

Auditory Attention to Space and Frequency Activates Similar Cerebral Systems

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PET was used to test the hypothesis that similar neural systems are involved in attending to spectral and to spatial features of sounds. In each of four conditions subjects heard tones varying randomly in frequency and location and responded to either the low- or the high-frequency stimuli, ignoring location, or to stimuli on the left or right, ignoring frequency. In comparison to a silent baseline, CBF increases were observed in auditory cortex bilaterally and in the right superior parietal, right dorsolateral frontal, and right premotor regions, with no modulation as a function of attentional condition. Analysis of regional covariation indicated a coordinated CBF response between the right parietal region and the right frontal and middle temporal regions. The data imply that auditory attention engages a network of right-hemisphere cortical regions for both spatial location and tonal frequency and support a model whereby auditory attention operates at a level at which separate features have been integrated into a unitary representation. © 1999 Academic Press

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INTRODUCTION

The ability to attend to distinct stimulus features, such as a red hat in a crowd or a clarinet in an orchestra, is central to the efficient processing of information in all sensory systems. In the auditory modality, evidence from experimental psychology has established that selective attention may be guided by both location and frequency cues (e.g., Dai *et al.*, 1991; Mondor and Bregman, 1994; Mondor and Zatorre, 1995; Spence and Driver, 1994). However, Mondor *et al.* (1998) found that listeners were unable to attend to the location of an auditory stimulus independently of its spectral characteristics and vice versa. This result implies that auditory objects, and not individual features, are subject to selection. If correct, this cognitive principle makes certain specific predictions about how neural processes may be involved in selective attention; in particular, it

would predict that attending to stimulus features which are integrated should result in similar patterns of cerebral activity, since these features are proposed to be analyzed preattentively. One principal goal of the present study, therefore, was to test this prediction directly.

Integrity of location and frequency does not necessarily imply that these features might not be independently registered at an early stage of processing (e.g., Melara and Marks, 1990), however. Thus, Woods *et al.* (1994) reported different event-related potential (ERP) scalp distributions for attending to location vs frequency, consistent with evidence that neurons within distinct cortical fields are sensitive to specific acoustic features (Rauschecker *et al.*, 1995). Although these data suggest that different neural mechanisms would be involved for different stimulus dimensions, Woods *et al.* (1994) also showed that features appear to be conjoined rapidly (within 130 ms). An enhancement in ERP amplitude has also been reported for attended over unattended stimuli (Hillyard *et al.*, 1973), and neuromagnetic recordings suggest that this modulation occurs within auditory cortex (Woldorff *et al.*, 1993).

Functional brain imaging studies have contributed to this question by examining the modulation of cortical activity as a function of attention. The findings have not been completely consistent, however: whereas some authors have reported an enhanced response in auditory cortical areas when subjects are instructed to attend to auditory targets (Alho *et al.*, 1999; Grady *et al.*, 1997; O'Leary *et al.*, 1996; Woodruff *et al.*, 1997), several other studies did not find such enhancement (Frith and Friston, 1996; Paus *et al.*, 1997; Tzourio *et al.*, 1997; Zatorre *et al.*, 1992). The reason for these discrepancies is not immediately apparent, but much may depend on the specific comparisons performed and especially on the nature of the attentional processes that might be elicited by the baseline tasks used. It is quite feasible that certain types of stimuli or situations engage sensory processing automatically and that no

further modulation of sensory regions is observed during active processing because the necessary perceptual information has been extracted fully. Thus, another goal of the present study was to examine the presence of modulation of auditory cortical areas as a function of specific features to be attended.

In addition to the involvement of sensory cortices in auditory attention, imaging data have implicated frontal and parietal systems as well. For example, using a sustained attention task, Paus *et al.* (1997) found evidence to dissociate arousal mechanisms, involving the thalamus, anterior cingulate, basal forebrain, and basal ganglia, from activity related to selective auditory attention, which was associated primarily with right parietal, frontal, and middle temporal areas. The contribution of right parietal and frontal regions to attention finds considerable support in the neuropsychological literature, as damage to these areas often leads to disturbances in visual spatial selective attention (Farah *et al.*, 1989; Mesulam, 1981; Posner *et al.*, 1984, 1987). Moreover, brain imaging data with visual and somatosensory attention tasks have also consistently implicated similar regions (Corbetta *et al.*, 1993; Pardo *et al.*, 1991), thus suggesting that this anatomical network subserves a supramodal attentional system.

The present study was designed specifically to examine the neural mechanisms involved in the control of auditory attention. To this end, listeners performed a task which required detection of tones of a specified frequency or at a specified spatial location while undergoing PET scanning. This design allowed us to evaluate the prediction (derived from the cognitive findings of Mondor *et al.*, 1998) that similar neural mechanisms should be involved in selection on the basis of each feature. Alternatively, if modulation of auditory cortical regions occurs as a function of the features attended, then changes in cerebral activity should be seen depending on which dimension is the focus of attention. Finally, we wished to test the prediction that engagement of auditory attention entails the participation of right-hemisphere parietofrontal regions, as has been reported for other modalities, and that these areas function in an integrated fashion as part of a distributed functional network for attention.

MATERIALS AND METHODS

Subjects

Eight healthy right-handed McGill University students (four of each sex, average age 22.4 years) volunteered for scanning after giving informed consent in accordance with ethical procedures established at our institute.

