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The neural networks underlying endogenous auditory covert orienting and reorienting

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Auditory information communicated through vocalizations, music, or sounds in the environment is commonly used to orient and direct attention to different locations in extrapersonal space. The neural networks subserving attention to auditory space remain poorly understood in comparison to our knowledge about attention in the visual system. The present study investigated whether a parietal–prefrontal right-hemisphere network controls endogenous orienting and reorienting of attention to the location of sounds just as it does for visual–spatial information. Seventeen healthy adults underwent event-related functional magnetic resonance imaging (fMRI) while performing an endogenous auditory orienting task, in which peripheral cues correctly (valid) or incorrectly (invalid) specified the location of a forthcoming sound. The results showed that a right precuneus and bilateral temporal–frontal network mediated the reorienting of auditory attention at both short and long stimulus onset asynchronies (SOAs). In contrast, the more automatic stage of auditory reorienting at the shorter SOA was associated with activation in a bilateral inferior parietal–frontal oculomotor network. These findings suggest that the reorienting of auditory attention is generally supported by a similar inferior parietal–frontal network as visual attention, but in both hemispheres. However, peripheral auditory cues also appear to elicit an automatic orienting response to the spatial location of a sound followed by a period of reduced processing of information that occurs in the same location later in time.

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The ability to orient attention to a sound located in space is fundamental to most organisms and is often under volitional (i.e., endogenous) control. For example, most organisms will purpose-

fully allocate attentional resources to a location in auditory space following the appearance of a sound. Numerous neuroimaging studies demonstrate that endogenous orienting and reorienting to a visual location are supported by a frontal–parietal network, which is biased for right hemisphere processing (Arrington et al., 2000; Corbetta et al., 2000; Corbetta and Shulman, 2002; Thiel et al., 2004). However, electrophysiological and behavioral research suggests that auditory information may be processed more rapidly than visual information (Eimer and Schroger, 1998; Ward, 1994), which may result in different patterns of functional activation in attention networks during auditory orienting tasks.

To our knowledge, no imaging studies have directly examined volitional orienting to auditory space, which is the focus of the present study. Instead, auditory orienting is presently understood in terms of neural systems that support selectively attending to auditory information, detecting changes in a stream of auditory information, attention to auditory motion, mismatch negativity, and sound localization (e.g., Griffiths et al., 1998; Lewis et al., 2000; Pugh et al., 1996; Downar et al., 2000; Molholm et al., 2005; Park et al., 2002; Schall et al., 2003; Tata and Ward, 2005). The most commonly used paradigm to study auditory attention in the neuroimaging literature is the localization task, in which the location of a sound is identified without prior information (i.e., a cue) about its location. Although most neuroimaging studies fail to demonstrate any clear hemispheric bias for sound localization in the primary auditory cortex (Alain et al., 2001; Maeder et al., 2001; Weeks et al., 2000; Zatorre et al., 1999, 2002), a right hemisphere bias has been reported in a parietal–prefrontal network, encompassing areas near the frontal eye fields (FEFs; Maeder et al., 2001; Zatorre et al., 1999, 2002; but see Bushara et al., 1999 and Weeks et al., 2000). Lesion and single cell recordings in animals also implicate parietal–prefrontal areas in auditory localization (Rauschecker and Tian, 2000; Recanzone, 2000; Romanski et al., 1999b), as well as the primary auditory cortex and the superior/inferior colliculi (Middlebrooks and Knudsen, 1984; Middlebrooks

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et al., 2002; Romanski et al., 1999a). These results have led some to conclude that the localization of auditory information is supported by a fronto-temporoparietal network, which may be analogous to the “where” network in visual attention (Rauschecker and Tian, 2000; Zatorre et al., 2002).

However, a large body of research in psychology demonstrates that different cognitive processes are recruited to perform localization (i.e., target detection) and spatial cueing (i.e., orienting to location) tasks, suggesting that our current understanding of the neuroanatomical substrates for auditory spatial cueing is incomplete. Although early research did not reliably show that auditory cues facilitated identification of auditory targets (Spence and Driver, 1994), this was likely due to the use of target detection (i.e., detecting the appearance of target) rather than localization (i.e., discriminating target location) paradigms (Rhodes, 1987; Schmitt et al., 2000; Spence and Driver, 1994) or due to low angles of cue–target eccentricity (Spence and Driver, 1994). It is now well established that both visual and auditory spatial cues, which correctly (i.e., valid trials) or incorrectly (i.e., invalid trials) predict the location of a forthcoming target, exert powerful effects on behavior and the assumed underlying cognitive processes of expectation, response preparation and reorienting (Mesulam, 1981; Mondor and Amirault, 1998; Mondor and Breau, 1999; Mondor and Zatorre, 1995; Posner, 1980, 1994; Posner and Peterson, 1990; Spence and Driver, 1994).

Specifically, when the ratio of valid to invalid cues is high, organisms purposefully allocate attention to the cued location through endogenous mechanisms. The expectancy that the cue will typically be informative of a target location results in an increased orienting response to the cued location, which facilitates reaction times so that response times are faster for validly than invalidly cued trials, even when the cue–target stimulus onset asynchrony (SOA) lasts for longer periods of time (Mueller and Rabbitt, 1989; Rafal and Henik, 1994). In exogenous orienting, peripheral cues with a low validity ratio are utilized, so that cognitive expectations about the cue are not developed. Still, peripheral cues produce facilitation on validly cued trials when the SOA is short (e.g., 100 ms) because the cue captures attention automatically. However, for longer SOAs, attention is inhibited at the cued location before target onset, resulting in slower responses for validly than invalidly cued targets (Mondor, 1999; Mondor et al., 1998; Posner et al., 1985).

Neuroimaging research indicates that these different attentional mechanisms also produce distinct patterns of neuronal activation. During endogenous spatial orienting, invalidly cued trials produce greater activation than validly cued trials in ventral regions of the right parietal lobes and frontal oculomotor areas (Arrington et al., 2000; Corbetta et al., 2000; Thiel et al., 2004). In contrast, valid endogenous cues produce greater activation than valid exogenous cues in the bilateral temporoparietal junction, left intraparietal sulcus (IPS), bilateral superior temporal gyrus, right middle temporal gyrus, and right FEF (Mayer et al., 2004a). Although endogenous and exogenous spatial orienting activate similar networks when the effects of cue validity are not considered, endogenous orienting results in more pronounced activation within the posterior parietal and temporo-occipital lobes, whereas exogenous orienting shows relatively more activation of right hemisphere resources (Kim et al., 1999). There is also evidence that attending to a location (i.e., spatial cueing) can be dissociated from target detection (i.e., localization) within the parietal lobe. Specifically, the IPS is more activated during spatial cueing,

whereas the temporoparietal juncture is more activated during target detection (Corbetta et al., 2000).

