Dissociation of Stimulus Relevance and Saliency Factors during Shifts of Visuospatial Attention

The control of visuospatial attention entails multiple processes, including both voluntary (endogenous) factors and stimulus-driven (exogenous) factors. Exogenous processes can be triggered by visual targets presented at a previously unattended location, thus capturing attention in a stimulus-driven manner. However, little is known about the relative role of stimulus salience and behavioral relevance for this type of spatial reorienting. Here, we directly assessed how salience and relevance affect activation of the frontoparietal attentional system, using either low-salience but task-relevant target stimuli or salient but task-irrelevant flickering checkerboards. We compared event-related functional magnetic resonance imaging responses for stimuli presented at the unattended versus attended side (invalid minus valid trials), separately for the 2 categories of visual stimuli.

We found that task-relevant invalid targets activated the frontoparietal attentional network, demonstrating that this system engages when target stimuli are presented at an unattended location, even when these have a low perceptual salience. Conversely, the presentation of high-salience checkerboards in one hemifield while endogenous attention was engaged elsewhere did not activate the attentional network. These findings indicate that task relevance is critical for stimulus-driven engagement of the attentional network when attentional resources are endogenously allocated somewhere else.

Keywords: attention, fMRI, relevance, salience, space, vision

Introduction

Traditional accounts of spatial covert orienting to a visual location consider 2 main aspects: the allocation of attention associated with expectation and voluntary behavior (endogenous attention) and stimulus-driven shifts of attention that are guided by the sudden and unexpected appearance of salient stimuli at an unattended location (exogenous attention). These 2 mechanisms are typically studied using the behavioral cueing paradigm first introduced by Posner (Posner 1980). In the endogenous version of this paradigm, a symbolic cue indicates the likely side for an upcoming peripheral visual target, thus prompting the subject to voluntarily direct covert attention to one side. A subsequent target appears on the cued side (e.g., 80% valid trials) or on the uncued side (20% invalid trials). Comparing reaction times (RTs) to targets on the cued versus uncued side reveals faster responses for targets on the cued side. This indicates that endogenous attention can facilitate processing of targets at the attended side and that it yields to some costs for targets presented at the unattended side. In the exogenous versions of this spatial cueing paradigm, salient but noninformative cues are presented at peripheral locations, either at the same position as the upcoming visual target (valid trials) or at a different location (invalid trials). Critically, in the exogenous protocol, the cued position is task irrelevant, and it does not predict the position of the upcoming target (i.e., valid and invalid trials are equally probable). This abolishes any strategic reason for the subject to voluntarily pay attention to the cues, instead emphasizing stimulus-driven, automatic mechanisms of spatial covert orienting. Exogenous studies also show that nonpredictive, task-irrelevant cues presented at the same location as the target can have a facilitating effect when the cue and the target are presented within a short time window (less than 300 ms, see Klein 2000). It should be noted that the main difference between endogenous and exogenous paradigms relates to the type of attentional allocation associated with the cue: task relevant and predictive for the endogenous versions versus task irrelevant, nonpredictive for the exogenous versions. On the other hand, spatial reorienting associated with invalid targets will always entail both stimulus-driven “saliency factors” (i.e., the sudden appearance of the target at the unattended location) and also task-related “relevance factors” (i.e., the subject has to respond to the target even if this is presented at the unattended location). Neuroimaging can help us to segregate these 2 factors because it allows us to measure stimulus-related processing even in the absence of any behavioral response. In particular, it is possible to study how the direction of spatial attention affects processing of visual stimuli that are task irrelevant, never requiring any judgment or overt response.

Early functional imaging studies on visuospatial attention indicated that endogenous and exogenous attention may rely on largely overlapping neural substrates, centered in and around the intraparietal sulcus (IPS) (Corbetta et al. 1993; Nobre et al. 1997; Gitelman et al. 1999; Kim et al. 1999). However, these studies employed blocked designs and were unable to dissociate cue-related versus target-related activity, therefore measuring brain activity likely to include combinations of endogenous and exogenous attentional processes. The introduction of event-related functional magnetic resonance imaging (fMRI) allowed for the separation of cue-related and target-related activities demonstrating that dorsal frontoparietal regions regulate endogenous spatial attention. These regions include the frontal eye fields (FEFs), IPS, plus visual areas (Corbetta et al. 1998; Kastner et al. 1999; Martinez et al. 1999; Kanwisher and Wojciulik 2000; Yantis et al. 2002). On the other hand, stimulus-driven reorienting for targets presented at the unattended side (invalid trials) has been mainly associated with the activation of ventral frontoparietal areas, constituted by the temporoparietal junction (TPJ) and the inferior frontal gyrus (IFG), and mostly lateralized to the right hemisphere (Arrington et al. 2000; Corbetta and Shulman 2002).

Initially it was put forward that the activation of TPJ and IFG related selectively to the exogenous shift of attention from the...
cued location to the previously unattended target location (e.g., see Arrington et al. 2000; Macaluso et al. 2002a). However, some evidence indicates that these ventral regions can activate also when such shifts do not take place (Corbetta et al. 2000). Corbetta and Shulman (2002) reported activation of TPJ and IFG during target detection both at the attended and unattended side (but still showing further enhancement when target detection occurred at the unattended side, i.e., invalid trials). The finding of activation of ventral regions for attended targets suggests a possible role of endogenous factors also within this part of the frontoparietal attentional system (see also Shulman et al. 2005). Thus, an absolute anatomical segregation of dorsal/endogenous versus ventral/exogenous attentional functions might be an oversimplification. Indeed, more recent work has focused on the dynamic interplay between dorsal and ventral parietal regions (Corbetta et al. 2005), suggesting that mechanisms of attention control are likely to require both parts of the attentional network.

