FMRI Correlates of Visuo-Spatial Reorienting Investigated With an Attention Shifting Double-Cue Paradigm

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Abstract: The control of visuo-spatial attention entails the joint contribution of goal-directed (endogenous) and stimulus-driven (exogenous) factors. However, little is known about the neural bases of the interplay between these two mechanisms. To address this issue, we presented endogenous (spatially informative) and exogenous (noninformative) visual cues sequentially within the same trial (double-cue paradigm) during fMRI, crossing factorially the validity of the two cues. We found that both endogenous and exogenous cues affected behavioral performance, speeding-up or slowing-down target discrimination when valid and invalid, respectively. Despite the double-cue paradigm maximizes the interplay between endogenous and exogenous factors, the two types of cue affected responses in an independent manner without any significant effect of congruence. The imaging data revealed increased activation in separate cortical areas following invalid endogenous and invalid exogenous cues. A fronto-parietal system was activated during invalid endogenous trials, whereas a region at the temporo-occipital junction was activated during invalid exogenous trials. Within both circuits, activity was unaffected by the validity of the other cue. These results indicate the existence of separate, noninteracting neural circuits for endogenous and exogenous reorienting of visuo-spatial attention. *Hum Brain Mapp* 30:2367–2381, 2009. © 2008 Wiley-Liss, Inc.

Key words: visual information processing; attentional capture; goal-directed; stimulus-driven; cue-target paradigm; event-related design; fronto-parietal network; dorsal; ventral; temporo-occipital cortex

INTRODUCTION

The ability to orient attention in space is a fundamental component of most conscious perceptual-motor processes. Spatial orienting can occur covertly, that is, without movements of the head or eyes, and it is typically directed towards a region of space that is behaviorally relevant (goal-directed attention) or that contains intrinsically salient stimuli (stimulus-driven attention). These two modes of attention control provide a mechanism for the selection of a wide spectrum of relevant information from the environment, enhancing the processing of sensory input at the attended location [e.g. Heinze et al., 1994; Luck et al., 1997;

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Martínez et al., 1999] and reorienting spatial attention toward potentially relevant stimuli presented at unattended locations [e.g. see Corbetta et al., 2008; Corbetta and Shulman, 2002]. Crucially, goal-directed and stimulus-driven factors jointly contribute to prioritize spatial selection of important locations [e.g. Fecteau and Munoz, 2006], although little is known about the neural bases of the interplay between the two mechanisms. This topic is strictly related to the long debated issue of the extent to which the anatomical substrate of the two mechanisms may overlap that yielded controversial conclusions so far, possibly depending on methodological factors.

Spatial cueing paradigms are the gold standard to investigate processes of covert orienting and reorienting [Posner, 1980; Posner and Cohen, 1984]. These paradigms typically come in one of two flavors. In the endogenous version, a symbolic cue (often a central arrow) predicts the location of a subsequent target in most of the trials (valid trials: 70%–80%), while cueing the incorrect location on the remaining trials (invalid trials: 30%–20%). These informative cues can be used to generate volitional allocation of attention, as assessed by measuring benefits in speed and accuracy of responses to targets at the cued location (valid trials) when compared with targets on the opposite side (invalid trials). It should be noted that both valid and invalid trials include the initial volitional allocation of attention, requiring interpretation of the symbolic cue, and the initial cue-related orienting response (i.e. disengaging from fixation, shifting, and engaging to the cued peripheral location). On the other hand, invalid trials are thought to selectively trigger a set of additional processes. These include disengaging from the cued location, shifting and re-engaging of spatial attention to the current target location. All these processes are components of the reorienting response to the invalidly cued target and are required as a consequence of the mismatch between expected and actual spatial position of the task-relevant target.

In the exogenous version, a salient peripheral cue is presented on the same side of the target (valid trials) or on the opposite hemifield (invalid trials) with equal probability. The peripheral cues capture attention in a fully stimulus-driven fashion, still producing the typical pattern of benefits and costs [for cue-target intervals shorter than 300 ms (Klein, 2000) or even shorter (Mele et al., 2008)] despite the absence of any predictive value. Although exogenous and endogenous (valid and invalid) trials basically involve the same operations, there are also several differences between them. An important one is that in valid trials exogenous cues (task-irrelevant stimuli), unlike endogenous cues, may drive pure stimulus-driven attention orienting without generating any spatial expectation as to the target location. Thereby, in invalid exogenous trials targets (task-relevant stimuli) still induce a stimulus-driven re-orienting response as in endogenous trials, but in absence of any breach of spatial expectation.

In the most practiced approach to the neuroimaging of spatial orienting, endogenous and exogenous spatial cueing conditions have been used on separate blocks of trials and

their relative neural correlates inferred by inter-block comparisons. With this method, early PET and fMRI studies revealed a substantially overlapping pattern of activation in the two attentional conditions which included a network of bilaterally distributed fronto-parietal regions [Corbetta et al., 1993; Gitelman et al., 1999; Kim et al., 1999; Nobre et al., 1997; Peelen et al., 2004; Rosen et al., 1999]. This led to the conclusion that goal-directed and stimulus-driven spatial attention are mediated by the same neural substrate, apparently in contrast with electrophysiological recordings in monkeys and behavioral observations in humans suggesting that distinct areas of the fronto-parietal system make a differential contribution to the spatial attention [cf. Corbetta and Shulman, 2002; for review]. However, it might be possible that the early neuroimaging studies were not able to tease apart the specific contribution of endogenous and exogenous factors; hence, overlapping activations would merely reflect their concurrent engagement in a given experimental condition [cf. Hahn et al., 2006; Kincade et al., 2005; Mayer et al., 2004]. Recently, event-related fMRI studies used a different approach and analyzed the activation related to the cue separately from that related to the target [Corbetta et al., 2000; Kincade et al., 2005]. This approach demonstrated some segregation between dorsal (IPS and FEF) and ventral (TPJ and IFG) fronto-parietal regions, with the former being primarily engaged by the endogenous cues [voluntary orienting, Kincade et al., 2005] and the latter activating in response to targets at invalid locations [stimulus-driven re-orienting towards task-relevant stimuli, see Corbetta et al., 2000; Kincade et al., 2005]. Importantly, in spatial cueing studies, a ventral activation was observed in invalid endogenous trials [Corbetta et al., 2000; Kincade et al., 2005], but not following the exogenous signals [Kincade et al., 2005]. Thus, these studies provided evidence that while during orienting of attention the dorsal network is recruited by both endogenous [see also Hopfinger et al., 2000] and exogenous signals [see also de Fockert et al., 2004], during reorienting of attention the frontoparietal attention network activates only for endogenous invalid trials [see also Corbetta et al., 2008 for a recent review on this point]. A dorsal-ventral segregation in the fronto-parietal network has also been observed in another study that examined separately the cue and target activity [Hahn et al., 2006]. Hahn and colleagues introduced a novel paradigm where endogenous and exogenous task-components were weighted to a greater or smaller degree in the different conditions, by means of a parametric manipulation of the predictability of the target location. In no-target trials, cue-dependent signal changes, increasing linearly with more precise spatial cueing, were found in a network comprising left intraparietal sulcus, left inferior and superior parietal lobule, bilateral precuneus, middle frontal gyri, and middle occipital gyri. Conversely, in target trials a different set of regions activated with decreasing target predictability (i.e. bilateral temporoparietal junction, cingulate gyrus, right precentral gyrus, right insula, fusiform and lingual gyri, cuneus). However, it should be noted that nei-