Collectively, the above research demonstrates dissimilarities in the control of different types of attention, which underscores the need for a study that specifically examines the neuronal correlates of endogenous auditory attention. In the present study, we used fMRI to image healthy adults as they performed an event-related auditory endogenous orienting task in which peripheral cues correctly specified the location of a forthcoming sound in 75% of the trials. Based on the endogenous visual attention literature, we hypothesized that endogenous auditory attention would be associated with a right-hemisphere lateralized frontal–inferior parietal network, which would be more activated following an invalidly than validly cued auditory location. We also examined whether auditory spatial-cueing effects would be greater at a short (100 ms) than a long (800 ms) SOA, secondary to more rapid processing of auditory than visual information (Eimer and Schroger, 1998; Ward, 1994).

Methods

Subjects

Seventeen (8 male, 9 female) strongly right-handed (mean Edinburgh Handedness Inventory score = $95.0\% \pm 10.2\%$) adult volunteers (mean age = 25.5 ± 4.0) participated in the study. Subjects with a history of neurological disease, major psychiatric disturbance, substance abuse, or psychoactive prescriptive medications were excluded. Informed consent was obtained from subjects according to institutional guidelines at the University of New Mexico.

Procedures

To identify the neural correlates of endogenous auditory orienting, subjects performed an auditory spatial-cueing task while undergoing fMRI on a 1.5 T Marconi-Picker scanner at the Veterans Affairs Medical Center in Albuquerque. Auditory stimuli consisted of two 100 ms monaural tone pips with a 10 ms linear onset–offset ramp, delivered directly into the subjects’ pinnae through 125 in. of plastic tubing. The tubing passed through headphones and separates earplugs before entering the pinnae to attenuate scanner noise. The first tone pip (1000 Hz) served as a cue, which correctly (i.e., valid trials) predicted the location of a second target tone pip (2000 Hz) on 75% of the trials to promote endogenous orienting (Fig. 1). On the remaining

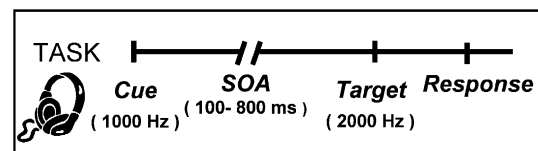


Fig. 1. A diagram of the events that occurred during cued trials. Headphones were used to present a 1000 Hz pure tone (the cue), which correctly predicted the location of a second 2000 Hz tone (the target) on 75% of trials and incorrectly predicted the location on 25% of the trials. The target pseudorandomly occurred after a stimulus onset asynchrony (SOA) of either 100 or 800 ms. Participants indicated the spatial location of the target by pressing a key with their right index (left target) or right middle (right target) finger.

25% of the trials, the cue incorrectly (i.e., invalid trials) specified the target location so that subjects had to reorient their attention upon the appearance of the target. The SOA between the cue and the target was either 100 or 800 ms, based on previous behavioral studies of auditory orienting (Mondor, 1999; Mondor and Zatorre, 1995; Spence and Driver, 1994) and imaging studies of visual attention (Mayer et al., 2004a). The order of trials was randomized.

Subjects were instructed to make a key press with their right middle finger for targets appearing in the right auditory space and right index finger for targets appearing in the left auditory space. A target localization paradigm was chosen to maximize the likelihood of observing cueing effects (Spence and Driver, 1994). The current design was based on paradigms from the cognitive behavioral literature in which endogenous auditory orienting is evoked using peripherally presented monaural predictive cues (60% to 80% validity ratio; Mondor, 1999; Mondor and Zatorre, 1995; Spence and Driver, 1994). In addition, catch trials were included to ensure that subjects were responding to the appearance of the target rather than the cue and to control for the effects of responding to a target. Catch trials consisted of a single binaural target tone pip that was not preceded by a cue. On catch trials, subjects responded by pressing both buttons. There were a total of 168 valid, 54 invalid, and 54 catch trials presented across three separate imaging runs. Subjects were informed of the ratio of valid to invalid cues prior to the start of the experiment and were encouraged to use this information to improve their performance.

Subjects were required to demonstrate 100% proficiency in verbally identifying the target and cue tone pip before entering the scanner. To minimize neuronal activation associated with eye movements, subjects were instructed to maintain fixation throughout the task on a white central fixation cross presented on a black background. Subjects viewed the fixation cross through an Avotech vision goggle system. Previous studies using eye-tracking devices have demonstrated that healthy subjects are capable of maintaining visual fixation during visual orienting tasks within the scanner (Gitelman et al., 2000; Mesulam et al., 2001) and during auditory tasks outside of the scanner (Spence and Driver, 1994).

The inter-trial interval was randomly jittered to allow for the best sampling of the hemodynamic response (Burock et al., 1998). This was accomplished by applying a random seed to the 2.0 s epochs (equivalent to repetition time) that contained cueing trials or only the fixation cross and then sorting all epochs by the random seed. In order to achieve a minimal inter-trial interval of 3.0 s (Glover, 1999), an additional constraint was applied to the data so that two trials requiring a response (e.g., cueing or catch trials) could not be presented consecutively. Trial length ranged from 4 to 10 s. This procedure also allowed for the establishment of the baseline resting state in the regression model, which corresponded to the neuronal activation associated with maintaining visual fixation on the central cross and ambient scanner noise from the switching of the gradients.

Subjects rested supine in the scanner with their head secured by chin and forehead straps and foam padding to limit head motion in the head coil. A non-ferrous key press device was positioned directly under the subject's right hand to record responses. Stimulus presentation, synchronization of stimulus events with the MRI scanner, and the collection of accuracy and reaction time (RT) data for offline analyses were achieved using Presentation

software. RT was measured from the onset of the target stimulus to the completion of a key press response.