Procedure

Three pure tones of frequencies 250, 1000, and 4000 Hz were synthesized on a personal computer. Tones had a duration of 200 ms, with 5-ms onset/offset ramps, and were presented over insert earphones randomly to the left ear, the right ear, or both ears. Tones were presented as a continuous random sequence to each subject, starting several seconds before scanning commenced and continuing until scanning was finished with an interstimulus interval of 800, 900, or 1000 ms, determined randomly on each trial. The variation in timing prevents anticipatory responses. Average intensity was set at 77 dB SPL(A), but varied randomly across trials over a range of ± 2.5 dB. This manipulation prevents subjects from using incidental intensity cues as a means of selecting the stimuli.

Performance was examined under five different scan conditions. In the Baseline condition listeners were not presented with any stimuli or task. In the Attend High condition, listeners were required to make a speeded detection response to the occurrence of the high-frequency (4000 Hz) tone, irrespective of its location. In the Attend Low condition, listeners responded to the occurrence of the low-frequency (250 Hz) tone irrespective of location. The random variation in intensity prevented the use of any perceived differences in loudness as a cue in these conditions. In the Attend Left condition, listeners responded to any tone that sounded from the left location, regardless of frequency, and similarly in the Attend Right condition, listeners responded to any tone that sounded from the right location. Thus, excluding the Baseline control condition, the actual stimulus information was identical across conditions; only the instructional set varied. The four active conditions were counterbalanced for order across subjects, who kept their eyes closed throughout all scans. Listeners made their detection responses by pressing a button on a computer mouse and were instructed to respond as quickly and accurately as possible. Fifty practice trials were given prior to beginning each condition; both reaction time and error rate were recorded online.

PET Scanning

PET scans were obtained with a Scanditronix PC-2048B 15-slice tomograph. The distribution of CBF was measured during each 60-s scan using the $H_2^{15}O$ water bolus method (Raichle *et al.*, 1983). MRI scans (160 1-mm-thick slices) were also obtained for each subject with a 1.5-T Phillips ACS system to provide anatomical detail. CBF images were reconstructed using an 18-mm Hanning filter, normalized for differences in global CBF, and coregistered with the individual MRI data (Evans *et al.*, 1992). Each matched MRI/PET data set was then linearly resampled into the standardized

stereotaxic coordinate system of Talairach and Tournoux (1988) via an automated feature-matching algorithm (Collins *et al.*, 1994). PET images were averaged across subjects for each condition, and the mean change image volume was obtained for each comparison; this volume was converted to a *t* statistic map, and the significance of focal CBF changes was assessed by a method based on three-dimensional Gaussian random-field theory (Worsley *et al.*, 1992; see below).

Analysis

The presence of significant changes in CBF was first established on the basis of an exploratory search, for which the *t* value criterion was set at 3.5 or greater. This value corresponds to an uncorrected *P* value of 0.0004 (two-tailed) and results in an average of 0.58 false positives per search volume of 200 resolution elements (dimensions of $18 \times 18 \times 7.6$ mm), corresponding approximately to the volume of gray matter scanned. Separate subtractions were performed for each of the four activation conditions minus the baseline, and the presence of CBF changes that exceeded the criterion in each subtraction was evaluated.

Because we were interested in the similarity of activity patterns across the four conditions, we also carried out a directed search within specific locations. Therefore, loci of CBF peaks are listed in Tables 2 and 3 if (i) they met the criterion of 3.5 or greater in any one of the individual subtractions or (ii) they did not meet this criterion, but exceeded a *t* value of 2.5 and were also within 7 mm or less of the location of a significant CBF change in one or more of the other subtractions. As a check on the validity of this approach, we performed an additional analysis, in which the CBF data from all four activation tasks were combined using a weighted average, and the baseline condition was subtracted from it. We then confirmed that all of the locations reported in Tables 2 and 3 were also present at a *t* value greater than 3.5 in the global analysis, within a radius of 7 mm. By using this strategy, we avoided likely false positives, since peaks close to but below the statistical criterion in any one of the four subtractions were all confirmed to be in spatial proximity to at least one significant location in the other three subtractions, as well as in the omnibus analysis that includes all the data.

Several subsidiary analyses were also performed. First, in order to test whether CBF changes were indeed essentially identical across the four attentional conditions, we compared the activation conditions directly to one another in pairs (Attend Left–Attend Right and Attend High–Attend Low). We also computed the compound comparison pitting the two spatial conditions against the two nonspatial ones [(Attend Left + Attend Right)–(Attend High + Attend Low)] to seek any differences related to the dimension to be attended.

Second, to test specifically whether there were any

significant differences in CBF within the region of the primary (as proposed by Alho *et al.*, 1999) or secondary (as proposed by Grady *et al.*, 1997) auditory cortices in the various conditions, we performed two region-of-interest analyses, one defining a region based on anatomical criteria, the other defining a region based on functional criteria. In one analysis, the CBF change within Heschl's gyrus was estimated by multiplying the normalized CBF volume for each of the four attentional conditions by a probability-weighted stereotaxic map of Heschl's gyrus within each hemisphere (Penhune *et al.*, 1996). This procedure yields an estimate of the normalized CBF value within a region most likely to include the primary auditory cortex for each individual; these values were then submitted to analysis of variance to examine modulation in CBF change as a function of condition and side. Another analysis estimated the CBF changes associated with activity in secondary auditory cortical areas; for this purpose the normalized CBF was extracted from spherical regions of interest (radius 8 mm) centered on the peak coordinates in secondary auditory regions (stereotaxic coordinates: $-37, -37, 14$ and $58, -31, 11$), as obtained in a comparison of all stimulation conditions to silence (see Results). These values were also submitted to analysis of variance to examine modulation as a function of attentional condition.

