

What is “Odd” in Posner’s Location-cueing Paradigm? Neural Responses to Unexpected Location and Feature Changes Compared

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Abstract

■ Within the parietal cortex, the temporo-parietal junction (TPJ) and the intraparietal sulcus (IPS) seem to be involved in both spatial and nonspatial functions: Both areas are activated when misleading information is provided by invalid spatial cues in Posner’s location-cueing paradigm, but also when infrequent deviant stimuli are presented within a series of standard events. In the present study, we used functional magnetic resonance imaging to investigate the distinct and shared brain responses to (i) invalidly cued targets requiring attentional reorienting, and (ii) to target stimuli deviating in color and orientation leading to an oddball-like distraction effect. Both unexpected location and feature changes were accompanied by a significant slowing of manual reaction times. Bilateral TPJ and right superior pa-

rietal lobe (SPL) activation was observed in response to invalidly as compared to validly cued targets. In contrast, the bilateral inferior occipito-temporal cortex, the left inferior parietal cortex, right frontal areas, and the cerebellum showed stronger activation in response to deviant than to standard targets. Common activations were observed in the right angular gyrus along the IPS and in the right inferior frontal gyrus. We conclude that the superior parietal and temporo-parietal activations observed here as well as previously in location-cueing paradigms do not merely reflect the detection and processing of unexpected stimuli. Furthermore, our data suggest that the right IPS and the inferior frontal gyrus are involved in attentional selection and distractor processing of both spatial and nonspatial features. ■

INTRODUCTION

Human lesion and functional imaging studies suggest that subregions of the parietal cortex are involved in covert reorienting of attention in space as well as in the detection of salient unexpected events (for reviews, see Husain & Nachev, 2007; Corbetta & Shulman, 2002). In particular, it has been suggested that the superior parietal lobe (SPL) is activated by spatial attention shifts (e.g., Yantis et al., 2002; Vandenberghe, Gitelman, Parrish, & Mesulam, 2001). The cortex adjacent to the intraparietal sulcus (IPS) (adjoining in most studies to the angular or the supramarginal gyrus) and the temporo-parietal junction (TPJ) (i.e., the posterior part of the superior temporal gyrus/superior temporal sulcus adjoining to the inferior parts of the angular or supramarginal gyrus) has been implicated in visuospatial attentional reorienting in response to invalid spatial cues (e.g., Giessing, Thiel, Rösler, & Fink, 2006; Vossel, Thiel, & Fink, 2006; Thiel, Zilles, & Fink, 2004; Arrington, Carr, Mayer, & Rao, 2000; Corbetta, Kincade, Ollinger,

McAvoy, & Shulman, 2000). Based upon these observations, it has been suggested that the IPS is involved in top-down attentional control (Corbetta & Shulman, 2002; Hopfinger, Buonocore, & Mangun, 2000), whereas the TPJ is supposed to signal the appearance of unexpected but behaviorally relevant stimuli occurring outside the current focus of attention to an IPS-frontal eye field (FEF) network (Corbetta & Shulman, 2002). Importantly, however, the TPJ has also been implicated in the detection of deviant stimuli in oddball paradigms even when no spatial reorienting of attention is required (e.g., Bledowski, Prvulovic, Goebel, Zanella, & Linden, 2004; Downar, Crawley, Mikulis, & Davis, 2000, 2001; Clark, Fannon, Lai, Benson, & Bauer, 2000; Linden et al., 1999). Albeit less consistently, activation adjacent to the IPS (in the angular gyrus, sometimes also extending into the superior parietal cortex) in response to oddball stimuli has also been reported (Bledowski et al., 2004; Downar et al., 2000, 2001; Marois, Leung, & Gore, 2000). Thus, these two subregions of the parietal cortex seem to subservise both spatial and nonspatial functions which cannot simply be captured by dorsal versus ventral stream dichotomies (Husain & Nachev, 2007).

Visuospatial attentional reorienting is usually investigated using Posner’s (1980) location-cueing paradigm, in

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which spatial cues predict the location of behaviorally relevant targets with a certain probability (typically ~80% validity in case of centrally presented cues). Subjects respond slower to invalidly as opposed to validly cued targets, and the reaction time (RT) difference is used as an indicator for the time needed to reorient attention in space. Likewise, in the analysis of functional imaging data, invalid trials are contrasted with valid trials to isolate those brain regions differentially involved in the reorienting of attention (Giessing et al., 2006; Vossel et al., 2006; Thiel et al., 2004; Arrington et al., 2000; Corbetta et al., 2000). However, invalid trials differ from valid trials not only with regard to the position of the target stimulus (occurring at the unexpected or the expected location, respectively) but also in the frequency of their occurrence (e.g., 80 vs. 20%), and thus, in unexpectedness and saliency. In a previous study (Vossel et al., 2006), we have shown that the proportion of valid to invalid trials (i.e., cue validity) affects reorienting-related activity in the right inferior parietal and temporo-parietal cortex. Activity in these areas was enhanced when subjects had to reorient attention in the context of a high as compared to a low cue validity condition, that is, when invalid trials were more infrequent and unexpected. Given that deviant stimuli in oddball paradigms elicit activation in similar brain regions, it thus remains to be investigated whether those areas, together with those identified in other studies employing location-cueing paradigms, indeed reflect spatial reorienting processes per se. Alternatively, those regions could respond to unexpected, infrequent, and salient events in general (Corbetta & Shulman, 2002).

Accordingly, the aim of the present functional magnetic resonance imaging (fMRI) study was to dissociate the neural correlates of visuospatial attentional reorienting and nonspatial visual oddball distraction. To address this question, we designed a paradigm in which we orthogonally manipulated the spatial cueing (valid and invalid) and task-irrelevant stimulus properties of the targets (resulting in both standard and infrequently occurring deviant target stimuli).

Because it has been shown that RT costs are likewise observed in location-cueing as well as in visual oddball paradigms when subjects are engaged in a primary task (i.e., in response to task-irrelevant stimulus changes; Berti & Schröger, 2004, 2006; Meinke, 2006; Meinke, Thiel, & Fink, 2006), subjects performed a discrimination task in which they had to make spatial frequency judgments of laterally presented target stimuli (sinusoidal gratings). The targets were preceded by spatial cues indicating their location correctly in 80% of the trials. Importantly, in 80% of all trials, the color and orientation of the target were held constant (standard targets), whereas both features changed in the remaining 20% of the targets (deviant targets). We tested for both distinct and common neural activity in response to changes in location (invalid vs. valid trials) and to changes in

orientation and color of the target (deviants vs. standards), respectively.

