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Functional Neuroimaging Studies in Asymmetric Hearing Loss

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Key Words

Asymmetric hearing loss · Bimodal stimulation · Cochlear implants · Neuroimaging · Positron emission tomography

Abstract

This article presents an analysis of the impact of functional neuroimaging studies (positron emission tomography, PET) in asymmetric hearing loss based on the clinical expertise obtained from a group of 21 patients. In these patients, PET studies are performed at rest and after auditory stimulation in order to measure the increase in brain activity in the ipsi- and contralateral cortex, providing supporting evidence to recommend a specific treatment and the side to implant. In conclusion, PET is a useful tool for selected cases in which information on the metabolic status of the auditory pathway can drive the decision regarding the treatment of the most appropriate ear. However, in view of our small sample, further research is needed to confirm our results in this topic.

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Introduction

Asymmetric hearing loss (AHL) is defined as a difference of 15 dB or greater at two consecutive frequencies or a greater than 15% difference in the speech discrimination test between ears. The most extreme case of this type of hearing loss is single-sided deafness (SSD).

Bimodal hearing, which is a combination of electrical stimulation of one ear with a cochlear implant (CI) and acoustic stimulation of the opposite ear by a hearing aid (HA), is now a new criterion for CI surgery and is an ideal treatment for some AHL cases. The benefits in speech perception in quiet and noisy environments from the bimodal stimulation have been well reported and are described and listed by Ching et al. [2004, 2007]. Different authors [Sanhueza et al., 2011; Morera et al., 2012; Firszt et al., 2014] have concluded that patients with AHL who are not typical CI candidates can benefit from using a CI in the poorer ear with continued use of a HA in the better ear.

AHL is a contemporary topic in otological discussions around the world, and it represents part of the challenge to restore binaural performance for a variety of cases. For patients with pre-/perilingual onset of sensorineural hearing loss (SNHL) who have no HA experience in the poorer ear, it may not always be possible to restore binaural hearing. Therefore, we aimed to determine whether or not the audiometric definition of AHL is equivalent at the level of the central auditory system organisation? With this in mind, we investigated patients with profound SNHL in one ear and prolonged auditory deprivation in our clinical practice, and the following five AHL types were identified according to the overall hearing condition with particular reference to that for the better hearing contralateral ear: (i) normal hearing in the contralateral ear; (ii) stable, moderate-to-severe SNHL in the contralateral ear; (iii) progressive hearing loss in the better ear, which has recently become severe to profound, showing benefit from a hearing aid; (iv) prelingual deafness with early unilateral CI, and (v) postlingual deafness with long-term use of a unilateral CI (an old device) possibly requiring an upgrade CI in the implanted ear in order to further improve speech discrimination or a sequential implant in the contralateral ear to facilitate bilateral hearing. Counselling these patients about the potential benefit that can be achieved after CI surgery in the ear with long-term auditory deprivation is of great importance. The question is: 'Can neuroimaging studies, such as positron emission tomography (PET), be a useful tool in the prediction of the CI outcome in AHL patients with unilateral, long-term deprivation?'

The introduction of new non-invasive functional neuroimaging techniques, such as functional magnetic resonance imaging (fMRI), single photon emission computed tomography (SPECT) and PET, have given us the opportunity to study the human cortex. There are some advantages and disadvantages of fMRI over PET in auditory cortex studies. On the one hand, for the PET study, radioactive injections are needed; on the other hand, MRI tests are longer and the noise can interfere with the results, plus there are restrictions for patients with CIs due to the interaction with the magnetic field. The increases in regional blood flow (H_2O_{15}) and metabolism (^{18}F FDG) because of 'metabolic entrapment' is what Magistretti et al. [1999] described as the analysis of the biochemistry that gives rise to imaging signals. He deduced some of the cellular and molecular events that accompany neuronal activity in the working brain, ultimately laying the groundwork for determining the biochemistry that underlies human cognition.