Interactions between endogenous and exogenous factors have been observed also in nonspatial contexts. For example, Downar and colleagues reported increased activity in TPJ (and IFG) when infrequent stimuli were attended and detected in one modality, compared with conditions when attention was focused to another modality and the same infrequent stimuli were ignored (Downar et al. 2001). Furthermore, activation of TPJ has also been found in a series of studies on attention to temporal intervals (Coull and Nobre 1998; Coull et al. 2000; Coull 2004). These studies did not require any shift of exogenous spatial attention, thus suggesting a more general function of TPJ associated with the resetting of expectations built during the cueing phase (e.g., Coull and Nobre 1998).

However, mere sensitivity to task relevance does not appear to fully explain activation of ventral frontoparietal regions. Salient stimuli (novel or infrequent events) presented in a behaviorally neutral context were also found to activate TPJ, even when the stimuli where presented passively and did not require any overt motor response (Downar et al. 2000, 2002). However, it should be noted that in these 2 experiments, the absence of a behavioral task may cause participants to treat the stimuli as “targets,” even if there was no explicit instruction to judge the task-irrelevant events. On the other hand, in the first study (Downar et al. 2000), subjects received trimodal stimulation simultaneously, thus the high sensory load should have discouraged subjects to treat salient events as targets. Also, the second study (Downar et al. 2002) found TPJ activation for passive viewing of equiprobable novel minus familiar events. As novel stimuli were presented as frequently as familiar events, there would be no specific reason to treat novel rather than familiar stimuli as targets. In any case, it appears difficult to draw any firm conclusion on the relative role of relevance and saliency in these studies because these 2 factors were not manipulated systematically by experimental design. One previous study (Downar et al. 2001) investigated explicitly the modulatory effect of stimulus relevance (i.e., detect vs. ignore) on brain activity associated with transient visual or auditory stimulus changes. This study found modulatory effects of stimulus relevance on TPJ activation, but it also showed relevance-independent effects within a subregion of TPJ. More importantly, all these previous studies did not address the topic of relevance versus saliency in the context of spatial reorienting.

As noted above, stimulus-driven attentional shifts associated with unpredictable peripheral cues are spatially specific, speeding up responses to targets presented at the same location, compared with targets on the opposite side. This spatial specificity is critical and specific to mechanisms of spatial selection. For instance, unspecific arousal effects could in principle be associated with oddball paradigms and stimulus-change paradigms (e.g., Downar et al. 2000). On the contrary, stimulus-driven effects in spatial attention can occur for unpredictable cues, that is, when valid and invalid trials are equally probable. In these situations, arousal or stimulus probability cannot explain the attentional effects that instead selectively relate to the position of the stimuli.

Only a few previous fMRI studies considered relevance/saliency effects in the context of spatial orienting. Serences and colleagues (Serences et al. 2005; Serences and Yantis 2006) investigated spatial reorienting of attention by salient stimuli while voluntary attention was focused to one or the other hemifield, but using salient stimuli that share properties with the target (contingent attentional capture). Serences’ work elegantly showed that task-irrelevant stimuli that share features with task-relevant targets compete for attention and modulate TPJ and IFG. However, it does not address the question of whether also salient, task-irrelevant stimuli that do not share any properties with the target would nonetheless capture attention automatically, as in the classical behavioral spatial cueing paradigms. Finally, Peelen et al. (2004) found coactivation of dorsal and ventral frontoparietal regions, irrespective of endogenous or exogenous spatial cueing. These results highlight again some overlap between ventral and dorsal attentional functions, and they suggest that salient onsets at peripheral locations may engage the frontoparietal attentional network, even when the stimuli are nonpredictive and task irrelevant.

Here we used fMRI to further investigate these issues. Within the same protocol, we aimed to dissociate the specific role of task relevance and stimulus salience during exogenous shifts of spatial attention. Although spatial attention was oriented endogenously toward one or the other hemifield, we presented either task-relevant but low-salience target stimuli (target “T,” requiring orientation discrimination and overt response) or salient, but now task-irrelevant visual stimuli (unilateral checkerboard). As in the classical behavioral paradigm, stimuli were presented either at the attended side (valid trials) or at the unattended side (invalid trials). To highlight stimulus-driven exogenous processes, we compared unattended minus attended trials, expecting activation of the frontoparietal attentional network (e.g., see Arrington et al. 2000; Corbetta et al. 2000; Macaluso et al. 2002a). Critically, here we could perform this comparison for 2 distinct categories of visual stimuli: low-salience, task-relevant target T or high-salience, but task-irrelevant checkerboards. If stimulus relevance is the critical factor for activation of the frontoparietal network, we should expect activation for the first comparison when attentional shifts occur toward a task-relevant stimulus (invalid minus valid target stimuli). Alternatively, if stimulus salience determines the engagement of this network (i.e., pure exogenous effect), the activation should be observed for the second comparison (unattended minus attended salient checkerboards).

Materials and Methods

Participants

Twelve right-handed healthy volunteers (9 males) participated in the study. After receiving an explanation of the procedures, all subjects gave
written informed consent. The study was approved by the independent Ethics Committee of the Fondazione Santa Lucia (Scientific Institute for Research Hospitalisation and Health Care).