ther this nor the studies mentioned above manipulated endogenous and exogenous cueing conditions as independent factors within the same trial. Thus, these studies could not directly investigate the interaction between the two types of signals during reorienting of spatial attention (i.e. the interplay between stimulus-driven reorienting towards a task-relevant target and stimulus-driven effects related to task-irrelevant exogenous cues).

In a recent behavioral study, Berger et al. [2005] combined both types of cues within a single trial (double-cue paradigm) and crossed factorially cue-type (endo/exo) and cue-validity (valid/invalid) seeking an interaction or independence between the endogenous and exogenous spatial processes. The results of this study revealed additive effects of both types of cues across a variety of visual detection and discrimination tasks, demonstrating that endogenous and exogenous signals jointly affect target processing, but also that they do so in an independent manner.

A few studies exploited this type of paradigm during ERPs (event-related potentials) or fMRI recording. Using ERPs, Hopfinger and West [2006] showed that exogenous and endogenous cues modulate evoked potentials independently, enhancing visual processing regardless of the spatial congruence of the other cue. Each signal was found to dominate a specific processing stage, namely an early stage for the exogenous cues (80–120 ms post stimulus onset) and a later stage for the endogenous cues (300–400 ms). In the time window between these two stages, ERPs were affected by both signals but in an independent manner. These ERP results provide evidence of the independence of endogenous and exogenous attention mechanisms, but they cannot identify the anatomical substrate underlying these separate effects because of the limited spatial resolution of ERP. Using fMRI, Thomsen et al. [Thomsen et al., 2005] presented nonpredictive peripheral cues and predictive central cues simultaneously on the same trial, conveying conflicting information about the likely target location. This showed greater behavioral costs for invalid exogenous when compared with invalid endogenous cues, with a corresponding activation of prefrontal cortex (cingulate gyrus, FEF, middle and inferior frontal gyri). However, the timing of the stimuli (the two cues were presented simultaneously for 200 ms, followed by a 300 ms delay between the cue and the target) was optimal for the engagement of exogenous processes, but unsuitable for the endogenous cues to develop their maximal effect. This could explain the rather surprising result of this study with greater costs for exogenous than endogenous invalid trials. Furthermore, this study included only conflicting-cues trials and therefore did not allow investigating the interplay between endogenous and exogenous spatial cues that would instead require the full factorial combination of cue-type and validity [cf. Berger et al., 2005].

In the present study, we used whole-brain event-related fMRI crossing factorially the validity of endogenous and exogenous cues in a double-cue paradigm (i.e. yielding congruent or conflicting conditions). Unlike previous studies

[Thomsen et al., 2005], here the timing of the stimuli was chosen so as to obtain optimal facilitatory effects for both types of cues. The stimulus onset asynchrony (SOA) between cues and target was selected to give the former enough time to develop a maximal facilitation [Müller and Rabbitt, 1989]. Moreover, to make it unlikely that exogenous facilitation would be replaced by inhibition of return (IOR) we used a fixed order of cue presentation (with endogenous cues always coming first) and asked participants to perform a forced choice visual discrimination rather than a simple RT task. Thus in our cue-sequence the endogenous signal has enough time to develop its own full effect (with a relatively long cue-to-target SOA, 1,400 ms see Methods), whereas the exogenous cue preceded the target by only a short SOA (100 ms). Using the reverse order, the exogenous cue would lead the target by at least the (long) SOA between endogenous cue and target. This would most probably result in IOR rather than exogenous facilitation [cf. Berger and Henik, 2000], although it has been demonstrated that with choice RTs, as used in the present study, a much longer SOA (well beyond the present 100 ms) than with simple RTs is needed for IOR to occur [e.g. Lupiáñez et al., 2001].

In keeping with previous behavioral findings, we predicted that the two cues would jointly affect the behavioral response to the target, but also that each cue would act independently yielding additive effects, with each invalid signal generating a similar cost irrespective of the validity of the other cue [see Berger et al., 2005]. The fMRI data should provide us with new insights on the neural basis of the interplay between endogenous and exogenous factors (joint effects, but independent mechanisms). We expected activation of the ventral fronto-parietal network for targets presented on the opposite side of the endogenously cued location [endogenous invalid trials; see Arrington et al., 2000; Corbetta et al., 2000; Kincade et al., 2005; Macaluso et al., 2002]. Critically, here for the first time we could investigate whether exogenous cues presented in the time window between the endogenous cue and the target would influence the reorienting process to the invalid endogenous signal. This might result in a further increase of activity in the ventral fronto-parietal network when the exogenous cue confirms the endogenously cued side (congruent double-cue trials, with both cues invalid). Alternatively, we may find that the validity of the exogenous cues does not modulate the ventral fronto-parietal network expected to activate for spatial reorienting in endogenous invalid trials. This would suggest a separation between the processing of task-relevant and task-irrelevant stimulus-driven signals (i.e. targets on invalid endogenous trials and exogenous cues), even when these occur within the same trial and both affect the behavioral performance.

METHODS

Participants

Twenty-two healthy volunteers (15 females; mean age 24 years) participated in the study. All participants were

right-handed and had normal or corrected (with contact lenses) visual acuity. All of them received an explanation of the procedure and gave written informed consent. The study was approved by the independent Ethics Committee of the Fondazione Santa Lucia (Scientific Institute for Research Hospitalization and Health Care).

