

Representation of Interaural Temporal Information from Left and Right Auditory Space in the Human Planum Temporale and Inferior Parietal Lobe

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The localization of low-frequency sounds mainly relies on the processing of microsecond temporal disparities between the ears, since low frequencies produce little or no interaural energy differences. The overall auditory cortical response to low-frequency sounds is largely symmetrical between the two hemispheres, even when the sounds are lateralized. However, the effects of unilateral lesions in the superior temporal cortex suggest that the spatial information mediated by lateralized sounds is distributed asymmetrically across the hemispheres. This paper describes a functional magnetic resonance imaging experiment, which shows that the interaural temporal processing of lateralized sounds produces an enhanced response in the contralateral planum temporale (PT). The response is stronger and extends further into adjacent regions of the inferior parietal lobe (IPL) when the sound is moving than when it is stationary. This suggests that the interaural temporal information mediated by lateralized sounds is projected along a posterior pathway comprising the PT and IPL of the respective contralateral hemisphere. The differential responses to moving sounds further revealed that the left hemisphere responded predominantly to sound movement within the right hemifield, whereas the right hemisphere responded to sound movement in both hemifields. This rightward asymmetry parallels the asymmetry associated with the allocation of visuo-spatial attention and may underlie unilateral auditory neglect phenomena.

Keywords: auditory motion, hemispheric asymmetry, inferior parietal cortex, interaural temporal processing, planum temporale

Introduction

Many sounds that are behaviorally relevant to humans, such as speech and music, contain predominantly low-frequency energy. The horizontal localization of these sounds mainly relies on the processing of interaural temporal disparities (ITDs; Wightman and Kistler, 1992), produced by path length differences from the sound source to the two ears, as low frequencies produce little or no interaural energy differences. Consequently, humans — and other mammals with good low-frequency hearing — have evolved a remarkable sensitivity to ITDs of the order of a few tens of microseconds (Durlach and Colburn, 1978). Sounds with the same energy at the two ears activate the auditory areas in both superior temporal cortices about equally strongly, even when the sounds are completely lateralized towards one or the other ear by means of ITDs (Woldorff *et al.*, 1999). This is probably why unilateral superior temporal lesions usually have surprisingly little effect on most auditory functions, such as the ability to understand speech or appreciate music (for a review, see Engelien *et al.*, 2001). In contrast, lateralized visual stimuli produce a largely contralateral response in early visual areas, and unilateral lesions in the

occipital cortex may lead to complete blindness in the contralesional hemifield. Unilateral superior temporal lesions do, however, often lead to deficits in sound localization (for a review, see Clarke *et al.*, 2000). Several studies reported selective sound localization deficits in the contralesional hemifield following superior temporal lesions in either hemisphere. Other studies described localization deficits in both hemifields after lesions in one (either the left or right) but not the other hemisphere (e.g., Zatorre and Penhune, 2001). The lesion results suggest that the processing of auditory spatial information differs from the non-spatial information, in that it is distributed asymmetrically across the two hemispheres.

In order to verify this notion, one would have to measure the responses to sounds that have the same energy at the two ears and that are lateralized solely by means of ITDs, because only in that way would any functional asymmetry in the observed responses not be confounded by the known anatomical asymmetry in the number of crossed and uncrossed excitatory projections in the ascending auditory pathway (Webster *et al.*, 1992). Unfortunately, animal physiological data on the representation of ITDs in auditory cortical areas are still scarce. A recent study by Fitzpatrick *et al.* (2000) suggests that, in the rabbit, the distribution of best ITDs (the ITD producing maximal discharge) is skewed towards the contralateral hemifield. The recordings of Fitzpatrick *et al.* are from the primary auditory cortex (PAC) and the distribution might look somewhat different in non-primary areas, particularly in areas belonging to the dorsal 'where' stream that is assumed to be specialized in auditory spatial processing in primates, including humans (for a review, see Rauschecker and Tian, 2000; Warren *et al.*, 2002; Warren and Griffiths, 2003). Moreover, the results of superior temporal lesions suggest that, in humans, any contralateral asymmetry in the representation of auditory space may be shifted somewhat towards one or the other hemisphere (e.g., Zatorre and Penhune, 2001; for a review, see Clarke *et al.*, 2000).

Deficits in sound localization may also be observed in patients with hemispatial neglect (Bellmann *et al.*, 2001). Chronic neglect most reliably occurs after right- and not left-hemisphere lesions. This asymmetry is generally explained by assuming that the left hemisphere deploys attention mainly within the right hemifield, whereas the right hemisphere deploys attention within both hemifields. In accordance with this notion are findings which show that parietal activations associated with the allocation of spatial attention, and more generally with global spatial processing, exhibit an asymmetry towards the right hemisphere (reviewed in Mesulam, 1999; Marshall and Fink, 2001). Moreover, auditory spatial processing has been found to activate parietal and frontal regions more strongly in

the right than in the left hemisphere (Griffiths *et al.*, 1998; Weeks *et al.*, 1999, 2000). It is unclear, whether a similar rightward asymmetry is also inherent in the preattentive, sensory processing of spatial information. In the auditory domain, the existing evidence from human lesion data (Clarke *et al.*, 2000; Zatorre and Penhune, 2001) and from neuroimaging and electrophysiological studies of auditory spatial processing (Baumgart *et al.*, 1999; Kaiser *et al.*, 2000; Warren *et al.*, 2002; Zatorre *et al.*, 2002a) are contradictory with respect to this question.