**Paradigm**

We used a variation of the classical spatial cueing task introduced by Posner (Posner 1980) to dissociate relevance-related and salience-related aspects of visuospatial covert orienting. With this aim, we added to the classical $2 \times 2$ design ("validity" [valid/invalid] x "side" [left/right]) the additional factor of "stimulus type" (task-relevant target vs. salient, but irrelevant checkerboards; see Fig. 1A). A symbolic central visual cue instructed the subjects to pay attention either to the left or to the right visual hemifield. Unpredictably, either visual targets for discrimination or task-irrelevant checkerboards were presented at peripheral locations. On target trials, 2 visual stimuli of different color were presented simultaneously in the 2 hemifields (bilateral presentation to minimize saliency effects). The color of the stimuli determined on what side subject had to perform the discrimination, thus determining the validity of the trial (80% valid, 20% invalid). On the remaining trials, a single high-contrast checkerboard was presented either on the attended side (50% attended checkerboard) or on the contralateral hemifield (50% unattended checkerboard). Direct comparison of invalid versus valid trials (separately for the 2 stimulus conditions) was used to study reorienting of visuospatial attention and any effect of stimulus relevance and/or stimulus salience on this. As the aim of the study was to investigate the differential activation for valid/invalid (attended/unattended) trials, we used a relatively fast event-related fMRI protocol (intertrial interval = 3-5 s). This optimized the detection sensitivity for the critical differential effects, but it did not allowed us to estimate brain activity in the absence of task-relevant target and task-irrelevant checkerboard. This would be required, for example, to assess common activation for all trial types or to study attentional modulation of baseline activity (e.g., Kastner et al. 1999).

**Stimuli and Task**

Subjects lay in the scanner and viewed the visual stimuli through a mirror system. Symbolic visual cues were presented centrally instructing subjects to attend left (leftward pointing arrows) or to attend right (rightward pointing arrows). Attention was blocked to one or the other side for 68 s. The central cues were displayed throughout the block, and participants were required to maintain central fixation. On 62.5% of trials, subjects were presented with visual stimuli for discrimination (target trials). On the remaining 37.5% of the trials, the visual stimuli were high-salience checkerboards that did not require any response. Target trials and checkerboard trials were intermixed in a random and unpredictable order (see Fig. 1B).

On target trials, 2 different color "Ts" (red and blue) were presented simultaneously at 8 degrees eccentricity left and right from central fixation for 100 ms. The orientation of the Ts could be either canonical or upside down, and this was independent in the 2 hemifields. One of the 2 Ts served as target for orientation discrimination. The relevant target T was defined according to color. For half of the subjects, blue Ts were relevant, and for the other half of the subjects, red Ts were relevant. For each subject, the relevant color remained the same throughout the scanning session, and the Ts in the other (irrelevant) color never required any discrimination or response. Subjects reported the orientation of the target T by pressing one of 2 buttons with the index or middle finger of the right hand (2 alternative forced choice). As for the classical endogenous version of the Posner paradigm, 80% of the target Ts were presented in the attended hemifield (valid trials) and 20% in the opposite hemifield (invalid trials). All Ts of the target color required a response, irrespective of whether they appeared at the attended side (valid target) or the unattended side (invalid target).

Randomly intermixed with the target trials (requiring discrimination and motor response), there were presentations of task-irrelevant high-salience checkerboards. Black and white checkerboard briefly flickered (200 ms) at 8 degrees visual angle (subtending 4.3 total degrees) in one hemifield only. Half of the checkerboards were presented in the attended hemifield (attended checkerboards) and half in the unattended hemifield (unattended checkerboards). The subject was instructed to ignore the checkerboards that never required any response.

Eleven subjects underwent 4 fMRI runs, and one subject underwent 3 runs only (for technical reasons). Each run lasted for approximately 7 min, during which 48 visual stimuli were presented in the left hemifield (24 valid target Ts, 6 invalid target Ts, 9 attended checkerboards, and 9 unattended checkerboards) and 48 visual stimuli in the right hemifield (with the same proportion as left-field stimuli). Irrespective of stimulus type, the intertrial interval was 4 s (range 3-5 s). Prior to the fMRI session, all subjects received a practice run of approximately 2 min training.

**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 blood oxygenation level-dependent imaging (3 x 3 mm, 2.5 mm thick, 50% distance factor, repetition time = 2.08 s, time echo = 30 ms), covering the entirety of the cortex.

**Data Analysis**

We used SPM2 (Wellcome Department of Cognitive Neurology) implemented in MATLAB 6.5 (The MathWorks Inc., Natick, MA) for...
data preprocessing and statistical analyses. For 11 participants, we acquired 816 fMRI volumes (612 for one participant, who underwent only 3 fMRI runs). After discarding the first 4 volumes of each run, all images were corrected for head movement. Slice-acquisition delays were corrected using the middle slice as reference. All images were normalized to the standard SPM2 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 subject were high-pass filtered at 220 s and prewhitened by means of autoregressive model AR(1).

Statistical inference was based on a random effects approach (Penny and Holmes 2003). This comprised 2 steps. First, for each subject, the data were best fitted at every voxel using a combination of effects of interest. These were delta functions representing the onsets of the 8 conditions given by the crossing of our $2 \times 2 \times 2$ factorial design (validity $\times$ side $\times$ stimulus type; see Fig. 1), convolved with the SPM2 hemodynamic response function. Parameters of motion were also included in the design matrix as covariates of no interest. Linear contrasts were used to determine responses for the 8 conditions, averaging across fMRI runs. This resulted in 8 contrast images per subject. The contrast images then underwent the second step, comprising a within-subject analysis of variance (ANOVA) that modeled the effect of the 8 conditions plus the main effect of subject. Finally, linear compounds were used to compare the condition effects, now using between-subjects variance (rather than between scans). Correction for nonspHERicity (Friston et al. 2002) was used to account for possible differences in error variance across conditions and any nonindependent error terms for the repeated measures.