METHODS

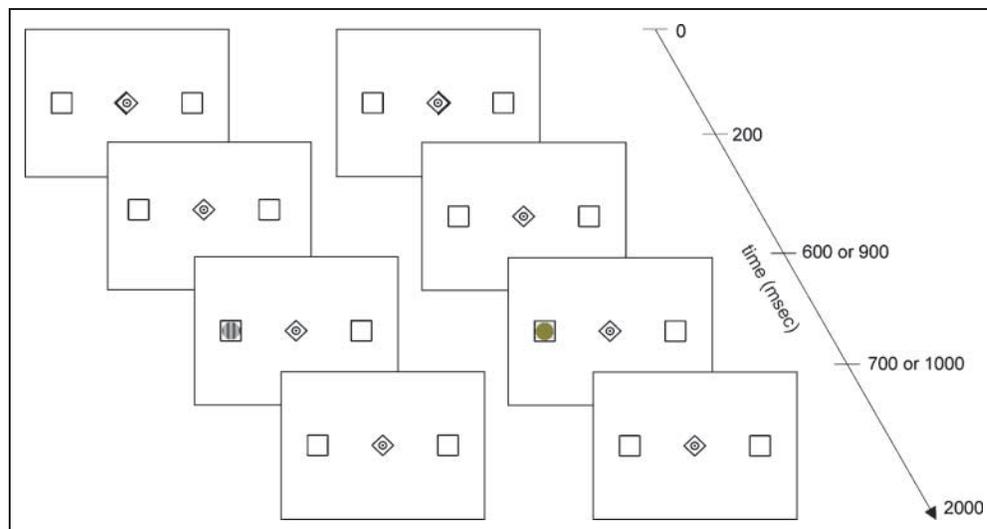
Subjects

Twenty-four subjects with no history of neurological or psychiatric disease gave written informed consent to participate in the study. Four subjects were excluded from further analysis due to excessive head movement during fMRI scanning. Therefore, data from 20 subjects were analyzed (9 men, 11 women; age range from 19 to 38 years; mean age = 26.15 years). All subjects were right-handed as indexed by a handedness inventory (Oldfield, 1971). Intact color vision was tested with an adaptation of the Ishihara color tables (Velhagen & Broschmann, 2003).

Stimuli and Experimental Paradigm

We used a location-cueing paradigm with central predictive cueing (Posner, 1980). The stimuli were shown on a TFT screen behind the MR scanner and were presented to the subjects by means of a mirror system. Viewing distance was approximately 245 cm. Subjects were presented with two horizontally arranged boxes (1° wide and 4° eccentric in each visual field; see Figure 1). A central diamond (0.5° eccentric in each visual field) was placed in between serving as a fixation point. Cues consisted of a 200-msec brightening of one side of the diamond depicting an arrowhead pointing to one of the peripheral boxes. The cue was followed by a target appearing for 100 msec in one of the boxes. To prevent temporal orienting, we used two randomly occurring cue–target intervals (400 and 700 msec). The cues were valid in 80% of the trials. The targets were circular sinusoidal gratings (0.9° eccentricity) with two different spatial frequencies (“fine” grating: 7 cycles per grating; “coarse” grating: 3 cycles per grating). Subjects were asked to report the spatial frequency of the target stimulus as quickly as possible by button presses with the index and middle fingers of their right hand. Fine and coarse gratings were presented randomly and with equal probability (i.e., 50%). The gratings could be either in grayscale or in red and green color and were presented with four possible orientations (0°, 45°, 90°, 135°). One specific combination of color and orientation (e.g., grayscale grating with 0° orientation; see Figure 1) was defined as the “standard target” which was presented in 80% of the trials. Twenty percent of the targets, however, were “deviants” in which both the color and the orientation of the gratings changed (e.g., red–green gratings with 45°, 90°, and 135° orientation). We varied both stimulus features of the targets in the deviant trials at the same time (i.e., both color and orientations) because this reliably produced RT costs in a behavioral

Figure 1. Experimental paradigm. Illustration of an exemplary event sequence during trials with a validly cued standard (grayscale grating, 0° orientation) and an invalidly cued deviant target (red–green grating, 45° orientation). Note that in this example other possible deviants were red–green gratings with either 90° or 135° orientation. The allocation of color and orientation to standards and deviants, respectively, was counterbalanced across subjects. Subjects were asked to fixate the central diamond throughout the experiment and to make spatial frequency judgments of the target stimuli (fine or coarse). The proportion of valid to invalid cues and standard to deviant targets was 4:1.



pilot study. Note that these variations were completely irrelevant for the task. Thus, a location-cueing paradigm was combined with a visual oddball paradigm (see Figure 1), resulting in a 2×2 design with the factors “cueing” (valid, invalid) and “target” (standard, deviant). In addition, approximately 2% of the experimental trials were “catch trials” in which only a cue, but no target, was presented to prevent anticipatory responses to the cues.

The allocation of the responding fingers (right index and middle fingers) to the two spatial frequencies (fine and coarse) as well as the allocation of color and orientation to standard and deviant targets, respectively, was counterbalanced across subjects. Subjects were informed about the different experimental conditions and completed a short practice session prior to performing the task in the MR scanner. Trials were presented every 2000 msec. The experiment consisted of 959 trials, including 320 “null events” (Josephs & Henson, 1999) where a baseline stimulus was displayed, leading effectively to variable stimulus-onset asynchronies (SOAs) (i.e., 2000 msec, 4000 msec, 6000 msec, etc.). The duration of the experiment was 34 min. The scanning session included two rest periods of approximately 1 min during which the word “pause” was shown on the display and the subjects were allowed to close their eyes. This was done to prevent deterioration of fixation ability due to exertion of the eyes. Restart of the task was indicated by a tone.