Finally, in order to test the hypothesized interaction between right parietal cortex and other right-hemisphere areas involved in a putative attentional network, a regional regression map which assessed the significance of a relationship between CBF values in a given region of interest with CBF in the entire volume was generated. This map should reveal all brain areas that show a coordinated CBF response with the CBF in the right parietal cortex. Because the procedure requires multiple observations per subject, and since few differences were observed across the four activation conditions, these were combined for this analysis. A spherical volume of interest (radius 6 mm) was centered on the average right parietal CBF peak position ($40, -59, 56$) in the combined volume; a linear function was then fit in which the parameter of interest was the slope of the function relating CBF in the volume of interest to CBF elsewhere in the brain, after removing the effect of subjects (Paus *et al.*, 1997). Assessment of significance was carried out by producing a *t* statistic map in the same manner as for the subtraction analysis (Worsley *et al.*, 1992).

RESULTS

Behavioral Results

All subjects understood the tasks and performed them easily and efficiently. As may be seen in Table 1, overall performance level was very high, with most

subjects performing near ceiling. There were no significant differences in the proportions of hits or false alarms across conditions. Analysis of variance was performed on the reaction times, which also were found not to differ significantly across conditions ($F(3,21) = 2.10, P > 0.10$).

Analysis of CBF Data: Subtractions

The first analysis consists of comparisons between each of the attentional conditions and the baseline. Foci of significant CBF increase and decrease are detailed in Tables 2 and 3, respectively, following the strategy outlined under Materials and Methods, and the most pertinent of these are illustrated in Fig. 1.

All four subtractions resulted in very similar patterns of CBF, as indicated in Table 2. In addition to the expected activations in auditory cortices bilaterally, and in primary and supplementary motor areas, CBF increases were also noted in the cerebellum and left thalamus. Of greatest interest to our hypotheses, three cortical sites within the right hemisphere also yielded significant activity; these were located within the superior parietal, premotor, and middorsolateral frontal regions (see Fig. 1, top). It is notable that the stereotaxic coordinates for all nine of these foci are very near one another in all four conditions. With only a single exception (the cerebellar peak in the Attend Right condition), every one of the activation sites in the individual subtractions corresponding to each attentional condition was confirmed to be within 7 mm of a significant ($t > 3.5$) CBF activation in the omnibus subtraction that included all four conditions together.

In addition to the nine consistent activation sites, there was a right inferior frontal area which yielded significant activation in the Attend Left condition only (Fig. 1, top). Although some activation was detected within this general location in the other conditions (see Table 2, focus 10), they either did not reach criterion for significance (Attend Right and High conditions) or were located more than 7 mm away from the peak in the omnibus analysis (this was true for the significant focus in the Attend Low condition). Thus, this one region seems to be engaged more variably and/or differentially across the four conditions.

TABLE 1

Behavioral Performance during Attentional Tasks

Attend condition	Mean reaction time (ms)	Mean proportion hits	Mean proportion false alarms
Left	561	0.98	0.008
Right	591	0.94	0.014
Low	567	0.98	0.010
High	585	0.99	0.005

TABLE 2

Stereotaxic Coordinates and Significance Level of Regions of Increased CBF in Each of the Four Attentional Conditions Compared to Baseline

Region	Attend condition	x	y	z	t
1. Left auditory cortex (41/42)	Left	-36	-35	18	4.50
	Right	-38	-35	14	5.78
	Low	-36	-37	11	5.23
	High	-39	-37	14	5.66
2. Right auditory cortex (42)	Left	58	-31	12	4.74
	Right	58	-33	11	4.72
	Low	58	-33	11	5.88
	High	60	-30	11	4.47
3. Left motor cortex (4)	Left	-46	-19	54	4.88
	Right	-39	-22	59	4.75
	Low	-43	-14	54	4.89
	High	-39	-19	58	3.96
4. SMA (6)	Left	-4	-2	60	6.58
	Right	-4	-4	60	6.89
	Low	-1	-2	60	6.76
	High	-4	-1	62	6.57
5. Cerebellum	Left	7	-57	-20	5.25
	Right	-9	-73	-35	3.25*
	Low	-1	-71	-20	3.49
	High	5	-71	-20	4.20
6. Left thalamus	Left	-9	-14	0	4.47
	Right	-17	-18	0	3.77
	Low	-9	-16	0	3.28
	High	-13	-14	0	3.63
7. Right superior parietal (7)	Left	39	-57	56	3.79
	Right	39	-60	56	3.08
	Low	39	-62	54	3.33
	High	43	-57	56	2.84
8. Right premotor (6)	Left	48	-2	47	5.02
	Right	50	-2	47	3.76
	Low	49	-1	47	3.41
	High	50	-1	48	3.62
9. Right dorsolateral frontal (46/9)	Left	38	36	23	3.80
	Right	36	29	21	3.37
	Low	39	29	24	4.05
	High	35	31	20	3.39
10. Right inferior frontal (47/10)	Left	42	42	-9	5.32
	Right	24	46	-6	2.73*
	Low	25	24	-7	3.56
	High	51	30	-9	3.08*

* t value did not meet significance by either exploratory or directed search criteria (see text).