Functional MR imaging

At the beginning of the scanning session, high resolution anatomic images were collected [TE (echo time) = 4.5 ms, TR (repetition time) = 15 ms, 25° flip angle, number of excitations (NEX) = 1, slice thickness = 1.2, FOV (field of view) = 25.6 cm, resolution = 256 × 256]. Echo-planar images were collected using a single-shot, gradient-echo echo-planar pulse sequence [TE = 37.3 ms; TR = 2000 ms; FOV = 25.6 cm; matrix size = 64 × 64]. Twenty-one contiguous sagittal 6-mm thick slices were selected to provide coverage of the entire brain (voxel size: 4 × 4 × 6 mm). Three time series were collected consisting of 225 sequential echo-planar images per series. A sparse sampling sequence with a clustered volume acquisition (Hall et al., 1999) was not employed in the current study as one of the primary goals was to perform an event-related study which closely followed the experimental parameters from the cognitive behavioral literature (i.e., shorter inter-trial intervals).

Image processing and statistical analyses

Functional images were generated using Analysis of Functional NeuroImages (AFNI) software package (Cox, 1996). Time series images were spatially registered in both 2- and 3-dimensional space to minimize effects of head motion. A correction for autocorrelations was not performed. A deconvolution analysis was used to generate one impulse response function (IRF) for each condition on a voxel-wise basis. Each IRF was derived relative to the baseline state (fixation) and based on the first 6 TRs post-stimulus onset. The coefficients for the images acquired 4.0 to 8.0 s post-stimulus onset from the cue, corresponding to the peak of hemodynamic response function (Cohen, 1997), were then divided by the coefficient for the baseline state to compute an index of percent signal change. Anatomical and functional images were then interpolated to volumes with 1 mm³ voxels, co-registered, converted to a standard stereotaxic coordinate space (Talairach and Tournoux, 1988), and blurred using a 4 mm Gaussian full-width half-maximum filter.

In order to investigate differences in neuronal networks during the various phases of orienting, a 2 × 2 (Validity × SOA) voxel-wise repeated-measures ANOVA was performed on the percent signal change data for the images corresponding to the peak of the hemodynamic response function. Planned comparison *t* tests were performed to test a priori hypothesis. To quantitatively examine whether there was a hemispheric bias in controlling endogenous auditory reorienting, we reversed (i.e., flipped) the order of the left–right row in our stereotaxically normalized data and conducted a 2 × 4 (Order × Condition) voxel-wise repeated-measures ANOVA. Specifically, the first factor corresponded to voxel order (flipped versus normal orientation) and the second factor corresponded to the four different conditions in the experiment (valid and invalid trials at the 100 and 800 ms SOA). A significance threshold corresponding to *P* < 0.001 was applied in combination with a minimum cluster size threshold of 0.25 ml to all of the data to minimize the likelihood of false positives (Forman et al., 1995). This probability threshold was established based on 10,000 Monte Carlo simulations demonstrating that the chance probability of obtaining a significant

activation cluster for an entire volume (Type I error) was less than 1×10^{-6} .

Results

Behavioral results

Behavioral accuracy for the task was very high as the majority of subjects performed perfectly or had three or less errors, suggesting that participants had no difficulty distinguishing cues from targets and no difficulty identifying target location while in the scanner. A 2×2 [Validity (Valid, Invalid) \times SOA (100, 800)] ANOVA was performed on the RT data to evaluate performance in the scanning environment for correct trials only (Fig. 2). The main effects of validity ($F_{1,16} = 66.15$, $P < 0.001$), SOA ($F_{1,16} = 61.22$, $P < 0.001$), and the validity by SOA interaction ($F_{1,16} = 23.05$, $P < 0.001$) were significant. Planned comparisons of the interaction indicated that RTs for valid trials were significantly faster than invalid trials at both the 100 ($t_{16} = 6.5$, $P < 0.001$) and 800 ms SOAs ($t_{16} = 6.3$, $P < 0.001$). The magnitude of the validity effect (invalid RT–valid RT) was significantly larger for the 100 than the 800 ms SOA ($t_{16} = 4.80$, $P < 0.001$), but this was primarily a result of the larger difference between invalid compared to valid trials across SOA ($t_{16} = -4.82$, $P < 0.001$).

In summary, the significant effect of cue validity at both SOAs demonstrates that subjects utilized endogenous mechanisms to allocate their attentional resources to the spatial locations of cues. However, the magnitude of the validity effect was larger at the 100 compared to 800 ms SOA, suggesting that auditory cues may elicit an automatic orienting of attention followed by decreased processing of cued auditory space over longer periods of time (Klein, 2000; Posner et al., 1985).

Functional results

A 2×2 (Validity \times SOA) ANOVA was performed to investigate the neural correlates of auditory orienting. Clusters of activation based on both parametric and spatial thresholds for the main effects of validity, SOA, and the validity \times SOA interaction are presented in Figs. 3–5 and Tables 1–3. Tables 1 and 2 tabulate the main effects of cue validity and SOA for clusters that were not involved in the interaction. Table 3 tabulates regions in which

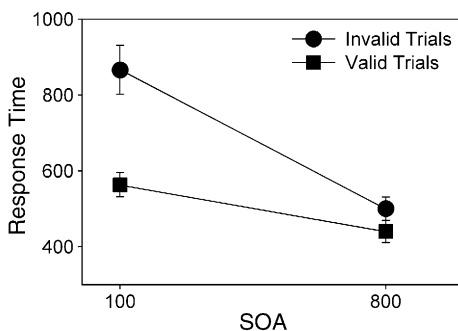


Fig. 2. Reaction time (RT) data for validly (filled square) and invalidly (filled circle) cued trials. The group mean of the median RT for valid trials was significantly faster than for invalid trials at both the 100 and 800 ms stimulus onset asynchrony (SOA). The difference between valid and invalid RTs was significantly reduced at the 800 ms SOA.

activation depended on the interaction between cue validity and SOA and summarizes the follow-up simple effect analyses of these interactions.

The first column of Table 1 and Fig. 3 summarize regions showing greater activation during covert reorienting than orienting (i.e., greater activation for invalid than valid trials) across both SOA periods. These regions included the left inferior frontal gyrus, right middle frontal gyrus (FEF; Brodmann area (BA) 6 and 8), left insula, bilateral middle and superior temporal gyri (BA 21 and 22), right precuneus (BA 7), left calcarine sulcus (BA 17), left pyramis, and right inferior sub-lunar lobule of the cerebellum. The second column of Table 1 and Fig. 3 indicates that the bilateral anterior cingulate gyrus (BA 24 and 32) and the left superior frontal gyrus (BA 8) demonstrated greater activation during covert orienting than reorienting (i.e., valid greater than invalid trials). However, examination of the impulse response functions in these areas (Fig. 3) shows that, for both regions, greater activation during valid trials was the result of deactivation during invalid trials.

