Interactions between Voluntary and Stimulus-driven Spatial Attention Mechanisms across Sensory Modalities

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Abstract

■ In everyday life, the allocation of spatial attention typically entails the interplay between voluntary (endogenous) and stimulus-driven (exogenous) attention. Furthermore, stimuli in different sensory modalities can jointly influence the direction of spatial attention, due to the existence of cross-sensory links in attentional control. Using fMRI, we examined the physiological basis of these interactions. We induced exogenous shifts of auditory spatial attention while participants engaged in an endogenous visuospatial cueing task. Participants discriminated visual targets in the left or right hemifield. A central visual cue preceded the visual targets, predicting the target location on 75% of the trials (endogenous visual attention). In the interval between the endogenous cue and the visual target, task-irrelevant nonpredictive auditory stimuli were briefly presented either in the left or right hemifield (exogenous auditory attention). Consistent with previous unisensory visual studies, activation of the ventral fronto-parietal attentional network was observed when the visual targets were presented at the un-cued side (endogenous invalid trials, requiring visuospatial re-orienting), as compared with validly cued targets. Critically, we found that the side of the task-irrelevant auditory stimulus modulated these activations, reducing spatial reorienting effects when the auditory stimulus was presented on the same side as the upcoming (invalid) visual target. These results demonstrate that multisensory mechanisms of attentional control can integrate endogenous and exogenous spatial information, jointly determining attentional orienting toward the most relevant spatial location. ■

INTRODUCTION

There are several ways of covertly (i.e., without eye movements) directing one's attentional resources to a particular position in the environment, involving both voluntary and stimulus-driven attention shifts. In the former case, usually referred to as endogenous attention, it has been argued that the available resources are "pushed" toward the stimulus location; in the latter case, usually referred to as exogenous attention, the available attentional resources have traditionally been thought of as being "pulled" by abrupt changes taking place in the environment (see Klein & Shore, 2000).

The neural bases of these modes of attentional orienting have been studied extensively in recent years, but mostly in a separate manner, that is, by presenting separate blocks of exogenous and endogenous trials (e.g., Natale, Marzi, Girelli, Pavone, & Pollmann, 2006; Serences et al., 2005; Rosen et al., 1999; Kastner, De Weerd, Desimone, & Ungerleider, 1998; Mangun, Buonocore, Girelli, & Jha, 1998; Corbetta, Miezin, Shulman, & Petersen, 1993; see also Kastner & Ungerleider, 2000). This liter-

ature seems to converge on the existence of a neuro-anatomical dissociation between the endogenous and exogenous orienting of spatial attention (e.g., Hopfinger & West, 2006; Mayer, Dorflinger, Rao, & Seidenberg, 2004; see Corbetta & Shulman, 2002, for a review; although see also Peelen, Heslenfeld, & Theeuwes, 2004; Kim et al., 1999; Nobre et al., 1997). Accordingly, *dorsal* fronto-parietal regions (i.e., the intraparietal sulcus [IPS] and superior premotor cortex) would be involved in voluntary shifts of spatial attention (e.g., Hahn, Ross, & Stein, 2006; Corbetta, Kincade, Ollinger, McAvoy, & Shulman, 2000). By contrast, a *ventral* fronto-parietal attention network (including the temporo-parietal junction [TPJ] and the inferior frontal gyrus [IFG]) has been associated with stimulus-driven shifts of attention; in particular, in conditions requiring spatial reorienting toward behaviorally relevant stimuli, such as targets presented outside the current focus of attention (i.e., invalid trials; e.g., Kincade, Abrams, Astafiev, Shulman, & Corbetta, 2005; Corbetta et al., 2000).

Several recent studies have started to investigate the interplay between voluntary and stimulus-driven attention control, which is likely to be the rule rather than the exception in everyday life. For instance, using a contingent attentional capture task (see Folk, Remington, &

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Johnston, 1992), Serences and Yantis (2007) found that activity in the IPS and dorsal premotor regions (frontal eye field) also increased following stimulus-driven shifts of attention, when these were triggered by task-irrelevant stimuli sharing some defining feature of the target stimuli. This demonstrates that activity in dorsal fronto-parietal regions (thought to be involved in endogenous attention) can be modulated in a stimulus-driven manner, but only when the task-irrelevant stimuli are potentially relevant from a behavioral point of view.

Endogenous and exogenous factors have also been found to interact in the ventral attentional system. For instance, Indovina and Macaluso (2006) demonstrated that when attention is voluntary focused on one side, perceptually salient but task-irrelevant stimuli presented in the opposite hemifield do not trigger stimulus-driven reorienting and the activation of the ventral fronto-parietal network. Conversely, task-relevant stimuli (i.e., targets) at the unattended side activated the ventral attentional network, even when these stimuli had low perceptual salience. Indeed, more recent models of visuospatial attentional control stress the key role that behavioral relevance plays for the activation of the ventral fronto-parietal system (see Corbetta, Patel, & Shulman, 2008). In particular, it has been suggested that the TPJ may act as a "circuit-breaker," disengaging endogenous (internal) processing in dorsal regions, but only when the unexpected external stimulus is potentially relevant and may require the reallocation of attention (Corbetta & Shulman, 2002). Consistent with this account, Shulman, Astafiev, McAvoy, d'Avossa, and Corbetta (2007) also reported deactivation of the TPJ during visual search, until the target was detected. Deactivation of the TPJ would enable the filtering out of distracter information, thus ensuring that stimulus-driven orienting does not occur toward currently irrelevant stimuli.

However, to our knowledge, no studies have as yet examined whether task-irrelevant stimuli in a sensory modality other than vision interact with ongoing endogenous processing in a similar way (i.e., affecting the TPJ only if behaviorally relevant). Given that the TPJ has been shown to respond to transient multisensory stimulation (i.e., visual, auditory, and tactile stimuli; see Downar, Crawley, Mikulis, & Davis, 2000, 2001), one may expect a similar role for TPJ irrespective of the sensory modality of the incoming input (see also Macaluso, Frith, & Driver, 2002, who showed common activation of the TPJ as a consequence of the reorienting of visual and tactile spatial attention, but only when *task-relevant* targets were used). On the other hand, several recent studies have shown that multisensory stimuli are remarkably effective in capturing spatial attention, causing disengagement of endogenous attentional resources even when entirely *task-irrelevant* (Santangelo, Ho, & Spence, 2008; Santangelo & Spence, 2007; see also Santangelo, Van der Lubbe, Olivetti Belardinelli, & Postma, 2008; Talsma & Woldorff, 2005). These results suggest that

the filtering out of task-irrelevant information in a multisensory context may be more difficult, and perhaps, accomplished by different neural circuits, as compared to situations involving unisensory visual selection.