In order to verify that the pattern of activation was largely identical across the four tasks, CBF was compared directly between pairs of attentional conditions. Comparison of Attend Left to Attend Right conditions did not yield any significant CBF activation in any of the first nine sites listed in Table 2, confirming that the CBF increases seen in these regions were essentially the same. It did demonstrate, however, a significant CBF change in the right inferior frontal region (x, y, z coordinates: 43, 42, -8; t value 4.28, corresponding to focus 10 in Table 2) and in an additional more dorsal right frontal area (39, 48, 18; $t = 3.64$). The reverse

TABLE 3

Stereotaxic Coordinates and Significance Level of Regions of Decreased CBF in Each of the Four Attentional Conditions Compared to Baseline

Region	Attend condition	<i>x</i>	<i>y</i>	<i>z</i>	<i>t</i>
1. Left middle temporal gyrus (37)	Left	-55	-56	-5	-6.31
	Right	-54	-57	-5	-3.98
	Low	-60	-56	-5	-5.41
	High	-55	-57	-5	-5.60
2. Left parahippocampal/fusiform (36/37)	Left	-24	-40	-23	-4.23
	Right	-28	-38	-11	-2.97*
	Low	-36	-42	-18	-4.08
	High	-43	-42	-15	-2.80*
3. Left superior occipital gyrus (19)	Left	-36	-76	26	-2.75
	Right	-29	-78	26	-3.73
	Low	-34	-81	24	-3.32
	High	-38	-76	26	-2.97
4. Precuneus (7)	Left	0	-31	45	-4.56
	Right	-4	-55	39	-4.34
	Low	5	-38	47	-3.66
	High	8	-45	48	-4.09
5. Posterior cingulate (23/30)	Left	-3	-52	18	-4.40
	Right	5	-59	11	-3.08*
	Low	0	-57	17	-3.10
	High	-5	-54	17	-4.38
6. Anterior cingulate (32)	Left	1	32	-8	-5.61
	Right	4	24	-15	-4.90
	Low	1	32	-8	-4.29
	High	-1	34	-8	-4.45
7. Left orbitofrontal (11)	Left	-36	25	-17	-5.01
	Right	-31	34	-17	-4.99
	Low	-31	34	-20	-4.26
	High	-29	36	-17	-4.26
8. Left inferior frontal (47)	Left	-42	36	-9	-4.26
	Right	-45	41	-5	-3.35
	Low	—	—	—	—
	High	-43	37	-5	-2.63
9. Left dorsolateral frontal (6/8)	Left	-31	17	54	-4.03
	Right	-29	18	51	-2.92
	Low	-28	17	54	-3.37
	High	-28	17	54	-3.00

* *t* value did not meet significance by either exploratory or directed search criteria (see text).

comparison (Attend Right vs Attend Left) yielded activity in two inferior frontal areas as well, one in the left orbital region ($-9, 44, -17$; $t = 3.72$) and another in the right medial frontal cortex ($16, 48, -6$; $t = 3.53$).

Subtraction of the Attend High vs Attend Low conditions also confirmed the absence of any CBF changes in the regions listed in Table 2.

The two spatial conditions (left/right) were also combined and compared against the combined nonspatial conditions (high/low). This analysis was consistent with the others, in showing no significant change in auditory cortices or any of the other regions listed in Table 2. Only three significant foci emerged from this analysis: two regions were found to be more active in the high/low conditions compared to the left/right, one in the left frontal operculum ($-29, 24, -9$, $t = 4.07$) and another in the left parahippocampal area ($-23, -26, -15$, $t = 3.60$); as well, a single significant focus was observed to show higher CBF in the pooled spatial conditions, in the medial parietal cortex ($4, -68, 57$, $t = 3.96$).