Data Acquisition

T2*-weighted echo-planar imaging (EPI) images with blood oxygen level-dependent (BOLD) contrast (ma-

trix size = 64×64 , voxel size = $3.1 \times 3.1 \times 3.0$ mm³) were obtained using a 3-T MRI System (Trio, Siemens, Erlangen, Germany). Additional high-resolution anatomical images (voxel size = $1 \times 1 \times 1$ mm³) were acquired using a standard T1-weighted 3-D MP-RAGE sequence.

Nine hundred seventeen EPI volumes of thirty-six 3-mm-thick axial slices were acquired sequentially with a 0.3-mm gap (repetition time = 2.2 sec, echo time = 30 msec). The first 5 volumes were discarded to allow for T1 equilibration effects. The data were preprocessed and analyzed with Statistic Parametric Mapping software SPM5 (Wellcome Department of Imaging Neuroscience, London; Friston et al., 1995; www.fil.ion.ucl.ac.uk/spm5.html). To correct for interscan movement, the images were spatially realigned to the first of the remaining 912 volumes and, subsequently, re-realigned to the mean of all images after the first step. Then, the mean EPI image for each subject was computed and spatially normalized to the Montreal Neurological Institute (MNI) single-subject template using the “unified segmentation” function in SPM5. The resulting parameters of a discrete cosine transform, which define the deformation field necessary to move the subjects data into the space of the MNI tissue probability maps, were then combined with the deformation field transforming between the latter and the MNI single-subject template. The ensuing deformation was subsequently applied to the individual EPI volumes as well as to the T1 scan, which was coregistered to the mean of the realigned EPIs beforehand. All images were hereby transformed into standard stereotaxic space and resampled at $2 \times 2 \times 2$ mm³ voxel size. The normalized images were spatially smoothed using an 8-mm full-width half-maximum Gaussian kernel to meet the statistical requirements of

the General Linear Model and to compensate for residual macroanatomical variations across subjects.

Statistical Analysis of Imaging Data

Data were analyzed with SPM5 employing a random effects model. Seven regressors were defined at the single-subject level (validly cued standard targets, invalidly cued standard targets, validly cued deviant targets, invalidly cued deviant targets, catch trials, missed/incorrect responses, pauses). The event types were time-locked to the onset of the target by a canonical synthetic hemodynamic response function (hrf) and its first-order temporal derivative. The six movement parameters of the realignment (rigid body translation in the x -, y - and z -plane as well as rotation around the x -, y -, and z -axis) were included in the design matrix as additional regressors. Data were scanwise globally scaled to reduce globally distributed confounding effects (Kiebel & Holmes, 2004) and high-pass filtered at 1/128 Hz. For each subject, four contrast images were created for each experimental condition (each trial type vs. baseline) and entered into a 1×4 within-subjects ANOVA (flexible factorial design in SPM5 including an additional factor modeling the subject means). Inhomogeneity of variance and correlation of measurement were estimated with a Restricted Maximum Likelihood (ReML) algorithm.

To isolate brain areas involved in the spatial reorienting of attention (i.e., to test for the main effect of the factor cueing), we used a directed t contrast comparing all invalid to all valid trials. Similarly, brain areas associated with nonspatial visual distraction were identified by contrasting all deviant with all standard trials (i.e., by testing for the main effect of the factor target). Interaction effects between these two factors were tested with two directed t contrast. Activations are reported at a statistical threshold of $p < .05$, corrected at cluster-level (cluster size estimated at voxel-level at $p < .001$, uncorrected) (Poline, Worsley, Evans, & Friston, 1997).

To isolate the distinct brain activations in response to spatial reorienting and oddball distraction, respectively, we used a masking procedure in which each main effect contrast ($p < .05$, corrected at cluster-level) was exclusively masked with the other contrast at a low statistical threshold ($p < .05$, uncorrected for multiple comparisons). Hence, with this procedure, only those voxels are tested for an effect in one contrast that fail to reach a level of significance of $p < .05$ (uncorrected) in the mask contrast.

To test for common neural activations, we used a conjunction analysis testing for the conjunction null hypothesis (Friston, Penny, & Glaser, 2005). As cluster-level inference can validly be applied to single statistic images only (and not to image intersections like in a conjunction), we used a threshold of $p < .001$, uncorrected (equivalent to a conjoint $p < 1 \times 10^{-6}$) and a cluster

threshold of 10 contiguous voxels when reporting the results of this analysis.

Region-of-interest (ROI) analyses of the TPJ were performed for the main effect of target as well as for the two interaction contrasts (WFU PickAtlas; Maldjian, Laurienti, Kraft, & Burdette, 2003). Here, the voxels of peak activation in both the left and right TPJ of the main effect contrast of the factor cueing were used as the center for two spheres with a radius of 8 mm serving as a single ROI mask. In other words, the ROI mask can be considered as a localizer for the tests of the remaining (orthogonal) contrasts of the 2×2 design (see, e.g., Friston, Rotshtein, Geng, Sterzer, & Henson, 2006 for a discussion on that topic). Activations of the ROI analyses are reported at $p_{\text{FWE}} < .05$ (family-wise error corrected for multiple comparisons within the search volume).

Statistical Analysis of Behavioral Data

RTs faster than 100 msec (i.e., anticipated responses) were excluded from the analysis. Median RTs were calculated for the four experimental conditions in each subject. These median RTs were analyzed with a repeated measure ANOVA with the factors “cueing” (valid, invalid) and “target” (deviant, standard). Omissions and incorrect responses were summed-up and expressed as percentage values. For the “catch trials,” false alarm responses were determined and transformed into percentage values. To rule out that the version of the experimental task across the subjects (i.e., the allocation of orientation and color to standard and deviant targets) affected the behavioral effects, we calculated separate one-way ANOVAs on the RTs and missed responses in standard trials as well as on the RT costs (RT invalid – RT valid trials and RT deviant – RT standard targets) comparing the four different standard orientations and the two colors of the standard.

