Acta Otorrinolaringol Esp. 2009;**60(3):**160-8

Acta Otorrinolaringológica Española

www.elsevier.es/otorrino

ORIGINAL ARTICLE

Results of a functional magnetic resonance study of the primary auditory cortex (I): general characteristics and individual outcomes

Luis M. Menéndez-Colino,[a,*] Josep Traserra,[b] Carles Falcón,[c] Joan Berenguer,[d] Teresa Pujol,[d] Joan Doménech,[b] and Manuel Bernal-Sprekelsen[b]

[a]*Servicio de Otorrinolaringología, Hospital Virgen de la Salud, Toledo, Spain*
[b]*Servicio de Otorrinolaringología, Hospital Clínic, Barcelona, Spain*
[c]*Unidad de Resonancia Magnética Funcional, Universidad de Barcelona, Barcelona, Spain*
[d]*Centro de Diagnóstico por la Imagen (CDI), Hospital Clínic, Barcelona, Spain*

Received October 2, 2008; accepted December 22, 2008

KEYWORDS
Functional magnetic resonance;
Auditory pathways;
Auditory cortex;
Hearing

Abstract
Objective: To demonstrate and investigate the activation patterns of the primary auditory cortex (Heschl's gyrus) using functional magnetic resonance imaging (fMRI).
Material and methods: Pure tone stimuli at 750 Hz and 2000 Hz were delivered to the right and left ear of 32 normal-hearing volunteers (18-49 years old) in 20-second on-off cycles. The fMRI data were obtained using a 1.5 Tesla scanner and processed with SPM2.
Results: For both tone frequencies, bilateral hemispheric activation was identified in the transverse temporal gyrus (Heschl's gyrus) in 29 subjects (90.62%) in response to pure tone stimuli with a probability level of $P<.001$. For monaural stimulation, bilateral hemispheric activation was observed with generally greater extent of activation in the Heschl's gyrus (HG) contralateral to the stimulated ear.
Conclusions: These results demonstrate that fMRI is a useful imaging technique to investigate the auditory cortex. The contralateral auditory cortex is more responsive than the ipsilateral cortex to tones presented monaurally.

*Corresponding author.
E-mail address: 34227lmc@comb.es o lmenendez@sescam.jccm.es (L.M. Menéndez-Colino).

0001-6519/$ - see front matter

PALABRAS CLAVE
Resonancia magnética funcional;
Vía auditiva;
Córtex auditivo;
Audición

Resultados en el estudio del córtex auditivo mediante resonancia magnética funcional (I): características generales y resultados individuales

Resumen
Objetivo: Investigar y demostrar los modelos de activación en el córtex auditivo primario mediante la resonancia magnética funcional (RMf).
Material y métodos: Se estimuló la audición, a 32 voluntarios normooyentes (intervalo de edad, 18-49 años), con tonos de 750 y 2.000 Hz en ciclos de 20 s de estimulación, seguidos por 20 s de reposo. Se empleó un escáner de RM de 1,5 T y la herramienta estadística SPM2.
Resultados: Para ambas frecuencias (750 y 2.000 Hz) en 29 de 32 sujetos (9.62%) se registró una activación cortical auditiva en la circunvolución de Heschl de ambos hemisferios con una $p < 0,001$. Ante la estimulación auditiva monoaural se ha registrado una activación cortical auditiva bilateral que, generalmente, fue mayor en el hemisferio contralateral al oído estimulado.
Conclusiones: Estos resultados demuestran que la RMf es una técnica de imagen útil para la investigación del córtex auditivo. La estimulación monoaural con tonos puros activa, predominantemente, el córtex auditivo contralateral.

Introduction

Within the auditory brain cortex we can distinguish one or more primary areas surrounded by secondary or association areas. The primary auditory cortex is located at the level of the temporal lobe in the transverse Heschl's gyrus (areas 41 and 42).

This large lobe is located below the lateral scissure and, on its outer side, presents three circumvolutions oriented obliquely: the superior, middle and inferior gyri. The superior temporal scissure is parallel to the lateral scissure, and caudally presents an ascending branch which ends in the angular circumvolution. At the external edge of the lateral scissure, several oblique circumvolutions form the transverse gyrus of Heschl; these transverse and relatively short circumvolutions, medial to the posterior part of the superior temporal gyrus, constitute the primary auditory cortex in humans. The primary auditory cortex or coniocortex is equivalent to area 41 of Brodmann, and corresponds to the first superior temporal gyrus. The paraconiocortex, included or not, according to different authors, in the primary auditory cortex, corresponds to area 42 of Brodmann and to the rest of transverse circumvolutions and the temporal plane, the smoothest portion of the superior surface of the temporal lobe and caudal to the transverse circumvolutions.[1,2]