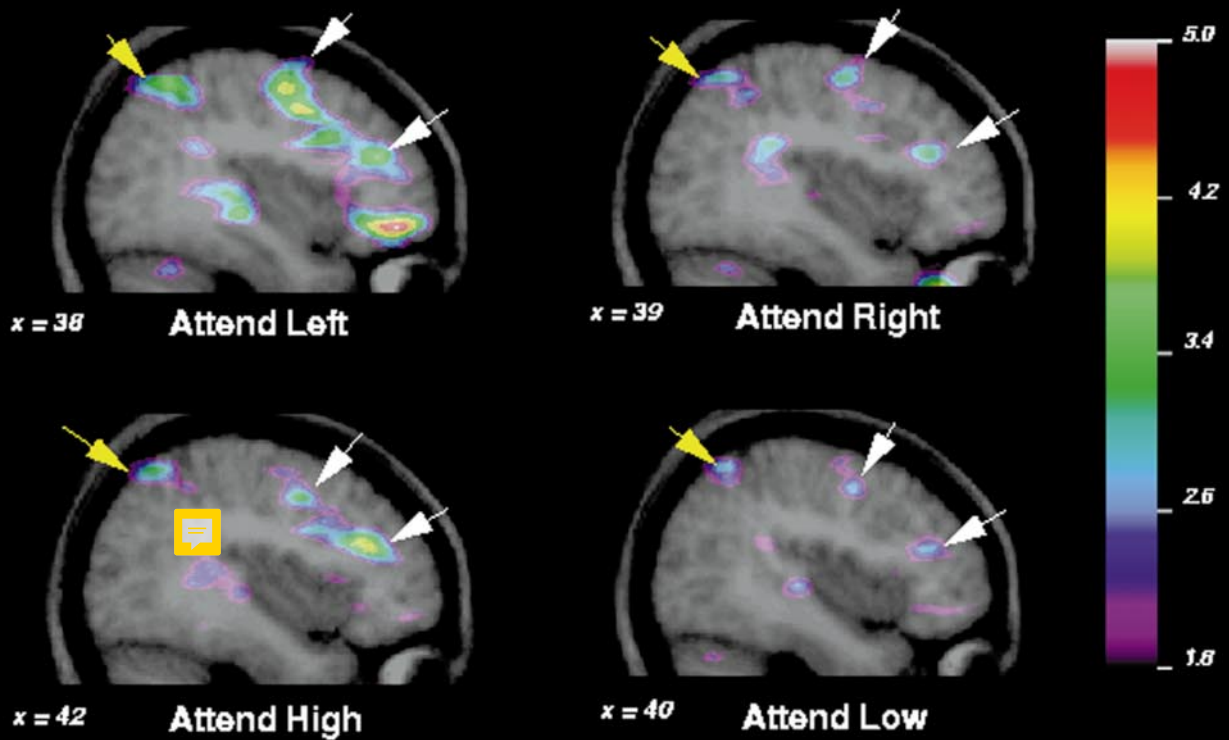
Table 3 lists the foci of significant CBF decrease in the subtractions of the baseline condition from each of the four attentional conditions. Once again, the pattern and location of changes were very similar across conditions. It is of interest that, with the exception of three midline sites (cuneus, anterior, and posterior cingulate, foci 4, 5, and 6), all the other foci of CBF decrease were located within the left hemisphere. It is also notable that many of the regions identified were located within regions thought to be important for visual function. As was the case for the CBF increases, the sites listed in Table 3 met the criterion of being within 7 mm of a significant site of CBF decrease in the omnibus subtraction pooling all the conditions, except in four instances, as noted in Table 3 (even in the latter cases, however, the coordinates are not very far from one another). None of the nine foci listed in Table 3 were found to correspond to significant CBF changes when the Attend Right and Left conditions were compared to each other nor when the Attend Low and High conditions were compared to each other.

Analysis of CBF Data within Auditory Cortex

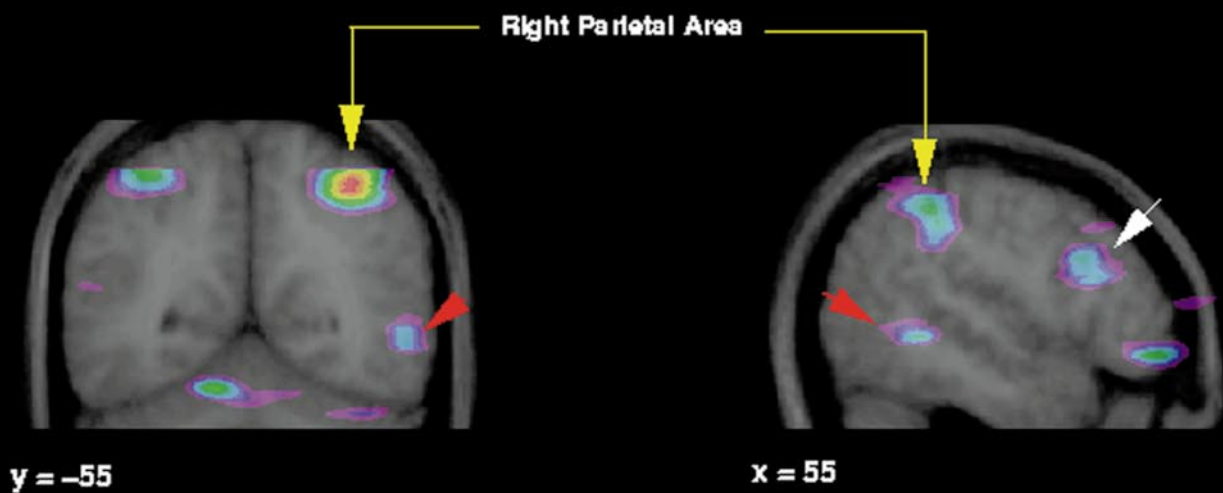
Normalized CBF values were extracted from probability-weighted maps of Heschl's gyrus (Penhune *et al.*, 1996; see Materials and Methods) within each hemisphere for each condition and were submitted to analysis of variance to determine if there were significant

FIG. 1. Top: Selected areas of significant CBF increase in the comparison of each of the four active attentional conditions to the silent baseline condition. The average PET subtraction images are shown superimposed upon averaged MRI scans. Each image corresponds to a sagittal slice through the right hemisphere (between 38 and 42 mm from midline, as indicated by the *x* coordinate). Changes in CBF are shown as a *t* statistic map, coded by the color scale shown at right. Yellow arrows indicate superior parietal region (focus 7 in Table 2). White arrows indicate premotor and dorsolateral frontal regions (foci 8 and 9 in Table 2). Bottom: Areas of significant positive covariation in CBF with activity in the right parietal area (indicated by the yellow arrows) for all attentional conditions pooled together. Visible in the coronal view, on the left, are the significant covariations obtained in the left parietal area and cerebellum (foci 4 and 5, respectively, in Table 4), as well as in the middle temporal region (focus 3 in Table 4), indicated by the red arrow. The middle temporal region, again indicated by a red arrow, is also visible on the sagittal view, shown on the right. In addition, this sagittal section illustrates regions of positive covariation in the right dorsolateral frontal region (focus 1 in Table 4), indicated by the white arrow, and a more inferior frontal region (focus 2 in Table 4) as well.