Eye Movement Control

Eye position was monitored during scanning with an MR-compatible infrared eye tracker (SensoMotoric Instruments SMI, Berlin, Germany). Eye movement data were analyzed to assure that the subjects were able to maintain eye fixation in response to the cue and the target stimuli. Therefore, the time interval between cue and target appearance and the time period after the appearance of the targets were analyzed. The latter analysis was performed separately for the four experimental conditions (i.e., validly and invalidly cued standard targets and validly and invalidly cued deviant targets) to control for differences in fixation performance between the conditions. Analysis was restricted to a time frame of 800 msec after target appearance (note that, on average, the response occurred within about 600 msec after target appearance).

For both analyses (time interval between cue and target and 800 msec time interval after target appearance), the amount of time in which the eye movements stayed within a range of two standard deviations was determined and transformed into a percentage value. As in the analysis of RTs, differences in fixation performance between conditions were tested with a 2×2 repeated measure ANOVA with the factors Cueing and Target.

RESULTS

Behavioral Data

None of the subjects showed any anticipated or false alarm responses. Missed and incorrect responses amounted together, on average, to 3.4% (± 0.58 SEM). The ANOVA of the median RTs yielded a main effect of the factor Cueing [$F(1, 19) = 24.56, p < .001; \eta_p^2 = .564$], reflecting slower responses to invalidly than to validly cued targets. Moreover, we observed a significant main effect of Target [$F(1, 19) = 95.26, p < .001; \eta_p^2 = .834$], reflecting the RT costs caused by deviant target stimuli. Thus, both invalid cues and deviant targets caused a significant prolongation of RTs. The Cueing \times Target interaction was not significant ($p > .3$) as the average magnitude of RT costs was almost of equal magnitude (RT of all invalid minus RT of all valid trials: mean \pm SEM: 28.3 ± 3.8 msec; RT of all deviant minus all standard trials: 34.1 ± 3.4 msec). The means of the median RTs for each experimental condition are depicted in Figure 2.

The RTs and missed responses in standard trials of the subjects did not significantly differ as a function of the orientation or of the color of the standard. This indi-

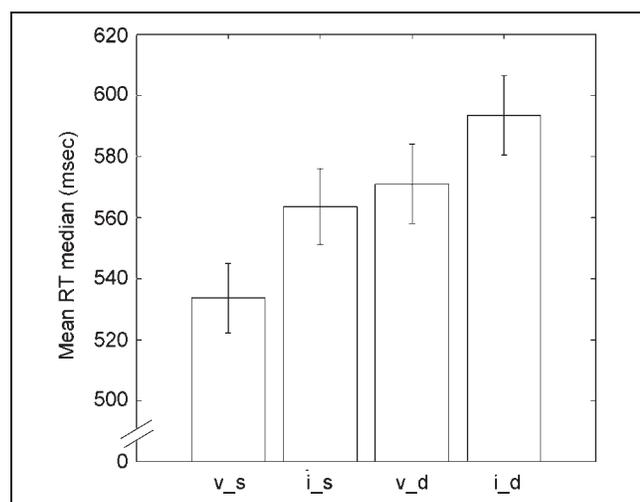


Figure 2. Behavioral data. Averaged median reaction times (RTs) and standard errors of the mean (SEM) for the four experimental conditions. v_s = validly cued standard targets; i_s = invalidly cued standard targets; v_d = validly cued deviant targets; i_d = invalidly cued deviant targets.

cates that task difficulty did not vary across the different versions of the experimental task. Moreover, neither the RT costs in response to invalidly cued targets nor the RT costs in response to deviant targets were significantly influenced by the orientation or color of the standard stimulus.

Eye Movement Data

The subjects spent $94.8 \pm 1.0\%$ (mean \pm SEM) of the time between cue and target appearance within a fixation zone of 2 SDs. There were no significant differences in fixation performance after target appearance between the four experimental conditions (validly cued standard targets: $96.0 \pm 0.8\%$, invalidly cued standard targets: $95.6 \pm 0.9\%$, validly cued deviant targets: $95.7 \pm 0.9\%$, invalidly cued deviant targets: $95.6 \pm 1.3\%$; all p values of the ANOVA terms $> .4$).

