mean activation-Left Cortex	15.19	9.42	9.93	16.10	1.81	19.00	17.94

Fig. 3. Mean right versus left cortices blood flow increase after acoustic stimulation.

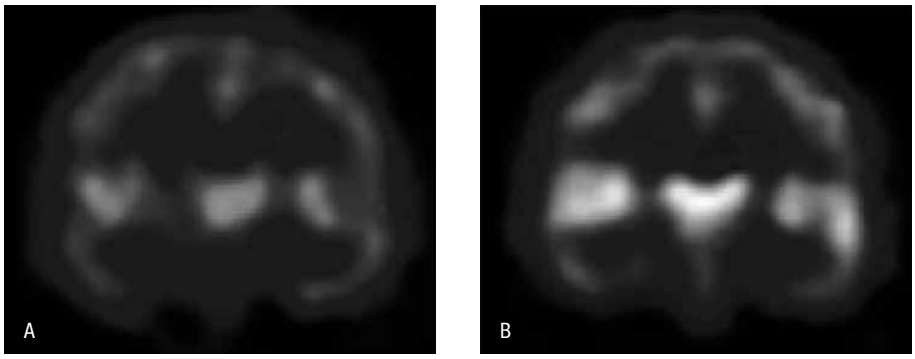


Fig. 4. Perfusion increment in Patient 6 (coronal view); A: Pre-stimulation slice, B: Post-subtraction slice.

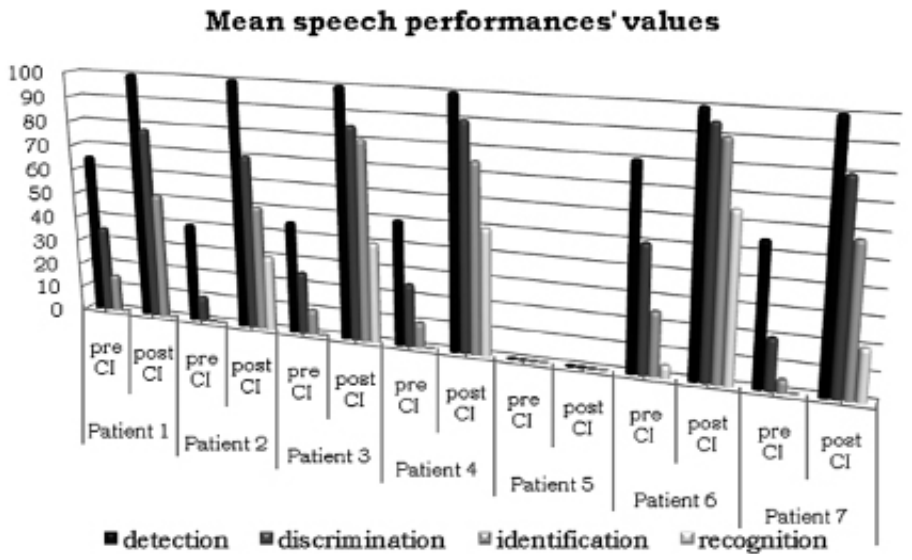


Fig. 5. Mean scores obtained in speech detection, discrimination, identification and recognition tests in each patient in the pre-surgical condition (with hearing aids) and at 24 months after cochlear implant activation.