In the present study, we used functional magnetic resonance imaging (fMRI) to investigate interactions between voluntary (endogenous) and stimulus-driven (exogenous) spatial attention, in a multisensory context (e.g., Olivetti Belardinelli et al., 2004). The participants discriminated the elevation (up vs. down) of a visual target (i.e., a flash of light) presented equiprobably to either side of fixation. A central-symbolic, spatially predictive visual cue[1] was used to direct voluntary attention toward the location of the upcoming visual target (i.e., endogenous valid trials) or toward the opposite side (i.e., endogenous invalid trials). After the presentation of the endogenous cue but prior to the onset of the target, a spatially nonpredictive burst of white noise was used to capture auditory attention exogenously (e.g., Spence, McDonald, & Driver, 2004), either toward the same or the opposite side of the visual target (i.e., exogenous valid and invalid trials, respectively). This allowed us to examine the interaction between endogenous visual attention and exogenous auditory attention. In particular, we asked whether the position of the task-irrelevant auditory cue would influence any process associated with the endogenous visuospatial cueing task. We expected faster responses as a consequence of both the validity of the endogenous cue (valid faster than invalid) and the spatial correspondence between the auditory stimulus and the subsequent visual target (same side/exogenous valid trials faster than opposite side/exogenous invalid trials; cf. Berger, Henik, & Rafal, 2005, for a purely visual equivalent of this "double cueing paradigm"). The imaging data will reveal whether such an interplay between endogenous and exogenous signals in the two different modalities can lead to a reduction of activity within the ventral fronto-parietal network (TPJ and IFG, previously associated with reorienting toward invalidly cued targets), when the exogenous cue anticipates the unexpected target location in endogenous invalid trials. Any interaction within this network would indicate that multisensory attention control integrates endogenous and exogenous spatial information from different senses, and further, that—unlike visual stimuli—auditory stimuli can also affect reorienting processes in the ventral fronto-parietal system when they are entirely behaviorally irrelevant.

METHODS

Participants

Seventeen right-handed volunteers (10 men, mean age = 25.3 years, range = 20–32 years) took part in the study. All were in good health, free of psychotropic or vasoactive medication, with no past history of psychiatric or

neurological disease. All had normal or corrected-to-normal (with contact lenses) vision, and normal hearing. After having received an explanation of the procedures, all of the participants gave their written consent. The study was approved by the independent Ethics Committee of the Santa Lucia Foundation (Scientific Institute for Research Hospitalization and Health Care).

Stimuli and Materials

Participants lay in the scanner in a dimly lit environment and viewed the visual stimuli via a mirror system (see Figure 1A). The fixation point consisted of a white cross (1.2° × 1.2°) presented centrally against a black background. The auditory stimuli consisted of 50 msec white noise bursts presented at a sound pressure level (SPL) of approximately 115 dB.[2] Sounds were presented by means of two rubber tubes (one on each side) conducing the sounds from two loudspeakers placed outside the MR room. The two rubber tubes were connected one to the left and one to the right side of the coil, and aligned horizontally with the fixation cross. Two optical fibers were inserted into each rubber tube at a vertical distance of approximately 30° from each other (the horizontal distance between left and right fibers was approximately 70°). Each optical fiber was connected to a yellow light-emitting diode (LED) that, flashing for 100 msec in one of the four locations (top-left, top-right, bottom-left, bottom-right), served as the visual target. The positioning of the rubber tubes and the LED allowed us to present task-irrelevant auditory stimuli and visual targets in close spatial proximity.

Procedure

Once inside the scanner, and prior to the start of the first fMRI run (i.e., without any background scanner noise), the participants had to perform a visual and auditory pretest in which they had to indicate the location of presentation of both the visual targets (top-left, top-right, bottom-left, bottom-right) and the sound bursts (left, right, and center; the latter was achieved by presenting sound bursts simultaneously from both sides). Participants had to reach 100% correct in this pretest before starting the fMRI acquisition.

In the fMRI experiment, each trial started with the presentation of a white fixation cross for 500 msec (see Figure 1B). Next, the cross changed color (either to gray, red, or green) until the end of the trial. The gray color did not provide any predictive information with regard to the side of presentation of the upcoming target (endogenous neutral cue). The other two colors (red or green) provided an endogenous cue indicating that the visual target would be presented on a given side in 75% of trials (valid trials), while on the remaining trials it would be presented on the opposite side (invalid trials). The participants were explicitly informed about
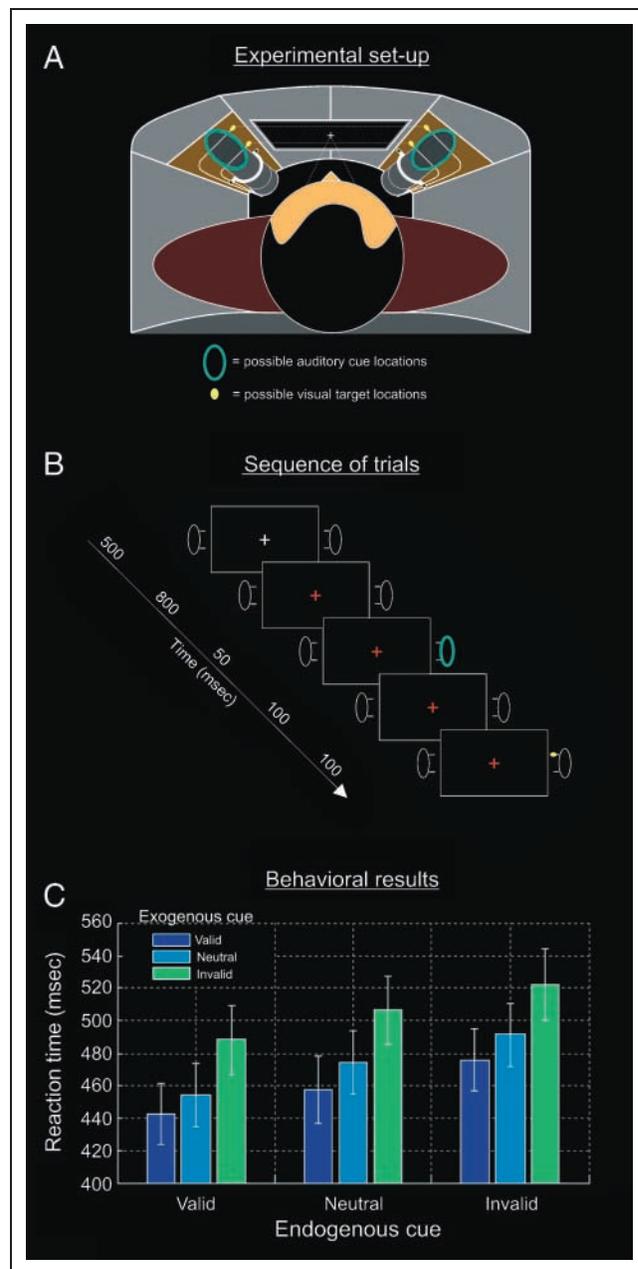

Figure 1. (A) Illustration of the experimental set-up. The fixation point consisted of a white cross presented on a central display. The auditory stimuli (bursts of white noise) were presented by means of two rubber tubes (one on each side of the fixation cross; see the green ellipses) conducting the sound generated by two loudspeaker cones. The rubber tubes were connected to the head coil, and aligned horizontally with the fixation cross. Two optical fibers connected to yellow LEDs and inserted into each rubber tube served as the visual targets. (B) Schematic diagram showing the time course of stimulus presentation. The change of color of the central fixation point (red or green) served as a symbolic cue to endogenously direct the participants' attention toward either the left or right side (color gray served as endogenous neutral trial). A burst of white noise presented equiprobably on either the left, right, or both sides served to exogenously orient spatial attention. Participants responded to the elevation (up vs. down) of the visual targets (LEDs). (C) RTs for the three types of endogenous cues (valid, neutral, and invalid) as a function of the three types of exogenous cues (valid, neutral, and invalid). The error bars represent the standard error of the means.

the percentage of validity of the endogenous cue. The association between color and likely target side was counterbalanced across participants. After 800 msec, a peripheral burst of white noise was presented on the left or right (exogenous peripheral cue), or from both loudspeakers (exogenous neutral cue) for 50 msec. This exogenous auditory cue was entirely spatially uninformative and participants were explicitly informed about this. One hundred milliseconds after the offset of the noise burst, one of the four LEDs was switched on for 100 msec. The participants were instructed to respond to all visual targets, pressing one of two response keys with the index finger to report the elevation of the visual target (e.g., left index finger for up targets and right index finger for down targets, or vice versa), regardless of target side and cueing condition. The participants alternated the fingers used to respond at the beginning of each run. The intertrial interval was 3.5 sec (range = 3–4 sec).