Table 2 lists regions showing an effect of SOA. The first column shows that the right cuneus (BA 19) was associated with greater activity during the shorter (100 ms) than the longer SOA (800 ms) period. Greater activation during the longer SOA was found in bilateral medial frontal gyrus (BA 6; supplementary motor area (SMA) proper), bilateral superior temporal gyri (BA 41 and 42) and the left inferior temporal gyrus.

Functional activity in several cortical areas depended on the interaction between cue validity and SOA (Table 3; Fig. 4). These areas included bilateral medial frontal gyrus spanning both the pre-SMA and SMA proper (BA 6), left middle frontal gyrus (FEF; BA 6), left parahippocampal gyrus, right insula (BA 13), bilateral inferior parietal lobes (BA 40), the left supramarginal gyrus (BA 40) and the left angular gyrus (BA 39). Fig. 4 displays this map and plots the percent signal change for selected regions.

Simple effect analyses were conducted to specify the nature of the interaction effects. These analyses consisted of voxel-wise paired t tests that were restricted to the spatial areas associated with the interaction effect and used the same parametric ($P < 0.001$) and spatial (250 ml) thresholds. The first group of simple effect analyses compared the effect of cue validity (valid versus invalid trials) at each SOA. The second group of tests compared the effect of SOA separately for valid and invalid trials. The three right-most columns of Table 3 summarize these results. This table shows that there was an effect of cue validity at the 100 ms SOA in all regions demonstrating an interaction effect, with the exception of the angular gyrus and one activation focus within the right insula ($x = 37$, $y = 20$, $z = 6$). In the majority of these regions, including the bilateral inferior parietal lobe, bilateral pre-SMA, left FEF, right insula ($x = 45$, $y = 4$, $z = 19$), and the left supramarginal gyrus, activation was greater during covert reorienting than orienting (i.e., invalid greater than valid). In contrast, activation in the left parahippocampal gyrus was greater for valid than invalid trials. However, this effect was due to deactivation from baseline levels during invalid trials. Despite the robust effects of cue validity during the 100 ms SOA, no effects of reorienting or orienting were found in these regions at the 800 ms SOA.

Simple effect analyses of reorienting (invalid) trials showed that activation was greater at the 100 ms than the 800 ms SOA in bilateral pre-SMA, right insula and the bilateral inferior parietal lobes (BA 40). On invalid trials, no areas showed greater activation at the 800 ms than the 100 ms SOA. These results contrasted with orienting (valid) trials in which activation was greater for the 800

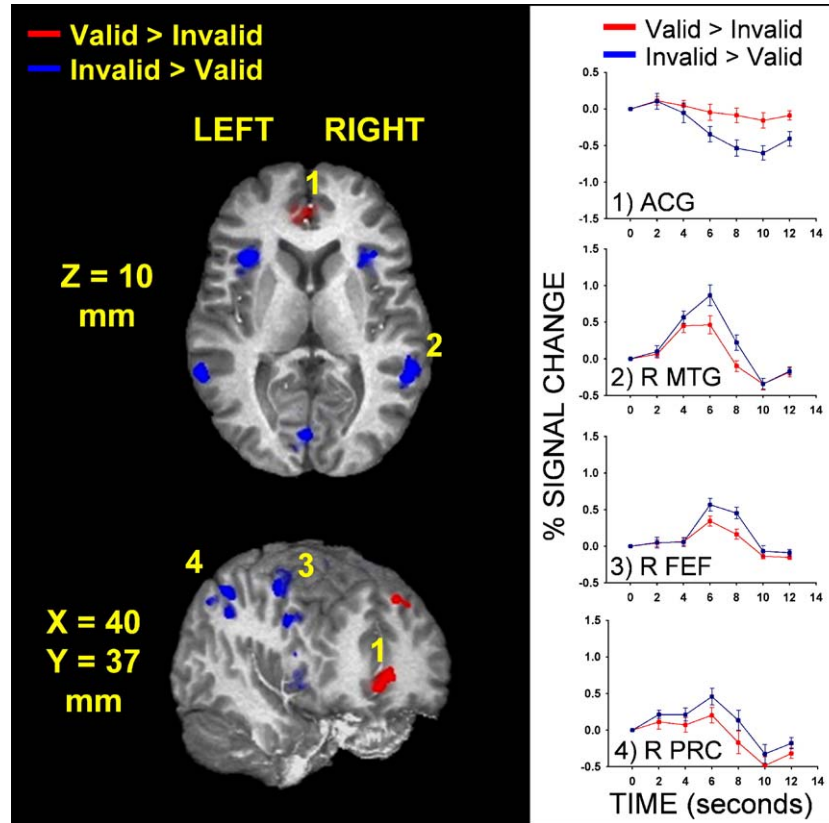


Fig. 3. Areas of activation during the orienting (validly cued trials) and reorienting (invalidly cued trials) of attention. The upper panel displays cortical activations corresponding to a slice 10 mm superior (z direction) to the origin (anterior commissure) in Talairach space. The lower panel displays a rendering corresponding to a slice 40 mm to the right (x direction) and 37 mm rostral (y direction) to the origin (anterior commissure). Increased activation was observed in the (1) bilateral anterior cingulate gyrus (ACG) and the left superior frontal gyrus during valid trials (red coloring). Attentional reorienting (blue coloring) was associated with activation in a temporal prefrontal network including right (2; R MTG) and left temporal cortex, right frontal eye field (3; R FEF), right precuneus, (4; R PRC) and left inferior frontal cortex. Separate impulse response functions are presented for valid and invalid trials for the right MTG, right FEF, right PRC, and bilateral ACG. Examination of the impulse response functions indicated that activation within the ACG and left superior frontal gyrus (impulse response function not pictured) was the result of significant deactivation from baseline during the invalid trials.

than the 100 ms SOA in the SMA proper and the left FEF. On valid trials, no areas showed greater activation for the 100 ms than the 800 ms SOA.