The central aim of the experiment was to test for the effect of shifting visuospatial attention associated with invalid trials and to assess whether any such effect was due to stimulus relevance (target trials) or stimulus salience (checkerboard trials) or any combination thereof. Thus, we directly compared invalid (unattended) minus valid (attended) trials (see Arrington et al. 2000; Corbetta et al. 2000; Macaluso et al. 2002a) for the 2 stimulus types (target trials and checkerboard trials), and we then statistically assessed any difference between these 2 patterns of activation using interactions between validity and stimulus type. For these comparisons, the SPM threshold was set to $P$ corrected $= 0.05$ (minimum cluster size $= 10$ voxels) considering the whole brain as volume of interest. In addition, we tested for attentional effects associated with validly cued stimuli to reveal any boosting of visual responses for attended versus unattended visual stimulations (e.g., see Heinze et al. 1994; Martinez et al. 1999). We assessed this for target trials comparing left- versus right-valid targets (and vice versa). Note that because during target trials the stimulation was always bilateral, this is not confounded with stimulus position, and instead it corresponds to the direct comparison of leftward versus rightward attention that is commonly used to reveal modulatory effects of spatial attention (e.g., Heinze et al. 1994; Hopfinger et al. 2000; Macaluso et al. 2002b). For checkerboard trials, we compared responses to attended-left minus unattended-left checkerboards (and the same for right checkerboards). These trial types consist of equivalent unilateral stimulations but with spatial covert attention allocated to different positions. For these modulatory effects of spatial attention on visual processing, the SPM thresholds were set to $P$ corrected $= 0.05$; considering as volume of interest, all voxels responding to contralateral visual stimulation (Worsley et al. 1996), where such effects would be expected (Heinze et al. 1994; Martinez et al. 1999). Areas responding to contralateral visual stimulation were identified comparing left minus right checkerboard and vice versa (see Fig. 3A and Table 2).

Results

Behavioral Data

Comparison of RTs for valid and invalid target trials demonstrated faster responses for target Ts presented at the cued location, indicating that participants complied with the instructions and directed attention to the cued hemifield. Mean RTs (in millisecond, $\pm$standard error of mean $[SEM]$) for target stimuli in the left hemifield were $772 (\pm26)$ for invalid targets versus $629 (\pm15)$ for valid targets; and in the right hemifield, RTs were $803 (\pm30)$ for invalid targets versus $643 (\pm11)$ for valid targets. A within-subject ANOVA revealed only the expected main effect of validity ($F_{1,11} = 78.8; \ P < 0.001$). Mean group percentage of correct response ($\pmSEM$) was $97.3\% ( \pm0.9\%$) for valid trials and $94.9\% ( \pm1.3\%$) for invalid trials, demonstrating that there was no speed/accuracy trade-off.
is, the same control condition used to reveal the attention network for invalid target trials. This additional analysis did not show any significant effect, even when the volume of interest was restricted to the areas activated for invalid versus valid targets trials (Fig. 2, yellow and white checkerboard-related bars). These results indicate that the activation of the fronto-parietal network for visual stimuli presented at the unattended location relates to the behavioral relevance of the stimulus (here low-salience target Ts, requiring orientation discrimination and manual response), rather than the pure stimulus-driven saliency effect typically associated with exogenous orienting.

The second question that we asked was whether there was some processing advantage for attended versus unattended stimuli (e.g., see Heinze et al. 1994; Martinez et al. 1999) and critically whether any such modulatory effect would apply to both target stimuli and task-irrelevant checkerboards or whether this would be selective for the task-relevant targets instead (as found for the invalid minus valid comparison, see Figure 2).
Table 1

Target trials: main effect of invalidity and invalidity by stimulus-type interaction

<table>
<thead>
<tr>
<th>x</th>
<th>y</th>
<th>z</th>
<th>P corrected</th>
<th>Z-score</th>
</tr>
</thead>
<tbody>
<tr>
<td>L angular gyrus/IPS</td>
<td>−30</td>
<td>−58</td>
<td>44</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>R angular gyrus/IPS</td>
<td>34</td>
<td>−68</td>
<td>38</td>
<td>&lt;0.001</td>
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<tr>
<td>L IFG</td>
<td>−42</td>
<td>6</td>
<td>32</td>
<td>&lt;0.001</td>
</tr>
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<td>R IFG</td>
<td>48</td>
<td>14</td>
<td>26</td>
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<tr>
<td>L precuneus</td>
<td>−8</td>
<td>−74</td>
<td>42</td>
<td>0.013</td>
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<tr>
<td>R precuneus</td>
<td>8</td>
<td>−60</td>
<td>52</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>L Insula</td>
<td>−32</td>
<td>24</td>
<td>−8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>R Insula</td>
<td>34</td>
<td>26</td>
<td>−4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>L pre-SMA</td>
<td>8</td>
<td>20</td>
<td>40</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>R pre-SMA</td>
<td>−6</td>
<td>18</td>
<td>46</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>L FEF</td>
<td>−30</td>
<td>4</td>
<td>54</td>
<td>0.007</td>
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<tr>
<td>R FEF</td>
<td>26</td>
<td>4</td>
<td>46</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 2