CBF Increases relative to baseline



CBF Co-variations



changes as a function of the different conditions. This analysis did not reveal any significant effect of condition nor was there any significant interaction between condition and side.

A similar analysis was carried out using spherical regions of interest centered on the areas of secondary auditory cortex found to be maximally active in the omnibus comparison of all stimulation conditions to silence (corresponding to foci 1 and 2 in Table 2). This analysis also failed to demonstrate any significant interaction between condition and side. These results therefore confirm the conclusion of the subtraction analyses that there was no significant modulation of CBF within the auditory cortices, either primary or secondary, as a function of the attentional manipulation.

Analysis of Covariation

The final set of results relates to the analysis of interregional covariation. As indicated under Materials and Methods, this analysis searches for all pixels which demonstrate a significant covariation in CBF relative to a pixel in the right parietal cortex. The results are shown in Table 4 and Fig. 1 (bottom). Of greatest relevance to the hypotheses, it was found that significant positive covariations occurred between the right parietal area and three right cortical regions, in the dorsolateral and inferior frontal lobe, and in the right middle temporal area (foci 1, 2, and 3 in Table 4). In addition, there was significant covariation between the right parietal region and a homologous left parietal locus; finally, a positive covariation was also observed in the left cerebellum (both visible in Fig. 1, bottom left).

Several of the sites identified in the covariation analysis appear to be related to regions identified in the subtraction analysis. In order to quantify the anatomical relation, we measured the vector distance between the average of each CBF covariation peak and the average CBF increases from the omnibus analysis of all attentional conditions combined. The anatomical location of the right dorsolateral frontal region (focus 1 in Table 4) seems to fall halfway between the right dorsolateral and right premotor foci that had been identified in the subtraction analysis (foci 8 and 9 in Table 2); the average position of the coordinates listed within focus 1 in Table 4 is about 7 mm from the midpoint of these two dorsal frontal regions from the subtraction analysis. Similarly, the covariation that emerged within the right inferior frontal cortex (focus 2 in Table 4) falls within less than 6 mm of the similar region (focus 10 in Table 2) identified in the subtraction analysis. Finally, the cerebellar area that yielded significant covariation (focus 5 in Table 4) was very close (<2 mm) in the y and z dimensions to the average cerebellar location in the combined subtraction analysis, but

TABLE 4

Stereotaxic Coordinates and Significance Level of CBF Covariations with CBF in Right Superior Parietal Region

Region	x	y	z	t
Positive covariations				
1. Right dorsolateral frontal (9/8)	39	20	39	4.11
	36	27	36	4.03
	48	15	29	3.72
	50	22	21	3.44
2. Right inferior frontal (47/11)	38	48	-15	4.38
	46	44	-9	4.18
3. Right middle temporal gyrus (21)	54	-49	-3	4.08
4. Left superior parietal (7)	-36	-49	54	4.23
5. Left cerebellum	-12	-59	-20	4.39
Negative covariations				
6. Anterior cingulate (32)	-4	34	-8	-5.01
7. Left orbitofrontal (11)	-32	20	-18	-3.65
8. Left insula	-34	-14	11	-3.76
9. Left temporal pole (38)	-36	1	-35	-3.69
	-50	5	-12	-3.57
10. Left lingual/fusiform gyrus (19/37)	-9	-62	-3	-3.72
	-31	-33	-11	-3.55
11. Right lingual/fusiform gyrus (19/37)	32	-50	-2	-4.20
	34	-37	-11	-3.56
12. Left superior occipital gyrus (19)	-43	-68	32	-3.54

differed in the lateral position, being located 17 mm farther to the left.

Analysis of negative covariations with the right parietal pixel yielded a total of seven regions. It is notable that most of these areas were located in the left hemisphere, apart from a midline anterior cingulate area, and the inferior lingual/fusiform gyrus region, which showed a bilateral response. As was the case with the positive covariations, some of the areas identified appeared to be in proximity to peaks of CBF decrease that had been observed in the subtraction analysis. The left orbitofrontal area (focus 7 in Table 4) was very close (<1 mm) in the x and z dimensions to the average location of CBF decrease in the combined subtraction of all attentional conditions (focus 7 in Table 3), although its location was 12 mm more anterior in the y dimension. Similarly, the anterior cingulate area (focus 6 in Table 4) was within 19 mm of a similar region seen in the subtraction (focus 6 in Table 3). Finally, the left superior occipital region (focus 12 in Table 4) was 17 mm away from a similar site among the CBF decreases (focus 3 in Table 3).