Hemispheric asymmetry in auditory reorienting

A 2×4 (Order \times Condition) repeated-measures ANOVA was performed to investigate hemispheric asymmetries in activation during endogenous auditory orienting (see Table 4). The percent signal change for the right (R) and left (L) hemisphere shows the nature of hemispheric differences. The results for the main effect of order showed greater activation in the left than the right hemisphere in the pre/post-central gyrus ($L = 0.45\%$; $R = 0.05\%$), premotor cortex ($L = 0.22\%$; $R = 0.06\%$), and putamen ($L = 0.20\%$; $R = 0.08\%$). In contrast, activation was greater in the right than left hemisphere in the dentate nucleus ($L = 0.09\%$; $R = 0.31\%$) and inferior cerebellar lobule ($L = 0.06\%$; $R = 0.16\%$). This pattern of hemispheric bias is most likely reflective of the right-hand motor response on every trial to identify the target location. The order by condition interaction showed four additional clusters of activation including the angular gyrus, cingulate gyrus, parahippocampal gyrus, and superior frontal gyrus. Follow-up t tests of this interaction, restricted to the areas of activation associated with the interaction term, were then conducted for the effect of order at

each of the four different conditions to determine the hemisphere that demonstrated greater activation. The results indicated that activation was greater in the right than left the hemisphere in the superior frontal gyrus ($L = -0.17\%$; $R = 0.11\%$), parahippocampal gyrus ($L = -0.12\%$; $R = 0.02\%$) and angular gyrus ($L = -0.24\%$; $R = 0.03\%$) only during the 100 ms invalid trials. However, the percent signal change shows that this right hemisphere bias was actually the result of left hemisphere deactivation in these structures.

Relationship between performance and brain activation

The behavioral results indicated that the time to reorient attention to an unexpected target location depended upon the SOA between the cue and the target. For this reason, our analysis examining the relationship between RT performance and brain activation focused on regions involved in the interaction. For this analysis, the validity effect at each SOA (i.e., invalid–valid 100 ms SOA; invalid–invalid 800 ms SOA) was first calculated for functional activity in the significant interaction clusters and for the RT data. Then, a multiple regression analysis was performed where the magnitude of the validity effect at each SOA within the interaction clusters was regressed on the respective RT data. Due to the documented role of parietal areas and the FEFs in attention

Table 1
Regions showing a main effect of cue validity that did not overlap with the interaction term

Region	Side	Invalid > Valid					Valid > Invalid				
		BA	x	y	z	Volume (μ l)	BA	x	y	z	Volume (μ l)
Frontal lobe											
Anterior cingulate	B						32	−4	39	1	1.650
Superior frontal gyrus	L						8	−15	37	44	0.259
Inferior frontal gyrus	L		−52	3	26	0.867					
Middle frontal gyrus (FEF)	R	6	32	−1	53	1.522					
Middle frontal gyrus	R	8	40	9	33	0.647					
Temporal lobe											
Insula gyrus	L		−34	16	4	1.679					
Middle temporal gyrus	R	21/22	54	−45	8	0.860					
Superior temporal gyrus	L	21/22	−59	−45	12	0.541					
Parietal lobe											
Precuneus	R	7	16	−68	36	0.400					
Occipital lobe											
Calcarine sulcus	L	17	−4	−80	5	0.618					
Cerebellum											
Pyramis	L		−28	−61	−27	0.314					
Semi-lunar lobule	R		21	−64	−41	0.265					

Note. Side refers to the hemisphere showing activation where B = bilateral, L = left, and R = right hemisphere. The Brodmann area (BA) and Talairach coordinates (x, y, z) are specified for each area of activation.

(Corbetta and Shulman, 2002), clusters from the left FEF and bilateral parietal lobes were entered first in the regression followed by a stepwise entry of the remaining clusters. The results indicated that the parietal areas and the left FEF accounted for a significant percent of the total variance ($F_{3,33} = 9.50$, $P < 0.005$; $R^2 = 0.39$, $P < 0.005$). However, within the remaining clusters, only the medial frontal gyrus accounted for additional significant variance in RTs ($F_{1,33} = 15.46$, $P < 0.005$; $R^2 = 0.21$, $P < 0.005$). Within the medial frontal gyrus, different patterns of activation were observed in the SMA proper and the pre-SMA in the simple effects analyses of the cue validity by SOA interaction (Fig. 5), suggesting that these structures may function in different capacities during the various stages of endogenous auditory orienting and reorienting. Altogether, 60% of the total variance in RTs was accounted for by activation in these four regions.

Discussion

Although multiple imaging studies have investigated the neural correlates of endogenous visual orienting (Arrington et al., 2000; Corbetta et al., 2000; Thiel et al., 2004) and auditory localization

(Alain et al., 2001; Maeder et al., 2001; Weeks et al., 2000; Zatorre et al., 1999, 2002), to our knowledge, this is the first fMRI study to examine endogenous orienting within the auditory modality. Contrary to our prediction of a right hemisphere parietal–frontal bias for reorienting, the results showed that auditory reorienting was mediated by a bilateral network consisting of the parietal lobes, medial frontal gyrus, FEFs, insula, and temporal cortex. However, activation within this reorienting network was strongly dependent on the length of time between the cue and the target, which may be a function of whether attention was modulated by more automatic processes. We now turn to a discussion of these findings.

A general network mediating the reorienting of auditory attention

Reorienting of auditory attention at both SOAs produced increased activation in a temporal–prefrontal network, including the left superior and right middle temporal cortex, right FEF and left inferior frontal gyrus, but also the right precuneus. The temporal–prefrontal network may aid in resolving spatial location and assist in the planning of ocular-reorienting movements to sounds. This proposal is consistent with reports of bilateral

Table 2
Regions showing a main effect of SOA that did not overlap with the interaction term

Region	Side	Short > Long					Long > Short				
		BA	x	y	z	Volume (μ l)	BA	x	y	z	Volume (μ l)
Frontal lobe											
Medial frontal gyrus	B						6	0	−9	52	0.546
Temporal lobe											
Superior temporal gyrus	R						21/22	52	−23	10	1.597
Superior temporal gyrus	L						21/22	−49	−25	10	0.810
Inferior temporal gyrus	L							−58	−18	−16	0.588
Occipital lobe											
Cuneus	R	19	16	−80	41	0.519					

Note. Side refers to the hemisphere showing activation where B = bilateral, L = left, and R = right hemisphere. The Brodmann area (BA) and Talairach coordinates (x, y, z) are specified for each area of activation.