Neural Data

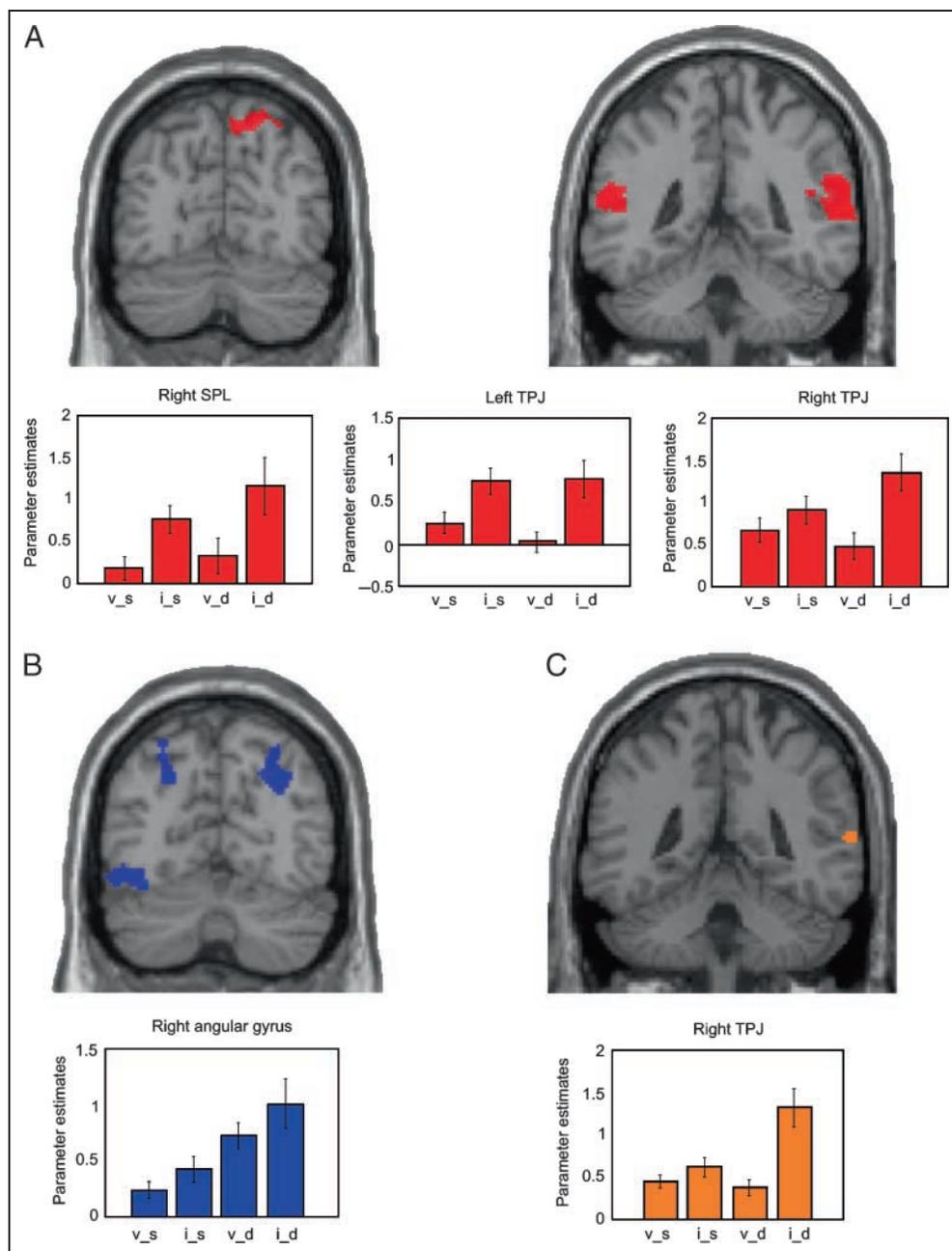
Visuospatial Attentional Reorienting

The comparison of all invalid versus all valid trials (i.e., testing for the main effect of cueing to isolate brain regions involved in visuospatial attentional reorienting) yielded activation in the posterior parts of the superior and middle temporal gyrus in both hemispheres (voxels of peak activation: $x = 66, y = -44, z = 11, Z = 5.17, 774$ voxels; $x = -58, y = -54, z = 13, Z = 4.92, 456$ voxels) (see Figure 3A). These activations, which adjoined to the inferior parietal lobe (IPL), will be referred to as the TPJ in the following sections of the article because these areas overlapped with regions that have been termed as the TPJ in prior studies (see, e.g., Arrington et al., 2000; Corbetta et al., 2000). Moreover, we observed activation in the posterior part of the middle temporal gyrus of the right hemisphere ($x = 44, y = -62, z = 13, Z = 4.39, 155$ voxels) and in the right SPL which extended into the IPS ($x = 18, y = -72, z = 57, Z = 3.95, 221$ voxels) (see Figure 3A). When masked exclusively with the main effect of target (deviants $>$ standards), all four regions survived the masking procedure (see Table 1 and Figure 4 [red]), suggesting that these brain areas were indeed involved in spatial reorienting of attention and not in the detection of infrequent events per se.

Visual Oddball Distraction

The contrast of all deviant versus all standard targets (i.e., the main effect of target) resulted in bilateral activation of the inferior temporal gyrus, which extended into inferior occipital areas as well as the fusiform gyrus ($x = -50, y = -62, z = -15, Z = 5.6, 573$ voxels; $x = 50, y = -58, z = -15, Z = 5.59, 169$ voxels). These activations will, in the following, be termed the

Figure 3. Neural data. (A) Neural activity related to visuospatial attentional reorienting (red) in the right superior parietal lobe (SPL) and the left and right temporo-parietal junction (TPJ). (B) Neural activity related to visual oddball distraction (blue) in the right angular gyrus (parts of the activation within left occipito-temporal cortex [OTC] and left inferior parietal lobe [IPL] are also depicted by the coronal section image). (C) Results of the ROI analysis of the TPJ of the interaction contrast (orange). (See legend of Figure 2 for other abbreviations.)



occipito-temporal cortex. Furthermore, the right inferior frontal gyrus ($x = 50, y = 36, z = 17, Z = 5.42, 438$ voxels), the right anterior insula ($x = 36, y = 20, z = -7, Z = 4.37, 135$ voxels), the right angular gyrus along the IPS ($x = 30, y = -68, z = 39, Z = 4.71, 465$ voxels) (see Figure 3B), the left IPL ($x = -42, y = -38, z = 53, Z = 4.57, 659$ voxels), and the left cerebellum ($x = -30, y = -36, z = -27, Z = 4.79, 127$ voxels) showed significantly stronger activation in response to deviant than to standard targets. Only the activation in the right angular gyrus/IPS did not survive the analysis with exclusive masking with the main effect of cueing (see Table 1 and Figure 4 [blue]).

Interaction Effects

At cluster-level inference, none of the two interaction contrasts ([invalidly cued standards > validly cued standards] > [invalidly cued deviants > validly cued deviants]; [invalidly cued deviants > invalidly cued standards] > [validly cued deviants > validly cued standards]) revealed any significant activations.

Region-of-interest Analyses

Because neither the main effect contrast of target (deviants > standards) nor the interaction contrasts revealed

Table 1. Brain Areas Involved in Visuospatial Reorienting of Attention and Visual Oddball Distraction and Results of the Conjunction Analysis