The current study uses functional magnetic resonance imaging (fMRI) to investigate how the interaural temporal information mediated by low-frequency sounds is represented in the auditory areas of the human superior temporal cortex. In order to isolate brain regions involved in interaural temporal processing, we compared the blood oxygen level-dependent (BOLD) responses to sounds that were matched in energy and spectral composition and differed solely in their interaural temporal properties. Our hypothesis was that lateralized sounds would yield a stronger activation in the contralateral superior temporal cortex as compared to midline sounds. Any contralateral asymmetry in the auditory cortical representation of sound laterality may or may not be superposed by a right-hemisphere dominance for auditory spatial processing.

Materials and Methods

Stimuli and Experimental Protocol

The experiment comprised a total of five sound conditions, as well as a silent condition. The sounds consisted of 50 ms bursts of noise, filtered to the low-frequency region (200–3200 Hz), where interaural temporal cues are most salient, and presented at a rate of 10 per s. All sounds had the same energy at both ears. They were delivered through electrostatic headphones, which produced minimal image distortions and passively shielded the subjects from the scanner noise. In three of the five sound conditions, labeled 'center', 'left static', and 'right static', the noise bursts were presented with static ITDs of 0, -500 or 500 μ s, respectively, so the perception was that of a stationary sound centered on the midline, or lateralized towards the left or right ear, respectively. By convention, a positive ITD means that the sound to the left ear is lagging the sound to the right ear, whereas a negative ITD denotes the reverse situation. In the remaining two sound conditions, labeled 'left moving' and 'right moving', the train of noise bursts moved back and forth between the midline and the left or right ear. The impression of movement was created by varying the ITD continuously between 0 and -1000 or 1000 μ s. The ITD variation was linear, with a rate of 1000 μ s per s, so it took 2 s for the sounds to move from the midline to the left or right ear and back to the midline again. The starting point of the movement was randomized from trial to trial.

The sparse imaging technique (Hall *et al.*, 1999) was applied to minimize the effect of the scanner noise on the recorded activity, and cardiac triggering (Guimaraes *et al.*, 1998) of image acquisition was used to reduce motion artifacts in the brainstem signal resulting from basilar artery pulsation. Each image acquisition was triggered by the first R wave of the electrocardiogram occurring after a 6.5 s period of either sound presentation or silence. No images were acquired during this 6.5 s period. Due to cardiac triggering, the exact repetition time of image acquisitions (TR) varied slightly over time and across subjects; the average TR amounted to 9.24 s. Five sound epochs containing the five sound conditions in pseudorandom order were alternated with a single silence epoch. Each epoch lasted ~46 s, during which the stimulus was presented five times. A total of 300 images were acquired per listener (50 for each condition).

Subjects were asked to listen to the sounds and take particular notice of their spatial attributes. To avoid that the subjects moved their eyes in the direction of the sounds, they were asked to fixate a cross at the midpoint of the visual axis and perform a visual control task. The task

was to press a button with the left or right index finger upon each occurrence of the capital letter 'Z' in either of two simultaneous, but uncorrelated, sequences of random one-digit numbers that were shown to the left and the right of the fixation cross. The numbers were presented for 50 ms once every 2 s.

fMRI Data Acquisition

Blood oxygen level-dependent (BOLD) contrast image volumes were acquired with a Siemens Vision 1.5 T whole-body scanner and gradient echo planar imaging ($T_R \approx 9.24$; $T_E = 66$ ms). Each brain volume consisted of twenty 4 mm slices with an interslice gap of 0.4 mm and an in-plane resolution of 3.125×3.125 mm², which were acquired in ascending order. At the beginning of each measurement, a high-resolution structural image was acquired using the 3-D MP-RAGE sequence. The midsagittal slice of the structural image was used to orient the slices of the functional images along the line between the anterior and posterior commissures. The functional slices were positioned so that the inferior colliculus (IC) in the midbrain was covered by the third slice.

Data Analysis

Structural and functional images were analyzed using SPM99 (<http://www.fil.ion.ucl.ac.uk/spm>). After realignment, slice time correction, coregistration with structural images, normalization and smoothing (10 mm full width at half maximum), the functional image time series of fourteen subjects, comprising a total of 4200 volumes, were subjected to a fixed-effects group analysis. The height threshold for activation was $t = 4.65$ ($P_{\text{voxel}} \leq 0.05$, corrected for multiple comparisons across the entire scanned volume). In Fig. 6, a cluster threshold ($P_{\text{cluster}} \leq 0.001$, corrected) was also used to illustrate the whole extent of the respective activations. The contrasts between the static lateralized sound conditions and the center condition failed to meet the threshold criterion of $t \geq 4.65$, but did produce significant superior temporal activation when a less stringent criterion was used ($t \geq 3.09$; $P_{\text{voxel}} \leq 0.001$, uncorrected). In these cases, a small volume correction was applied within bilateral spheres of 15-mm radius centered on the plana temporale (PT; dashed outlines in Fig. 3a,b). The position of PT was approximated as 10 mm posterior and lateral, and 5 mm superior to the 'center of gravity' of the probability map of Heschl's gyrus (HG) for the fourteen subjects who participated in the experiment (see Table 1 for Montreal Neurological Institute coordinates). The probability map was constructed by labeling HG in both hemispheres of each subject using the MRICro software (<http://www.psychology.nottingham.ac.uk/staff/crl/micro.html>). For that, the area between the face of HG and the connecting line between the first transverse sulcus and Heschl's sulcus, or the sulcus intermedius in the case of a duplicate HG, was marked in