Table 3
Regions showing a validity \times SOA interaction and follow-up simple main effect analyses (*t* tests)

Region	Side	Validity \times SOA					Valid vs. Invalid (100 ms SOA) ^a		100 > 800 SOA (invalid trials)		800 > 100 SOA (valid trials)	
		BA	<i>x</i>	<i>y</i>	<i>z</i>	Volume (μ l)	BA	Volume (μ l)	BA	Volume (μ l)	BA	Volume (μ l)
Frontal lobe												
Medial frontal gyrus ^b	B	6	0	6	50	3.430	Pre-SMA	3.100	Pre-SMA	1.761	SMA	1.141
Middle frontal gyrus (FEF)	L	6	-31	-6	54	1.168	*	1.148			*	0.594
Temporal lobe												
Parahippocampal gyrus ^b	L		-27	-33	-14	0.304	*	0.269				
Insula	R		45	4	19	1.013	*	0.783	*	0.296		
Insula	R	13	37	20	6	0.265						
Parietal lobe												
Inferior parietal lobe	R	40	38	-44	47	1.865	*	1.387	*	0.397		
Inferior parietal lobe	L	40	-42	-46	45	0.561	*	0.532	*	0.554		
Supramarginal gyrus	L	40	-31	-50	37	0.666	*	0.606				
Angular gyrus	L	39	-48	-66	29	0.271						

Note. There was no effect of cue validity for the 800 ms SOA for any of regions showing a cue validity \times SOA interaction. Side refers to the hemisphere showing activation where B = bilateral, L = left, and R = right hemisphere. The Brodmann area (BA) and Talairach coordinates (*x*, *y*, *z*) are specified for each area of activation.

Asterisks indicate that the center of mass of the region remained unchanged in the simple main-effects analyses.

^a For the valid versus invalid 100 ms SOA simple main-effect analysis, all areas demonstrated greater activation for invalid than valid trials, with the exception of the parahippocampal gyrus, which showed the opposite effect of cue validity.

^b The medial frontal gyrus included activation foci in pre-SMA and SMA proper.

temporal and middle and inferior frontal activation during auditory localization tasks (Alain et al., 2001; Maeder et al., 2001; Weeks et al., 2000; Zatorre et al., 1999, 2002). In addition, the extensive connectivity between frontal oculomotor areas and the caudal belt of the auditory cortex provides the anatomical means by which these areas can function as a network (Romanski et al., 1999a; Russo and Bruce, 1994). However, temporal–frontal networks are also involved in cued, covert shifts of visual–spatial attention (Corbetta et al., 2000; Gitelman et al., 1999; Kim et al., 1999; Mayer et al., 2004a,b; Thiel et al., 2004), suggesting that this network may not be specific to processing auditory information, but rather may be more generally involved in shifts of attention irrespective of stimulus modality.

This network might also encode stimulus location and hold this information in a working memory buffer for later processing (Martinkauppi et al., 2000; Pasternak and Greenlee, 2005; Rama and Courtney, 2005). Indeed, the results from the SOA analysis showed greater bilateral temporal activation during the long SOA period where working memory demands should be the greatest. The precuneus, which is widely associated with memory encoding and retrieval (Prabhakaran et al., 2000), may participate in this network given its interconnectivity with inferior frontal, temporal, and occipital cortices (Krause et al., 2000), all of which showed greater activation when attention was reoriented. Increased precuneus activation during reorienting may be due to the demands placed on encoding sounds when the spatial location occurs in an unexpected location.

A network mediating the reorienting of attention at short SOAs

Unlike the findings from visual–spatial reorienting (Arrington et al., 2000; Corbetta et al., 2000; Thiel et al., 2004), the right inferior parietal cortex was not biased for modulating reorienting to auditory space at both SOAs. Instead, we found that a bilateral inferior parietal–medial frontal and left FEF network was only activated during reorienting trials at the 100 ms SOA. Moreover, a

direct comparison between the left and right hemisphere did not reveal any areas of asymmetric activation within the traditional attentional network. Although a similar network supports other aspects of auditory attention in humans (Downar et al., 2000; Pugh et al., 1996; Zatorre et al., 1999, 2002), this is the first study to implicate these structures for endogenous auditory reorienting at short SOAs. Activation in this inferior parietal–frontal network also explained a large portion of the RT variance, which further suggests its preeminence in auditory reorienting.

In vision, the right inferior parietal cortex is thought to regulate disengagement of spatial attention (Corbetta et al., 2000; Friedrich et al., 1998). Our results extend these findings by suggesting that the inferior parietal lobes function in a similar capacity to control the disengagement of auditory attention but do not exhibit as strong a hemispheric bias for reorienting to auditory space. Corbetta and colleagues have suggested that endogenous visual reorienting to an unattended location following invalid cues activates both a dorsal (e.g., superior parietal lobe, intraparietal sulcus) and ventral (e.g., temporoparietal juncture, supramarginal gyrus) frontoparietal attentional network (Corbetta and Shulman, 2002; Kincade et al., 2005). This contrasts with our results showing that endogenous auditory reorienting is associated with activation only in the ventral frontoparietal network, as defined by Corbetta's group.

Reduced activation in the inferior parietal lobes at the 800 ms SOA during covert reorienting was unexpected given that cue validity effects are typically larger at longer SOAs in endogenous visual–spatial attention (Mueller and Findlay, 1988; Mueller and Rabbitt, 1989; Rafal and Henik, 1994). In vision, reduced or absent validity effects are more commonly reported under exogenous orienting conditions, in which unexpected changes in a peripheral stimulus elicit an automatic orienting response to the stimulus location followed by a period of reduced processing, or even active inhibition at longer SOAs, for stimuli appearing in the same location (Klein, 2000; Posner et al., 1985). Although the endogenous orienting paradigm in the present study has been extensively validated in the cognitive literature, could the