For some years, functional SPECT and PET studies have been conducted during the performance of complex tasks, such as auditory discrimination of tonal intensity and language that required the subject's attention through which the activation of the auditory cortex, frontal association cortex and lateral occipital cortex could be demonstrated [Mazziotta et al., 1982; McLaughlin et al., 1992]. During verbal stimulation, Zatorre et al. [1992] noticed using PET that discrimination of phonetic structures led to an increased activity in part of Broca's area of the left hemisphere, which suggested a

Table 1. Summary of the clinical features for subjects studied with PET and results

Pat. No.	Age, years	Mean PTA/% disyllabic words/type		Radiotracer	PET results		Suggested treatment	CI results
		PE	BE		at rest	after stim.		
1	39	115 dB/0%/Pre	85 dB/85 % HA/Post	¹⁸ F-FDG	Hypo	ND	CI in PE + HA BE	Not implanted
2	30	120 dB/0%/Pre	96 dB/50% HA/Peri	¹⁸ F-FDG	Hypo	1/1	CI PE + HA BE	Open set, summation
3	27	110 dB/0%/Pre	88 dB/90% HA/Pre	¹⁸ F-FDG	Hyper	1/1	CI PE (uncertain)	Not implanted
4	37	115 dB/10%/Peri	108 dB/70% HA/Peri	¹⁸ F-FDG	Hypo	1/1	CI PE + HA BE	Open set, summation
5	67	117 dB/0%/Peri	71 dB/85% HA/Post	¹⁸ F-FDG	Hypo	-1/1	CI PE + HA BE	No open set
6	59	111 dB/0%/Pre	43 dB/100% HA/Post	¹⁸ F-FDG	Hyper	1/1	CI PE (uncertain)	Not implanted
7	52	97 dB/0%/Post MH (O)	86 dB/95% HA/Post MH (O)	¹⁸ F-FDG	Hyper	1/1	CI? Codacs? PE	Not implanted
8	72	120 dB/0%/Peri	88 dB/58% HA/Post	¹⁸ F-FDG	Hyper	1/1	CI PE (uncertain)	Not implanted
9	28	120 dB/0%/Peri	78 dB/90% HA/Peri	¹⁸ F-FDG	Hyper	1/1	CI PE + HA BE	No open set, summation
10	48	56 dB/20% HA/Post, THI: 88	72 dB/75% HA/Peri	¹⁸ F-FDG	Hyper	1/1	CI PE (tinnitus)	Not implanted
11	57	90 dB/0%/long Post	42 dB/86% HA/Post	¹⁸ F-FDG	Hypo	-1/1	CI PE + HA BE	Not implanted
12	31	120 dB/0%/Post	3d B/100% (SSD)	¹⁸ F-FDG	Hypo	-1/1	CI PE or BCI	BCI
13	69	120 dB/0%/Peri	63 dB/40% HA/Post (AN)	¹⁸ F-FDG	Hyper	-1/1	No CI PE, follow-up	
14	41	78 dB/16%/Post (HI)	71 dB/6%/Post (HI)	¹⁸ F-FDG	Hypo	-/-	No CI, central deafness	
15	54	121 dB/0%/long Post	88 dB/82% HA/Post	¹⁸ F-FDG	Hyper	-1/1	No CI PE	
16	48	106 dB/10% HA/Post	87 dB/50% HA/Post	¹⁸ F-FDG	Hyper	1/1	CI PE	Not implanted
17	75	120 dB/0%/Pre	92 dB/45% HA/Post	H ₂ O ₁₅	Hypo	-1/1	CI PE + HA BE	Open set
18	33	110 dB/0%/Peri	92 dB/75% HA/Peri	H ₂ O ₁₅	Hypo	1/1	CI PE + HA BE	Open set, no summation
19	67	110 dB/0%/Pre	110 dB/75% HA/Pre	¹⁸ F-FDG	Hypo	-1/1	CI BE	Open set
20	54	120 dB/0%/Post	98 dB/90% HA/Post	¹⁸ F-FDG-H ₂ O ₁₅	Hyper	1/1	CI PE + HA BE	Open set, summation
21	23	108 dB/0%/Peri	17 dB/90% (SSD)	¹⁸ F-FDG	Hyper	1/1	CI PE	Not implanted

1/1 = Activation of both cortices; -1/1 = activation of the contralateral cortex to the ear where the stimulus was performed; BE = better ear; PE = poorer ear; mean PTA = 0.5–4 kHz in dB; Pre = prelingual; Post = postlingual; Peri = perilingual; Hypo = hypometabolism; Hyper = hypermetabolism; ND = no data; BCI = bone conduction implant; summation = auditory benefit from CI and HA; uncertain = uncertain prognosis after implantation; MH = mixed hearing loss; AN = acoustic neuroma; O = otosclerosis; HI = head injury; stim. = stimulation; THI = Tinnitus Handicap Inventory [Herráiz et al., 2001].

role for articulatory recoding in phonetic perception and processing changes in pitch-produced activation of the right prefrontal cortex. More recently, Zatorre and Belin [2001] confirmed the specialisation of the auditory cortex: the left-hemisphere auditory cortex for rapid temporal processing and the right-hemisphere belt cortical areas for spectral processing. Some years later, this theory was confirmed using fMRI [Jamison et al., 2006].