The temporal plane, behind the paraconiocortex, and the posterior part of the superior circumvolution include area 22, which extends towards the operculum and inferior parietal lobe. This area in the left hemisphere is known as Wernicke's area or the speech area. It is a centre of auditory understanding, where lesions cause an aphasia fundamentally characterized by a deficit in the understanding of the words which are heard. For some authors, this area extends to all the inferior parietal lobe: area 39, angular lobe, and area 4. supramarginal lobe. Areas 39 and 40 are polymodal areas, of integration of sensory information, auditory, visual, and somesthetic, which therefore correspond to the secondary auditory cortex of non-human primates and other mammals. All cortical areas are interconnected with the auditory cerebral cortex of the contralateral hemisphere through the corpus *callosum*. Within each hemisphere, the arcuate fascicle is the main route of auditory association. This fascicle connects Wernicke's area and the parietal lobe with Broca's area or *area triangularis* of the inferior frontal gyrus. Broca's area includes areas 44 and 45 of Brodmann and is the motor centre for language.

In summary, the primary auditory cortex (area 41) corresponds to Heschl's gyrus (HG) in its medial part, and according to some authors, is also part of Brodmann area 42 (lateral part of HG) and the secondary auditory or association cortex is formed by area 22 (*planum polare* and *planum temporale*); for some authors this area extends to the complete inferior parietal lobe; area 39, angular lobe, and area 4. supramarginal lobe.[3]

From the point of view of neuroimaging, the term brain activation refers to the fast and concomitant biochemical and biophysical changes of neurons, the basic functional units of the brain, in relation to its activity. Recent developments in magnetic resonance imaging (MRI) based on the possibility of detecting changes in blood oxygenation and those related to the rapid acquisition of images have led to techniques that can measure, in the entire brain and non-invasively, the physiological processes believed to be related to neuronal activity. These new techniques are known as functional MRI (fMRI). Increased regional brain activity carries with it a local increase in perfusion and metabolism. This relationship has been tested with high-resolution optical images,[4] blood flow studies using positron emission tomography (PET)[5,6] and fMRI studies.[7]

The objectives to meet during the present study were:

— Definition of auditory stimulation protocols (paradigms) and implementation of the proposed auditory fMRI project, which was already partially published.[8]

— Demonstrate the ability to record and clearly separate, through fMRI, the brain activity related to the perception of auditory stimuli from other concurrent brain activity.
— Evaluation of possible differences in cortical response with regard to age, gender, presentation of the sound stimulus and frequency of the stimulus, to establish parameters of auditory cortical activity in subjects with normal hearing that can serve as reference for studies of auditory cortical activity in patients with alterations in hearing.
— Assess the degree of reproducibility of the auditory fMRI.

Material and methods

Study subjects

This study was conducted with a sample of 32 volunteer subjects with normal hearing, of both genders, aged between 18 and 50 years. A sample of 32 subjects was considered, as it was estimated that it would be sufficiently representative to establish the parameters of normality. The 32 subjects were divided into two groups: group A (between 18 and 34 years) and group B (between 35 and 50 years).

The age was limited to 50 years because above this age, presbyacusis phenomena may occur to distort the results; this age group may be the subject of a subsequent study.

Each of the volunteers signed an informed consent before the fMRI testing, reflecting their agreement to participate in the study.

Inclusion criteria

— Voluntary subject, with no medical-surgical neurological or otolaryngeal history, especially without a history in middle and inner ear.
— Subjects of 18-50 years of age with no history of claustrophobia or other reasons that prevent the practice of fMRI (pacemakers, ferromagnetic material ...).
— Subjects with otolaryngology and audiological examination within normal range.

Exclusion criteria

— Patient with history of middle and inner ear surgery (ventilation tubes, tympanoplasty, neurectomy, etc).
— Patients under 18 years of age or 50 or more years of age, with a history of claustrophobia or other reasons preventing the practice of fMRI (pacemakers, ferromagnetic material...).
— Patients with an auditory alteration in the otolaryngeal examination (tone threshold audiometry with a frequency threshold greater than 25 dB).
— Patients with Ménière's disease, otosclerosis or chronic middle ear infections.
— Professionals exposed to environmental and/or work-related noise.
— Patients with hearing aids.
— Patients with language disorders.
— Patients with a history of recent severe head injury.

Material

For this study we prepared the following resources:

1. MRI equipment (1.5 T) from the Centre for Diagnostic Imaging (CDI) at the "Hospital Clínic de Barcelona."
2. Audio system compatible with MRI, necessary for the auditory stimulation of the brain cortex.
3. IBM compatible PC Pentium IV and the statistical tool SPM (Statistical Parametric Mapping) necessary for processing the images obtained by fMRI.
4. Laptop with programme generating the necessary sound files as paradigms for stimulation of the auditory cortex. The composition of these sound files is detailed in the methodology.

The equipment in points 3 and 4 was obtained through the co-operation of the Amplifon S.L. company.

Type of study and methods

This is a prospective longitudinal, controlled clinical-experimental trial in volunteer patients with normal hearing (normal tonal audiometry), between 18 and 50 years of age.