All participants underwent four fMRI runs. Each run lasted approximately 8 min. Overall, each participant completed 288 endogenous valid trials (96 exogenous valid, 96 exogenous neutral, 96 exogenous invalid), 192 endogenous neutral (64 exogenous valid, 64 exogenous neutral, 64 exogenous invalid), and 96 endogenous invalid trials (32 exogenous valid, 32 exogenous neutral, 32 exogenous invalid).

Eye Movement Recording

The eye position of participants was recorded during fMRI using an ASL eye-tracking system, adapted for use in the scanner (Applied Science Laboratories, Bedford, MA; Model 504, sampling rate 60 Hz). Eye-position traces were examined for each trial in a temporal window starting 200 msec before the onset of the endogenous cue and lasting till 200 msec after the offset of the visual target. Failures to maintain fixation were identified as changes in horizontal eye position greater than ±2° of visual angle.

Magnetic Resonance Imaging

A Siemens Allegra (Siemens Medical Systems, Erlangen, Germany) operating at 3 T and equipped for echo-planar imaging (EPI) acquired functional magnetic resonance (MR) images. A quadrature volume head coil was used for radio-frequency transmission and reception. Head movement was minimized by mild restraint and cushioning. Thirty-two slices of functional MR images were acquired using BOLD imaging (3×3 mm, 2.5 mm thick, 50% distance factor, repetition time = 2.08 sec, time echo = 30 msec), covering the entirety of cortex.
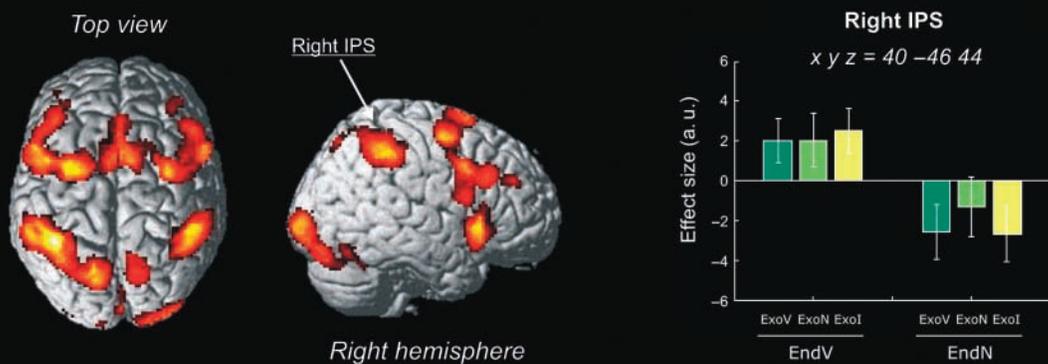
Data Analysis

We used SPM5 (Wellcome Department of Cognitive Neurology) implemented in MATLAB 7.1 (The MathWorks,

Natick, MA) for data preprocessing and statistical analyses. For all participants, we acquired 1000 fMRI volumes. After having discarded the first 4 volumes of each run, all images were corrected for head movements. Slice-acquisition delays were corrected using the middle slice as a reference. All images were normalized to the standard SPM5 EPI template, resampled to 2 mm isotropic voxel size, and spatially smoothed using an isotropic Gaussian kernel of 8 mm FWHM. Time series at each voxel for each participant were high-pass filtered at 220 sec and pre-whitened by means of autoregressive model AR(1).
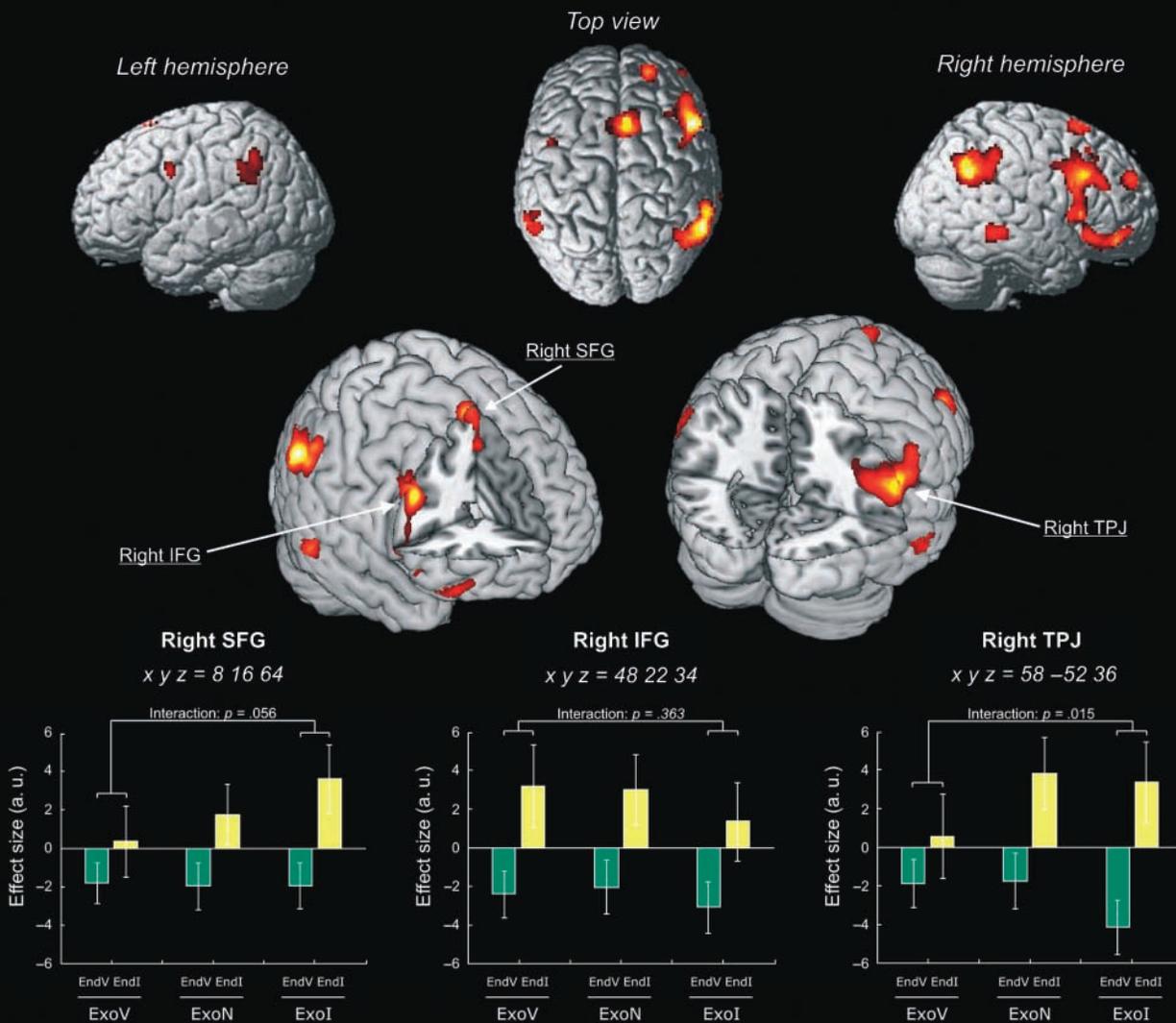
Statistical inference was based on a random effects approach (Penny & Holmes, 2004). This comprised two steps. First, for each participant, the data were best-fitted at every voxel using a combination of effects of interest. These were delta functions representing the onsets of the 18 conditions given by the crossing of our $3 \times 3 \times 2$ factorial design (endogenous validity [valid, neutral, invalid]; exogenous validity [valid, neutral, invalid]; target side [left, right]), convolved with the SPM5 hemodynamic response function. The onset of the hemodynamic response function was aligned with the onset of the target, with duration = 0. Onsets of trials in which an erroneous response or an eye movement occurred were included in the design matrix as covariates of no interest, but excluded from any further analysis. Linear contrasts were used to determine responses for the 18 conditions of interest, averaging across the four fMRI runs. This resulted in 18 contrast images per participant. The contrast images then underwent the second step, comprising a within-participant ANOVA that modeled the effect of the 18 conditions plus the main effect of participant. Finally, linear compounds were used to compare the condition effects, now using between-participants variance (rather than between scans). Correction for nonsphericity (Friston et al., 2002) was used to account for possible differences in error variance across conditions (given, for instance, by the different number of endogenous valid versus invalid trials) and any non-independent error terms for the repeated measures.