DISCUSSION

Cortical Network for Auditory Attentional Processing

The findings of the present study indicate that the performance of an auditory attentional task engages a specialized network of right-hemisphere regions, as predicted on the basis of both neuropsychological and

neuroimaging data. In particular, the joint participation of right parietal, frontal, and temporal cortex is indicated by the analysis of covariation, which supports the hypothesis that these regions function in a coordinated manner as part of a distributed functional network for the deployment of attention. Other regions showing significant CBF increases which were not part of this network include areas likely related to the motor response (primary motor cortex, SMA, cerebellum), the auditory cortices, and a region within the left thalamus. The activity in this latter structure may be related to a nonspecific arousal mechanism which would be engaged while performing the task. This interpretation is strengthened by findings from a previous study (Paus *et al.*, 1997) in which precisely the same thalamic region was observed to decrease over time during performance of an auditory vigilance task; as in the present data, the thalamic response did not covary with right cortical regions, thus suggesting a functional dissociation. A similar conclusion on the role of left thalamic intralaminar nuclei was reached by Kinomura *et al.* (1996) using visual and somatosensory detection tasks.

In keeping with the predictions derived from cognitive behavioral studies (Mondor *et al.*, 1998), one of the main findings from the present study is that changes in CBF were very similar when subjects attended to spatial or to spectral features of the auditory input. The highly consistent pattern of CBF increases (and decreases) that emerges across the four attentional conditions indicates that there is little difference in the mechanisms that underlie behavioral performance as a function of the features that must be attended. This finding is indicated not only by the comparisons of each condition with the silent baseline, which yielded similar areas of activity, but also by the comparisons of active conditions to one another, which showed no differences in CBF in the areas in question. It should be emphasized that these latter subtractions do not involve a baseline task and are hence free from any problems of interpretation associated with choice of baseline. In the current study, the subtractions with the baseline condition, presented in Tables 2 and 3, serve primarily to identify the entire network of areas active.

One possible exception to the conclusion that attentional conditions yielded similar brain activation pertains to the most ventral right frontal region (focus 10 in Table 2), which was strongly active during the Attend Left condition, but only variably present in the other conditions. Furthermore, direct comparison of Attend Left vs Right yielded a significant CBF increase in the same right ventrolateral site, whereas Attend Right vs Left yielded an activation site in the left orbitofrontal area. It is therefore possible that there may be some reciprocal activity in the ventral frontal

cortex, contralateral to the side of space to be attended. None of the other cortical areas showed any evidence of such modulation, however. In particular, there was no evidence for modulation of activity of parietal cortex as a function of side to be attended, as has been reported with certain visual attentional tasks (Corbetta *et al.*, 1993). However, participation of left superior parietal cortex was indicated by the covariation analysis, even though it did not show significantly greater CBF above the baseline condition. Thus, both left and right parietal areas may play a role, but it appears to be unrelated to the side of space to be attended.

The conclusion that there is a functional asymmetry favoring a right-hemisphere cortical network for auditory attention also finds ample support in the literature; importantly, several studies have suggested that right parietal and frontal regions are responsible for attentional processes across several modalities (Belin *et al.*, 1998; Farah *et al.*, 1989; Mesulam, 1981; Pardo *et al.*, 1991; Paus *et al.*, 1997; Posner *et al.*, 1984). Thus, the findings reported in the present study are best interpreted as reflecting the engagement of a supramodal attentional system that responds to conjoined stimulus features. In this context, it is of interest to consider that the anatomical inputs to the superior parietal cortex in the rhesus monkey come from polymodal cortical regions, including the superior temporal sulcus (Mesulam *et al.*, 1977), consistent with the idea that highly processed sensory representations are involved in attentional selection. It is therefore feasible to hypothesize that the right middle temporal gyrus region revealed by the covariation analysis in the present study (focus 3 in Table 4, visible in Fig. 1, bottom right) may be related to this type of integrated sensory input.

The important role of the right prefrontal cortex in subserving attentional processes was also revealed by this study. The right premotor area (focus 8 in Table 2) is a few millimeters lateral to the average location of a region functionally identified as the human frontal eye field (Paus, 1996), an area which also receives efferent input from the superior parietal cortex (Barbas and Mesulam, 1981). It seems clear from the present results and previous data as well, however, that this region is functionally implicated in attentional processes not only in the visual modality but also when stimuli in other modalities must be attended (e.g., Belin *et al.*, 1998; Pardo *et al.*, 1991; Paus *et al.*, 1997) or when attention is allocated to temporal cues as well as to spatial location (Coull and Nobre, 1998). What remains unclear is whether this dorsal frontal region is active because it subserves a higher-order role in attentional processing, related perhaps to action based on multisensory environmental cues, or whether it represents the engagement of a specifically visual system for eye movements, but which can be recruited by auditory or other nonvisual cues.

Pattern of CBF Decreases

The pattern of CBF decreases observed in the subtraction analysis consistently revealed similar areas in all four attentional conditions, adding further support to the claim that attending to spectral or spatial stimulus features recruits similar neural mechanisms. Moreover, many of the areas of CBF decrease uncovered in the subtraction analysis were similar to those found in the negative covariations, suggesting that these areas are functionally related in a complementary manner. Except for midline cingulate and precuneus regions, the CBF decreases were located in the left hemisphere, suggesting a possible reciprocal relation between activity patterns across the two hemispheres. Furthermore, many of these regions are located in cortical areas related to higher-order visual processes; it is possible, therefore, that there may be functional suppression of visual processing when attention must be allocated to auditory events. This conjecture finds some support from studies in which attention to one or another modality is manipulated directly, as CBF decreases have often been reported in the regions associated with processing the modality that is not attended (Haxby *et al.*, 1994; Kawashima *et al.*, 1995; Paus *et al.*, 1997; Woodruff *et al.*, 1996). The relationship between areas involved in processing various sensory modalities and attention is likely to be more complex than a simple reciprocity, however: in particular, several studies have observed CBF increases in visual cortical areas when subjects are presented with auditory stimuli, even with their eyes closed (Démonet *et al.*, 1994; Zatorre *et al.*, 1994, 1996). It is therefore clear that additional information will have to be obtained before this issue can be clarified.