All subjects in the study had a full medical history taken and an otologic examination comprising: oto-microscopy, tympanometry, and tone threshold audiometry of the air and bone routes. Once it was verified that the previous tests were within normal ranges, each subject received an fMRI consisting in:

— Sagittal locators.
— Axial anatomical slices (10) in sequence enhanced in T1 of the region under study (temporal cortex).
— Sequences of auditory function in the 10 axial slices. The acquisition parameters were TE=60 ms; TR=2000 ms; delay =8000 ms for the paradigm.
— 3D structural image (slice thickness of 1.5 mm) to locate the exact anatomical region of the activation patterns. The paradigm used involved alternating periods of silence of 20 s and 20 s of auditory stimulation, with 4 different types of stimuli that are applied cyclically for 8 min and 20 s (3 phases) with an intensity of 86 dB SPL: 750 Hz in the left ear, 750 Hz in the right ear, 2000 Hz in the left ear, and 2000 Hz in the right ear, all of them formed by discontinuous tones of 125 ms of duration.

Preparation and statistical analysis of the data

The neurofunctional images have been recorded in DICOM format (individual files each corresponding to a volume slice) and converted to Analyze 7.5 format using the MRICRO programme (software developed by Chris Rorden; www.psychology.nottingham.ac.uk) and 50 volumetric files of 10 slices were obtained (covering the auditory cortex), from the original 500.

All treatments carried out on these functional image volumes were performed using the statistical tool SPM2 (Statistical Parametric Mapping, software from Wellcome Department of Cognitive Neurology, Institute of Neurology, London; http://www.fil.ion.ucl.ac.uk/spm; with the programme Matlab 6.5 MathWorks, Natick, United States). The images have been processed using a Pentium IV processor with Windows 98 operating system.

The first volume (corresponding to the initial 10 s for the stabilization of the signal) of each subject was discarded and the remaining 49 were used for further analysis. The SPM is a digital tool allowing statistical analysis of information collected in medical imaging. The neurofunctional images have been subjected to identical pre-treatment in all cases, consisting of motion correction, spatial normalization and smoothing.

Statistical verification is then obtained using the general linear model to see in which parts of the brain the variations in image intensity during the test correlate with phases of auditory stimulation.

Results

General characteristics

The first tests of auditory fMRI were started in April 2002 and, after trying several paradigms in 15 different subjects, a paradigm for auditory stimulation was successfully established and installed on a PC laptop. A total of 40 fMRI tests were carried out on 32 volunteer subjects. In the end, 8 of them underwent a second control test of auditory fMRI to assess the reproducibility of the test. In 3 different subjects the fMRI had to be interrupted due to the emergence of claustrophobic feeling, without any further consequence or complication. The average age (standard deviation) of the 32 subjects was 34.75 (8.67), with an interval of 23-49 years. Of the 32 volunteers, 17 were women and 15 men. By age sub-group, 16 were included in group A (18-34 years), 8 males and 8 females, and 16 in group B (35-49 years), 7 males and 9 females. Of the 32 subjects, 30 were right-handed and 2 left-handed (one 27 year-old male and one 23-year-old female).

Individual results

Of the 32 volunteer subjects tested for auditory fMRI, statistically significant bilateral activation was observed in the primary auditory cortex in 29 and in the other 3 subjects no activation was observed. In other words, in 90.62% of the cases cortical activation has been observed in response to auditory stimulation with the paradigm used in the study. A statistical threshold of $P<.001$ has been used in this result. Figure 1 and Table show the probability of activation of different points (voxels) or contiguous regions of voxels (clusters) corresponding to a volunteer with normal hearing, ie the probability that the time evolution of that Voxel or cluster is random (null hypothesis) or is influenced by the periods of auditory stimulation and rest of the paradigm used. Therefore, a very low value indicates that it is very unlikely that the temporal evolution of that voxel is random and it is concluded that that voxel or cluster has been activated during the auditory stimulation (paradigm).