First, we seek to highlight the dorsal and the ventral attentional networks associated with the endogenous visuospatial cueing task. We tested for the main effect of endogenous valid versus endogenous neutral trails in order to identify the areas involved in processing of the predictive central cue and the associated voluntary orienting toward the expected target location. Next, we tested for the main effect of endogenous invalid versus valid trials, identifying areas involved in the reorienting of visuospatial attention toward the behaviorally relevant visual target (cf. Indovina & Macaluso, 2006; Macaluso et al., 2002; Arrington, Carr, Mayer, & Rao, 2000; Corbetta et al., 2000). For these comparisons, the SPM threshold was set to *p-corrected* = .05 at cluster level (cluster extent estimated a *p-uncorrected* = .001), considering the whole brain as the volume of interest (see Figure 2A).

A Main effect of Endogenous orienting: Valid versus Neutral trials

Top view

Right IPS

Right hemisphere

Right IPS
x y z = 40 −46 44

B Main effect of Endogenous reorienting: Invalid versus Valid trials

Left hemisphere

Top view

Right hemisphere

Right SFG

Right IFG

Right TPJ

Right SFG
x y z = 8 16 64
Interaction: p = .056

Right IFG
x y z = 48 22 34
Interaction: p = .363

Right TPJ
x y z = 58 −52 36
Interaction: p = .015

Next, we tested our main prediction by looking for any modulatory effect of the task-irrelevant auditory stimuli, within the reorienting network. For this, we created ROIs extracting average BOLD signals (MarsBar 0.41, ''MARSeille Boîte À Région d'Intérêt'' SPM toolbox) from the regions that showed a main effect of invalid versus valid endogenous trials (see Figure 2B). For each region, we tested for the interaction between the validity of the endogenous cue (valid/invalid) and the spatial correspondence between the auditory stimulus and the subsequent visual target (same/opposite side, resulting in valid/invalid exogenous trials). It should be noted that main effects and interactions are orthogonal and, therefore, our ROI selection procedure was unbiased. We tested whether endogenous invalidity (invalid minus valid target trials) was modulated by the validity of the exogenous cue (i.e., [EndI/ExoI − EndV/ExoI] > [EndI/ExoV − EndV/ExoV]). We expected that the cost of reorienting visual attention from the cued location to the uncued target location (and any associated brain activation for endogenous invalid trials) should decrease when the auditory stimulus anticipated the target side (e.g., stimulus sequence: *cue left–sound right–target right*, compared with: *cue left–sound left–target right*).

In addition to this critical prediction, we also tested for the main effect of the invalidity of the exogenous task-irrelevant auditory signals (whole-brain analyses, *p-corrected* = .05, at cluster level; cluster extent estimated a *p-uncorrected* = .001), and for any interaction between endogenous and exogenous spatial processing within areas showing such main effect (using ROIs analyses; see Figure 3A). Finally, we also assessed whether endogenous and exogenous signals jointly contributed to the processing of the lateralized visual targets. Accordingly, we directly compared trials with target stimuli in one or the other hemifield (i.e., main effect of target side, irrespective of endogenous and exogenous attention), expecting posterior activation in the hemisphere contralateral to the target side (whole-brain analyses, *p-corrected* = .05, at voxel level). Within these regions (ROIs analyses), we then tested whether there was any boosting of target-related activity[3] when both endogenous and exogenous cues signaled the same valid target location (e.g., *cue left–*

sound left–target left), compared with the two cues signaling opposite locations (e.g., *cue left–sound right–target left*). Formally, this was assessed as an interaction between endogenous and exogenous validity, using only trials with targets on one or the other side (e.g., for right-side targets: [endL/exoL − endR/exoL] > [endL/exoR − endR/exoR]; see Figure 3B).

RESULTS

Behavioral Data

Trials on which the participants responded in under 100 msec (anticipations) or failed to respond within 1200 msec of target onset (misses), and trials in which participants responded erroneously or made an eye movement were excluded from the analysis. Premature responses and misses occurred seldom (an average of 0.3% of trials). Eye movements and errors occurred on 5.4% and 6.4% of trials, respectively.

A three-way within-participants ANOVA with the factors of endogenous validity (valid, neutral, and invalid), exogenous validity (valid, neutral, and invalid), and side of target presentation (left or right) was performed on the RT data. This revealed significant main effects of both endogenous [$F(2, 32) = 14.3$, $p = .001$] and exogenous validity [$F(2, 32) = 46.0$, $p < .001$], indicating that participants responded more rapidly when the cue (endogenous or exogenous) was valid (459 and 462 msec, respectively) than when it was neutral (473 and 479 msec, respectively; $ps < .001$), which, in turn, resulted in faster responses than when the cue was invalid (506 and 496 msec, respectively; $ps < .005$). Importantly, this significant effect of validity for the exogenous cues implies that the participants successfully processed the position (left vs. right) of the auditory stimulus, despite the background noise produced by the MR scanner. There was neither a main effect of side of target [$F(4, 16) < 1$, ns] nor any interaction between the three factors [$F(4, 64) < 1$, ns], thus suggesting that although both modes of attention jointly affected target processing, they acted in an independent manner (see Figure 1C).