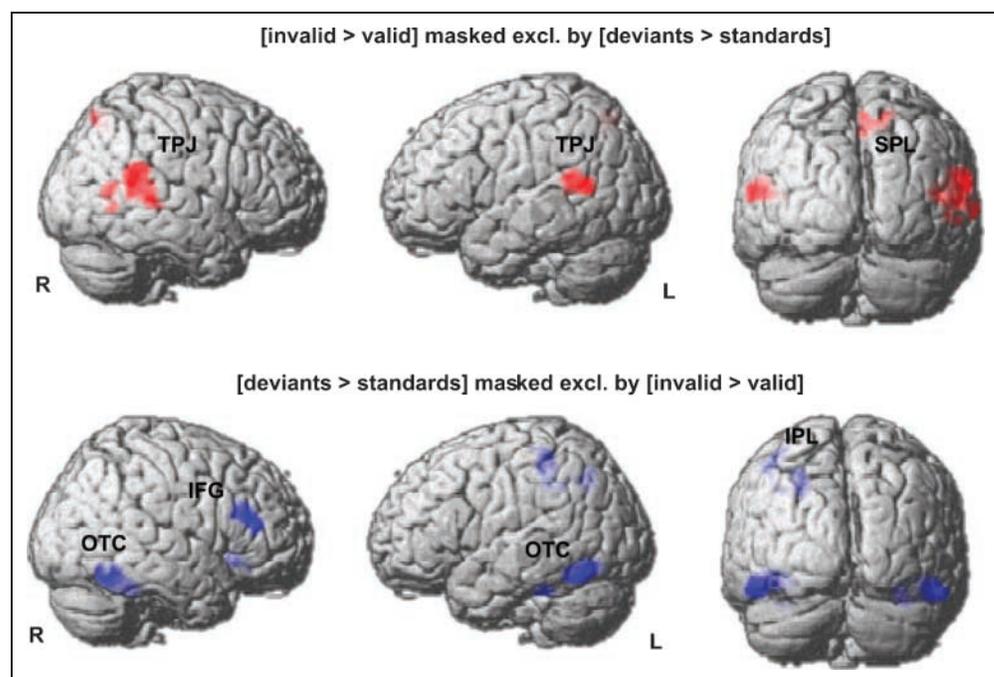
Region	Side	MNI Coordinates			Voxels	Z Score
		x	y	z		
<i>[Invalid > Valid] Masked Exclusively by [Deviant > Standard]</i>						
Superior/middle temporal gyrus	R	66	-40	9	655	5.15*
	L	-58	-54	13	413	4.92*
Posterior middle temporal gyrus	R	44	-62	13	148	4.39
Superior parietal lobe (SPL)	R	20	-72	59	145	3.93
<i>[Deviant > Standard] Masked Exclusively by [Invalid > Valid]</i>						
Inferior frontal gyrus	R	50	36	17	372	5.42*
Insula	R	36	20	-7	132	4.37
Inferior parietal lobe (IPL)	L	-42	-36	53	428	4.28
Inferior occipito-temporal cortex, fusiform gyrus	L	-50	-62	-15	547	5.60*
	R	50	-58	-17	680	5.44*
Cerebellum	L	-30	-36	-27	127	4.79
<i>Conjunction: [Invalid > Valid] ∩ [Deviant > Standard]</i>						
Inferior frontal gyrus	R	54	12	41	10	3.38
Angular gyrus, IPS	R	32	-66	51	21	3.38

*Activations denoted with an asterisk are also significant after applying a family-wise error correction for multiple comparisons at the voxel-level.

any activation within the TPJ in the whole-brain analyses at cluster-level inference, we conducted additional ROI analyses for this anatomical region. Even this more lenient analysis did not yield a main effect of target. How-

ever, an effect was found in the right TPJ for one of the interaction contrasts ($[invalidly\ cued\ deviants > invalidly\ cued\ standards] > [validly\ cued\ deviants > validly\ cued\ standards]$) ($x = 66, y = -44, z = 9, Z = 3.95,$

Figure 4. Neural data. Results of the analyses with exclusive masking. Distinct neural correlates of visuospatial attentional reorienting (red) and visual oddball distraction (blue). TPJ = temporo-parietal junction; SPL = superior parietal lobe; IFG = inferior frontal gyrus; OTC = occipito-temporal cortex; IPL = inferior parietal lobe.



31 voxels) (see Figure 3C). As indicated by the BOLD signal changes in this region, a difference in neural activity was observed between deviant and standard trials in invalid rather than in valid trials. In other words, the right TPJ showed relatively enhanced activity in response to deviant targets only when they appeared at the unexpected location.

Conjunction Analysis

The conjunction analysis testing for common activations of the two main effect contrasts (i.e., for a logical AND) yielded two activation clusters in the right inferior frontal gyrus and in the right angular gyrus adjacent to the IPS (see Figure 5 and Table 1). As revealed by the BOLD signal changes in the four experimental conditions (see Figure 5 for the IPS), these two regions showed higher activity in trials with invalidly cued standards (location change only) and validly cued deviants (feature change only) when compared to trials with validly cued standards. The activity was highest in trials with invalidly cued deviants (location and feature change).

DISCUSSION

In this fMRI study, we included elements of an oddball paradigm within the context of Posner's location-cueing paradigm in order to dissociate the neural correlates of visuospatial attentional reorienting and visual oddball distraction as well as to reveal shared neural processes. While performing a spatial frequency judgment of a sinusoidal grating, subjects were presented with unexpected changes in the location and/or the color and orientation of the target stimuli. At the behavioral level, both invalid spatial cueing and the occurrence of deviant targets resulted in a significant slowing of RTs. Importantly, both experimental conditions produced RT costs which were equal in magnitude. At the neural level, spa-

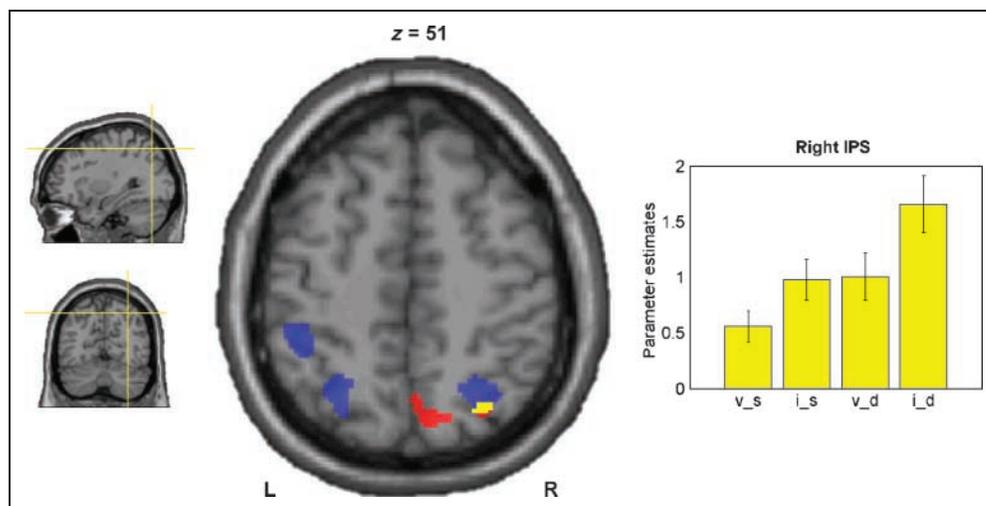
tial reorienting of attention was accompanied by activation of bilateral temporo-parietal as well as right superior parietal brain areas. In contrast, bilateral inferior temporal and occipital areas, the right angular gyrus, as well as inferior parietal and right frontal regions, showed stronger activation in response to deviant than to standard targets. Interaction effects were observed in an ROI analysis of the TPJ. A conjunction analysis revealed common activations of the two contrasts in the right inferior frontal gyrus and in the angular gyrus along the IPS.