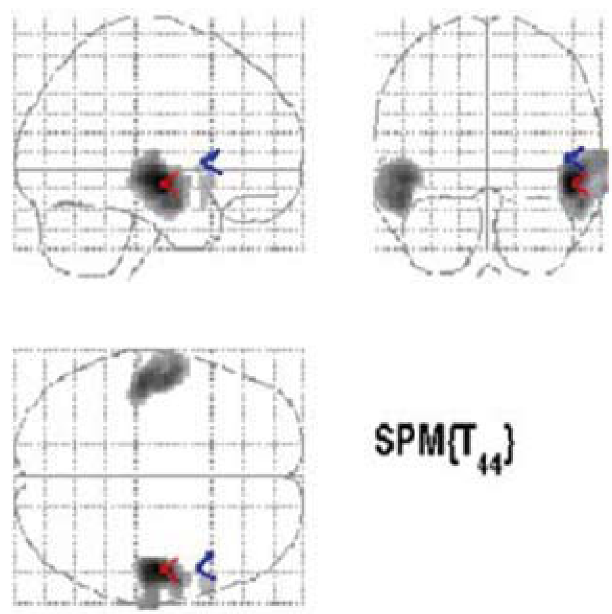
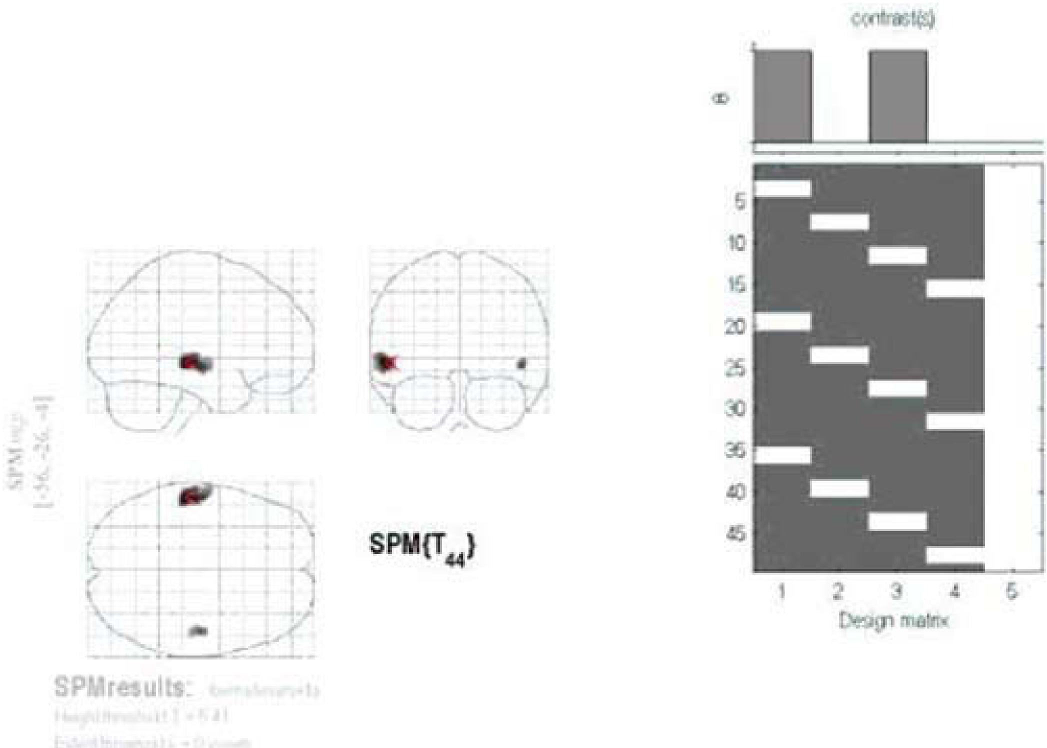


Figure 1 Glass brain of a volunteer with normal hearing, with bilateral register of temporal cortical activity (auditory cortex) higher in the right hemisphere in the three orthogonal projections.

Table 1 Probabilities of activation of clusters of the volunteer with normal hearing in Figure 1

Set-level		Cluster-level			Voxel-level							
P	c	$p_{corrected}$	k_E	$p_{uncorrected}$	$p_{xxx\text{-}corr}$	$p_{xxx\text{-}corr}$	7	(Z)	$p_{uncorrected}$	x,y,z, mm		
.995	5	.000	1460	.000	.000	.000	10.39	7,35	.000	50	–12	–0
					.000	.000	7.10	5,77	.000	56	–4	–18
					.029	.000	5.60	4,90	.000	60	–16	4
		.000	1276	.000	.000	.000	7.77	6,13	.000	–50	–24	–4
					.000	.000	7.49	5,90	.000	–52	–10	–16
		.350	80	.036	.967	.020	3.70	3,50	.000	54	12	–16
					.909	.021	.76	.40	.000	50	16	–6
		.964	20	.266	.994	.024	3.71	3,44	.000	50	10	2
		1.000	2	.752	1.000	.065	3.30	3,10	.001	–64	–26	4



Statistics: *p-values adjusted for search volume*

set-level p	set-level c	cluster-level $p_{corrected}$	cluster-level k_E	cluster-level $p_{uncorrected}$	voxel-level $p_{FWE-corr}$	voxel-level $p_{FDR-corr}$	voxel-level T	voxel-level $(Z_≡)$	voxel-level $p_{uncorrected}$	x,y,z {mm}
0.001	2	0.000	326	0.000	0.000	0.000	8.56	6.53	0.000	-56 -26 -8
					0.000	0.000	7.71	6.10	0.000	-54 -16 -6
		0.000	69	0.000	0.001	0.000	6.99	5.78	0.000	48 -16 -4

table shows 3 local maxima more than 8.0mm apart

Height threshold: T = 5.41, p = 0.000 (0.050)
Extent threshold: k = 0 voxels, p = 1.000 (0.050)
Expected voxels per cluster, <k> = 3.450
Expected number of clusters, <c> = 0.05
Expected false discovery rate, <= 0.00

Degrees of freedom = [1.0, 44.0]
Smoothness FWHM = 10.3 10.9 11.1 {mm} = 5.2 5.4 5.6 {voxels}
Search vol: 1083712 cmm; 135464 voxels; 691.0 resels
Voxel size: [2.0, 2.0, 2.0] mm (1 resel = 156.24 voxels)

Figure 2 Glass brain, table of probabilities of another volunteer with normal hearing, when applying auditory stimulation to the right ear.