Paradigm

Figure 1A shows a schematic depiction of one trial that started with a central informative cue signaling the most likely location of the target (validity: 75%; also note that to minimize automatic orienting we used complex multicolor endogenous cues, see below). Directional central cues were used on 67% of trials, whereas endogenous neutral (spatially non-predictive) cues were used in the remaining trials. After 1,300 ms, a noninformative peripheral cue (50% valid, 50% invalid) was briefly flashed in one hemifield and was immediately followed by the target stimulus. Accordingly, the design was $3 \times 2 \times 2$: endogenous side (left, right or neutral) $\times$ exogenous side (left/right) $\times$ target side (left/right). These conditions yielded endogenous valid and invalid trials, with congruent or incongruent exogenous cues (see also Fig. 1B). The task of the subject was to discriminate the orientation of the target, irrespective of validity, congruence, and side of cues. All conditions were randomly intermixed.

Stimuli and Task

The visual stimuli were back-projected on a screen behind the magnet. Subjects laid in the scanner and viewed the visual display through a mirror mounted on the MRI headcoil (total display size 14 degrees of visual angle, $1,024 \times 768$ screen resolution, 60 Hz refresh rate). Stimulus presentation was controlled with Cogent2000 (www.vislab.ucl.ac.uk/Cogent/). During the inter trial interval (ITI), the display consisted of two dark-gray arrowheads in the centre of the screen (subtending 1×1 degrees), and two dark-gray boxes (each 2×2 degrees wide) located 5 degrees to the right and to the left of centre. At the beginning of each trial, the arrowheads became colored, one yellow and one magenta. Before MR scanning, each subject was instructed to pay attention to one color only (yellow or magenta), because this would predict the likely location of the target on 75% of the trials. The central cues were presented for 500 ms and, then, dimmed again to gray for 800 ms before displaying the peripheral cue for 100 ms. This exogenous cue consisted of a brightening and thickening of one of the two boxes. At the offset of the peripheral cue, the target was presented for 100 ms.

The SOA between cues and target was fixed and selected to give each cue enough time to develop an optimal effect [Müller and Rabbitt, 1989]. In particular, there was a 1,400 ms SOA (500 ms cue duration plus 800 ms

background plus 100 ms exogenous cue duration) between endogenous cue and target and a 100 ms SOA between exogenous cue and target (corresponding to the duration of the exogenous cue). Endogenous orienting of attention was likely to start and develop at the offset of the central cue, as subjects had to first process the complex multicolor central cue. Therefore, central and peripheral cues were likely to develop their maximal effects at the time of presentation of the target (i.e. 1,400 and 100 ms after the onset of the endogenous and exogenous cues, respectively).

The target was similar to the capital letter “E” pointing either upwards (i.e. an “E” tilted 90° anti-clockwise) or downwards (90° clockwise tilt). The task of the subject was to report the up/down orientation of the target by pressing as quickly and correctly as possible one of two adjacent buttons arranged vertically on a keyboard. The two index fingers were used to press the buttons one for upward and the other for downward stimuli. Stimulus-response mapping was always compatible (i.e. upper button for “up” and lower button for “down” responses). The hand used to press the up/down keys changed across fMRI-runs of the same subject, following an ABAB order. The duration of one trial was 3,500 ms (range: 3,000–4,000 ms).

Each participant completed a total of 576 trials, with 72 repetitions for each of the four endogenous valid conditions (left/right endogenous cues, with exogenous cues congruent or incongruent), 24 for each of the four endogenous invalid conditions (left/right endogenous cues, with exogenous cues congruent/incongruent), and 48 for each of the four endogenous neutral conditions (with left/right and valid/invalid exogenous cues). The imaging session was divided into four separate fMRI-runs, each with 144 trials. Before MR scanning, each subject practiced the task outside the scanner for 288 trials.

Image Acquisition

A Siemens Allegra (Siemens Medical Systems, Erlangen, Germany) operating at 3T and equipped for echo-planar imaging (EPI) acquired functional magnetic resonance 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 (3×3 mm, 2.5 mm thick, 50% distance factor, repetition time = 2.08 s, time echo = 30 ms), covering the entirety of the cortex.

Eye Tracking

Eye position on the screen was recorded during fMRI using an ASL eye tracking system that was adapted for the use in the scanner (Applied Science Laboratories, Bedford, MA; Model 504, sampling rate 60 Hz). Eye-position traces were examined in a 2,000 ms window, beginning

Figure 1.

A: Schematic depiction of the series of events occurring during one trial. At the beginning of the trial, a central multicolor cue signaled the most likely side (validity: 75%) of the target (the right or left hemifield, according to the instruction of paying attention to the yellow or the magenta arrow, respectively). After 1,300 ms a noninformative peripheral cue was briefly (100 ms) flashed in one hemifield. At the offset of the exogenous cue, the target stimulus was displayed for 100 ms. The target was a symbol resembling a tilted “E,” pointing upwards (like in the example) or downwards. The task of the subject was to discriminate the up/down orientation of the target. **B:** The experimental design, combining factorially cue-type (endogenous [Endo] and exogenous [Exo]) by cue-validity (valid, invalid, and neutral; the latter for endogenous cues only). For simplicity, the

additional factor of “target side” is not shown here. Also, the conditions’ labels refer to subjects that were instructed to attend to the yellow arrowhead. **C:** Behavioral performance during fMRI scanning. Blue bars in the graph represent mean RTs (plus standard errors) for each of the six combinations given by the crossing of validity and cue-types (averaging across left/right side). Errors (bars in magenta) comprised incorrect responses, misses, anticipations, and retards. White and yellow bars represent costs (invalid minus valid trials) for exogenous and endogenous cues, under the different levels of the other cue. Data show overall larger costs for endogenous than exogenous cues. Importantly, the size of these effects was unaffected by the validity of the other cue (except for the costs of invalid exogenous cues under endogenous neutral conditions, see the main text).

200 ms before the onset of the endogenous cue and ending 400 ms after the onset of the target. Loss of fixation was identified as change in horizontal eye position exceed-

ing $\pm 2^\circ$ of visual angle for at least 100 ms. Eye position was not monitored in one participant because of technical problems with the eye-tracking system.

Data Analysis

Inclusion criteria

Behavioral and imaging data were analyzed for subjects who showed reliable effects of the endogenous cues, thus demonstrating to comply with the instruction of paying attention to the relevant-color central cues. Four subjects were excluded as they did not show any cost related to the endogenous cues (mean valid trials = 670 [85] ms; mean invalid trials = 668 [80] ms). In addition, we only analyzed data of subjects who were able to perform the task with good accuracy, while maintaining central fixation. The discrimination task was relatively difficult, requiring to judge the position of the horizontal segment of the target (which crossed the shorter vertical segments and could be positioned slightly above or below the mid-line, see Fig. 1) in peripheral vision, while ignoring any intervening exogenous task-irrelevant cue. Four subjects were excluded due to excessive loss of fixations or incorrect responses. We evaluated each subject's performance straight after fMRI scanner and assigned the color schedule to the next subjects so as to maintain the balance between the subjects attending yellow and magenta arrows. Thus, for the final analyses we retained fourteen (9 females, mean age 23.7 years) out of the twenty-two participants, half of whom attended to yellow and half to magenta cues.