Figure 2. (A) Voluntary orienting of visuospatial attention following the centrally presented predictive cue (endogenous valid vs. endogenous neutral trials). Left: Surface-rendered projections of statistically significant activations, overlaid on the SPM5 template (threshold *p-corrected* = .05, at cluster level; images are displayed with a minimum cluster size of 50 voxels), showing a bilateral *dorsal* fronto-parietal network for the endogenous orienting of spatial attention. Right: Signal plot for the right IPS. The signal plot shows the estimated activity for endogenous valid and endogenous neutral trials, for each of the different levels of auditory stimuli (exogenous valid, neutral, invalid; in the figure: ExoV, ExoN, ExoI, respectively). (B) Reorienting of visuospatial attention associated with the main effect of endogenous invalid trials. The projections illustrate statistically significant activations for endogenous invalid target trials minus endogenous valid target trials (threshold *p-corrected* = .05, at cluster level; images are displayed with a minimum cluster size of 50 voxels), showing activation of a *ventral* fronto-parietal network. Top: Surface-rendered projections of the activations overlaid on the SPM5 template. Central and bottom: Coronal sections and signal plots for right anterior and posterior regions activated by the endogenous invalid trials. The signal plots show the estimated activity for endogenous invalid (yellow bars) and endogenous valid (green bars) target trials, across the different levels of exogenous validity (valid, neutral, or invalid). The plots demonstrate the involvement of these regions during the reorienting of visuospatial attention toward task-relevant visual targets. Critically, in the right TPJ (and right SFG), this reorienting effect was larger when the task-irrelevant auditory signal confirmed the endogenously cued side (Bar 6) compared to the condition when audition anticipated the new target location (Bar 2). In all signal plots, the level of activation is expressed in arbitrary units (a.u., ±90% confidence interval).
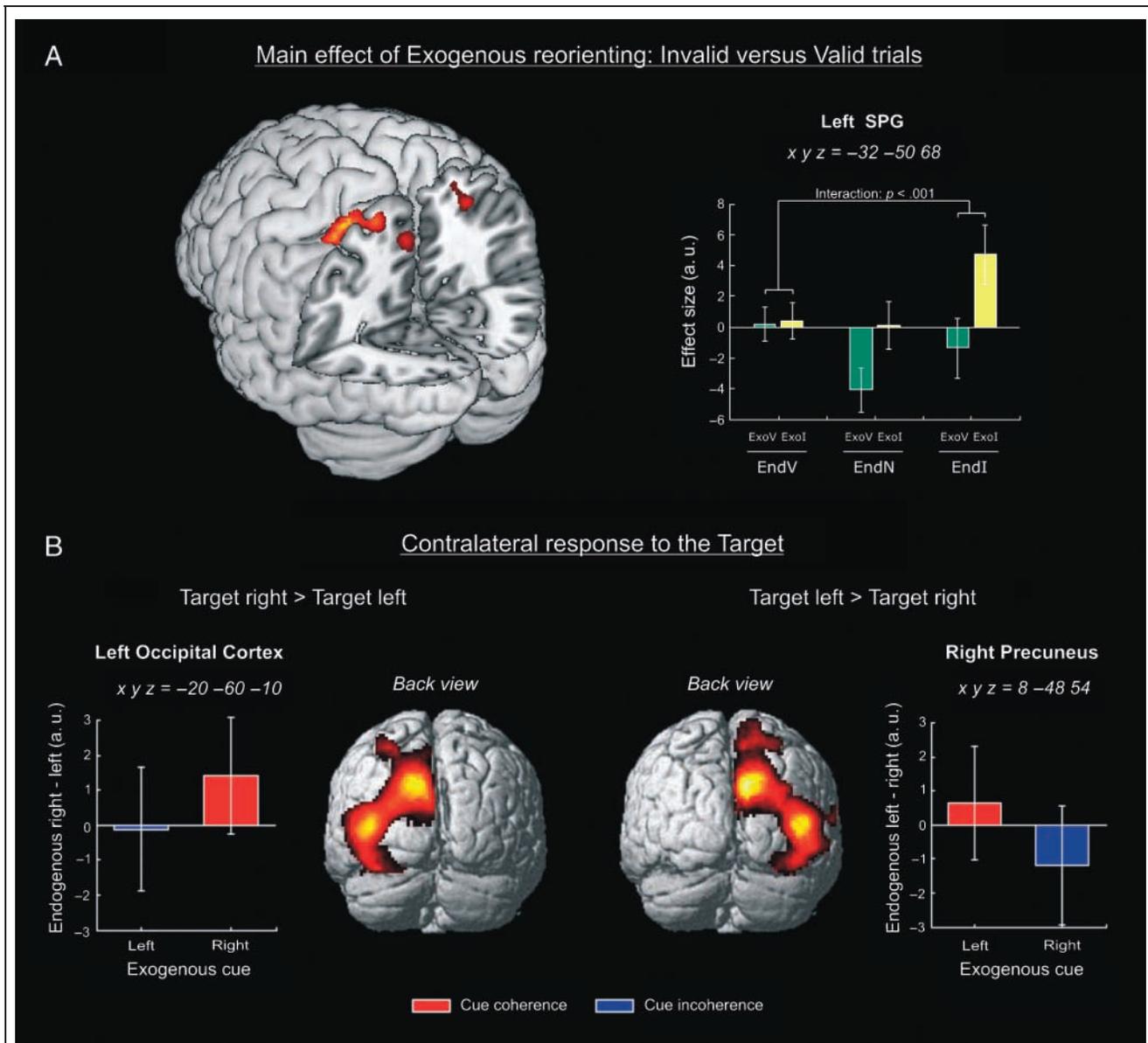
Figure 3. (A) Reorienting of visuospatial attention for exogenous invalid trials. Left: Coronal section showing statistically significant activations for exogenous invalid trials minus exogenous valid trials (threshold *p-corrected* = .05, at cluster level; images are displayed with a minimum cluster size of 50 voxels). Right: Signal plot for the left posterior region activated by the exogenous invalid trials. The plot shows the estimated activity for exogenous invalid (yellow bars) and exogenous valid (green bars) target trials in the different types of endogenous trial (valid, neutral, invalid; in the figure: EndV, EndN, EndI, respectively), demonstrating the involvement of this region in the reorienting of visuospatial attention toward the location of the forthcoming target following the presentation of an invalid auditory cue. In the left SPG endogenous and exogenous signals interacted just as found in the TPJ. Indeed, the reorienting effect was larger when the task-irrelevant auditory signal confirmed the endogenously cued side (Bar 6) compared to the condition when audition anticipated the new target location (Bar 2). (B) Main effect of target side. Surface-rendered projections of the activations associated with the presentation of trials containing right visual targets or left visual targets (left and right panels, respectively), overlaid on the SPM5 template. The signal plots show the estimated activity when the exogenous cue was coherent (same side) or incoherent (opposite side) with the endogenous cue. These results demonstrate that activity in occipito-parietal regions contralateral to the target location was greatest when both the endogenous cue and the task-irrelevant auditory cue signaled the same contralateral location (i.e., when they were both valid). In all signal plots, the level of activation is expressed in arbitrary units (a.u., ±90% confidence interval).

fMRI Data

Main Effect of Endogenous Orienting

To highlight the brain regions involved in the processing of the predictive central cues and the associated shifts of endogenous attention toward the expected target location, we compared endogenous valid minus endogenous neutral trials (irrespective of sound position). This comparison revealed the expected activation of the *dorsal* fronto-parietal network, including regions in and around the IPS, plus several clusters in the frontal lobe (see Figure 2A and Table 1). These anterior clusters