Thus, the red line shows the probability that the voxel indicated by the red arrow in the glass brain is <.001 and, therefore, is very likely to have been activated. Similarly, the probability of randomly finding that cluster with that pattern of activity-rest by chance is virtually zero.

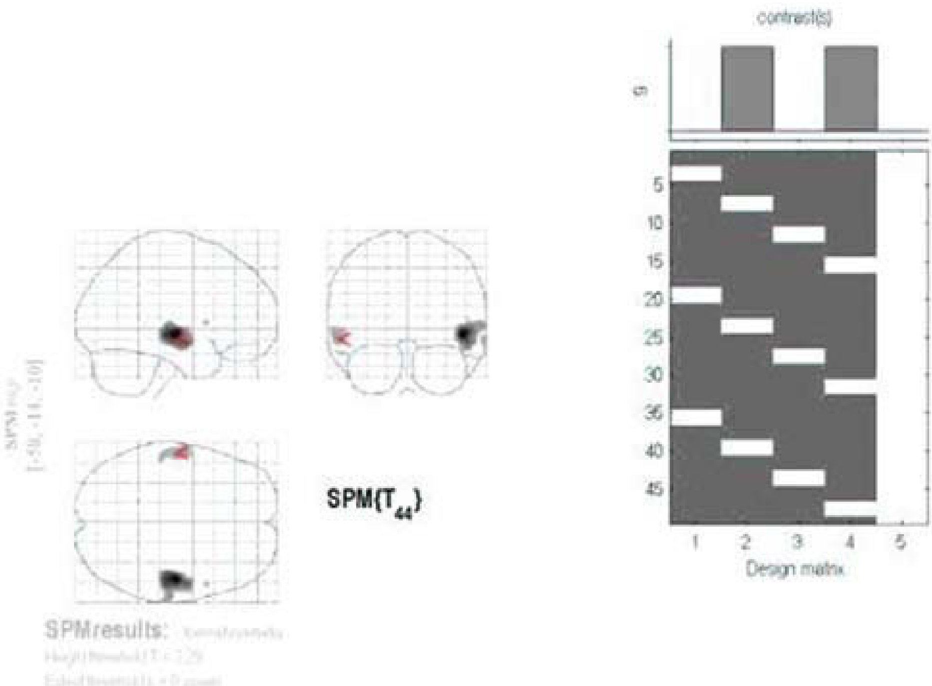
On the other hand, the blue line shows that the probability of the voxel indicated by the blue arrow in the glass brain is 0.994, that is, there is a 99.4% chance (96.4% in the cluster) of finding that voxel (cluster) randomly in the brain with that behaviour. This indicates that no conclusion can be drawn as to whether the voxel follows the pattern of activation-rest or has a random behaviour.

The 3 subjects (9.38%) in whom no statistically significant cortical activation was observed (*P*<.001) were males of 28, 27 and 47 years of age, and like all subjects in the study, showed a normal audiometry.

In analyzing the results of the 32 subjects, which are obtained with monaural stimulation of the right ear, bilateral cortical activation was recorded in 29 cases (90.6%) and no cortical activation was observed in 3 (9.4%).

Of the 29 (90.6%) cases with bilateral cortical activation, in 27 (84.3%), it is greater on the side which is contralateral to the stimulated ear, that is, in the left hemisphere, and in 2 of the 32 subjects (6.3%) the observed cortical activation was also bilateral, but higher on the side ipsilateral to the stimulated ear, ie higher in the right hemisphere (Figure 2).

Figure 2 shows the glass brain and the table of probability of activation of different voxels and clusters or set of voxels of volunteer with normal hearing, after auditory stimulation of the right ear. The glass brain shows that the recorded cortical activation is bilateral, although greater in



Statistics: *p-values adjusted for search volume*

set-level		cluster-level			voxel-level					x,y,z {mm}
p	c	$p_{corrected}$	k_E	$p_{uncorrected}$	$p_{FWE-corr}$	$p_{FDR-corr}$	T	($Z_{\equiv}$)	$p_{uncorrected}$	
0.999	4	0.000	795	0.000	0.000	0.000	10.36	7.34	0.000	48 -14 -4
					0.001	0.000	6.87	5.63	0.000	52 -8 -12
					0.333	0.005	4.65	4.17	0.000	64 -20 2
		0.008	224	0.001	0.305	0.004	4.69	4.20	0.000	-58 -14 -10
					0.898	0.028	3.96	3.64	0.000	-56 -26 -4
		0.972	12	0.363	0.744	0.016	4.17	3.81	0.000	66 -24 -10
		0.996	5	0.569	0.999	0.086	3.48	3.25	0.001	52 10 4