multaneous bilateral acoustic stimulation from 2.08% to 13.75% in the right temporal areas, and from 1.81% to 19.00% in the left temporal areas. In patients 4, 6 and 7, a clearer inter-hemispherical activation asymmetry was observed, whereas in patient 5 there was no significant cortical activation after acoustic stimulation in comparison with the baseline SPECT. In this patient, in fact, baseline and post-stimulation tomograms were essentially superimposable. Neuropsychological and audiological functional pre-surgical assessments of this patient showed severe deficiency of auditory and language skills, which were also related to the absence of adequate rehabilitation of speech and refusal to use hearing aids. Therefore, in agreement with parents, it was decided to suspend the implantation. Consistent with the brain activation data obtained, patients who showed a greater activation of the left cerebral cortex were implanted on the right side (patients 1, 4, 6 and 7), while those with a greater responsiveness of the right temporal auditory areas were implanted on the left side (patients 2 and 3). In fact, it has been extensively demonstrated that the human acoustic pathway has a mainly crossed activation, so that stimulating the right ear mostly causes activation of the auditory cortex of the left hemisphere, and vice versa. Figure 5 shows a summary of the performance of auditory perception in each subject enrolled. Data refer to the last speech therapist's assessment before implantation with hearing aids and to the speech evaluation performed at 24 months after CI activation. Tests were administered in hearing mode with a conversational voice intensity. A correlation could be seen between the amount of cortical perfusion detected by SPECT and the results of auditory performance tests obtained by implanted patients. An improvement of auditory function performance tests, evaluated as increased rates of detection, discrimination, identification of vowels and consonants and recognition of words and phrases 2 years after CI activation, appeared to be considerable especially in those patients who had, pre-operatively, a higher increase of blood

flow from baseline in all tomograms of temporal auditory cortex areas. In particular, it can be noticed that a substantial percentage gain in recognition of sentences and words, compared to the pre-implant scores, occurred in subjects (patient 4 and 6) who showed a greater increase of cortical blood flow in tomograms closer to the median line (18.75 mm and 26.25 mm), i.e. at higher frequencies, according to current knowledge on tonotopics. We also noted that the performances seem even more related to the activation of the most medial tomograms, corresponding to medium-high frequencies. This finding is consistent with the well-known importance of these frequencies in speech understanding.

Discussion

A recent review stated that "the indications for CI in adults with pre-lingual deafness and prognostic factors should be analyzed on a case-by-case basis. Factors to be taken into account are mainly progression of deafness, use of hearing aids and rehabilitation (and in particular the methodology of rehabilitation), results with hearing aids, patient motivations and psychological aspects" [3]. Given the extreme variability of auditory outcomes, it can be assumed that functional neuroimaging can be considered as a critical factor for preoperative evaluation.

Functional neuroimaging can provide a non-invasive and reliable assessment of the features of the cerebral cortex. In particular, SPECT has largely proved to be an extraordinarily useful tool in recognition and description of human cerebral cortex activation patterns in response to different types of stimuli [6]. Currently, the value of SPECT in candidacy assessment for CI and prediction of their efficacy is still hypothetical. To strengthen its contribution, it would be necessary to correlate the functional information provided by pre-implantation imaging with post-implantation performances. SPECT was used in the evaluation of regional cerebral blood flow changes in the auditory cortex after acoustic stimulation [11-13]. However, there are only a few reports of SPECT-based auditory function assessment in severe-to-profound hearing impaired CI candidates [7 9]: in addition, there are no SPECT studies on auditory cortex activation in patients undergoing cochlear implantation, performed with multi-frequency acoustic stimuli administered through headphones in a bilateral and simultaneous way. It has been demonstrated that SPECT can provide reliable and objective information about the degree of a supposed hearing loss, or about hearing levels at low frequencies, particularly in patients with profound hearing loss [14]; this is of great importance, as other investigations among those commonly performed in the pre-implantation study of profoundly deaf patient, do not offer any objective assessment of the residual hearing at low frequencies. SPECT also allows assessment of the overall functioning of the auditory brain cortex, by generating qualitative and semi-quantitative data, which can be performed both before surgery and during follow-up of CI recipients [9]. In 2001, Roland chose SPECT to evaluate the activation of the auditory cortex of three post-lingual bilateral deaf CI candidates, using complex stimuli consisting of a videotaped story, in auditory-visual modality (mono-and binaurally presented, with hearing aids/CI) and in visual-only modality. The authors suggested that changes in the auditory cortex responsiveness in pre- vs. post-surgery conditions are related to improvements in speech perception scores; moreover, individuals with better outcome showed a more robust cortical response than subjects with poor outcome [15].