Imaging data

We used SPM5 (www.fil.ion.ucl.ac.uk) implemented in MATLAB 7.1 (The MathWorks, Natick, MA) for data preprocessing and statistical analyses. For all participants, we acquired 1,000 fMRI volumes, 250 for each run. The first four image volumes of each run were discarded to allow for stabilization of longitudinal magnetization, leaving a total of 984 volumes per subject. Preprocessing included rigid-body transformation (realignment) and slice timing to correct for head movement and slice acquisition delay. Slice-acquisition delays were corrected using the middle slice as reference. All the images were normalized to the standard SPM5 template and spatially smoothed with a Gaussian filter of 8 mm full-width at half maximum (FWHM) to increase the signal-to-noise ratio.

We used a conventional SPM approach to estimate the effects associated with the experimental design on a voxel-by-voxel basis using the general linear model. 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 12 conditions given by the crossing of our $3 \times 2 \times 2$ factorial design (endo cue [left/right/neutral] $\times$ exo cue [left/right] $\times$ target side [left/right], averaging across "up/down" targets), convolved with the SPM5 hemodynamic response function. In addition, for each subject, trials with losses of fixation or incorrect responses were modeled as separate event-types and excluded from any further analysis (10.7% of trials rejected

in total). Linear contrasts were used to determine responses for the 12 conditions of interest, averaging across the fMRI runs. This resulted in 12 contrast images per subject. The contrast images underwent a second step (group-analysis), comprising a within-subject analysis of variance (ANOVA) modeling the effect of the 12 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 aim of the study was to investigate visuo-spatial reorienting when cue and target were presented on opposite sides (invalid trials), critically examining these effects for the endogenous and exogenous cues and assessing whether any such effect is influenced by the validity of the other cue (validity by cue-type interaction). Thus, we compared trials containing invalid versus valid endogenous cues, collapsing across the validity of the exogenous cues; and we contrasted all trials containing invalid versus valid exogenous cues, irrespective of the validity of the endogenous cues. Within these regions, we then tested for cue-type by validity interactions, and we contrasted invalid minus valid endogenous (or exogenous) trials, separately for trials with valid and invalid exogenous cue (or valid, invalid, and neutral endogenous cue). Importantly, the direct comparison of invalid versus valid trials allowed us to compare conditions that are well-matched in term of "low-level processes" (similar stimulation and motor requirements during cue and target periods in all conditions) as well as some "higher level processes," such as interpretation of the central cue (e.g. arbitrary association of color and side), covert discrimination of peripheral targets (while maintaining central fixation), voluntary shift of attention toward the cued location, holding task rules in working memory, and performance monitoring.

In addition, we tested for the effect of the volitional deployment of spatial attention contrasting valid endogenous trials versus neutral endogenous trials (i.e. informative versus noninformative central cues). Note that unlike the direct comparison of invalid minus valid endogenous trials (where the two trials started differing only upon presentation of the target), in this comparison several factors may contribute to the activation pattern, including the strategic decision to shift voluntary attention toward the cued location and the maintenance of covert attention to one side while waiting for the target stimulus. However, the sensory stimulation during endogenous neutral trials differed only very little from valid/invalid cues, entailing just a slightly different spatial arrangement of the colored-lines that formed the central cue (see Fig. 1). On the other hand, the analogous contrast (spatially-directed vs. neutral trials) for the exogenous cues would have entailed major sensory differences between conditions (e.g. using simultaneous brightening/thickening of the two boxes in the left and

right hemifields, as exogenous neutral cues). Because of that, here we choose not to include this type of trials (exogenous neutral), focussing on spatially congruent/incongruent exogenous cues instead.

Finally, we analyzed side-specific effects in occipital visual cortex to reveal possible synergic action of the validity of the two cues in boosting visual responses. We highlighted contralateral visual areas responding to the lateralized stimulation comparing trials with left versus right targets (and vice versa), and we then assessed responses within these region as a function of the side of the two cues. Critically, in our design the side of the exogenous cue and the side of the target were manipulated in an orthogonal manner. Therefore, we could compare all trials containing left targets (half of which included left exogenous cues and half included right exogenous cues) with all trials containing right targets (again, with half including left-side and half including right-side exogenous cues). This allowed us to test for the effect of target side, irrespective of the position the exogenous cues (i.e. subtracting out the contribution of the peripheral exogenous cues). Analogous contrasts tested for the effect of left minus right (and right minus left) exogenous cues, subtracting out any effect related to the target side.

For all comparisons, the SPM threshold was set to P -corrected < 0.05 at the cluster level (cluster size estimated at voxel-level threshold of P -uncorrected $= 0.001$), considering the whole brain as volume of interest.

RESULTS

Behavioural Data

For the behavioral analyses, mean RTs were calculated collapsing across left/right target side and excluding incorrect responses, misses, anticipations (RTs < 140 ms), and retards (RTs $> 1,500$ ms). Overall, we discarded 4.2% of trials, without any difference between the conditions (see also Fig. 1C, in magenta). A within-subject 3×2 ANOVA tested for the main effect of endogenous validity (valid, invalid, and neutral), the main effect of exogenous validity (valid, invalid), and the interaction between the two factors (which is equivalent to the effect of congruence of the two cues). This revealed significant main effects for both the endogenous ($F(2, 26) = 30.1, P < 0.001$) and the exogenous cue ($F(1,13) = 36.4, P < 0.001$). Endogenous valid cues speeded up responses when compared with neutral cues (mean [SD]: valid 576 [70] ms, neutral 596 [81] ms; $t(13) = 4.1, P < 0.001$), whereas the invalid cues slowed down the RTs (invalid 661 [94] ms; invalid vs. neutral $t(13) = 5.7, P < 0.001$). The exogenous valid cues speeded up responses when compared with exogenous invalid cues (596 [78] ms versus 626 [81] ms, $t(13) = -6, P < 0.001$), confirming a reliable facilitation at the cued location also for nonpredictive peripheral signals.