table shows 3 local maxima more than 8.0mm apart

Height threshold: T = 3.29, p = 0.001 (1.000)
Extent threshold: k = 0 voxels, p = 1.000 (1.000)
Expected voxels per cluster, <k> = 15.006
Expected number of clusters, <c> = 9.88
Expected false discovery rate, <= 0.13
Degrees of freedom = [1.0, 44.0]
Smoothness FWHM = 10.3 10.9 11.1 {mm} = 5.2 5.4 5.6 {voxels}
Search vol: 1683712 cmm; 135464 voxels; 801.0 resels
Voxel size: [2.0, 2.0, 2.0] mm (1 resel = 156.24 voxels)

Figure 3 Glass brain, table of probabilities of another volunteer with normal hearing, when applying auditory stimulation to the left ear.

the contralateral area (left hemisphere) to the stimulated ear (right ear).

In analyzing the results of the 32 subjects, obtained with monaural stimulation of the left ear, bilateral cortical activation was observed in 28 subjects (87.5%) and in 4 (12.5%) no statistically significant cortical activation was observed. Of the 28 subjects (87.5%) with bilateral cortical activity registration, this bilateral activation was greater in the contralateral area to the stimulated ear in 25 of them (78.1%), in other words, in the right hemisphere (Figure 3) and in 3 (9.4%) the observed cortical activation was also bilateral, but greater in the area ipsilateral to the stimulated ear, ie greater in the left hemisphere.

Figure 3 shows the glass brain and the table of probability of activation of different voxels and clusters or set of voxels of another volunteer, after auditory stimulation of the left ear.

In the case of the 2 left-handed individuals (a 27-year-old male and a 23-year-old female), the activation after auditory stimulation, registered at the cortical level, was bilateral.

With monaural stimulation of the right ear, both subjects showed bilateral activation which was greater in the contralateral area to the stimulated ear, that is, in the left hemisphere. With monaural stimulation of the left ear, both subjects showed bilateral activation which was greater in the contralateral area to the stimulated ear, ie in the right hemisphere.

It is possible to obtain high-resolution or three-dimensional images of the activation recorded at the cortical level, characterized by great brightness (Figure 4).

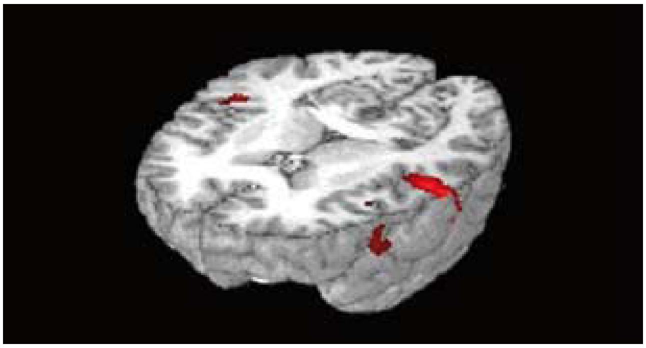


Figure 4 Three-dimensional image of a volunteer with normal hearing, showing bilateral activation of the primary auditory area in the temporal lobe. Axial slice.

Discussion

Elaboration of the paradigm

In April, 2002, the initial auditory fMRI tests began to be carried out at the Hospital Clínic in Barcelona, thanks to an agreement between the otolaryngology service and the CDI, and the backing of the company Amplifon Ibérica S.L. During the first 6 months the auditory stimulation paradigm was determined. In order to do this, different types and sequences of fMRI were tested as well as auditory stimuli in a pilot study on 15 different subjects. The first tests used auditory stimuli applied via an analogue audiometer and standard fMRI sequences without finding a reproducible cortical activity level. Auditory stimuli were also used through a reading of text, and resulted in an activation of the auditory area, both of the primary and association areas, and therefore this type of stimulation was dismissed since the objective was stimulation only in the primary auditory area.

In developing the auditory stimulation paradigm, the background noise produced by the MRI scanner (96 dB SPL) had to be taken into account, because this noise causes auditory stimulation in the subject under study and contaminates the cortical activation produced by the auditory stimulation paradigm used.

To avoid this problem, tests were carried out with different parameters and periods of stimulation/rest, until a paradigm was obtained that caused a targeted activation of the auditory cortex.

This paradigm consists of alternating periods of 20 s of silence and 20 s of auditory stimulation, with 4 different types of stimuli that occur cyclically during 8 min and 20 s: 750 Hz in the left ear, 750 Hz in the right ear, 2000 Hz in the left ear and 2000 Hz in the right ear, all of them formed by discontinuous tones lasting 125 ms and with an intensity of 86 dB SPL. The acquisition parameters were: TE=60 ms; TR=2000 ms; delay =8000 ms for the paradigm.