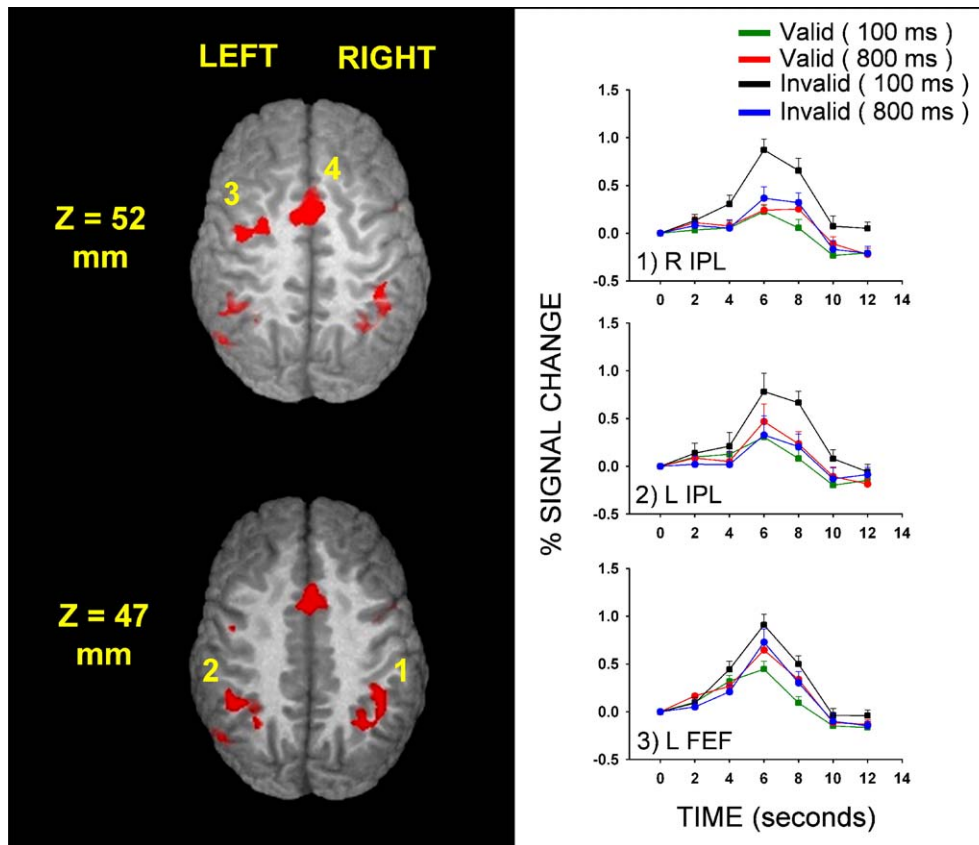


Fig. 4. Areas of activation in the validity by stimulus onset asynchrony (SOA) interaction term. The two slice locations correspond to 52 and 47 mm superior (z direction) to the anterior–posterior commissure plane in Talairach space. The bilateral inferior parietal lobes (1; R IPL: 2; L IPL), left frontal eye field (3; L FEF), and medial frontal gyrus (4) all demonstrated activation that was dependent on cue type and SOA. Impulse response functions are presented for validly and invalidly cued trials at the 100 and 800 ms SOAs for the inferior parietal areas and left FEF. In all areas, the magnitude of neuronal activation appeared to be the largest for invalidly cued trials at the 100 ms SOA. At the 800 ms SOA, there were no significant differences in the magnitude of the impulse response function for valid and invalid trials.

peripheral auditory stimuli used in the current experiment have generated a mixed pattern of exogenous and endogenous orienting despite the high ratio of valid (75%) to invalid (25%) cues?

Support for this hypothesis comes from both the cognitive literature on auditory orienting and from our functional and behavioral results. In the current study, the magnitude of the

Table 4
Regions showing hemispheric differences in the hemodynamic response

Region	Side	Main effect of order					Order × Condition effect				
		BA	x	y	z	Volume (μl)	BA	x	y	z	Volume (μl)
Frontal lobe											
Pre/Post-central gyrus	L	4/3	-40	-25	50	4.142					
Premotor cortex	L	31	-5	-14	47	1.130					
Cingulate gyrus	R						32	4	24	40	0.340
Superior frontal gyrus ^a	R							17	45	21	0.256
Temporal lobe											
Angular gyrus ^a	R						39	41	-71	27	0.719
Parahippocampal gyrus ^a	R							26	-33	-12	0.568
Subcortical											
Putamen	L		-29	-9	-2	0.334					
Cerebellum											
Dentate nucleus	R			16	-49	-20					2.989
Inferior semi-lunar lobule	R			13	-64	-38					0.442

Note. Side refers to the hemisphere showing greater activation where L = left and R = right hemisphere.

The Brodmann area (BA) and Talairach coordinates (x, y, z) are specified for each area of activation.

^a The results of simple effects tests indicated that the hemispheric effects were significant only for the invalid 100 ms SOA condition and were secondary to deactivation of homologous left hemisphere regions.

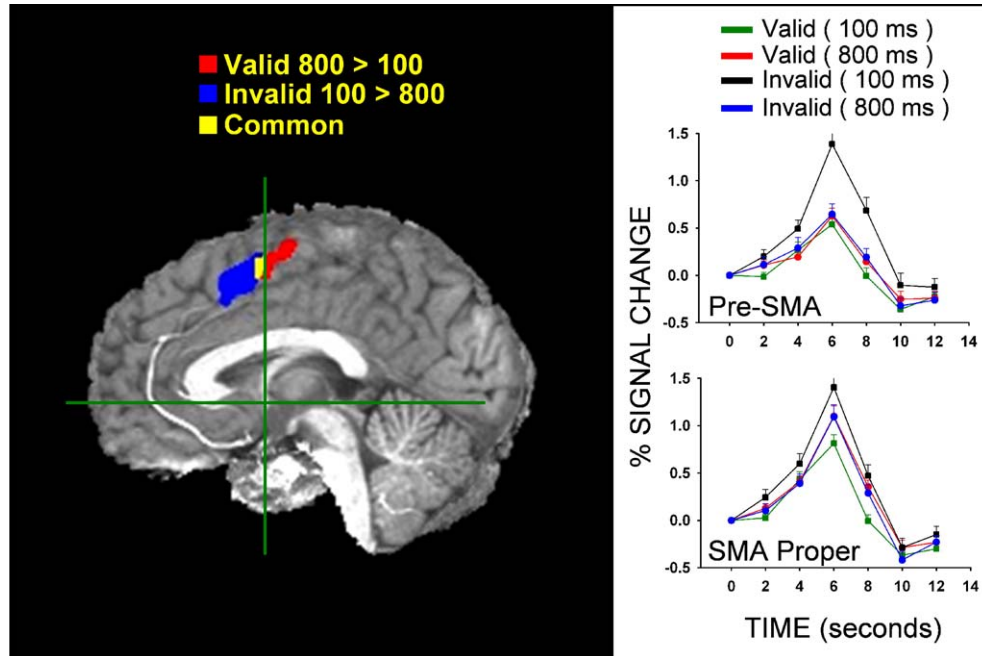


Fig. 5. Activation within the medial frontal gyrus. The green cross is aligned with the anterior commissure, corresponding to the origin in Talairach space, and divides the medial frontal gyrus into the pre-supplementary motor area (pre-SMA) and SMA proper. Examination of the impulse response functions suggests that the pre-SMA was activated during the conflict mediation stages of invalid 100 ms (blue coloring) trials. The SMA proper demonstrated increased activation during the 800 ms compared to 100 ms valid trials (red coloring), but examination of the impulse response functions suggests that this structure was also active during both invalid trials. A small area of overlap (yellow coloring) was observed during both of the comparisons.

validity ratio was reduced at the longer SOA. A similar reduction in the validity effect at longer SOAs has also been reported in previous behavioral studies of endogenous auditory reorienting (Mondor, 1999). Other supporting evidence shows that inhibitory processes occur with predictive, peripheral auditory cues at very long SOAs (Mondor, 1999) and that centrally presented auditory cues (i.e., words) do not produce as large an orienting response as peripheral cues (i.e., tones) at shorter SOAs (Quinlan and Bailey, 1995). At short SOAs, shifts in attention to cued locations are also difficult to inhibit when peripheral auditory cues are administered (Spence and Driver, 1994), suggesting that both exogenous and endogenous processes are at work.