The 3×2 ANOVA also showed a significant interaction between the endogenous and exogenous cue validity ($F(2,$

$26) = 5.15, P = 0.013$). This was due to the small costs of invalid exogenous cues when the endogenous cue was neutral (see Fig. 1C). However, neutral endogenous cues do not require any focusing of attention to one spatial location and, therefore, are unsuitable to investigate the interactions between the endogenous and exogenous spatial factors in attention control. Accordingly, we performed a second 2×2 ANOVA, now dropping the neutral level of endogenous cues. This replicated the two main effects of cue validity (both P -values < 0.001), but now the interaction was not significant ($F(1, 13) = 1.8, P = 0.2$). To further confirm the independence of endogenous and exogenous cueing effects, we tested for the effect of invalidity (invalid minus valid trials) of each cue type as a function of the validity of the other cue (see Fig. 1C, white and yellow bars). Overall, endogenous cues yielded larger costs than exogenous cues (about 80 ms vs. 30 ms, respectively), although the size of these effects was unaffected by the validity of the other cue (except for the effect of the exogenous cues under neutral endogenous cues, see above).

In summary, RT during MR scanning is in good agreement with previous behavioral evidence [see Berger et al., 2005]. We found that both the endogenous and the exogenous valid cues speed up target discrimination, but they do so in an independent manner without any significant effect of cue congruence (i.e. interaction cue-type by validity).

FMRI Data

Spatial reorienting following endogenous invalid cues

The initial analysis concerned the effect of invalid minus valid endogenous cues, irrespective of the validity of the exogenous cues. This comparison aimed at highlighting the neural circuits underlying reorienting of attention when spatial resources were first voluntarily focused in one hemifield, but the target was then presented in the opposite hemifield. A significant signal increase was found within a distributed network of fronto-parietal areas, which appeared to include parts of both the dorsal and ventral fronto-parietal attention system [see Fig. 2A and Table I; cf. also Corbetta and Shulman, 2002]. Foci of activation were found in the inferior parietal cortex bilaterally (including the angular gyrus, the supra-marginal gyrus, and the posterior part of the superior temporal cortex) and in almost the entirety of the premotor cortex in the frontal lobe. Activation extended from the inferior frontal gyrus (a key region of the ventral attentional system) dorsally to the middle frontal gyrus and to the FEF.

The signal plots in Fig. 2A show that reorienting of endogenous attention was unaffected by stimulus-driven processes triggered by the exogenous cues. Indeed, the increase of activation both in dorsal and ventral structures was independent from the validity of the peripheral non-predictive cues (compare bars 1 and 2 versus bars 5 and 6, for valid exogenous trials; and bars 3 and 4 versus bars 7

Figure 2.

A: Spatial reorienting following endogenous invalid cues. Surface-rendered sagittal projections of statistically significant activation for invalid minus valid endogenous trials, overlaid on the SPM5 anatomical template. Signal increase was found within a distributed network of cortical areas, including both dorsal and ventral fronto-parietal regions. Signal plots show the estimated activity for Endo_{INV} and Endo_{VAL} (invalid and valid endogenous) trials, both with Exo_{VAL} and Exo_{INV} (valid and invalid exogenous cues) and for targets on the left or right side (Tg_{LEFT}/Tg_{RIGHT}). The signal plots demonstrate greater activation for endogenous invalid compared to valid trials, irrespective of the validity of the

exogenous cue and the target side. Activity is adjusted to a mean of zero and is plotted in arbitrary units (a.u., error bars are 10% confidence interval). FEF, frontal eye field; AngG, angular gyrus; TPJ, temporo-parietal junction. **B:** Spatial reorienting following exogenous invalid cues. Brain activity related to reorienting after an invalid deployment of exogenous attention revealed by the direct comparison of invalid versus valid exogenous trials (Exo_{INV} minus Exo_{VAL}). Surface-rendered projections show bilateral activation of the posterior part of the middle temporal gyrus, around the temporo-occipital junction (P -uncorrected < 0.001).

and 8, for invalid exogenous trials; in Fig. 2A). To further explore possible interplays between the effects of the two cues, we computed cue-type by validity interactions (corresponding to the effect of cues coherence). This did not reveal any significant effect within this network, which

was also unaffected by reorienting after invalid exogenous cues (see also below). To confirm that endogenous invalid trials affected activity in these regions irrespective of the validity of the exogenous cues, we compared invalid against valid endogenous trials (cost of endogenous reor-

TABLE I. Spatial reorienting following endogenous invalid cues (invalid > valid trials)

Main effect								sME exo V				sME exo I			
Area	Clust size (in voxels)	<i>P</i> -corr	Hemisph	MNI coordinates			Z-scores	MNI coordinates			Z-scores	MNI coordinates			Z-scores
				<i>x</i>	<i>y</i>	<i>z</i>		<i>x</i>	<i>y</i>	<i>z</i>		<i>x</i>	<i>y</i>	<i>z</i>	
SMA	2,565	<0.001	M	6	10	68	4.75	0	12	66	3.66	6	8	68	4.10
FEF			L	−10	16	66	5.05	−8	14	68	4.03	−10	18	64	3.97
			R	24	8	56	5.30	18	16	60	3.46	24	8	56	5.76
SPL	2,043	<0.001	L	−8	−68	54	4.65	−6	−62	52	3.96	−10	−68	52	3.56
			R	8	−64	54	4.22	8	−62	54	3.43	10	−70	54	3.46
AngG			R	56	−42	36	4.67	56	−44	34	3.22	54	−44	40	4.03
TPJ			R	58	−44	20	4.48	54	−46	18	4.21	58	−44	22	2.74
MFG	1,347	<0.001	R	44	12	32	4.65	42	12	32	3.84	44	10	22	3.40
IFG			R	54	18	2	4.25	54	20	0	3.17	58	20	4	3.38
AngG	656	<0.001	L	−58	−48	34	4.45	−58	−48	32	2.99	−58	−50	36	3.82
IPS			L	−36	−46	44	3.77	−38	−46	42	3.19	−32	−46	46	2.92

Group effect (P -corrected for multiple comparisons at cluster level), considering the whole brain as the volume of interest. Main effect of endogenous invalidity; and simple main effects, with valid exogenous cues (sME exo V) and with invalid exogenous cues (sME exo I). MNI coordinates in millimeters. M, medial; L, left; R, right. AngG, angular gyrus; FEF, frontal eye field; IFG, inferior frontal gyrus; IPS, intra-parietal sulcus; MFG, middle frontal gyrus; SMA, supplementary motor area; SPL, superior parietal lobule; TPJ, temporo-parietal junction.

ienting), separately for trials with valid and invalid exogenous cues. All areas showed consistent effects for these additional comparisons (simple main effects; cf. Table I columns on the right side).