Table 1. Main Effect of Endogenous Orienting

	x	y	z	Cluster Size	p Corrected	Z score
L IPS	−42	−50	46	3923	<.001	6.18
L Precentral G	−30	0	62	7880	<.001	6.11
L IOG	−30	−88	−16	1387	<.001	5.93
R IPS	40	−46	44	1293	<.001	5.26
R Precuneus	12	−70	52	476	.002	5.03
R Insula	34	22	4	3201	<.001	6.14
R Precentral G	42	8	38	1159	<.001	4.49
R IOG	28	−96	0	2359	<.001	5.03

Anatomical locations, peak coordinates in MNI space (Montreal Neurological Institute), and statistical values for the direct comparison of endogenous valid versus endogenous neutral trials (irrespective of sound position/validity). p values are corrected for multiple comparisons at the cluster level, considering the whole brain as the volume of interest. L/R IPS = left/right intraparietal sulcus; L/R Precentral G = left/right precentral gyrus; L/R IOG = left/right inferior occipital gyrus; R Precuneus = right precuneus; R Insula = right insula.

included the superior frontal gyrus (SFG) extending to the precentral gyrus; and the middle and inferior frontal gyri (MFG and IFG), extending into the insula. In the occipital lobe, clusters of increased activity were found in the inferior occipital gyrus, the fusiform gyrus, and the cuneus. In addition, the caudate and the putamen also activated for valid versus neural trials. As illustrated in the signal plot reported in Figure 2A, greater activity was observed for endogenous valid than neutral trials (i.e., Bars 1 to 3 vs. 4 to 6), irrespective of the type of auditory exogenous cue (as would be expected for regions processing any predictive cue that occurred before any auditory signal). These findings are in line with previous studies showing an involvement of these regions in the voluntary shifting and holding of visuospatial attention on the location of the forthcoming target (e.g., Kelley, Serences, Giesbrecht, & Yantis, 2008; Molenberghs, Mesulam, Peeters, & Vandenberghe, 2007; Macaluso, Eimer, Frith, & Driver, 2003).

Main Effect of Endogenous Reorienting

Our critical comparisons concerned activity within the ventral fronto-parietal network, previously shown to activate selectively for behaviorally relevant stimuli (e.g., Indovina & Macaluso, 2006; Kincade et al., 2005). Here we tested for the first time whether multisensory interactions between endogenous visual attention and exogenous auditory attention may modulate the activity of this network. First, we used the main effect of endogenous invalidity (endogenous invalid minus valid trials, irrespective of sounds) to highlight regions involved in reorienting of attention toward behaviorally relevant tar-

gets presented at the unattended location. This revealed the expected activation of the *ventral* fronto-parietal network (see Figure 2B and Table 2) including the TPJ and the ventral part of the supramarginal and angular gyri. In the frontal lobe, activation was observed in the superior and inferior frontal gyri, extending ventrally into the central and subcentral gyri, and to the lateral fissure and the frontal operculum. This network was predominant in the right hemisphere, but was also present in the left hemisphere at a lower threshold. The signal plots show, on average, greater activity for endogenous invalid than valid trials (compare yellow vs. green bars in Figure 2B). Nonetheless, it is evident that the size of the reorienting effect in the TPJ and the SFG changed as a function of the type of task-irrelevant auditory stimulus that was delivered between the endogenous cue and the task-relevant visual target (i.e., Bar 2–1 [sound and target on the same side] vs. Bar 6–5 [sound and target on opposite sides]).

This modulation was formally assessed within the three regions that showed a significant main effect of endogenous invalidity (i.e., right SFG, right IFG, and right TPJ). These analyses revealed that reorienting from the endogenously cued location to the target location interacted with exogenous invalidity in the right TPJ ($t = 2.17$, $p = .015$). The same interaction was almost significant in the right SFG ($t = 1.59$, $p = .056$) but not significant in the right IFG ($t = 0.62$, $p = .363$). Thus, in the right TPJ (and to some extent in the right SFG), the endogenous invalidity effect (i.e., the yellow bar minus the green bar in the signal plot) was larger when the

Table 2. Main Effect of Endogenous and Exogenous Reorienting

	x	y	z	Cluster Size	p Corrected	Z score
Main Effect of Endogenous Reorienting: Invalid vs. Valid Trials						
R SFG	8	16	64	500	<.001	4.42
R IFG	48	22	34	1414	<.001	5.04
R TPJ[a]	58	−52	36	938	<.001	5.06
Main Effect of Exogenous Reorienting: Invalid vs. Valid Trials						
L SPG[a]	−32	−50	68	100	.035	4.18

Anatomical locations, peak coordinates in MNI space, and statistical values for the main effect of endogenous reorienting (invalid minus valid trials, irrespective of sound position/validity); and for the main effect of exogenous reorienting (invalid minus valid trials, irrespective of endogenous in-/validity). p values are corrected for multiple comparisons at the cluster level, considering the whole brain as the volume of interest. R SFG = right superior frontal gyrus; R IFG = right inferior frontal gyrus; R TPJ = right temporo-parietal junction; L SPG = left superior parietal gyrus.

[a]ROI analyses revealed in these regions significant interactions between endogenous and exogenous signals (see Results section for more details), indicating that multisensory signals can interact to jointly control the distribution of attention in space.

auditory exogenous cue was also invalid (i.e., congruent with the endogenous cue and confirming the cued side; e.g., *cue left–sound left–target right*) than when the auditory cue was valid (i.e., incongruent with the endogenous cues, but anticipating the correct location of the upcoming visual target: e.g., *cue left–sound right–target right*).

Main Effect of Exogenous Reorienting

Together with reorienting processes associated with the spatial relationship between the predictive central cue and the target, we also investigated the main effect of exogenous invalidity, comparing trials when the non-predictive sound was on the same side as the visual target (exogenous valid trials) versus trials with sound and target on opposite sides (exogenous invalid trials). This showed activation of the superior parietal gyrus (SPG) in posterior parietal cortex (see Figure 3A and Table 2). The SPG was more active in the left hemisphere, although at a lower threshold, a similar region activated in the right hemisphere. Just as for the TPJ, the SPG was not immune to the influence of the other cue (i.e., the endogenous cue, in this case). An ROI analysis of the left SPG showed that the exogenous reorienting (invalidity) effect interacted significantly with the endogenous invalidity ($t = 3.19$, $p < .001$). More specifically, the exogenous invalidity effect (i.e., yellow minus green bars in Figure 3A) was larger when the endogenous cue was also invalid (and therefore congruent with the exogenous cues) than when the endogenous cue was valid (i.e., incongruent with the exogenous cues).

Contralateral Response to the Lateralized Visual Targets

Finally, we investigated how the two cues (endogenous visual and exogenous auditory) influenced activity related to the lateralized visual targets. The direct comparison of right-target trials and left-target trials showed widespread activation of occipito-parietal regions in the left hemisphere, contralateral to the target side (see Figure 3B and Table 3). Activations included the lingual gyrus, the middle occipital gyri, plus medial regions extending from the cuneus (and the anterior portion of the calcarine sulcus) to the superior occipital gyrus and the precuneus. The reverse comparison (left-target minus right-target trials) revealed activation in symmetrical occipito-parietal regions of the right hemisphere (see Figure 3B and Table 3).