Our functional imaging findings and those of others also suggest that peripheral cues may elicit both endogenous and exogenous orienting responses. In exogenous visual attention, reorienting of attention during longer cue–target SOAs is associated with reduced activation in the frontoparietal attention network (Kincade et al., 2005; Mayer et al., 2004b). This reduction in activation may be secondary to a mixture of both inhibition and facilitation at the longer SOA (Mayer et al., 2004b) or may be due to a decrease in the behavioral relevance of cues under more exogenous conditions (Kincade et al., 2005). The current experiment also found increased activation in the SMA proper and left FEF at the longer SOA during valid trials. A similar network, consisting of the supplementary eye fields (SEFs), located in the SMA proper (Grosbras et al., 1999), and the FEFs, has been posited to mediate an inhibitory mechanism in exogenous visual attention (Lepsien and Pollmann, 2002; Mayer et al., 2004b). Activation of this frontal–oculomotor network in our study further suggests that a mixture of inhibition and facilitation may have occurred at the longer SOA.

The prospect that different attentional mechanisms operate during endogenous auditory reorienting was also suggested by the distinct patterns of activity in regions of the medial frontal gyrus, which was the only structure that predicted unique variance in RTs, in addition to the variance accounted for by the ventral parietal–FEF network. Two distinct clusters within the SMA emerged from the interaction (Fig. 5), which suggests different roles for each of the clusters in auditory reorienting. The SMA proper (SEFs) showed greater activation during the 800 ms than the 100 ms SOA, but only on valid trials. These findings may reflect increased inhibition or planning of overt eye movements when either consciously anticipating a sound in an expected location (800 ms valid trials) or when reorienting to a sound in an unexpected location (invalid trials). In contrast, activation within the pre-SMA was greater for invalid than valid trials during the more automatic phase of attentional reorienting and during invalid trials at the shorter SOA. This pattern of pre-SMA activation may be the result of the greater demands placed on conflict mediation (Garavan et al., 2003) or response preparation when a target appears in an unexpected location immediately following the cue.

Finally, deactivation was also found during auditory reorienting in the bilateral anterior cingulate gyrus (BA 32/24), left superior frontal gyrus (BA 8), left parahippocampal gyrus, and left angular gyrus in both the orienting and the hemispheric asymmetry comparisons. Deactivation is not typically reported in visual orienting but is common in neuroimaging research. Task-induced deactivation has been reported for the anterior cingulate and superior frontal gyrus (McKiernan et al., 2003) as well as the parahippocampus (Harrington et al., 2004) and may reflect increased difficulty in processing invalidly cued targets. However, more research is needed to elucidate the exact mechanism of deactivation during auditory orienting tasks.

The current study has several limitations. First, due to the relatively poor temporal resolution of the hemodynamic response, it is difficult to determine whether differences in brain activation between covert reorienting and orienting are the result of orienting attention to auditory space, target processing, or an interaction between these processes (Corbetta et al., 2000; Kincade et al., 2005). Future experiments on auditory orienting might employ longer SOAs to distinguish these processes. Second, eye movements were not monitored in our experiment so that patterns of activation within the oculomotor network may be related to increased overt eye movements. However, we do not think this is a compelling explanation of our findings for two reasons. First, if subjects did not consistently maintain fixation, one might expect FEF activation to be greater at longer SOAs regardless of cue validity, which was not found. Second, there is ample evidence that healthy individuals are capable of maintaining fixation during covert auditory orienting tasks (Spence and Driver, 1994) and in the scanner environment during visual orienting tasks (Gitelman et al., 2000; Mesulam et al., 2001).

Summary

The results from the present study and from previous studies of visual orienting suggest both similarities and differences in the neuronal networks that mediate auditory and visual reorienting. In general, visual and auditory reorienting appears to be mediated by a similar ventral frontoparietal network including the inferior parietal lobe and frontal oculomotor areas (Corbetta and Shulman, 2002). However, activation of this network during auditory reorienting was not right hemisphere lateralized as it is for visual reorienting. Rather, when hemispheric biases were found, they were typically associated with the motor response or were the result of deactivation during covert reorienting at the 100 ms SOA. Exceptions were subtle differences in hemispheric biases for reorienting during the different SOA periods. In the frontal lobes, the right FEF was more active during invalid than valid trials, irrespective of SOA. However, the left FEF was more activated during reorienting only at the 100 ms SOA (i.e., validity \times SOA interaction). The inferior parietal lobes in both hemispheres supported the reorienting of auditory attention during invalid trials at the 100 ms SOA, but the right precuneus mediated reorienting at both SOAs. Collectively, these findings suggest that auditory reorienting does not exhibit selective engagement of right frontal and parietal resources as does visual reorienting. An increased dependence on a more bilateral network may be needed to resolve the spatial location of auditory information because it requires a complex integration of sound characteristics and head positioning information (Spence and Driver, 1994).

We also found that endogenous auditory reorienting effects on both functional and behavioral data were more robust at the shorter SOA during a relatively more automatic stage of reorienting. At the longer SOA, we observed reduced cue validity effects, selective activation of inhibitory structures during valid trials, and reduced functional activation during covert reorienting trials. Thus, similar to the behavioral and functional findings during exogenous visual attention (Lepsien and Pollmann, 2002; Mayer et al., 2004b), auditory cueing with peripheral stimuli may result in an automatic orienting to a sound's location in space followed by a reduction in cue

facilitation at longer SOAs, even when endogenous conditions are employed. The more automatic nature of orienting and reorienting attention to auditory than visual information may explain why response times are typically faster for auditory than visual stimuli and why auditory information is more difficult to ignore (Eimer and Schroger, 1998; Mayer and Kosson, 2004; Ward, 1994; Ward et al., 2000). Future studies that directly compare auditory orienting with peripheral cues under both exogenous (50% validity ratio) and endogenous (75% validity ratio) conditions are needed to more directly evaluate whether volitional and automatic orienting of auditory attention are supported by distinct neural networks.

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