Checkerboard trials: main effect of stimulus side

<table>
<thead>
<tr>
<th>x</th>
<th>y</th>
<th>z</th>
<th>P corrected</th>
<th>Z-score</th>
</tr>
</thead>
<tbody>
<tr>
<td>L medio/ventral occ.</td>
<td>−8</td>
<td>−88</td>
<td>−4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>L lateral occ.</td>
<td>−44</td>
<td>−72</td>
<td>2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>L dorsal occ.</td>
<td>−20</td>
<td>−98</td>
<td>16</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>x</th>
<th>y</th>
<th>z</th>
<th>P corrected</th>
<th>Z-score</th>
</tr>
</thead>
<tbody>
<tr>
<td>R medio/ventral occ.</td>
<td>12</td>
<td>−84</td>
<td>−4</td>
<td>&lt;0.001</td>
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<tr>
<td>R lateral occ.</td>
<td>50</td>
<td>−66</td>
<td>0</td>
<td>&lt;0.001</td>
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<tr>
<td>R dorsal occ.</td>
<td>30</td>
<td>−86</td>
<td>22</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Note: Group effect | P ≤ 0.05 voxel level corrected, considering the whole brain as the volume of interest. MNI coordinates in millimeters. AngG/IPS: angular gyrus / intraparietal sulcus; IFG: inferior frontal gyrus; SMA: supplementary motor area; FEF: frontal eye fields. L/R: left/right hemisphere.

Table 3

Target (invalid > valid) minus checkerboard (invalid > valid)

<table>
<thead>
<tr>
<th>x</th>
<th>y</th>
<th>z</th>
<th>P corrected</th>
<th>Z-score</th>
</tr>
</thead>
<tbody>
<tr>
<td>L angular gyrus/IPS</td>
<td>−32</td>
<td>−56</td>
<td>40</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>R angular gyrus/IPS</td>
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<td>−64</td>
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</tr>
<tr>
<td>L IFG</td>
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<td>6</td>
<td>34</td>
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</tr>
<tr>
<td>R IFG</td>
<td>52</td>
<td>18</td>
<td>12</td>
<td>0.038</td>
</tr>
<tr>
<td>L precuneus</td>
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<td>−64</td>
<td>50</td>
<td>0.016</td>
</tr>
<tr>
<td>R precuneus</td>
<td>8</td>
<td>−58</td>
<td>52</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>L Insula</td>
<td>−32</td>
<td>26</td>
<td>−8</td>
<td>0.226</td>
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<tr>
<td>R Insula</td>
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<td>26</td>
<td>−4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>L pre-SMA</td>
<td>8</td>
<td>16</td>
<td>44</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>R pre-SMA</td>
<td>−6</td>
<td>18</td>
<td>48</td>
<td>0.006</td>
</tr>
<tr>
<td>L FEF</td>
<td>0.015</td>
<td>5.60</td>
<td></td>
<td></td>
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<tr>
<td>R FEF</td>
<td>24</td>
<td>6</td>
<td>48</td>
<td>0.006</td>
</tr>
</tbody>
</table>

Note: Group effect | P ≤ 0.05 voxel level corrected, considering the whole brain as the volume of interest. Montreal Neurological Institute coordinates in millimeters. L/R, left/right hemisphere; occ., occipital cortex.

above). Because of prior hypothesis concerning the modulatory effects of visuospatial attention on visual processing (e.g., Heineze et al. 1994; Martinez et al. 1999; Hopfinger et al. 2000, 2001), we selectively tested for any such effect in visual areas contralateral to the attended side. Visual areas responding to contralateral stimulation were first highlighted by directly comparing checkerboard stimulation in one versus the other hemifield. As expected, this revealed activation of ventral, lateral, and dorsal occipital cortices, plus the calcarine fissure; with all activations contralateral to the stimulated hemifield (see Fig. 3A).

Within these areas we tested for any modulation of stimulus-related activity by spatial attention. For the target trials, we compared valid-left versus valid-right target trials (and vice versa), using a procedure commonly applied to reveal spatial attentional modulation during bilateral stimulation (e.g., Heineze et al. 1994; Hopfinger et al. 2000; Macaluso et al. 2002b). This showed that activity in ventral occipital cortex was higher for attention to the contralateral versus the ipsilateral hemifield (see Fig. 3B and Table 3). Figure 3B depicts the anatomical location of the regions showing this attentional modulation and the level of activity in these areas for the 4 conditions involving target trials. Note that during target trials, the visual stimulation was always bilateral and thus the physical stimulation was equivalent in all 4 conditions. Nonetheless greater activity was observed for attended stimuli presented in the contralateral hemifield (red bars in Fig. 3B).

Our data regarding target trials (see Fig. 3B) replicate previous findings showing attentional modulation in visual cortex contralateral to the attended visual stimulus (e.g., for a review, see Hopfinger et al. 2001). More interesting in the context of the present study was to investigate whether the direction of endogenous attention had any effect on the processing of the task-irrelevant checkerboards. Note that unlike target-stimuli, checkerboards were presented unilaterally, and therefore, we could not directly compare attended-left checkerboards versus attended-right checkerboards because this would compare physically different visual stimuli. Instead, we compared brain activity for checkerboards on one side (e.g., left checkerboard) during blocks of leftward versus rightward attention. This demonstrated that the direction of endogenous attention also affected processing of the task-irrelevant checkerboards, with higher activity in contralateral occipital cortex for attended versus unattended checkerboards (see Fig. 3C and Table 4). Figure 3C shows the anatomical location and the level of activity for the regions where attention had a modulatory influence on checkerboard processing. Maximal activity was observed for attended checkerboards presented in the contralateral hemifield (see red bars in Fig. 3C). In addition, we also tested for any nonspatial effect for attended checkerboards (main effect of attended minus unattended checkerboards, irrespective of left/right hemifield). This comparison showed increased activity in the right putamen, but the effect did not fully meet our criteria for statistical significance (cluster size smaller than 10 voxels). Thus, although checkerboards flashed at the unattended position were ineffective in engaging the frontoparietal attentional network, they were processed differentially in the visual cortex depending on the current direction of attention. We found greater activity in contralateral occipital cortex for checkerboards at the attended minus unattended side. Therefore, spatial attention that was voluntarily lateralized to one side to discriminate target Ts was effective in selecting not just task-relevant target stimuli, but it also affected processing of the task-irrelevant checkerboards.
Discussion