Within these areas (ROI analyses), we investigated whether the spatial coherence between the two cues (i.e., when both endogenous and exogenous cues pointed to the same side as the upcoming target) yielded an increased activation for the target, as compared to when the two cues indicated opposite locations. These analy-

Table 3. Main Effect of Target Side

	x	y	z	Cluster Size	p Corrected	Z score
Target Left Minus Target Right						
R Cuneus/AntCalS	16	−74	24	5898	<.001	>8
R middle Occ G	48	−74	8			
R Lingual G	22	−60	−10			
R Precuneus[a]	8	−48	54	137	<.001	6.24
Target Right Minus Target Left						
L Cuneus/AntCalS[a]	−8	−78	24	5885	<.001	>8
L middle Occ G[a]	−46	−82	4			
L Lingual G[a]	−20	−60	−10			
L IPL	−30	−50	56	35	.002	5.34

Anatomical locations, peak coordinates in MNI space, and statistical values for the main effects of the target side (left minus right, and right minus left; irrespective of the cueing condition), considering the whole brain as the volume of interest. *p* values are corrected for multiple comparisons at the voxel level, considering the whole brain as the volume of interest. L/R Cuneus = left/right cuneus; L/R AntCalS = left/right anterior calcarine sulcus; L/R middle Occ G = left/right middle occipital gyrus; L/R Lingual G = left/right lingual gyrus; R Precuneus = right precuneus; L IPL = left inferior parietal lobule.

[a]ROI analyses revealed interactions between endogenous and exogenous signals in these regions (see Results section for further details), suggesting that multisensory (audiovisual) attentional control operates (at least in part) by biasing processing in visual sensory cortex in favor of target stimuli at the expected location.

ses did not reveal any significant effect after correction for multiple comparisons, but did show the expected trends with greater activity for coherent than incoherent cueing conditions. In the left hemisphere, the modulatory effect of the endogenous cue (cue right > cue left) on right target was found only when the exogenous cue was also presented on the right side (see red bar in Figure 3B, left; $t = 1.54$, $p = .063$; stimulus sequence: *cue right–sound right–target right*). The right hemisphere was more active for endogenous valid than invalid left targets, but only when the sound burst was also on the left side (see red bar in Figure 3B, right; $t = 1.53$, $p = .063$; corresponding to *cue left–sound left–target left*).

DISCUSSION

Here we examined for the first time whether *task-irrelevant auditory* stimuli are filtered out just as has previously been shown for task-irrelevant visual stimuli (Shulman et al., 2007; Kincade et al., 2005; Indovina & Macaluso, 2006; see also Corbetta & Shulman, 2002), or whether instead they interact with the voluntary deployment of visuospatial attention. We therefore investigated the neural basis of voluntary and stimulus-driven

attentional shifts using a multisensory spatial double-cueing visuospatial paradigm, in which an auditory exogenous cue (i.e., nonpredictive and task-irrelevant) was presented in the time interval between a spatially predictive endogenous cue and the task-relevant visual target.

The behavioral data demonstrated that both the endogenous visual cue and the exogenous auditory cue affected target discrimination performance, with faster RTs when both cues indicated the correct target location. These two spatial cueing effects summed linearly, suggesting separate mechanisms of voluntary and stimulus-driven attentional control (e.g., Müller & Rabbitt, 1989). Consistent with this point of view, we observed some neuroanatomical dissociation between the two modes of spatial attentional reorienting. Comparing endogenous invalid versus valid trials, we found the expected activation of the ventral attentional system (including the TPJ and IFG) for reorienting of visual attention toward task-relevant invalidly cued targets. On the other hand, comparing exogenous invalid versus valid trials, we found activation of the SPG, relating to exogenous spatial reorienting following a task-irrelevant auditory stimulus. But critically, the imaging data also showed that within both the TPJ and the SPG, the two types of cues interacted, jointly affecting the activation of these areas. These findings indicate that, in the current multisensory context, entirely task-irrelevant auditory cues can interact with ongoing visuospatial endogenous processing.

The role of the ventral attentional system in attention control has been studied extensively for the visual modality (Arrington et al., 2000; Corbetta et al., 2000; see also Corbetta & Shulman, 2002). One key finding to emerge from this literature is that only task-relevant stimuli (i.e., visual targets or distracters that share some relevant features with the targets, e.g., the color) trigger visuospatial reorienting and engage the TPJ, whereas task-irrelevant stimuli appear to be filtered out and do not activate the TPJ (Shulman et al., 2007; Indovina & Macaluso, 2006; Kincade et al., 2005; see also Corbetta et al., 2008). However, the main finding of the present study is that the spatial location of an entirely task-irrelevant auditory stimulus can affect activity of this network. In particular, we observed greater activation in the TPJ when both the endogenous visual cue and the exogenous auditory cue required a shift of spatial attention (i.e., when the trial was invalid with respect of both the spatially predictive endogenous cue and the nonpredictive auditory cue) as compared to when only the endogenous cue was invalid (see Figure 2B). The interaction between cues presented in different sensory modalities is consistent with a supramodal role of the TPJ in attention control. The TPJ has been shown to respond to transient stimuli in different sensory modalities (i.e., visual, auditory, and tactile; see Downar et al., 2000, 2001) and to be active during spatial reorienting toward task-relevant tactile targets in a related spatial cue-

ing paradigm (Macaluso et al., 2002). Our current results with task-irrelevant auditory stimuli extend these findings and previous work involving unisensory visual attentional selection, demonstrating that auditory stimuli can engage attentional control processes mediated by the TPJ and are not filtered out as irrelevant visual distracters (see Shulman et al., 2007; Indovina & Macaluso, 2006; Corbetta & Shulman, 2002).

The exact neural mechanisms mediating the role of ''relevance'' in the ventral attentional system during visuospatial reorienting are still largely unspecified. Corbetta et al. (2008) recently suggested that task-related signals from the dorsal attentional network and/or prefrontal regions (possibly via subcortical loops) may mediate relevance effects in the ventral system. A key result of our study is that—unlike visual exogenous cues (see e.g., Natale, Marzi, & Macaluso, 2008)—auditory cues seem to bypass this ''filtering mechanism'' and to affect activity in the ventral attentional system, even when fully task-irrelevant. We suggest that a fundamental difference between unisensory and cross-sensory situations relates to how the brain registers the spatial alignment of the two stimuli (exogenous cue and target). In the unisensory (visual) case, this can occur within a single frame of reference (e.g., retinotopic maps of space), whereas registering the alignment of stimuli in different modalities requires a higher degree of spatial integration. We speculate that the latter involves more complex neural circuits (possibly including both cortical and subcortical structures, e.g., the superior colliculus) and that this may allow bypassing ''filtering mechanisms,'' as previously suggested for the within-modality situation.