Activity in Auditory Cortices

As predicted, the results from the present study did not reveal any modulation of neuronal activity in primary or secondary auditory cortices as a function of the stimulus features that were to be attended. Neither the direct comparison of the attentional conditions to one another nor the analysis of CBF change within the anatomically defined region of Heschl's gyrus or of functionally defined areas of secondary cortex revealed any evidence for such modulation. It is entirely possible, of course, that differential neuronal events do take place within the auditory cortices as a function of attention, but that these occur on a time scale to which PET is insensitive (as suggested by ERP studies, e.g., Woods *et al.*, 1994; Woldorff *et al.*, 1993). Frith and Friston (1996), who also reported no modulation of auditory cortex in a cross-modal attentional task, proposed that the difference between ERP and PET results could be reconciled if the reported ERP modulations

primarily reflect degree of synchrony between many sources, rather than amount of neural activity.

Although several imaging studies of auditory attention concur with our finding of no change in auditory cortices as a function of attentional instruction, others have reported increases in primary (Alho *et al.*, 1999) or extraprimary (O'Leary *et al.*, 1996; Grady *et al.*, 1997) cortices associated with attentional manipulations. The reason for these discrepancies may depend on the nature of the attentional processes that might be elicited by the tasks used in the various studies. This may also depend very much on rate of stimulus presentation, with relatively slow rates, such as used in the present study, leading to automatic and complete feature processing, while relatively fast rates might lead to early selection reflected by increased CBF in auditory cortex (Alho *et al.*, 1999; but see Frith and Friston, 1996, for evidence that rate of presentation does not interact with attention).

These factors may explain why Zatorre *et al.* (1992, 1996) observed no changes in STG regions when subjects were asked to respond to stimuli containing certain characteristics, compared to a baseline in which subjects were instructed to listen to the same stimuli but were not asked to respond. These findings contrast, however, with a similar fMRI study by Grady *et al.* (1997) in which subjects were asked to count the number of occurrences of a given target word, compared to a baseline in which the same stimuli were presented but no target was specified. These investigators observed a greater area of activation in left secondary auditory cortical regions, although there was considerable intersubject variability in the effect, as well as in the precise areas that showed modulation. One possible factor that cannot be discounted is that there may be some influence of the fMRI acoustic artifact on the processing elicited: it may be more attentionally demanding to perform a counting task during fMRI scanning than it would be in the quiet environment of PET. Thus, results may differ in the two situations because additional attentional processes may be engaged when subjects are performing a task in which the stimuli must be perceptually segregated from the background noise (see also Griffiths *et al.*, 1998).

The lack of differential STG activity in the Attend Left vs Attend Right conditions of the present study would also seem contradicted by the PET data of O'Leary *et al.* (1996), who did observe contralateral changes as a function of ear to be attended in a dichotic task. The difference in this case may relate to the very different situation of listening to isolated stimuli one at a time versus listening to auditory information presented dichotically. In the case of stimuli presented individually in silence, preattentive mechanisms could be engaged in an automatic manner, whereas in a dichotic situation, an active inhibitory mechanism may

be needed to suppress information coming from the irrelevant channel, which would otherwise be processed by the putative preattentive mechanism. Tzourio *et al.* (1997) also compared attend left to attend right conditions while subjects heard sequences of tones and did not observe any significant modulation of CBF in auditory regions, although a nonsignificant trend was noted. In summary, therefore, the existing findings would seem to indicate that attentional modulation of STG areas may occur, but only under certain conditions, such as when fast rate of presentation is used or when competing stimuli are present simultaneously.

The similarity in CBF in auditory cortex across attentional conditions in the present study is consistent with several other imaging studies that also reported no changes in temporal cortex as a function of attentional instructions (Frith and Friston, 1996; Paus *et al.*, 1997; Zatorre *et al.*, 1992). The recent data of Belin *et al.* (1998) are particularly relevant here: they observed activity within the right posterior superior temporal area in an auditory intensity discrimination task, along with right parietal and frontal regions. Most importantly, however, they reported no modulation of CBF in the temporal cortex as a function of task difficulty (as measured with psychophysical indices), whereas activity in right frontal and parietal regions increased parametrically with increasing difficulty. Thus, these findings converge with those of the present study in indicating a constant, task-independent activation of superior temporal auditory cortical regions, which is functionally dissociable from the right parietofrontal distributed network.

Our interpretation of this result is that it reflects an automatic stimulus feature extraction process, which occurs preattentively. According to the model of Mondor *et al.* (1998) there is an initial stage of feature integration which occurs prior to selection and allows selection to operate on the basis of auditory streams. This preattentive process by which distinct acoustic features of a stimulus are conjoined into auditory "objects" has been termed auditory stream segregation by Bregman (1990); we propose that the invariant auditory cortical activation that we and others have observed reflects this process. We further propose that it is these streams that are subject to selection by attentional mechanisms. The observation that the same attentional network appears to be recruited for either spatial location or tonal frequency supports a model such as that offered by Mondor *et al.* (1998), in which the selection of auditory information is accomplished via an attentional template which incorporates both spectral and spatial parameters.

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