Neural Data

Temporo-parietal Junction

In the present study, activation of the TPJ was observed when comparing invalidly and validly cued target stimuli, that is, in response to unexpected location changes requiring reorienting of attention. Although this activation was found in both hemispheres, it was more pronounced in the TPJ of the right hemisphere. This finding is consistent with other imaging studies investigating the neural mechanisms underlying visuospatial reorienting of attention which either observed right-hemispheric (Vossel et al., 2006; Thiel et al., 2004; Arrington et al., 2000; Corbetta et al., 2000) or bilateral (Giessing et al., 2006; Kincade, Abrams, Astafiev, Shulman, & Corbetta, 2005) activation in this area when contrasting invalid and valid trials in the location-cueing paradigm. Because the TPJ activation in the present study survived the exclusive masking with the contrast comparing the infrequently occurring deviants to the standard targets, it is unlikely that the activation here and in previous studies is caused by the increased unexpectedness of invalid trials per se. The activation in this study, moreover, overlapped with a region within the TPJ that shows stronger reorienting-related activation when the cue is highly valid and invalid trials, thus are presented with a very low frequency (Vossel et al., 2006). The present results, therefore,

Figure 5. Neural data. Common neural activation for visuospatial attentional reorienting and visual oddball distraction in the parietal cortex. Blue: main effect of Cueing (invalid > valid); Red: main effect of Target (deviants > standards). Note that the results without exclusive masking are depicted. Yellow: results of the conjunction analysis. IPS = intraparietal sulcus. (See legend of Figure 2 for other abbreviations.)



provide further support for the hypothesis that the susceptibility of the TPJ to cue validity reflects changes in the effort needed for attentional reorienting as predicted by attentional gradient models (Madden, 1992) rather than the processing of infrequent events in general.

Indeed, the TPJ did not show suprathreshold activation in deviant as compared to standard trials when tested for a main effect of target (neither in the whole-brain nor in the ROI analysis). In contrast, the bilateral inferior occipito-temporal cortex, the right angular gyrus, as well as left parietal and right frontal areas (including the anterior insula adjacent to the orbito-frontal cortex), were activated by deviant more than by standard targets. The activation in the latter regions is in accord with a recent model of visual object recognition, which proposed that the orbito-frontal cortex is involved in the top-down modulation of the activity in occipito-temporal visual areas (Bar et al., 2006). It could be assumed that the activity in these areas was enhanced in deviant trials because the unexpected feature change interfered with the target recognition (coarse or fine), and thus, required more top-down control. The missing main effect of target in the TPJ, however, contrasts with other fMRI studies that observed (mostly bilateral) TPJ activation when subjects had to detect infrequently occurring “odd” events (Bledowski et al., 2004; Downar et al., 2001; Clark et al., 2000; Linden et al., 1999). Note, however, that in these studies, the subjects were explicitly instructed to attend to these events and to respond accordingly by different button presses or to silently count the deviant stimuli (Linden et al., 1999). Exceptions to this are two studies in which subjects had to passively view sensory changes (Downar et al., 2000) or in which stimulus changes were presented in both task-relevant and task-irrelevant dimensions (Downar et al., 2001), and the TPJ was activated. However, in the study of Downar et al. (2000), activation of the TPJ was only observed when analyzing auditory and multimodal stimulus changes, but not in the unimodal contrast capturing the neural response to visual transitions. The findings of this latter analysis of unimodal contrast changes resembled the results of the present study, in that fusiform and occipital as well as right superior parietal brain areas were activated. In the second study by Downar et al. (2001), it was observed that one subregion of the TPJ in the supramarginal gyrus showed sensitivity to the relevance of the stimulus changes, whereas another in the superior temporal gyrus did not. However, the task-irrelevant stimulus changes in that study still had a response suppression component resembling go/no-go paradigms (Downar et al., 2001), and thus, the results cannot perfectly be compared to the present study.

In contrast to all of the abovementioned studies, the subjects in our study were engaged in a target discrimination task (spatial frequency judgment) in which the location, the color, and the orientation of the target were irrelevant with regard to the required response (fine

or coarse grating). In other words, both unexpected changes in the location as well as in the color/orientation of the target could be regarded as two different forms of expectation violation or visual distraction and both conditions were accompanied by almost equally high RT costs. One reason for the missing main effect of target within the TPJ could be that, unlike the color and orientation of the target, the location was explicitly cued. Although we presented both valid and standard trials with 80% probability, and thus, biased the expectation of the subjects with regard to both properties of the target stimulus, visual short-term memory (VSTM) load could have been affected differentially. In particular, one could argue that, in contrast to the color/orientation of the target, the (cued) location had to be maintained in the subjects' VSTM on a trial-by-trial basis. Indeed, it has been shown that VSTM load impairs the ability of subjects to detect unexpected task-irrelevant sensory changes (i.e., impairs stimulus-driven attention) by suppressing activity in the TPJ (Todd, Fougny, & Marois, 2005). It could thus be speculated that, in the present study, VSTM load could have suppressed activation of the TPJ for the feature change (different dimension), but not for the location change (same dimension as in VSTM).

Interestingly, we found evidence for a Cueing \times Target interaction effect within the right TPJ in an ROI analysis. Here, the right TPJ responded stronger to the invalidly cued deviant than to the invalidly cued standard targets when compared to the validly cued conditions (i.e., a visual oddball effect was only present in the invalid trials; see Figure 3C). The appearance of the target at the invalid location presumably triggered an attention shift by suspending the suppression of the activity in the TPJ (see also below for further discussion of the role of the TPJ). It could be argued that under these conditions, the filtering function of the TPJ was overall reduced, thus evoking a stronger response for the deviant than for the standard stimuli. The absence of the visual oddball effect in valid trials, however, somewhat corroborates the evidence against a general recruitment of the TPJ by rare unexpected events.