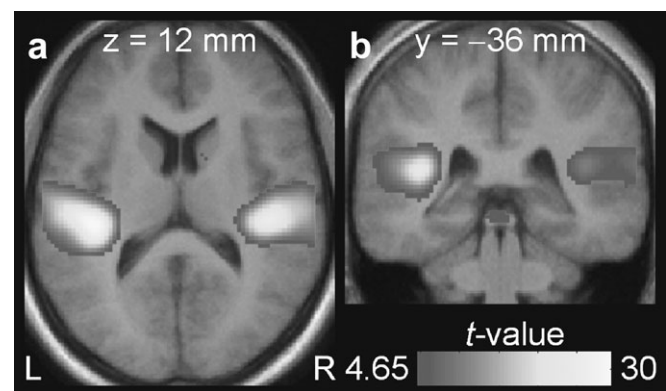


Figure 1. Activation for the contrast between all sound conditions and silence, rendered onto the average structural image of the group. Axial section at $z = 12$ mm showing bilateral activation on the supratemporal plane (a), coronal section at $y = -36$ mm showing activation in IC (b). The color scale gives the t -value for the comparison between the BOLD responses to the sound conditions and silence. Activation was thresholded at $t = 4.65$ ($P_{\text{voxel}} \leq 0.05$, corrected). A color version of this figure is available as online supplementary material.

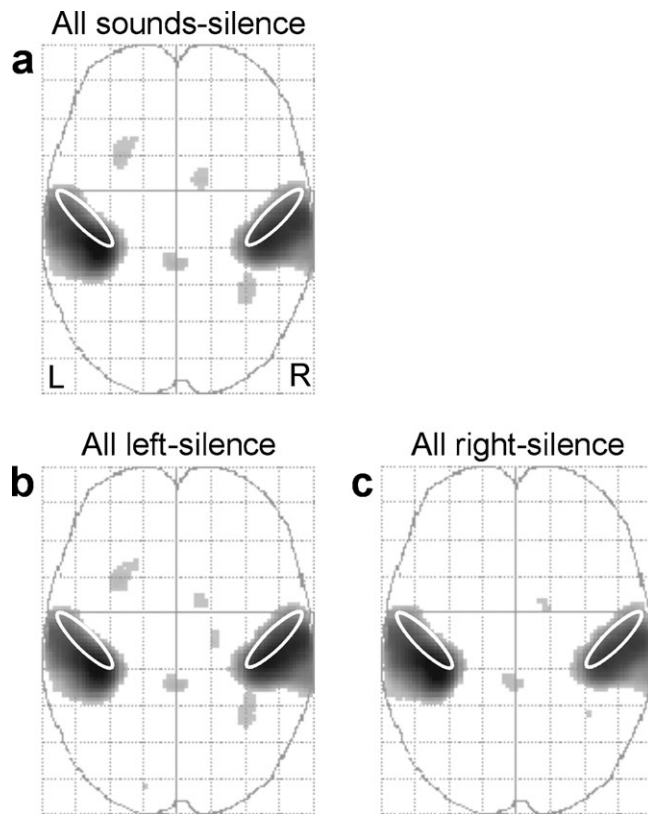


Figure 2. Contrasts between lateralized sounds and silence. The two lower panels show the axial projection of the activations to the contrasts between all left- (*b*) and all right-lateralized sounds (*c*) versus silence for a height threshold of $t = 4.65$ ($P_{\text{voxel}} \leq 0.05$, corrected). For a comparison, the upper panel shows the activation to the all sounds versus silence contrast, replotted from Figure 1. The light-gray ellipses mark the approximate position of HG. When contrasted against silence, the lateralized sounds produced a largely symmetric response.

Table 1
MNI coordinates and t -values of auditory activation foci

Contrast	Brain region	Coordinates x, y, z	t	P_{voxel} (corrected)
All sounds-silence	Left STG	-40, -28, 12	29.36	<0.001
	Right STG	46, -24, 10	25.36	<0.001
	IC	-2, -36, -8	6.24	<0.001
All left-center	Right PT	54, -24, 10	5.62	0.001
All right-center	Left PT	-46, -28, 6	5.45	0.001
Left static-center	Right PT	56, -24, 8	4.42	0.002 ^a
Left static-center	Left PT	-62, -28, 20	3.65	0.032 ^a
Left moving-center	Right PT/TPJ/IPL	64, -32, 14	6.35	<0.001
Right moving-center	Left PT/TPJ/IPL	-56, -26, 12	6.61	<0.001
	Right PT/TPJ/IPL	66, -34, 16	5.92	<0.001
Right-left moving	Left PT/TPJ	-54, -28, 12	4.70	0.04

STG: superior temporal gyrus; PT: planum temporale; TPJ: temporo-parietal junction; IPL: inferior parietal lobe. Unless marked, probabilities were corrected for multiple comparisons within the entire scanned volume. Only the most significant voxel of each activation cluster is listed.

^aProbabilities based on a hypothesis-driven (Warren *et al.*, 2002; Zatorre *et al.*, 2002a) volume of interest analysis in a sphere of 15 mm radius centered at 56, -28, 12 mm (right PT) or -55, -30, 12 mm (left PT).

successive coronal slices of the individual structural scans between the posterior and the anterior edge of HG. The individual marked volumes of fourteen subjects were then averaged to produce a probability map of HG.