Visual targets can attract spatial attention both because of their relevance for a behavioral task and because of their emergence from the environment, a property that is referred to as "stimulus salience" (Yantis and Jonides 1990; Corbetta and Shulman 2002; Peelen et al. 2004; Kincade et al. 2005; Serences et al. 2005). The purpose of this study was to directly assess how relevance and salience affect activity within neural networks associated with stimulus-driven control of spatial attention. To separate relevance and salience effects, we presented 2 types of visual stimuli during a classical spatial cueing paradigm. These were either low-salience targets that required discrimination and overt response or salient but task-irrelevant checkerboards. We found that task-relevant targets presented at the unattended side activated a frontoparietal network, even when we employed low-salience stimuli (bilateral stimulation, with target defined only according to color). On the contrary, high-salience checkerboards not requiring any overt response did not activate this network. Nonetheless, the direction of endogenous spatial attention affected processing of both task-relevant targets and task-irrelevant checkerboards, boosting activity in contralateral occipital cortex for all stimuli presented on the attended side. We conclude that task relevance rather than stimulus salience determines the activation of the frontoparietal attentional system, that is, only for task-relevant stimuli presented at the unattended side (invalid target trials).

The present finding of frontoparietal activation for invalid versus valid target trials is consistent with previous studies that used similar comparison (Corbetta et al. 2000, Arrington et al. 2000; Macaluso et al. 2002a). Unlike previous studies that cued attention to one or the other side on a trial-by-trial basis, here, attention was sustained on one side for blocks of 68 s. However, both behavioral data and imaging results demonstrated the expected effects of validity confirming that the subjects complied with instructions (see also Indovina and Macaluso 2004). Critically, here we show that the activation of the frontoparietal network for stimuli presented at the unattended side (invalid trials) relates to task relevance rather than stimulus salience. Thus, the attentional network activated for low-salience targets but not for high-salience task-irrelevant checkerboards.

Modulation of frontoparietal cortex by relevance factors has been previously demonstrated in nonspatial contexts, as in oddball paradigms (e.g., Clark et al. 2000; Downar et al. 2001). For example, Clark et al. (2000) examined brain activity associated with rare targets requiring overt motor response versus rare distracters that did not require any response, showing increased activity in inferior frontoparietal regions selectively for task-relevant target trials. Our current data are consistent with these previous results, but here we extend these findings to the context of spatial reorienting. Although oddball paradigms may share some features with spatial cueing paradigms (e.g., both addressing interactions between subject’s expectation and the actual sensory input), spatial orienting studies specifically focus on the role of stimulus position. This is a critical difference because the position also of task-irrelevant stimuli (e.g., brightening of a peripheral box) can act as a spatial cue, affecting judgment of subsequent targets (see classical exogenous spatial cueing paradigm; e.g., Klein 2000).

Recent imaging work (Shulman et al. 2003; Peelen et al. 2004; Kincade et al. 2005) addressed the role of task relevance using endogenous or exogenous spatial cueing paradigms. An endogenous cue is by definition task relevant, instructing the subject to voluntarily shift attention towards the most probable target location. On the other hand, an exogenous cue is a salient stimulus that automatically captures attention but it is not predictive of target location, hence, it can be considered task irrelevant. Peelen et al. (2004) investigated endogenous versus exogenous mechanisms of attention manipulating the type of cue (endogenous or exogenous). In order to subtract target-detection components, they compared both valid and invalid trials versus neutral trials (i.e., trials without any cue). This revealed activation of the right IFG, EFs, supplementary motor area, anterior cingulate cortex, TPJ, and precuneus, irrespective of the type of cue. This suggested that a common network regulates exogenous and endogenous spatial attention (see also Gitelman et al. 1999; Kim et al. 1999). Accordingly, it might be inferred that also task-irrelevant salient stimuli (exogenous cues) can engage the attentional network. However, it should be noted that for both exogenous and endogenous cues, valid and invalid trials were pooled together, and it is therefore difficult to establish the contribution of the invalid targets to these activations. In principle, common activation for the 2 cueing conditions might result from processes associated with invalidly cued targets (for analogous confounds arising for blocked designs, see also Gitelman et al. 1999; Kim et al. 1999; Rosen et al. 1999).

Kincade et al. (2005) separated cue and target activity avoiding any issue concerning possible confounds between cue-related and target-related processes. In different trials, nonpredictive exogenous cues or predictive endogenous cues were presented before visual targets for sensory discrimination. Analyses of brain activity associated with the different types of cue revealed a network of dorsal frontoparietal regions that was more active for endogenous than for exogenous cues. Ventral frontoparietal regions showed only weak activation during the cue period, and somewhat surprisingly larger activity was observed for endogenous than exogenous cues (cf., Corbetta and Shulman 2002). Analyses of target-related activity revealed the expected activation of the ventral regions for invalidly cued targets (see also Arrington et al. 2000; Corbetta et al. 2000), but only when the target followed an endogenous cue. The authors concluded that dorsal frontoparietal areas are primarily associated with voluntary control of spatial attention, whereas the activation of ventral regions may relate to the detection of mismatches between expectancy and sensory input and to any resetting processes associated with this (see also Corbetta and Shulman 2002). Thus, the conclusions of this study emphasize the importance of task relevance over stimulus saliency, both for dorsal and ventral frontoparietal regions.