Spatial reorienting following exogenous invalid cues

Brain activity related to reorienting following a pure stimulus-driven signal was examined by contrasting trials containing invalid versus valid exogenous cues. None of the dorsal or ventral regions involved in reorienting of endogenous attention showed increased activation for reorienting following invalid exogenous cues. The comparison invalid minus valid exogenous cues was associated with signal increase in the posterior part of the middle temporal gyrus, around the temporo-occipital junction (see Fig. 2B). However, this effect did not fully survive correction for multiple comparisons and it is reported here as a statistical trend only (P -uncorrected < 0.001). All the same, the symmetrical activation in the two hemispheres suggests that this effect did not arise by chance. This effect of invalid exogenous cues was present irrespective of the validity of the endogenous cue (i.e. no difference in the pattern of activation when comparing exogenous costs obtained in valid, invalid, and neutral endogenous conditions). These results, together with the above effects on invalid endogenous trials indicate a functional segregation of endogenous and exogenous mechanisms for reorienting of visuo-spatial attention (cf. Fig. 2 A,B).

Orienting of endogenous spatial attention

Together with the reorienting processes (invalid minus valid trials), our design also enabled us to explore the brain activity related to voluntary deployment of attention. To do that, we contrasted endogenous valid versus endog-

enous neutral trials, thus comparing activity in trials where central cues directed attention to the target location versus trials containing spatially nonpredictive central cues. Activation was observed bilaterally in both the anterior and posterior part of the dorsal fronto-parietal attentional network [see Fig. 3A and Table II; cf. also Corbetta and Shulman 2002]. The anterior cluster of activation was found at the junction of the precentral sulcus and the superior frontal sulcus and may include the FEF [Paus, 1996]. The posterior cluster included the SPL, extending into anterior and inferior segments of IPS. Additionally, this comparison revealed activation of the supplementary motor area (SMA).

The signal plots in Fig. 3 show that the endogenous deployment of attention was unaffected by the exogenous cues presented thereafter, regardless of whether conveying coherent (valid) or incongruent (invalid) signals. This was further confirmed by comparing valid against neutral endogenous trials (endogenous benefit), separately for conditions with valid exogenous cues (compare bars 1 and 2 versus bars 5 and 6, in Fig. 3) and invalid exogenous cues (compare bars 3 and 4 versus bars 7 and 8). The same pattern of activation was found for both types of exogenous cues.

Side-specific effects in occipital visual cortex

Finally, we identified visual areas responding to lateralized visual stimuli by examining activation within these regions as a function of target and cue side. As expected, these comparisons showed increased activation in occipital areas contralateral to the stimulated hemifield, see Figure 4. Activation associated with the targets was seen in dorso-lateral and ventral occipital cortex, comprising the inferior, middle, and lateral gyri (all P -corrected < 0.001). The lateralized, nonpredictive exogenous cues activated similar

Figure 3.

Orienting of endogenous spatial attention. Top panel: Surface-rendered sagittal projections of statistically significant activation for valid endogenous trials minus neutral endogenous trials overlaid on the SPM5 anatomical template. Increased activity was observed bilaterally in the dorsal fronto-parietal network. Central and bottom panels: Signal plots showing estimated activity for Endo_{VAL} and Endo_{NEUT} (valid and neutral endogenous) trials, both with Exo_{VAL} and Exo_{INV} (valid and invalid exogenous cues)

and for targets on the left or right side (Tg_{LEFT}/Tg_{RIGHT}). The plots demonstrate greater activation for valid (bars 1 to 4) than neutral (bars 5 to 8) endogenous trials, irrespective of the validity of the exogenous cue and the target side. Activity is adjusted to a mean of zero and is plotted in arbitrary units (a.u., error bars are 10% confidence interval). FEF, frontal eye field; SPL, superior parietal lobule; L, left; R, right.

areas (all P -corrected < 0.001 ; cf. also overlaid projections for targets [red] and exogenous cues [green] on the coronal sections, in Fig. 4A,B). Signal plots revealed that activity in each hemisphere corresponded to the linear sum of the activation associated with exogenous cues and targets, without

any significant synergic action of the two cues. This yielded a maximal activation in occipital cortex when both the exogenous cue and the target were presented in the contralateral hemifield (see bars 1, 5, and 9 in Fig. 4A, for the left hemisphere; and bars 2, 6, and 10 in Fig. 4B, for the right hemisphere).

TABLE II. Orienting of endogenous spatial attention (valid > neutral trials)

Area	Cluster size (in voxels)	<i>P</i> -corrected	Hemisphere	MNI coordinates			Z-scores
				<i>x</i>	<i>y</i>	<i>z</i>	
SMA	1,472	<0.001	M	−2	−2	62	4.5
FEF			L	−28	−4	56	7.2
SPL	1,498	<0.001	L	−20	−64	60	5.8
ant IPS			L	−30	−52	56	6.7
inf IPS			L	−32	−38	44	3.7
FEF	930	<0.001	R	28	−2	54	6.4
SPL	728	<0.001	R	26	−62	64	4.7
inf IPS			R	32	−36	40	3.7

Group effect (*P*-corrected for multiple comparisons at cluster level), considering the whole brain as the volume of interest. MNI coordinates in millimeters. M, medial; L, left; R, right. Ant/inf IPS, anterior/inferior segment of the intraparietal sulcus; FEF, frontal eye field; SMA, supplementary motor area; SPL, superior parietal lobule.

sphere). Nonetheless one should note that the overlapping activation may indicate that the same neural population responded both to task-irrelevant exogenous cues and to targets, providing a possible substrate for the behavioral advantage observed for exogenous valid trials (i.e. when both stimuli are on the same side, see also Fig. 1C).

DISCUSSION

We used whole-brain event-related fMRI and a spatial double-cueing paradigm to investigate behavioral and BOLD responses to endogenous and exogenous attentional signals that were concurrently presented on the same trial. We obtained behavioral evidence of the functional independence of spatial reorienting mechanisms following goal-directed (endogenous) and stimulus-driven (exogenous) signals. Both exogenous and endogenous cues affected RTs to peripheral targets, but with each cue developing its own typical effect without interacting with the other. The influence of the two cues on performance added up linearly and generated largest benefits and costs in trials where they were congruent as compared to trials with conflicting cues. Functional imaging data showed that only reorienting signals following endogenous invalid cues modulated activity in the ventral fronto-parietal attentional network. On the other hand, exogenous invalid cues affected activity in the occipito-temporal junction. The pattern of activation associated with each signal was independent from the effect (valid/invalid) of the other cue. These findings suggest a separation of endogenous and exogenous mechanisms for the reorienting of spatial attention.