Subjects

Fourteen right-handed subjects (six male, eight female), between 22 and 33 years of age, with no history of hearing disorder or neurological

disease participated in the experiment after having given informed consent. The experimental procedure was approved by the local ethics committee.

Results

Comparison between All Sounds and Silence

The BOLD response produced by all five sound conditions (center, left and right static, left and right moving) was compared to the response produced by the silent condition to reveal regions sensitive to the noise stimuli used in the current experiment. The contrast yielded three clusters of significant activation in the auditory pathway, one large cluster in each supratemporal plane (Fig. 1*a*) and a smaller cluster spanning both inferior colliculi in the midbrain (Fig. 1*b*). The MNI coordinates and t -values of the most significant voxels in these activation clusters are listed in Table 1. The activation in the supratemporal plane comprised the region of HG and extended onto the PT, which is the part of the supratemporal plane posterior to HG.

The lateralized sounds produced a largely symmetric response when contrasted against the silence condition (Fig. 2). The activation patterns for the contrasts between all left- (Fig. 2*b*) and all right-lateralized sounds (Fig. 2*c*) versus silence were similar to the activation pattern produced by the all sounds versus silence contrast (Fig. 2*a*). This is in accordance with the results of Woldorff *et al.* (1999), who also contrasted lateralized sounds against a silent baseline and found no significant inter-hemispheric differences in activation strength. The light-gray ellipses in Figure 2 mark the approximate position of HG in the group of 14 listeners.

Differential Sensitivity to Lateralized Sounds: Contralateral Asymmetry

Contrasts between sound conditions and silence would be expected to represent all brain areas that are sensitive to the sounds or to one of the sounds' various perceptual attributes. In order to isolate those regions that are involved in interaural temporal processing and examine their response to lateralized sounds, the response to all left- or all right-lateralized sounds (left static/moving or right static/moving) was compared with the response to the central sound (center). Figure 3*a,b* shows that the lateralized sounds produced a stronger contralateral response compared to the central sound. The activation to the all left versus center contrast was largely confined to the right supratemporal plane (Fig. 3*a*), whereas the main area of activation in the all right versus center contrast was in the left supratemporal plane (Fig. 3*b*). The differential activation produced by the lateralized sounds was largely limited to the PT (Fig. 3*a,b*, Table 1). The PT has previously been implicated with the processing of spatial sound attributes and sound movement in humans (Baumgart *et al.*, 1999; Warren *et al.*, 2002; Zatorre *et al.*, 2002a). In the monkey, non-primary auditory fields posterior to PAC have been shown to form a posterior-dorsally directed processing stream that is assumed to be specialized in auditory spatial processing (Rauschecker and Tian, 2000).

In order to assess the relative contributions of the static and moving sound conditions to the activation in PT, each of the lateralized sound conditions (left/right static/moving) was contrasted separately against the center condition. Figure 3*c,d* shows that the moving sounds (cross-hatched bars) produced a consistently stronger activation in PT than the static sounds

(hatched bars). In fact, neither the left static versus center contrast nor the right static versus center contrast produced any activation that exceeded the threshold criterion of $t = 4.65$, corresponding to a P -value of ≤ 0.05 , corrected for multiple comparisons across the entire scanned volume. However, using a more lenient threshold criterion ($t = 3.09$; $P_{\text{voxel}} \leq 0.001$, uncorrected) and a hypothesis-driven (Warren *et al.*, 2002; Zatorre *et al.*, 2002a) volume of interest analysis revealed that the left static versus center and right static versus center contrasts produced a significant activation in the PT of the respective contralateral hemisphere (see Table 1); there was no significant activation of the corresponding region in the ipsilateral hemisphere. The search volumes for these analyses were spheres of 15 mm radius centered on the left and right PT; they are marked by black dotted outlines in Figure 3a,b. The position of PT in each hemisphere was approximated as 10 mm posterior and lateral, and 5 mm superior to the center of HG, which was derived from the averaged map of HG for the fourteen subjects who participated in this experiment (see Materials and Methods).