Whereas Kincade et al. (2005) elegantly separated cue-related and target-related processes studying endogenous versus exogenous effects in the cueing phase, here we investigated relevance versus saliency factors in relation to target processing. Kincade reported activation of TPJ for invalid targets following an endogenous cue (Kincade et al. 2005). However, this study could not assess whether these invalidity effects related to the saliency of the target or its relevance because all invalid targets appeared suddenly at the unattended side and they required discrimination and response. In our paradigm, we separated task relevance and saliency effects presenting either low-salience targets that required discrimination and overt response or salient but task-irrelevant checkerboards. Note that here stimulus-driven processes (checkerboards) will interact with the
Figure 3. Effects of spatial attention on visual stimuli presented at the attended location. The direction of spatial attention boosted responses for stimuli presented at the attended side irrespective of task relevance (i.e., modulation observed both for task-relevant target trials and for task-irrelevant checkerboards). (A) We identified brain regions representing the attended location, comparing brain activity for checkerboards presented in the left hemifield (in blue) or in the right hemifield (in red). Surface-rendered activation overlaid on the SPM02 anatomical template (threshold: \( P \) corrected = 0.05), demonstrating activation of occipital cortex contralateral to the stimulated visual hemifield. Note that target Ts were presented at the same location as the task-irrelevant checkerboards and that left and right visual locations were marked throughout the fMRI run (see also Fig. 1B). (B) Leftward versus rightward attention (and vice versa) for target trials. We compared brain activity for valid-left versus valid-right target trials (see white lines in the 2 signal plots), demonstrating increased activity in occipital cortex contralateral to the attended side. Note that on target trials, the stimulation was always bilateral and that therefore this comparison is not confounded with any difference in the sensory stimulation (or motor response). The signal plots display the estimated activity for all target trials (valid/invalid, contralateral/ipsilateral), showing maximal activity for valid targets presented in the contralateral hemifield (see red bar). Blue crosses on coronal sections indicate voxels from which signal was extracted. (C) Leftward versus rightward attention (and vice versa) for checkerboard trials. To highlight any modulation of checkerboard-related activity according
endogenous attentional state in a way that is more similar to invalid targets than to processes associated with exogenous cues in previous studies (e.g., Kincade et al. 2005). We minimized any saliency effect during invalid target trials, presenting visual stimuli on the left and right hemifield simultaneously (target defined by color only). Thus, the position of the target at the unattended side still determined the invalidity of the trial (i.e., a stimulus-driven effect), but this was uncoupled from any saliency effect relating to the sudden appearance of a single stimulus outside the focus of attention. Our data show that also in this condition, task relevance rather than pure exogenous saliency determines the activation of the frontoparietal network. Accordingly, salient high-contrast and high-luminance checkerboards presented at the unattended location did not activate this network.

The frontoparietal network activated for invalid target trials included several clusters (see Fig. 2). In premotor cortex, we found activation both in dorsal and ventral regions. Dorsally, one cluster was located at the intersection of the superior frontal sulcus with the precentral sulcus, and it may correspond to the FEF (Petit et al. 1997). The coactivation of both ventral and dorsal anterior regions for invalid targets is in fact a common finding, with several previous studies reporting analogous effects (see Arrington et al. 2000; Indovina and Macaluso 2004; Kincade et al. 2005). In parietal cortex, we found activation of a region that included the lower bank of the IPS and extended ventrally in the angular gyrus. Our activation was located more dorsally than the anatomical location reported in other studies that interested mainly the supramarginal gyrus and the posterior part of the superior temporal sulcus (Corbetta et al. 2000; Macaluso et al. 2002a; Kincade et al. 2005). However, our parietal peak was only about 10 mm distance from Arrington et al. (2002), who also reported activation of the angular gyrus for invalid minus valid targets, and found a general pattern of frontoparietal activation very similar to the one reported here for the right hemisphere (cf., Fig. 2 here, and Fig. 4 in Arrington et al. 2002).

It might be argued that in fact our parietal activation may correspond to part of the dorsal rather than the ventral attentional network. This is indeed difficult to rule out, especially because we did not find any segregation of ventral versus dorsal network within the current experiment. However, we should note that our intraparietal activation did not extend posteriorly and superiority in the superior parietal lobule (Brodmann area 7) that is associated with voluntary attentional control (Corbetta et al. 1993; Kastner et al. 1999; Wojciulik and Kanwisher 1999; Corbetta and Shulman 2002; Simon et al. 2002; Yantis et al. 2002). Further, dorsal areas typically show attentional modulations that are specific for the position of the target (contralateral greater than ipsilateral responses, e.g., Schluppeck et al. 2006; Sereno et al. 2001), whereas here we did not find any spatially specific effect in the frontoparietal network. Nonetheless, we cannot exclude that our stimulus configuration engaged endogenous resources during invalid target trials. Target Ts were defined according to color, and therefore, it was not only the position of the visual stimulus that determined the validity of the trial but also a combination of stimulus to the direction of endogenous spatial attention, we compared activity for attended minus unattended checkerboards, in one or the other hemifield (see white lines in the 2 signal plots). This revealed that activity in occipital cortex contralateral to the checkerboard position was higher when endogenous attention was also focused there (attended checkerboard) compared with trials involving the same visual stimulation, but now with endogenous attention directed in the ipsilateral hemifield (unattended checkerboard). The signal plots show the estimated activity for all checkerboard trials (attended/unattended, in the left or right hemifield), highlighting maximal activity for contralateral checkerboards presented at the attended location (see red bar). Blue crosses on coronal sections indicate voxels from which signal was extracted. TgL/TgR, target left/target right; CkL/CkR, checkerboard left/checkerboard right; AttL/AttR, attend left/attend right.