This delay is necessary to record the cortical activation due solely to the stimulus presented through the headphones, since the activation due to the noise produced by the resonance scanner when acquiring images disappears during the delay (8000 ms=8 s) and is not recorded in the image.

Thus, in testing, there is a period (20 s) in which there is auditory stimulation and another one of rest (20 s) in which the MRI machine records the cortical activity produced by the previous period of auditory stimulation.

Aside from the need to develop a "good paradigm" that produces cortical activation of a specific area, the auditory cortex in this case, it must be borne in mind that the "attention" of the subject during the test run is a determinant factor in the registration of cortical activity, as demonstrated by some studies reported in the literature. Thus, Czisch et al[9] compared cortical activity in 14 subjects with normal hearing during the periods of wakefulness and sleep, and noted that during all stages of sleep (REM and non-REM), the cortical activity due to acoustic stimulation was lower than during the period of wakefulness. This would indicate that during sleep the processing of external stimuli is not abolished but can be significantly altered compared to the wakeful state. These findings are similar to the results of studies on the influence of attention on the activation of primary sensory areas carried out by Somers et al[10] and Watanabe et al.[11] In contrast, other authors such as Porter et al[12] observed a similar auditory cortical activation during sleep and during wakefulness, requiring further studies to attempt to explain the discordant results between these studies.

Individual results

The individual results showed auditory cortical activation in 29 (90.62%) subjects and in 3 (9.38%), there was no recorded cortical activity. This does not mean that in the case of these 3 subjects there was no cortical activation in the auditory cortex, but instead that the signal recorded by the resonance scanner, due to the auditory stimulation, was not sufficiently intense and therefore was different from the signal recorded by the resonance scanner during the period of rest or without stimulation.[13,14]

One possible reason explaining why the signal recorded by the resonance scanner due to auditory stimulation is not sufficiently intense is that the attention of the subject during the test was low; several authors have noted that the attention of the subject increases significantly the extent and magnitude of activation of the auditory cortex.[15]

In the analysis of the monaural activation by the right ear, we recorded bilateral cortical activity in the auditory cortex in 90.6% of cases (29/32), and this activity was greater in the contralateral area to the stimulated ear (left auditory cortex) in 84.3% of cases, and in 6.3% the cortical activity in the auditory cortex was bilateral, but greater in the area ipsilateral to the stimulated ear (right auditory cortex), with $P<.001$.

In 9.4% of cases (3/32) no statistically significant auditory cortical activation was recorded ($P<.001$).

With respect to monaural stimulation by the left ear, we recorded bilateral cortical activity in the auditory cortex in 87.5% of cases (28/32), and this activity was greater in the contralateral area to the stimulated ear (right auditory cortex) in 78.1% of cases and in 9.4% the cortical activity in the auditory cortex was bilateral, but greater in the area ipsilateral to the stimulated ear (left auditory cortex) with a $P<.001$.

In 12.5% of cases (4/32) no statistically significant auditory cortical activation was recorded (*P*<.001).

These results are consistent with studies carried out using electroencephalography (EEG) and magnetoencephalography (MEG), in which it has been observed that, with a monaural auditory stimulation, the projections towards the contralateral auditory cortex take precedence over the ipsilateral.[16]

Greater cortical activation contralateral to the stimulated ear is also due to complex excitatory and inhibitory mechanisms in the auditory pathway. Thus, studies in animals using evoked responses have shown that binaural stimulation produces a neural response in both brain hemispheres which is greater than the sum of 2 monaural stimulations.[17]

In a study using fMRI, the auditory cortical activation by monaural auditory stimulation in both ears was 30% lower than the activation by binaural stimulation, indicating that there is some inhibitory or excitatory mechanism in the auditory pathway. A lateralization in the auditory cortical activation was also noted, as in the results obtained, and this activation was predominant in the hemisphere contralateral to the stimulated ear.[18]

In the individual analysis of the two left-handed subjects, there was no difference in the method of activation of the auditory cortex, thus with the monaural stimulation the auditory cortex is bilaterally activated, although less than the contralateral. These results contradict the theory of some authors that left-handed individuals tend to present a greater activation of the right auditory cortex, and right-handed individuals, a greater activation of the left auditory cortex.[19] These results are not significant due to the small number of left-handed subjects; therefore, more studies are needed to investigate this possible difference between left-handed and right-handed individuals.

The possibility of obtaining high-resolution three-dimensional images for each volunteer enables us to obtain a precise location of the auditory cortex. This information could be used as pre-operative reference in surgery of tumours or other illnesses affecting the temporal lobe.[20]

Conclusions

We can summarize in three points the conclusions drawn from the results obtained and presented:

— Auditory fMRI is a non-invasive test allowing monitoring of the activation of the auditory cortex after stimulation of the sensorineural auditory pathway in subjects with normal hearing.
— The application of a paradigm for auditory stimulation and adequate acquisition and delay rest times are essential to record and separate cortical activation by auditory stimulation from the cortical activation by the noise of the device and other concurrent brain activity.
— In assessing the results obtained, it appears that monoaural stimulation of a subject with normal hearing produces a bilateral activation of the auditory cortex, and the tendency is for that activation to be greater in the area contralateral to the stimulated ear.