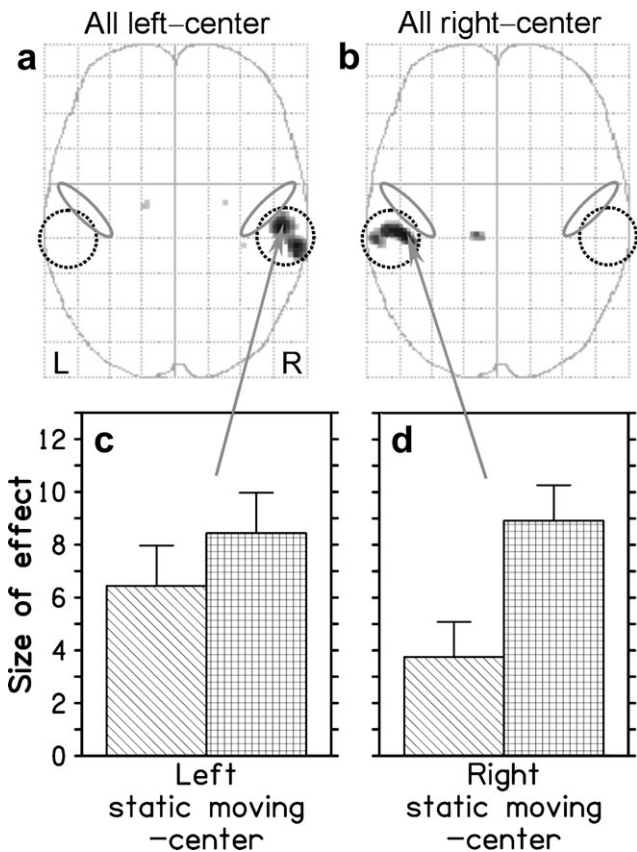


Figure 3. Contrasts between the lateralized sounds and the central sound. The upper panels show the axial projection of the activation to all left-lateralized (a) and all right-lateralized sounds (b) relative to the central sound; the height threshold was $t = 4.65$ ($P_{\text{voxel}} \leq 0.05$, corrected). The differential activation to the lateralized sounds was confined to the contralateral PT. (c, d) The relative contributions of the static and moving sounds to the contrasts shown in (a, b). (c) The contrast-weighted beta-values for the left static versus center (hatched bar) and left moving versus center contrasts (cross-hatched bar) at the most significant voxel in the all left versus center comparison (gray arrow pointing to a). (d) The analogous analysis for the right-lateralized sounds. The moving sounds activated the PT more strongly than the static sounds. The black, dotted outlines in panels a and b mark the regions used for the volume of interest analyses of the left and right static versus center contrasts (see text).

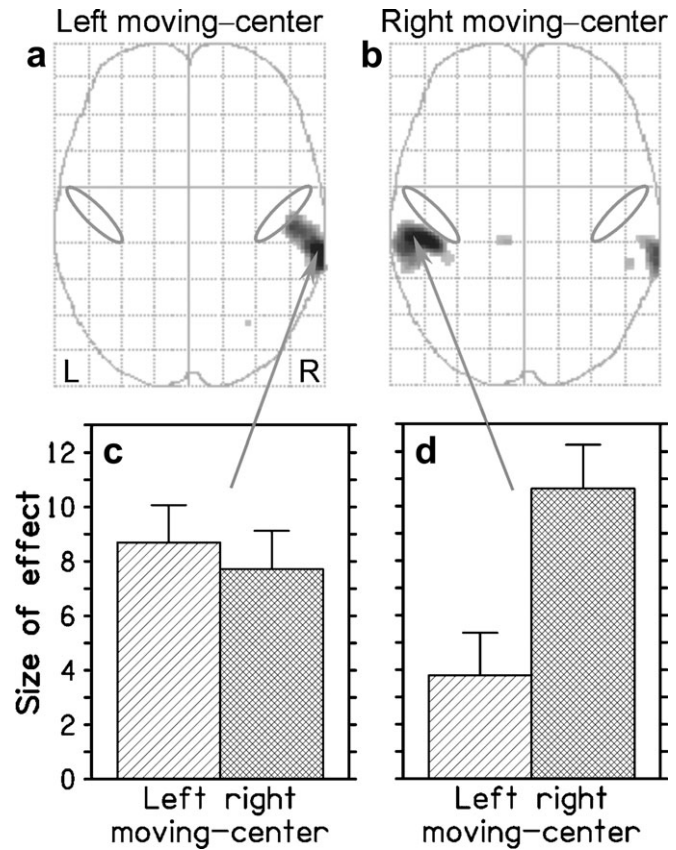


Figure 4. Contrasts between the moving sounds and the central sound. The upper panels show the axial projection of the activation to the left moving sounds (a) and the right moving sounds (b) relative to the central sound, thresholded at $t = 4.65$ ($P_{\text{voxel}} \leq 0.05$, corrected). The lower panels show the contrast-weighted beta-values for the left moving versus center (hatched bar) and right moving versus center contrasts (cross-hatched bar), evaluated at the most significant voxels in the left moving versus center (c) and right moving versus center comparisons (d), which were located in the right and left PT, respectively (gray arrows in a and b). The analysis shows that the right PT was activated by both the left and right moving sounds (c), whereas the left PT predominantly responded to the right moving sounds (d).

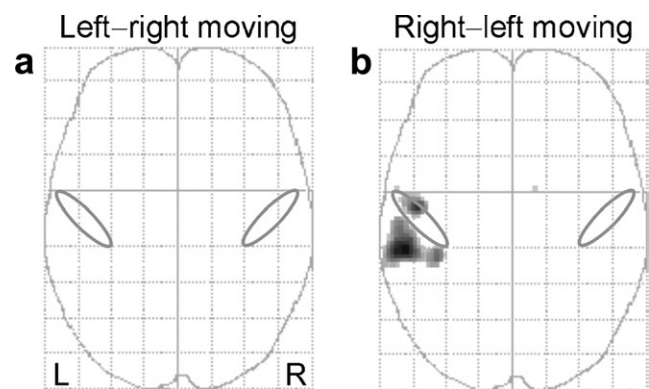


Figure 5. Activation to the contrasts between the left and right moving sounds in axial projection. The activation was thresholded at $t = 3.09$ ($P_{\text{voxel}} \leq 0.001$, uncorrected) and masked with the all sounds versus silence contrast to reveal all significant voxels in the auditory cortices. Whereas the right moving versus left moving contrast yielded a significant activation in the left PT (b), the left moving versus right moving contrast produced no activation in either PT (a) corroborating the notion of a right-hemisphere dominance in auditory motion processing.