### Table 3

<table>
<thead>
<tr>
<th>Checkerboard (valid &gt; invalid)</th>
<th>Right checkerboard</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>P corrected</th>
<th>Z-score</th>
</tr>
</thead>
<tbody>
<tr>
<td>L medio/ventral occ.</td>
<td>−28</td>
<td>−80</td>
<td>−10</td>
<td></td>
<td>0.073</td>
<td>3.52</td>
</tr>
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### Table 4

<table>
<thead>
<tr>
<th>Checkerboard (valid &gt; invalid)</th>
<th>Left checkerboard</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>P corrected</th>
<th>Z-score</th>
</tr>
</thead>
<tbody>
<tr>
<td>R medio/ventral occ.</td>
<td>10</td>
<td>−86</td>
<td>0</td>
<td></td>
<td>0.032</td>
<td>3.50</td>
</tr>
</tbody>
</table>

Note: Group effect $P \leq 0.05$ voxel level corrected, considering as volume of interest the region showing a main effect of checkerboard side (see Table 2). Regions outside this volume of interest are reported when surviving correction for multiple comparisons considering the whole brain as volume of interest (in italics). Montreal Neurological Institute coordinates in millimeters. L/R, left/right hemisphere; occ., occipital cortex.
configuration and task instruction (i.e., what color was task relevant). The need to match sensory input with internal representations regarding the relevant color could in principle explain the engagement of endogenous resources. However, even this would not be incompatible with activation of the ventral network, where endogenous effects have been previously reported in the context of cue processing (Kincade et al. 2005) and nonspatial tasks (e.g., Clark et al. 2000; Downar et al. 2001). Overall, our findings are more consistent with an engagement of the ventral rather than dorsal attentional system (localization below the IPS, activation for invalid targets, lack of any spatial modulation). However, it is important to note that a strict segregation of attentional functions in dorsal (voluntary) and ventral (automatic) processing may not fully capture the complexity of the system. Indeed, recent models of attention-control stress the critical interplay between the 2 systems (Corbetta et al. 2005).

Our data demonstrate that low-salience targets at the unattended side engaged frontoparietal regions, whereas no such activation was found for salient but task-irrelevant checkerboards. The finding that salient nontarget stimuli (here checkerboard) failed to engage this system might seem surprising at first. One possible explanation is that in the current experimental setting, task-irrelevant checkerboards failed to capture spatial attention. Here we did not have any behavioral measure to confirm this (checkerboards never required any discrimination or response), but previous behavioral studies have shown that attentional capture by salient stimuli can interact with current endogenous processes (Yantis and Jonides 1990) and current task set (e.g., see Serences et al. 2005). For example, Yantis and Jonides (1990) demonstrated that the interference caused by the sudden onset of a distracter stimulus can be greatly diminished if endogenous attention is highly focused. We suggest that in our experiment, spatial attention was highly focused indeed, in particular because on target trials visual stimuli were presented bilaterally and subjects were required to process the target while ignoring the concomitant distracter (nontarget T on the opposite hemifield).

Evidence for focused attention during our experiment also comes from the analyses of brain responses to stimuli presented at the attended side. Although previous studies using trial-by-trial cueing consistently activated the frontoparietal network for invalid trials, generally, they did not report any boosting of responses for target stimuli presented at the attended location (e.g., see Arrington et al. 2000; Corbetta et al. 2000; Macaluso et al. 2002a; Kincade et al. 2005). Instead, such effects are larger when subjects direct attention toward one location to discriminate target stimuli while distracters are presented simultaneously in the visual scene (Heinze et al. 1994; Kastner and Ungerleider 2001; Macaluso et al. 2002b; but see also Martinez et al. 1999). Here we found strong modulation of target-related activity in visual occipital cortex according to the direction of endogenous attention (see Fig. 3B). Furthermore, we found that also visual activity associated with task-irrelevant checkerboard was modulated according to the direction of endogenous attention (see Fig. 3C). This suggests that top–down modulatory signals that are thought to bias activity in visual areas (e.g., see Kastner and Ungerleider 2001) can affect processing of visual stimuli presented in the attended hemifield, irrespective of their behavioral relevance. The relatively fast stimulus presentation rate in our event-related study did not allow us to explicitly investigate top–down preparatory activity, which instead would require longer periods of MR scanning without any stimulation. However, the finding of attentional modulation of checkerboard-related activity indicates that endogenous spatial attention can affect processing of task-irrelevant stimuli. Thus, although checkerboards were ineffective in engaging the frontoparietal network when presented at an unattended location, they were treated differentially by the brain depending on the direction of attention (i.e., greater activity for attended vs. unattended checkerboards, in the contralateral occipital cortex). Further, these modulatory effects demonstrate that any sustained increase of baseline activity (e.g., Kastner et al. 1999) did not prevent us from detecting checkerboard-related responses and/or any attentional effects related to these task-irrelevant stimuli (see also main effect of checkerboard stimulation, Fig. 3A).

Conclusions

In summary, our results show that when attention is voluntarily focused on one side, a salient but task-irrelevant stimulus appearing unpredictably in the opposite visual hemifield is not sufficient to activate the frontoparietal network related to stimulus-driven shifts of spatial attention. On the contrary, task-relevant targets at the unattended side activate this attentional network, even when these have low perceptual salience. These findings indicate that task-related processes strongly interact with stimulus-related factors during control of spatial attention. Thus, when attention is highly focused in one visual hemifield, salient stimuli at an unattended location are ineffective in triggering frontoparietal attentional processes, if they do not have any behavioral significance.

Supplementary Material

Supplementary material can be found at: http://www.cercor.oxfordjournals.org/.

Notes

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