The current findings are also consistent with the view that the more an invalid location is cued (both endogenously and exogenously in our case), the more activity will be seen in the TPJ as spatial attention is reoriented when the target is presented at the uncued location. In other words, both cues jointly contribute to the commitment of spatial attention at one location, requiring more reorienting resources when the target is presented on the opposite side. Albeit only borderline significant, the finding of maximal contralateral responses in occipito-parietal regions for visual targets that followed two coherent valid cues (see Figure 3B) is also consistent with this proposal. In left occipital cortex (including the lingual gyrus, the parieto-occipital fissure, and the cuneus) and right occipito-parietal cortex (i.e., right precuneus), greater activations were observed when both cues correctly indicated the side of occurrence of the target (i.e., when they were both valid). This result suggests that multisensory (audiovisual) attentional control operates (at least in part) by biasing the processing in visual sensory cortex in favor of target stimuli at the expected location (e.g., McDonald, Teder-Salejarvi, Di Russo, & Hillyard, 2003; Macaluso, Frith, & Driver, 2000; see Macaluso, 2006, for a review). There are several possible candidate mechanisms for mediating multisensory

effects in putatively unisensory areas. These include feedback signals from higher-order areas (e.g., McDonald et al., 2003; Calvert, 2001; Macaluso et al., 2000); direct influences via direct anatomical connections between unisensory areas (e.g., Foxe & Schroeder, 2005); or via subcortical routes, such as nonspecific thalamic inputs (see Schroeder et al., 2003; see also Schroeder, Molhom, Lakatos, Ritter, & Foxe, 2004). Although our data do not allow us to discriminate between these different proposals, the finding of concomitant spatial interactions in the TPJ and in occipito-parietal regions may support the hypothesis that high-order temporo-parietal multisensory regions mediate these cross-sensory influences in visual cortex (e.g., Teder-Salejarvi, Di Russo, McDonald, & Hillyard, 2005; McDonald et al., 2003; Macaluso et al., 2000; see Macaluso & Driver, 2006, for a review).

To some extent more surprising was the finding of stimulus-driven reorienting effects in superior parietal cortex (see Figure 3A). Superior parietal cortex has been typically associated with control of endogenous visual attention (e.g., Molenberghs et al., 2007; Yantis et al., 2002; Vandenberghe, Gitelman, Parrish, & Mesulam, 2001; see also Husain & Nachev, 2006; Corbetta & Shulman, 2002). Indeed, here also we found activation of the most posterior part of the IPS and the SPG in response to the predictive visual cues (see Figure 2A, comparing valid vs. neutral endogenous cues). However, anterior to this, we found a region that responded more on exogenous invalid than valid trials (see Figure 3A), with some further modulation by the endogenous cue. Some previous studies also reported effects of auditory and audiovisual attention in superior parietal cortex (see Avillac, Olivier, Denève, Ben Hamed, & Duhamel, 2004; Shomstein & Yantis, 2004). For example, Shomstein and Yantis (2004) found that voluntary shifts of attention between vision and audition produced an increment of activity in the posterior parietal cortex; and similar regions showed increased activation in intramodal auditory spatial attention tasks involving both the endogenous (e.g., Mayer, Harrington, Adair, & Lee, 2006; Shomstein & Yantis, 2006; Wu, Weissman, Roberts, & Woldorff, 2006) and exogenous deployment of attention (Mayer, Harrington, Stephen, Adair, & Lee, 2007). In addition, Foxe, Simpson, and Ahlfors (1998), using high-density EEG recordings, highlighted the involvement of anticipatory parietal suppression mechanisms when their participants were cued to selectively attend to an upcoming auditory stimulus and ignore a concurrent visual stimulus (see also Fu et al., 2001). Furthermore, intracranial recordings in humans have shown that superior parietal cortex constitutes an auditory–visual convergence area (Molholm et al., 2006). The present result appears to be consistent with this framework. Our results indicate that SPL not only receives convergent projections from vision and audition, but also that endogenous visual attention and exogenous auditory attention may interact within this region. We found a greater activation in the SPG when

both cues required a shift of attention (i.e., when they were both invalid) as compared to when only the exogenous cue was invalid. Thus, the pattern of activation in the SPG was similar to that reported in the TPJ, but with a greater overall impact of auditory exogenous attention.

Our current observations of significant interactions between voluntary visual orienting and stimulus-driven auditory spatial attention in the TPJ (and SPG) adds to the current debate over whether stimulus-driven effects in spatial attention are truly automatic (e.g., Santangelo & Spence, 2008, for a review). Some behavioral studies have suggested that the exogenous orienting effects elicited by irrelevant visual onsets dissipate when attention is focused elsewhere (Santangelo, Olivetti Belardinelli, & Spence, 2007; Theeuwes, 1991; Yantis & Jonides, 1990), whereas others have reported contradictory findings (Santangelo, Ho, et al., 2008; Mazza, Turatto, Rossi, & Umiltà, 2007; Santangelo & Spence, 2007; Berger et al., 2005; Van der Lubbe & Postma, 2005; Müller & Rabbitt, 1989). Researchers have now acknowledged that several factors can determine the impact of exogenous cues when endogenous attention is already focused elsewhere. For example, Berger et al. (2005) showed that exogenous visual cues could capture attention regardless of endogenous attention in a simple spatial discrimination task, but not when subjects were engaged in a difficult spatial discrimination task. In two recent behavioral studies using multisensory stimuli, Santangelo, Ho, et al. (2008) and Santangelo & Spence (2007) showed that under conditions of high perceptual load (i.e., when attentional resources were fully engaged in a primary visual task), multisensory but not unisensory cues interfered with the ongoing endogenous processing associated with the primary task. Here we confirmed the distinctive role of multisensory interactions in the control of spatial attention, demonstrating that fully task-irrelevant auditory stimuli can influence activity in the TPJ associated with the primary endogenous visuospatial cueing task. These results are consistent with some automaticity of the exogenous orienting of spatial attention, at least in the multisensory context studied here.

In summary, we examined for the first time the fMRI correlates of multisensory interactions between voluntary visual attention and stimulus-driven auditory attention, with the two modes of spatial orienting engaged in the same trial. We found that the ventral fronto-parietal attentional network activated in response to endogenous invalid versus valid trials, when participants' attention was reoriented toward task-relevant visual targets. Critically, the side of the auditory stimuli modulated these reorienting effects, reducing activity in the TPJ when the task-irrelevant auditory stimulus anticipated the location of the upcoming (invalid) visual target. These results demonstrate that endogenous and exogenous multisensory signals can interact to jointly control the distribution of attention in space.

Acknowledgments

Notes

1. It is worth noting here that most of the abovementioned studies have typically induced a highly focused attentional state in their participants by means of the presentation of a spatially informative central arrow cue. However, a growing body of evidence now suggests that noninformative central arrow cues (Ristic & Kingstone, 2006; Tipples, 2002; Hommel, Pratt, Colzato, & Godijn, 2001; see also Spence & Driver, 1996), as well as a wide variety of other symbolic cues (see Gibson & Kingstone, 2006), may also trigger exogenous orienting, likely due to the overlearning of their meaning. Given that arrow cues may induce exogenous as well as endogenous shifts of spatial attention, their use may therefore not provide a particularly appropriate means of studying performance in the focused attentional state. For this reason, we used in the present study pure symbolic endogenous cues (i.e., a color associated with a spatial location; see Figure 1).

2. This sound level was implemented in order to guarantee sound discriminability regardless of the background noise produced by fMRI scans (approximately 103.7 dB SPL, A weighted measurement inside the head coil; Siemens Magnetom Allegra 3-T MR Imaging System: Evaluation Report No. MHRA 03026, Tab. 49, p. 30). The participants wore earplugs throughout the runs.

3. Note that although target-related responses were computed using trials that included both types of cues, all cue-related effects (i.e., endogenous/exogenous and valid/neutral/invalid) were fully matched in these comparisons.

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