**Differential Sensitivity to Moving Sounds:
Right-hemisphere Dominance**

Unlike the contrasts between the static sounds and center, the contrasts between the moving sounds and center did reach the predefined threshold criterion of $t = 4.65$ (Fig. 4*a,b*, Table 1). The activation produced by the left moving versus center contrast was largely confined to the right hemisphere (Fig. 4*a*), whereas the right moving versus center comparison produced a more bilateral pattern of activation, comprising a larger activation cluster in the left hemisphere and a smaller cluster in the right hemisphere (Fig. 4*b*). This suggests a right-hemisphere dominance in the processing of sound movement, in the sense that movement-sensitive auditory areas in the right hemisphere represent movement in both hemifields, whereas the corresponding areas in the left hemisphere predominantly represent movement within the right hemifield. The lower panels in Figure 4 corroborate this conjecture. In the right PT (Fig. 4*c*),

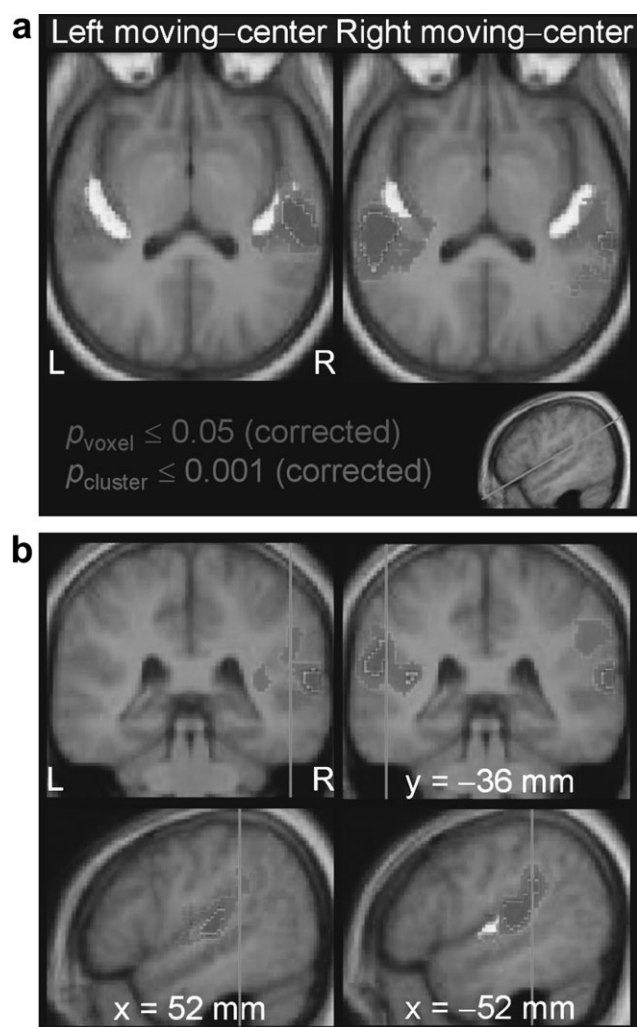


Figure 6. Differential activation to the moving sounds rendered onto the average structural image of the group. Red: voxels with t -values of 4.65 or larger ($P_{\text{voxel}} \leq 0.05$, corrected). Green: voxels with t -values of 3.09 or larger ($P_{\text{voxel}} \leq 0.001$, uncorrected) that were located in clusters of highly significant size ($P_{\text{cluster}} \leq 0.001$, corrected). In (*a*), the location and orientation of the section is shown in the small inset at the bottom. The locations of the coronal and sagittal sections shown in (*b*) are indicated by brown, vertical lines in the images themselves. The white highlight shows the 50% probability map of HG for the group of subjects. A color version of this figure is available as online supplementary material.

the differential response to the right moving sounds (cross-hatched bar) is almost as large as the response to the left moving sounds (cross-hatched bar). In contrast, the differential response of the left PT to the left moving sounds (hatched bar in Fig. 4*d*) is much smaller than the left-PT response to the right moving sounds (cross-hatched bar in Fig. 4*d*). In order to verify the effect statistically, we calculated the contrasts between the right moving and left moving sound conditions and vice versa. If the right moving sounds produce a reliably stronger left-hemisphere activation than the left moving sounds, but the left and right moving sounds activate the right hemisphere similarly strongly, the right moving versus left moving contrast should yield a significant activation in the left hemisphere, but the left moving versus right moving contrast should yield no significant activation in either hemisphere. Figure 5 shows that this was indeed the case. In order to reveal all significantly activated voxels in the auditory cortices, even those which would be insignificant at the corrected level, the activation in Figure 5 was thresholded at $t = 3.09$ ($P_{\text{voxel}} \leq 0.001$, uncorrected) and masked with the all sounds versus silence contrast; the uncorrected P -value of the mask was set to 0.001. Even with this relatively lenient threshold criterion, the left moving versus right moving contrast yielded no activation in either hemisphere (Fig. 5*a*). In contrast, the right moving versus left moving contrast produced a significant activation in posterior auditory regions of the left hemisphere, parts of which even surpassed the more conservative threshold criterion of $t = 4.65$ ($P_{\text{voxel}} \leq 0.05$, corrected; see Fig. 5*b* and Table 1).

Figure 6*a* shows how the differential activation to moving sounds is distributed on the supratemporal plane. The red color marks voxels with t -values of 4.65 or larger ($P_{\text{voxel}} \leq 0.05$, corrected). The green color depicts the whole extent of the respective activation clusters ($t \geq 3.09$; $P_{\text{voxel}} \leq 0.001$, uncorrected). The white highlight shows a 50% probability map of HG for the group of subjects (see Materials and Methods). The shape of the activation to moving sounds is roughly triangular in both hemispheres and comprises the lateral half to two-thirds of the PT. Some activation to the moving sounds overlaps parts of HG medially and laterally, however, there is little or no movement-related activity on the central part of HG, which is the site of the PAC in humans (Rademacher *et al.*, 2001).