Several PET studies have demonstrated that improvement in speech perception after CI surgery cannot be expected in patients who have had no hypometabolism in the auditory cortex before receiving the implant. These findings are related to neuroplasticity phenomena. Fallon et al. [2008] reported that the central auditory system is not immutable and has a remarkable capacity for plasticity changes, even into adulthood, as a result of changes in afferent inputs. In prelingual, bilateral, profound SNHL cases, duration of deafness prior to implantation has an influence on both auditory cortical activation and speech perception outcomes following cochlear implantation, and it is known that the extent and amount of hypometabolism in temporal lobes determine whether those regions remain available for auditory language in prelingually deaf children [Lee et al., 2007] and that hypometabolism in temporal cortices of deaf subjects indicates a latent susceptibility to auditory restoration via a CI [Arbizu et al., 1999; Giraud et al., 2001; Lee et al., 2001; Cervera-Paz et al., 2009].

AHL makes it difficult to identify a sound source, localise sounds in space and understand in noisy environments. Firszt et al. [2006] demonstrated the utility of modern neuroimaging tech-

niques in functional investigations of the human auditory system by providing additional insight as to how the cortical auditory pathways change with experience related to sound deprivation and sound experience. However, published studies with respect to imaging refer to cases of bilateral deafness; there are no reports in the literature that provide information on the activation and organisation of the auditory central nervous system in AHL, in which one ear has either not been stimulated or has suffered a long period of auditory deprivation.

Based on our clinical experience obtained in a group of CI candidates examined using PET, the aim of the present study is to demonstrate the established methodology and decision process with particular reference to CI candidates with AHL, and 2 representative cases are briefly reviewed from our sample including 21 patients.

Clinical Experience and Study Methodology

Twenty-one patients with AHL presenting as potential CI candidates in our CI programme, with a variety of hearing loss types, were examined using PET.

Table 1 summarises the clinical features, types of PET scan performed, results obtained and speech discrimination results after cochlear implantation in the cases when it was indicated and the patient agreed to proceed.

Based on the clinical expertise obtained in these subjects, the following study methodology is proposed: PET studies were performed using a high-resolution scanner (ECAT EXACT HR+, Sie-

Fig. 1. PET results at rest and after right-ear (RE) stimulation. LE = Left ear; n.s. = non-significant.

mens) using ^{18}F -FDG tracer. Scanning was performed on 2 consecutive days in patients who underwent the ^{18}F -FDG PET study. Subjects were scanned at rest and during monaural auditory stimulation of both ears, separately, using audible disyllabic words as stimuli (i.e. +15 dB over auditory thresholds). PET images obtained at rest and during auditory stimulation were subtracted to create images where the value for each voxel represented the areas of significant increase in brain activity (>2 SD). Basal neuronal activity (at rest) was compared with a database of normal-hearing people in the primary and association auditory cortex and related with auditory processing cortical areas (Brodmann areas 41, 42, 21 and 22, available from hearing-unrelated studies).

Case Reports

Patient 1. A 28-year-old female presented with congenital profound SNHL in the left ear (mean pure-tone average, PTA, 0.5–4 kHz, 120 dB HL) with 0% speech discrimination for disyllabic words, and 10 years of progressive SNHL in the right ear reaching a profound SNHL 2 years earlier (mean PTA, 0.5–4 kHz, 92.5 dB HL). A HA used in the right ear resulted in 65% discrimination for disyllabic words. Otological or CT scan abnormalities were not present. The patient requested a CI to improve speech discrimination.

During the PET study, the basal status showed hypometabolism in the left auditory cortex and an increase in activity in the right cortex, contralateral to the poorer ear. After acoustic stimulation of the right ear, the better-functioning ear, a significant increase in metabolism was shown in the left cortex with no significant changes in the right cortex. Stimulation of the left ear showed no changes in the metabolic activity of the right or left cortex compared to basal activity (fig. 1).

The recommendation was a CI in the right ear, the ‘better ear’. The decision was prompted by two main facts: firstly, the results of PET advised against implantation in the poorer ear and, secondly, the history of progressive hearing loss and, therefore, expect-

tations of worsening in hearing in the short term added to the fact that better speech discrimination was expected with a CI than a HA. The latter favours the implantation in the right ear. At the 7-year follow-up, the patient demonstrated speech discrimination scores of 84% for disyllabic words and 100% for CID (Central Institute for the Deaf) sentences in the CI-treated right ear.