Our behavioral data are in line with findings from a previous study that used the double-cue paradigm [Berger et al., 2005] and demonstrated that functional independence between the exogenous and endogenous attention generalizes across a variety of visual-motor tasks; see, for a direct comparison with our study, the fourth experiment and, specifically, the condition where SOA between the exogenous cue, and target was 100 ms. However, one should consider that behavioral data alone are insufficient to

assess whether the neural mechanisms underlying goal-directed and stimulus-driven attention are subserved by anatomically distinct circuits.

Our fMRI data highlighted a bilateral activation of the dorsal fronto-parietal network when attention was deployed following an endogenous signal (see Fig. 3, spatially-predictive versus neutral non-predictive cues). The involvement of dorsal fronto-parietal regions in endogenous spatial attention is in agreement with previous data of activity increase in these regions following presentation of informative cues [e.g. Corbetta et al., 2000; Hahn et al., 2006; Hopfinger et al., 2000; Kincade et al., 2005]. Here, we also found activation of the dorsolateral aspect of the premotor cortex, including putative human FEF [Paus, 1996] and the IPS/SPL in the posterior parietal cortex. These regions are key nodes of a bilaterally distributed circuit that contributes to the top-down control of spatial attention [Corbetta and Shulman, 2002]. Its prominent role in generating signals for covert shifts of visual attention in space is long-acknowledged [e.g. Perry and Zeki, 2000; Yantis et al., 2002]. Recent studies [Kelley et al., 2008] have thrown light on the specific contribution of distinct sub-components of the dorsal system (all responding to endogenous cues in the present study) to the different operations involved in voluntary shifts of attention. Specifically, medial regions of premotor cortex (including SEF) and SPL would generate transient activity for disengaging attention from fixation and moving it to a new location [Kelley et al., 2008; see also Yantis et al., 2002]. By contrast, activity in lateral premotor regions (FEF) and IPS would represent sustained maintenance of peripheral attention [Kelley et al., 2008]. This functional modularity is also consistent with the differential role of the dorsal parietal areas in remapping attentional priorities when a target appears to a new spatial location. Thus, SPL would track the locus of spatial attention by encoding changes in spatial co-ordinates [Molenberghs et al., 2007], whereas IPS (and FEF) would index the current locus of attention in the visual field and, ultimately, guide targeted motor interactions with the environment [Serences and Yantis, 2007]. This

Figure 4.

Side-specific effects in occipital visual cortex. Brain activity related to the processing of (A) left-sided targets revealed by the direct comparison of left versus right targets trials (Tg_{LEFT} minus Tg_{RIGHT}) and (B) right-sided targets revealed by the comparison of right versus left targets trials (Tg_{RIGHT} minus Tg_{LEFT}). Surface-rendered projections both in A and B show activation of dorso-lateral and ventral occipital cortex contralateral to the stimulated hemifield. The coronal sections, showing overlaid projections for activity related to A left targets and left exogenous cues (Exo_{LEFT} minus Exo_{RIGHT}) and B right targets and right exogenous cues (Exo_{RIGHT} minus Exo_{LEFT}), indicates that targets and cues acti-

vated similar areas. Signal plots show estimated activity for Tg_{LEFT} and Tg_{RIGHT} , both with Exo_{VAL} and Exo_{INV} (valid and invalid exogenous cues) and for $Endo_{VAL}$, $Endo_{INV}$ and $Endo_{NEUT}$ (valid, invalid and neutral endogenous) trials. The plots demonstrate maximal activation in occipital cortex when both the exogenous cue and the target were presented in the contralateral hemifield (see bars 1, 5, and 9 in A, for the left hemisphere; and bars 2, 6, and 10 in B, for the right hemisphere). Activity is adjusted to a mean of zero and is plotted in arbitrary units (a.u., error bars are 10% confidence interval). IOG, inferior occipital gyrus.

would also comprise encoding of behavioral valence of sensory changes in a spatially selective manner [Molenberghs et al., 2007] and engaging in working memory processes to support task performance [e. g. La Bar et al., 1999; Sala et al., 2003].

In keeping with previous studies, we found activation of more ventral fronto-parietal regions when a mismatch between expectation and sensory input occurred, that is, in trials with invalid endogenous cues [cf. Arrington et al., 2000; Corbetta et al., 2000; Kincade et al., 2005; Macaluso et al., 2002]. The foci of activation included the middle and inferior gyri in the frontal cortex, the angular gyri in the parietal cortex, and the TPJ at the intersection between the inferior parietal lobule and the superior temporal gyrus. All these regions are part of the ventral attention system specialized for the detection of unexpected events [e.g. Corbetta et al., 2000], with the TPJ that has been described as a circuit-breaker for ongoing processes in the dorsal system, redirecting attentional resources toward novel sensory events [Corbetta and Shulman, 2002; Corbetta et al., 2008]. Our data highlight that the pattern of fronto-parietal activation observed during reorienting to targets after invalid endogenous signals was unaffected by exogenous cues, regardless of whether there was spatial congruence or incongruence between the two cues (no validity $\times$ cue-type interaction). Thus, the effect of reorienting from an endogenously cued location to the target location was similar when the exogenous cues confirmed the cued location (congruent, invalid exogenous cues) as when these drove attention toward the target location in a stimulus-driven manner (incongruent, valid exogenous cues). This indicates that both dorsal and ventral fronto-parietal attentional regions are seemingly unaffected by salient but task-irrelevant exogenous signals. The present data are in line with evidence obtained in a previous study [Kincade et al., 2005] by comparing target-related activity after invalid endogenous and exogenous cues presented in separate blocks of trials. Importantly, our data extend previous results showing that even in the context of a double-cue paradigm the ventral fronto-parietal network activates only for reorienting toward stimuli that are strictly related with the task. This was true despite the fact that the double-cue paradigm maximizes the interplay between endogenous and exogenous mechanisms of attention control, triggering both types of processes within the same trial.

Our fMRI findings are also consistent with a growing body of evidence indicating that effectiveness of external signals in triggering fronto-parietal attentional processes largely depends on factors related to the ongoing task setting, rather than to mere sensory salience [Indovina and Macaluso, 2007; Kincade et al., 2005]. For example, fMRI studies of visual detection and discrimination showed that only unexpected targets [e.g. Corbetta et al., 2000; Kincade et al., 2005] or distracters with task-relevant properties [Serences et al., 2005] engage the ventral attentional system (right IFG and TPJ). In addition, TPJ was found to deactivate in response to irrelevant distracters [Shulman et al.,

2003], with larger deactivation when subsequent targets were detected than missed [Shulman et al., 2007]. Furthermore, the set of potentially interfering stimuli filtered out by TPJ [Shulman et al., 2007] was proven to substantially vary according to the presence of a behavioral context [Downar et al., 2001] and its demands [Todd et al., 2005].