The differential activation to moving sounds also comprised the temporo-parietal junction (TPJ) and extended into regions of the inferior parietal lobe (IPL; Fig. 6*b*). The uncorrected significant activation ($t \geq 3.09$; $P_{\text{voxel}} \leq 0.001$, uncorrected; green in Fig. 6) in the PT and IPL formed contiguous clusters in both hemispheres. The parietal activations to the left moving versus center and right moving versus center contrasts were located at MNI coordinates 54, -38, 30 ($t = 3.66$) and -56, -36, 26 mm ($t = 5.48$), respectively. Similar to the supratemporal activation, the inferior parietal activation to the left moving versus center contrast was confined to the right hemisphere (left panels in Fig. 6*b*), whereas the inferior parietal activation to the right moving versus center contrast was essentially bilateral (right panels in Fig. 6*b*), albeit with lesser significance on the ipsilateral side ($t = 4.9$ at 54, -38, 30 mm versus $t = 5.48$ at -56, -36, 26 mm).

The moving sounds produced no differential activation in the IC. In view of the much lower t -values of the IC activation in the all sounds versus silence contrast compared to the AC activation (Table 1), however, the lack of IC activation in the differential sound contrasts may be a mere threshold effect.

Activations Outside ‘Classical’ Auditory Structures

The contrasts between sound conditions and silence, and between the lateralized sounds and center also produced some activations in structures outside the ‘classical’, or unimodal, auditory structures of the superior temporal cortex (see Figs 1–4). The most significant activation outside the superior temporal cortex in the all sounds versus silence contrast was located at the base of the inferior frontal sulcus in the left hemisphere, close to the junction between the inferior frontal and precentral sulci ($t = 5.42$; $P_{\text{voxel}} \leq 0.05$, corrected at -28, 16, 22 mm). In the contrast between all lateralized sound conditions and the center condition, the most significant activation outside the superior temporal lobe was in the left thalamus ($t = 4.8$; $P_{\text{voxel}} \leq 0.05$, corrected at -10, -8, 4 mm) and the left and right pulvinar ($t = 4.47$; $P_{\text{voxel}} \leq 0.001$, uncorrected at -12, -26, -4 mm and $t = 4.31$; $P_{\text{voxel}} \leq 0.001$, uncorrected at 10, -24, -4 mm). These activations may, at least in part, be related to the fact that subjects were asked to perform a visual control task whilst listening to the sounds (see Materials and Methods). Performing the control task would be expected to be more difficult during the sound conditions than during the silence condition, because subjects had to divide their attention between the auditory and visual modalities. Moreover, the spatial foci of auditory and visual attention were disparate during the lateralized sound conditions, and subjects had to suppress the temptation to move their eyes in the direction of the sounds in order to do the visual task.

Discussion

The current data show that the internal representation of interaural temporal information mediated by lateralized sounds is predominantly contralateral in the human superior temporal cortex (Fig. 3). All sounds used in the current experiment had the same energy at the two ears and the impression of laterality or movement was created solely by interaural temporal manipulations, which are inaudible when listening to each ear separately. This means that the observed asymmetry was unconfounded by the known asymmetry in the number of crossed and uncrossed excitatory projections in the ascending auditory pathway (Webster *et al.*, 1992), and must be a result of the interaural temporal processing of the sounds. ITD processing involves comparing the temporal structure of the signals from the two ears on a sub-millisecond scale. This comparison must be accomplished in the brainstem (Oertel, 1997; Joris *et al.*, 1998), because the spike discharges of auditory cortical neurons do not exhibit the temporal precision that would be necessary to convey timing differences on that fine a scale (Lu *et al.*, 2001; Eggermont, 2002). The current data suggest that the left and right auditory hemifields are recreated as a result of this subcortical recoding of interaural temporal information. This conjecture is consistent with electrophysiological (Brandt *et al.*, 2002; Grothe 2003) and lesion data (Furst *et al.*, 1995, 2000; Pratt *et al.*, 1998) from the brainstem.

Representation of Spatial Attributes in Stationary Sounds

The stationary lateralized sounds used in the current experiment produced a significant, albeit small activation increase in the PT of the respective contralateral hemisphere compared to the central sound. In contrast, Zatorre *et al.* (2002a) observed no reliable cerebral blood flow change (measured with PET)

associated with variations in the spatial attributes of stationary sounds, at least not when the sounds were presented sequentially as in the present study. This discrepancy may be due to the inferior sensitivity of PET relative to fMRI, or to the fact that the spatial ranges of the sounds used by Zatorre *et al.* were centered around the midline, and thus always comprised equal parts of both hemifields, which means that Zatorre *et al.* were basically unable to detect the contralateral tuning that was observed in the current study. In the latter case, Zatorre *et al.*'s findings suggest that there is no differential spatial tuning within each hemisphere, and that different ITDs/lateral positions within each hemifield are coded non-topographically. Recent physiological data suggest that ITDs may be coded by the activity level in two broadly tuned hemispheric channels (McAlpine *et al.* 2001; McAlpine and Grothe, 2003), or by the timing of action potentials (e.g. first-spike latency) in neurons with broad spatial tuning to the contralateral hemifield (Furukawa and Middlebrooks, 2002; Middlebrooks *et al.*, 2002). The current data are consistent with both of these hypotheses.