Conflict of interests

The authors have indicated there is no conflict of interest.

References

1. Webster DB. An overview of mammalian auditory pathways with an emphasis on humans. In: Webster DB, Popper AN, Fay RR, editors. The mammalian auditory pathway: Neuroanatomy. New York: Springer-Verlag; 1992. p. 1-22.
2. Winer JA. The functional architecture of the medial geniculate body and the primary auditory cortex. In: Webster DB, Popper AN, Fay RR, editors. The mammalian auditory pathway: Neuroanatomy. New York: Springer-Verlag; 1992. p. 222-409.
3. Morosan P, Rademacher J, Schleicher A, Amunts K, Schormann T, Zilles K. Human primary auditory cortex: cytoarchitectonic subdivisions and mapping into a spatial reference system. Neuroimage. 2001;13:684-701.
4. Frostig RD, Lieke EE, Ts'o DY, Grinvald A. Cortical functional architecture and local coupling between neuronal activity and the microcirculation revealed by in vivo high-resolution optical imaging of intrinsic signals. Proc Natl Acad Sci U S A. 1990;87:6082-6.
5. Fox PT, Mintun MA, Raichle ME, Herscovitch P. A noninvasive approach to quantitative functional brain mapping with H2 (15)O and positron emission tomography. J Cereb Blood Flow Metab. 1984;4:329-33.
6. Mazziotta JC, Huang SC, Phelps ME, Carson RE, MacDonald NS, Mahoney K. A noninvasive positron computed tomography technique using oxygen-15-labeled water for the evaluation of neurobehavioral task batteries. J Cereb Blood Flow Metab. 1985;5:70-8.
7. Kwong KK, Belliveau JW, Chesler DA, Goldberg IE, Weisskoff RM, Poncelet BP, et al. Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation. Proc Natl Acad Sci U S A. 1992;89:5675-9.
8. Menéndez-Colino LM, Falcón C, Traserra J, Berenguer J, Pujol T, Herrera O, et al. Vanguardia en el estudio del córtex auditivo. Demostración de su activación mediante resonancia magnética funcional. Acta Otorrinolaringol Esp. 2004;55:247-51.
9. Czisch M, Wetter TC, Kaufmann C, Pollmacher T, Holsboer F, Auer DP. Altered processing of acoustic stimuli during sleep: reduced auditory activation and visual deactivation detected by a combined fMRI/EEG study. Neuroimage. 2002;16:251-8.
10. Somers DC, Dale AM, Seiffert AE, Tootell RB. Functional MRI reveals spatially specific attentional modulation in human primary visual cortex. Proc Natl Acad Sci U S A. 1999;96:1663-8.
11. Watanabe T, Harner AM, Miyauchi S, Sasaki Y, Nielsen M, Palomo D, et al. Task-dependent influences of attention on the activation of human primary visual cortex. Proc Natl Acad Sci U S A. 1998;95:11489-92.
12. Portas CM, Krakow K, Allen P, Josephs O, Armony JL, Frith CD. Auditory processing across the sleep-wake cycle: simultaneous EEG and fMRI monitoring in humans. Neuron. 2000;28:991-9.
13. Jancke L, Shah NJ, Posse S, Grosse-Ryuken M, Muller-Gartner HW. Intensity coding of auditory stimuli: an fMRI study. Neuropsychologia. 1998;36:875-83.
14. Friston KJ, Frith CD, Frackowiak RS, Turner R. Characterizing dynamic brain responses with fMRI: a multivariate approach. Neuroimage. 1995;2:166-72.
15. Grady CL, van Meter JW, Maisog JM, Pietrini P, Krasuski J, Rauschecker JP. Attention-related modulation of activity in primary and secondary auditory cortex. Neuroreport. 1997;8:2511-6.

16. Loveless N, Vasama J P, Makela J, Hari R. Human auditory cortical mechanisms of sound lateralisation: III. Monaural and binaural shift responses. Hear Res. 1994;81:91-9.
17. Barth DS, Kithas J, Di S. Anatomic organization of evoked potentials in rat parietotemporal cortex: somatosensory and auditory responses. J Neurophysiol. 1993;69:1837-49.
18. Scheffler K, Bilecen D, Schmid N, Tschopp K, Seelig J. Auditory cortical responses in hearing subjects and unilateral deaf patients as detected by functional magnetic resonance imaging. Cereb Cortex. 1998;8:156-63.
19. Millen SJ, Haughton VM, Yetkin FZ. Functional magnetic resonance imaging of the central auditory pathway following speech and pure-tone stimuli. Laryngoscope. 1995;105:1305-10.
20. Ojemann JG, Miller JW, Silbergeld DL. Preserved function in brain invaded by tumor. Neurosurgery. 1996;39:253-8.