Patient 2. A 60-year-old male presented with a history of meningitis at 3 months of age: progressive SNHL in the right ear (mean PTA, 0.5–4 kHz, 117.5 dB HL) since 14 years of age with 0% speech discrimination for disyllabic words and progressive hearing loss in the left ear over the last 35 years with a stable SNHL (mean PTA, 0.5–4 kHz, 71.85 dB HL). He used a HA since age 10 years. Speech discrimination for disyllabic words with the HA was 75%. MRI showed no abnormalities.

At rest PET demonstrated hypometabolism in both auditory cortices. Stimulation of the left ear, the better-functioning ear, showed an increase in metabolic activity of both cortices compared to the basal status mainly on the contralateral cortex (fig. 2).

Based on these results demonstrating hypometabolism in both auditory cortices in the basal condition and an increase in metabolism in both cortices after stimulation of the left (better-functioning) ear, the recommendation was to provide a CI in the right ear. This way, bimodal stimulation was provided: the poorer ear (right ear) was stimulated with the CI, while the left ear continued to be stimulated with a HA. At the 7-year follow-up, the speech discrimination results were 71% for disyllabic words with the CI-treated right ear, 84% with the HA-treated left ear and 96% with both ears using bimodal stimulation (CI and HA).

Discussion

Animal studies have shown a modification in the auditory cortex (cortex plasticity) in AHL subjects compared to normal-hearing subjects [Cheung et al., 2009]. Kral et al. [2013] studied white cats suffering from AHL implanted at an early and late age, and compared the subsequent plasticity following chronic CI stimula-

Fig. 2. PET results at rest and after left-ear (LE) stimulation. RE = Right ear.

Fig. 3. Algorithm summarising possible scenarios obtained with PET and their hypothetical outcome.

tion with local field potentials. The plasticity mechanism was similar at all ages, only the extent of the effect faded with increasing age, with faster progression at the ipsilateral hemisphere.

Neuroimaging can determine if the duration of deafness prior to implantation influences both auditory cortical activation and speech perception outcomes following CI surgery. The study by Giraud and Lee [2007] concluded that the auditory brain organisation (metabolism) assessed with PET immediately before CI surgery can efficiently predict subsequent speech outcome, and resting metabolism in the deaf brain can be a fairly good indicator of speech performance after auditory rehabilitation. In their study, they have proven that PET is a very useful exploratory tool, which is not only able to visualise the well-known time-dependent cross-modal reorganisation of auditory temporal cortices but also adaptive higher cognitive mechanisms.

In our experience, PET can be a useful tool for predicting CI outcome in cases of AHL in whom one ear has either not been stimulated or has suffered a long period of auditory deprivation.

PET studies suggest that when studying an ear that has suffered a long period of hearing deprivation, a good prognostic indicator may be the hypometabolism of the contralateral auditory cortex in the basal situation (at rest) and an increase in activity in both cortices after auditory stimulation of the better-functioning ear (fig. 3). Hypometabolism in the basal situation indicates that the primary auditory areas have not suffered ‘colonisation’ by the visual system based on cross-modal plasticity mechanisms described by Lee et al. [2001], i.e. they remain functional when facing stimulation via a CI. An increase in the activity in both cortices after stimulating the better-functioning ear (and not only an increase in the contralateral cortex) suggests the potential responsiveness of

the contralateral auditory cortical areas facing stimulation with a CI in the poorer ear, which has suffered a long period of auditory deprivation. However, in order for this to happen, a functional brainstem auditory pathway is required that is capable of conducting the stimulations from the implanted cochlea to the auditory areas in the cortex both ipsi- and contralateral to the treated ear. Different authors [Trune, 1982; Perier et al., 1984; Steward and Rubel, 1985; Hashisaki and Rubel, 1989; Pasic and Rubel, 1989; Moore, 1990] have described changes in a number of neurons, the size of the neuronal soma and synapsis density at different prethalamal auditory pathway centres following the destruction of the cochlea in neonates of different animal species, which could adversely affect the auditory rehabilitation of these patients.

The cases presented here belong to an ongoing study that is currently recruiting subjects that belong to any of the five hearing loss patterns described earlier in this paper. Our aim is to further evaluate the information from PET scans obtained before implantation and the ensuing decision process, and to compare the post-operative results from speech discrimination outcomes and repeated PET scans in our group of subjects. Ultimately, analyses of the findings may help to further support clinical guidelines in the management of such cases.

Disclosure Statement

The authors declare no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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