Specialized Auditory ‘Where’ Processing Stream

Unlike the sound versus silence contrasts, none of the differential sound contrasts (lateralized versus central sound conditions) yielded any activation in the region of the PAC on HG. Rather, the differential activations to the static lateralized and moving sounds were largely confined to non-primary auditory regions posterior to HG. In the monkey, (at least) two different auditory processing streams have been distinguished on the basis of distinct patterns of cortico-cortical connections (Romanski *et al.*, 1999; Kaas and Hackett, 2000; Lewis and Van Essen, 2000). Based on physiological results in non-human primates (Rauschecker, 1998; Rauschecker and Tian, 2000; Tian *et al.*, 2001) and brain imaging data in humans (Warren *et al.*, 2002; Warren and Griffiths, 2003), it was proposed that the anterior-ventrally directed stream is specialized in the processing of non-spatial sound features (‘what’), whereas the posterior-dorsally directed stream is concerned with auditory spatial processing (‘where’). The current data are consistent with this hypothesis, suggesting that, in humans, interaural temporal information is projected posteriorly from PAC into PT, and then further posteriorly from PT to the TPJ and into the IPL (see, however, Budd *et al.*, 2003). In the current experiment, changes in the sounds’ spatial attributes were unconfounded with changes in their monaural spectro-temporal properties, as would have been the case, had lateralization been mediated by filtering with head-related transfer functions (Wightman and Kistler, 1993). This means that the observed activations in PT cannot be attributed to the processing of ‘spectral motion’ (Belin and Zatorre, 2000). It is important to bear in mind, however, that the notion of a specialized ‘where’ stream remains conjectural as long as the mechanisms by which auditory spatial information is processed are not properly understood. In particular, it is conceivable that regions in the putative anterior ‘what’ stream encode sound location by action potential timing rather than by firing rate (Furukawa and Middlebrooks, 2002). In this case, auditory spatial processing in these regions would not be associated with any increase in BOLD signal and would thus be undetectable with fMRI. Evidence that auditory cortical regions anterior to HG may indeed be involved in sound localization comes from human lesion data (Zatorre and Penhune, 2001).

Auditory Motion Processing

In addition to posterior temporal regions (PT), the differential response to the moving sounds also comprised regions in the inferior parietal lobe, supporting the hypothesis that auditory spatial processing is subserved by a temporo-parietal network extending from the PT and PTO into the IPL (Rauschecker and Tian, 2000; Warren *et al.*, 2002; Warren and Griffiths, 2003). The posterior temporal activation to the moving sounds probably reflects the preattentive, sensory processing of time-varying spatial cues, whereas the inferior parietal activation may be related to higher-order processes associated with the conscious perception of movement (Griffiths *et al.*, 1998, 2000). Previous studies suggest that the IPL may be involved in the attentional tracking of the moving stimulus through space, or the integration of auditory spatial cues into multimodal spatial representations (Bushara *et al.*, 1999; Downar *et al.*, 2000; Bremmer *et al.*, 2001). The notion that the inferior parietal activation reflects attentional or supramodal aspects of motion processing is supported by the fact that lesions in the IPL and, in particular, the TPJ are a frequent cause of the hemispatial neglect syndrome, which is known to be a supramodal deficit that may affect the visual, auditory and somatosensory modalities (Corbetta and Shulman, 2002; Halligan *et al.*, 2003).

Both the posterior temporal and the inferior parietal activation to moving sounds exhibited a relative rightward asymmetry, in the sense that the right hemisphere was activated to similar degrees by sounds moving within the left or right hemifields, whereas the left hemisphere was predominantly activated by sounds moving within the right hemifield. These results indicate that the functional hemispheric asymmetry in the sensory representation of interaural temporal information parallels the asymmetry associated with attentional and supramodal components of spatial processing. Hemispheric functional asymmetries have also been observed in melody and speech processing in the auditory pathway (Patterson *et al.*, 2002; Zatorre *et al.*, 2002b). In these cases, one hemisphere appears to devote more neuronal resources to the respective task than the other hemisphere. In the case of auditory motion processing, on the other hand, the functional difference between the hemispheres seems to be more a qualitative rather than a quantitative one, in that auditory motion processing is more global in the right hemisphere and more local in the left hemisphere. In this sense, the hemispheric asymmetry in auditory motion processing resembles the asymmetry in the processing of global and local aspects of visual stimuli (Fink *et al.*, 1996, 1997; Marshall and Fink, 2001). The difference does not mean that the left hemisphere plays a lesser role in auditory space perception than the right hemisphere in neurologically intact subjects. In the current data, the left-hemisphere activation to the right moving sounds was stronger (Fig. 4) and spanned a larger area (Fig. 6) than the right-hemisphere activation to the left moving sounds. In the case of unilateral lesion, however, the right hemisphere would be expected to be better prepared to take over the function of the left hemisphere than *vice versa*. The observed asymmetry in the auditory motion processing may thus underlie the reported disparities in the auditory spatial deficits following unilateral temporal or parietal lesions in the left versus the right hemisphere (Bellmann *et al.*, 2001; Zatorre and Penhune, 2001).

Supplementary Material

Supplementary material can be found at: <http://www.cercor.oupjournals.org/>

Notes

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