Our data are also congruent with lesion studies employing the location-cueing paradigm in stroke patients. Here, it has been demonstrated that, in particular, lesions within the right TPJ lead to a deficit in attentional reorienting, as these patients show disproportionate slow RTs when a contralesional target is preceded by an invalid cue (Friedrich, Egly, Rafal, & Beck, 1998). In addition, activation of the left TPJ was found in the present study indicating bilateral reorienting-related activity as previously observed in the studies by Giessing et al. (2006) and Kincade et al. (2005), for example. The functional significance of the left TPJ for attentional reorienting is, so far, poorly understood, as the chronic spatial neglect syndrome is typically related to lesions within temporo-parietal and inferior parietal areas of the right hemisphere (Halligan, Fink, Marshall, & Vallar, 2003;

Mort et al., 2003; Corbetta & Shulman, 2002). In the acute phase of a stroke, however, symptoms of neglect are also often observed following left hemisphere lesions. Recent studies demonstrated that regions within the right and left TPJ show changes in reorienting-related activity in patients with neglect across different stages of recovery (Corbetta, Kincade, Lewis, Snyder, & Sapir, 2005), and that the functional connectivity between areas of the left and right TPJ correlates with missed responses and RTs in invalidly cued contralateral targets in the location-cueing paradigm in acute neglect patients (He et al., 2007).

Superior Parietal Lobe and Intraparietal Sulcus

The right SPL showed significantly higher activation in response to invalidly as compared to validly cued targets. As in the TPJ, the activation in this area was still present after explicitly masking the contrast with the comparison of deviant and standard targets. This result is consistent with previous studies as it has been shown that superior parietal areas are involved in spatial attention shifts (Kelley, Serences, Giesbrecht, & Yantis, 2008; Molenberghs, Mesulam, Peeters, & Vandenberghe, 2007; Yantis et al., 2002; Vandenberghe et al., 2001). It could thus be argued that spatial reorienting of attention in the location-cueing paradigm draws on activation of both ventral (TPJ) and dorsal (SPL) parietal areas, and that these activations persist even after subtracting effects evoked by unexpected and infrequently occurring salient stimuli. Although these two regions showed similar profiles in the current study (see Figure 3A), there is evidence in the literature that the SPL and the TPJ may have differential roles in attentional reorienting. The SPL has been implicated in voluntarily directing shifts of attention between peripheral locations (e.g., Kelley et al., 2008; Yantis et al., 2002). The TPJ region has been proposed to signal the appearance of relevant stimuli occurring outside the current focus of attention to dorsal parietal areas, thus initiating the attention shifts (Corbetta & Shulman, 2002). Conversely, deactivation of the right TPJ during visual search tasks has been related to the filtering of distractor stimuli, that is, to the prevention of inappropriate attention shifts (Shulman, Astafiev, McAvoy, d'Avossa, & Corbetta, 2007). It has to be noted, however, that with the present paradigm, we cannot differentiate between different subprocesses of attentional reorienting (e.g., disengaging, shifting, and engaging attention; Posner, 1980) any further.

Another region in the right parietal cortex adjacent to the IPS showed activation when testing for the common effects of spatial reorienting and visual oddball distraction with a conjunction analysis (see Figure 5). This is in line with the finding that the IPS is involved in both spatial and nonspatial attentional processes (Coull & Frith, 1998). The IPS activation overlapped with an area that has recently been attributed to the recalibration

of attentional weights of an attentional priority map (Molenberghs et al., 2007). Thus, it could be speculated that the changes in location and color/orientation of the target stimulus in the present study required an appraisal of task relevance and, accordingly, a readjustment of attentional weights. Resembling our results, Molenberghs and colleagues also reported dissociations between the functions of the SPL and of a more inferior region adjacent to the IPS. Although the SPL generally responded to spatial shifts of attention, the IPS was activated by feature changes even when no spatial shift was required (see also Weidner, Pollmann, Müller, & von Cramon, 2002). Other studies showed activation of the IPS elicited by distractor stimuli in three stimulus oddball paradigms (i.e., including standards, distractors, and behaviorally relevant targets; Bledowski et al., 2004) or by irrelevant stimuli occurring in the opposite peripheral visual field (Vandenberghe et al., 2005). Moreover, a recent study by Geng et al. (2006) demonstrated that the IPS is involved in the on-line attentional selection of competing visual stimuli. Therefore, the IPS seems to be involved in selecting task-relevant stimulus features as well as in isolating these features from potential distractions, may they be spatial or nonspatial. Applied to the present study, the IPS activation could thus reflect the refocusing of attention on the spatial frequency of the grating, which is particularly required in case of invalidly cued targets and deviant targets.

Furthermore, we observed coexistent activation in the right inferior frontal gyrus within the prefrontal cortex when contrasting deviant and standard targets as well as in the conjunction analysis. The prefrontal cortex has been shown to be responsible for maintaining goal-relevant information as well as for the control of distractibility (for a review, see e.g., Miller, 2000), and it has been proposed that this region accordingly transmits bias signals to other brain systems (like, probably, the IPS). Moreover, our result is consistent with ERP studies investigating the electrophysiological brain responses to deviant stimuli in patients with frontal and parietal lobe damage. According to Daffner et al. (2000, 2003), frontal lobe damage disrupts the novelty P300 component, indicating a deficient allocation of attentional resources to novel events. Reductions of the P300 amplitude were also observed in patients with damage to the parietal lobe, which may subserve the updating of internal models of the stimulus environment after novel or deviant stimuli (Daffner et al., 2003).

Conclusion

In sum, our data show that neural activation related to visuospatial attentional reorienting, as assessed with the location-cueing paradigm (invalid > valid trials), is not congruent with neural responses to deviant as compared to standard stimuli, and thus cannot only be attributed to the processing of unexpected salient stimuli

per se. Only the right IPS and the inferior frontal gyrus seem to subserve both spatial attentional reorienting and nonspatial visual distraction processes.

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