Altogether, our data support the anatomical model of human attention proposed by Corbetta and colleagues [2002; 2008], according to which the dorsal fronto-parietal system would be involved in spatial orienting, being specialized to prepare, maintain, and reprogram attentional sets associated with goal-directed stimulus-response selection. Some evidence suggests that the dorsal system can be engaged by exogenous, task-irrelevant signals as well [e.g. de Fockert et al., 2004; Kincade et al., 2005]. Here, we could not test for the specific effect of deployment of exogenous attention because our design did not include neutral exogenous trials. Nevertheless, we show that the pattern of activity within the dorsal system in response to endogenous cues did not change as a function of the validity of the exogenous cues. Thus, the spatial congruence between endogenous and exogenous cues did not yield any increased activation in the dorsal system, as expected if both types of cue would share a common neural substrate (but see also data revealing a possible differential effect of the distinct components of the exogenous orienting response, namely IOR versus facilitation, to activation within the dorsal system, cf. [Mayer et al., 2004]).

The present data confirm the segregation of dorsal and ventral attention systems during spatial orienting also with a double-cueing paradigm. As already noted (see Introduction), this was previously shown by separately analyzing cue and target related activity. Instead, here we crossed factorially the validity of endogenous and exogenous spatially-directing cues, thus avoiding some of the limitations associated with the separation of cue and target activity on a single trial basis [e.g. unexpected trial interruption in designs that used cue-only trials, e.g. Hahn et al., 2006; Macaluso et al., 2003; or changes of orienting strategy in studies that used very long cue-to-target intervals e.g. see Hopfinger et al., 2000; Kastner et al., 1999; Kincade et al., 2005].

It remains to be addressed at what stage the exogenous cues exerted their influence, as observed in the present behavioral data with a significant effect of exogenous cue validity (see Fig. 1C). When contrasting brain activity in trials with invalid versus valid exogenous cues, we observed bilateral activation of the posterior part of the middle temporal gyrus around the temporo-occipital junction (see Fig. 3B), although this effect did not reach full statistical significance (but note the symmetrical activation in the two hemispheres). These activations are potentially relevant because they suggest that the exogenous cues were processed, and even that their spatial relation with the subsequent target had an effect on brain activity (i.e. differential activation for invalid minus valid exogenous cues). This seems to rule out the hypothesis that the exogenous cues did not influence activity in the fronto-parietal system sim-

ply because they were entirely filtered out under conditions of focused endogenous attention (i.e. following a spatially-predictive endogenous cue). This hypothesis would also predict a different pattern of activation for invalid minus valid exogenous trials under conditions with neutral when compared with those with valid/invalid endogenous cues. On the contrary, our analysis comparing activation for invalid minus valid exogenous cues as a function of the validity of the endogenous cues did not reveal any difference in the pattern of activation for the three contrasts; $\text{Endo}_{\text{VAL}}/\text{Exo}_{\text{INV}} - \text{Endo}_{\text{VAL}}/\text{Exo}_{\text{VAL}}$, $\text{Endo}_{\text{INV}}/\text{Exo}_{\text{INV}} - \text{Endo}_{\text{INV}}/\text{Exo}_{\text{VAL}}$, and $\text{Endo}_{\text{NEUT}}/\text{Exo}_{\text{INV}} - \text{Endo}_{\text{NEUT}}/\text{Exo}_{\text{VAL}}$. Finally, our behavioral data show that the validity of the exogenous cues was present under all endogenous cueing conditions (even with numerically larger effects under conditions with valid/invalid than neutral endogenous cues, see Fig. 1C), again in contrast with the hypothesis that the exogenous cues were entirely filtered out in conditions of focused endogenous spatial attention.

Activation of the temporo-occipital cortex has been previously reported in studies of covert spatial attention. Gitelman et al. found activation of this region comparing an endogenous spatial cueing task versus a central attention baseline ([Gitelman et al., 1999], although note that valid and invalid trials could not be separated in this early blocked-fMRI study). The authors suggested that this region might provide a node of integration between ventral and dorsal streams for moving the focus of attention across the visual scene. In keeping with this suggestion, one possibility might be that when processing of task-relevant information engages the fronto-parietal system, as in the current study, then temporo-occipital cortex might independently process task-irrelevant exogenous signals. Interestingly, the temporo-occipital region activating for invalid exogenous trials in the present study colocalizes well with motion-sensitive areas as identified in human brain [DeYoe et al., 1996]. Thereby, one might also speculate that this activation relates to the processing of two peripheral events (cue and target) appearing in rapid succession at different spatial locations.

Another possible explanation for the behavioral effects associated with the validity of the exogenous cues (cf. Fig. 1C) is that they affected target processing at a relatively early stage within occipital visual cortex. This would be in keeping with ERP evidence obtained in another recent study that used the double-cue paradigm [Hopfinger and West, 2006; see the introduction for details]. Indeed, we found that exogenous cues activated contralateral occipital regions largely overlapping those activated by the targets, with maximal activation when both exogenous cue and target were on the same side (i.e. exogenous valid trials; see Fig. 3). Of course, this suggestion should be taken with some caution because of the inherent sensory confounds associated with the rapid presentation of the two stimuli (exogenous cue and target) at the same location, which is also likely to generate complex interactions between suppression and amplification in the fMRI responses [Murrey and Wojciulik, 2004; Murrey et al., 2006].

In summary, our results show that endogenous and exogenous factors independently influence reorienting of spatial attention even when concurrently engaged on the same trial. Focusing of endogenous attention according to spatially predictive cues produces facilitation in performance and activation of dorsal structures of the fronto-parietal attentional network. Ventral fronto-parietal regions are additionally recruited for redirecting attention toward task-relevant stimuli (targets) when these are presented at an unexpected location (invalid endogenous trials). By contrast, task-irrelevant peripheral cues did not affect activity within these (dorsal and ventral) fronto-parietal networks, despite also these cues affected target discrimination. These exogenous signals are likely to exert their influence at early stages of sensory processing affecting activity in occipital and temporo-occipital cortices. These results indicate the existence of separate neural circuits for the processing of the endogenous and exogenous signals that jointly contribute to the reorienting of spatial attention toward a previously unattended location.

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