Among the patients enrolled in our study, patient 6 showed, in the post-stimulation scan, a significant asymmetry in the cortical brain activation in response to bilateral and simultaneous acoustic stimulation, with a prevalent activation of the left temporal cortex (19.00 vs 13.09). Considering the contralateral prevalence of auditory pathways, in the patients under examination the right ear is obviously the starting side of more responsive and preserved neural networks, if compared to the contralateral side, and therefore more suitable to optimize the performance of CIs. The validity of this approach is supported by the percentage gain in auditory tests performed by CI recipients. The best result in terms of verbal recognition performancs at 24 months from implantation was achieved by the same patient: in fact, he showed the highest activation and asymmetric inter-hemispheric response, and also the best score of perfusion increase in response to activation in correspondence of the most medial tomograms, representative of high frequencies. Patient 5 showed weak cortical activity after acoustic stimulation, confirming his clinical assessment of severe auditory and speech deficiency, which put in doubt the opportunity to perform cochlear implantation. Thus, this kind of activation pattern (strong response to acoustic stimulation and high inter-hemispheric asymmetry) is likely correlated with functional outcome (the more the perfusion increment and asymmetry, the better the performances achieved), although more patients should be studied to give statistical power to our findings. From this point of view, SPECT shows excellent potential to become a factor for selecting long-deprived profoundly deaf CI candidates: the proof of the persistence of excitable neural circuits through acoustic stimulation, measured as significant increase in blood flow in the temporal areas in response to specific stimuli, gives rise to the realistic possibility of CI benefits on auditory function.

Conclusions

Long-standing sensorineural hearing loss is generally considered to be a contraindication for cochlear implantation, because neural degeneration in the spiral ganglion and the possibility of trans-synaptic degeneration are considered to be associated with unsatisfactory clinical outcome. Prolonged hearing loss causes atrophy of cochlear nuclei: cochlear electrical stimulation seems to prevent, at least in part, degeneration of peripheral and central au-

ditory pathways induced by deafness [16]. For this reason, deaf people with a brief history of profound auditory deprivation show less degeneration of nervous structures, and also show a greater benefit from CI use compared to long-term deprived deaf CI recipients. In fact, the two main predictors of successful CI use are the duration and onset of deafness, in relation with the age of language acquisition. However, some subjects, despite of long deprivation, have shown satisfactory results from CI use. This phenomenon can be explained by the persistence of nerve connections that keep a certain potential for cortical function. SPECT may be suitable for assessing the existence of adequate cortical responses in order to have a realistic expectation about the gain of hearing from CI surgery. Another interesting use in this field is the opportunity to register cortical activation in response to electrical stimulation. Taking into account these data, we could predict the future use of this method in the study of bilateral deaf patients, in which acoustic stimulation could not be used to activate the auditory pathways and centres: any changes in brain metabolism can therefore be investigated through SPECT using electrical currents that directly activate the 8th pair of cranial nerves by trans-tympanic stimulation. This would make it possible to appreciate cortical perfusion gradients that cannot be obtained with acoustic stimulation, thereby demonstrating the possible continuity of auditory pathways, even though small and underactive, which could be still stimulated by the CI. In the light of these considerations, we believe that SPECT may be useful in assessing the auditory cortex patterns of activation in response to acoustic stimuli and, perhaps in the future, to electrical stimuli. Analysis through SPECT can indeed provide valuable elements of assessment to help predict the real possibility of recovery in pre-lingually patients undergoing cochlear implantation, to select the most suitable side to receive the CI, and to verify the integrity of retro-cochlear auditory pathways in the absence of auditory threshold by using electrical stimulation.

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Address for correpondence: Sara Giannantonio, Institute of Otorhinolaryngology, Catholic University of the Sacred Heart, l.go A. Gemelli 8, 00168 Rome, Italy. Tel. +39 06 30154439. Fax +39 06 3051194. E-mail: sara_giannantonio@yahoo.it