# Control networks and hemispheric asymmetries in parietal cortex during attentional orienting in different spatial reference frames

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**Neuropsychological research has consistently demonstrated that spatial attention can be anchored in one of several coordinate systems, including those defined with respect to an observer (viewer-centered), to the gravitational vector (environment-centered), or to individual objects (object-centered). In the present study, we used hemodynamic correlates of brain function to investigate the neural systems that mediate attentional control in two competing reference frames. Healthy volunteers were cued to locations defined in either viewer-centered or object-centered space to discriminate the shape of visual targets subsequently presented at the cued locations. Brain responses to attention-directing cues were quantified using event-related functional magnetic resonance imaging. A fronto-parietal control network was activated by attention-directing cues in both reference frames. Voluntary shifts of attention produced increased neural activity bilaterally in several cortical regions including the intraparietal sulcus, anterior cingulate cortex, and the frontal eye fields. Of special interest was the observation of hemispheric asymmetries in parietal cortex; there was significantly greater activity in left parietal cortex than in the right, but this asymmetry was more pronounced for object-centered shifts of attention, relative to viewer-centered shifts of attention. Measures of behavioral performance did not differ significantly between the two reference frames. We conclude that a largely overlapping, bilateral, cortical network mediates our ability to orient spatial attention in multiple coordinate systems, and that the left intraparietal sulcus plays an additional role for orienting in object-centered space. These results provide neuroimaging support for related claims based on findings of deficits in object-based orienting in patients with left parietal lesions.**
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## Introduction

Selective attention enables us to focus awareness on a subset of the information present in a typical visual scene. Attention may be

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captured by events in the world in a bottom-up manner, but may also be deployed voluntarily to locations or objects using top-down control systems. The neural mechanisms responsible for the voluntary orienting of visual attention have been the subject of intense research over the past decade (Corbetta et al., 1993, 1995; Gitelman et al., 1999; Heinze et al., 1994; Hopfinger et al., 2000; Kastner et al., 1999; Martinez et al., 1999; Nobre et al., 1997; Weissman et al., 2002; Woldorff et al., 2004). A growing body of evidence suggests that a network of brain regions including superior frontal and posterior parietal cortices are involved in our ability to voluntarily direct attention, although it is unclear how this network is recruited in the face of differing demands placed on the attentional orienting system under different circumstances. For instance, how are the neuronal networks that underlie voluntary attention engaged when attention is deployed in different visual frames of reference?

Neuropsychological studies of hemispatial neglect patients have consistently demonstrated that visual selective attention can be anchored in one of several visual frames of reference (Behrmann, 2000). Although neglect has traditionally been defined as the inability to orient to, or appreciate information from, the "contralesional" visual field (e.g., the left visual field in patients with right parietal damage), recent evidence suggests that the neglected side of space need not be defined retinotopically. Orienting deficits have been observed within viewer-centered (Karnath et al., 1998; Kooistra and Heilman, 1989), environment-centered (Ladavas, 1987), and object-centered (Behrmann and Moscovitch, 1994; Driver et al., 1993; Marshall and Halligan, 1993) coordinate systems. Some patients show deficits that are grounded in multiple reference frames simultaneously (Calvanio et al., 1987; Farah et al., 1990), while still others appear to exhibit neglect in different reference frames depending on the nature of the task being performed (Behrmann and Tipper, 1999; Vuilleumier et al., 1999).

The neural systems that mediate our ability to orient attention in different frames of reference are not well understood. Some studies have reported results that are consistent with partial segregation of function. Fink et al. (1997a), for example, reported that object- and viewer-centered attention engaged a largely overlapping fronto-

parietal network, but that object-based attention resulted in increased activity in left striate and prestriate cortex, whereas viewer-based attention resulted in greater activity in the right dorsolateral prefrontal cortex as well as the right tempo-parietal junction. Marois et al. (1998), using fMRI, reported that object-based attention led to increased activity bilaterally in lateral occipital and fusiform gyri, but also in the medial superior frontal gyrus.

Egly et al. (1994a) have advanced a "hemispheric specialization" hypothesis, arguing that viewer-based and object-based spatial attention may rely more heavily on the right and left posterior parietal cortices, respectively. Using a visual pre-cueing paradigm, they demonstrated that normal observers were more severely impaired at shifting attention to a new object-based location (following an invalid cue) than to a new viewer- or space-based location. In addition, the difference in reaction times costs (between object- and viewer-based shifts) for locations in the contralesional visual field was much greater for patients with damage to the left parietal cortex relative to the right parietal cortex. Similarly, patients with a severed corpus callosum showed greater reaction time costs in the right visual field for shifts of attention to new object-based locations relative to viewer-based locations (following an invalid cue), but showed similar reaction time costs for such shifts in the left visual field (Egly et al., 1994b). These findings suggest that the two cerebral hemispheres are differentially involved in our ability to deploy attention in different visual frames of reference, and that our ability to orient in object-centered space relies more heavily on inferior parietal structures in the left hemisphere.

An alternative hypothesis is that the attentional control system has access to multiple frames of reference, and that the same neural circuitry underlies our ability to orient visual attention in multiple coordinate systems. Consistent with this "multiple frames" hypothesis is a recent study by Behrmann and Tipper (1999), which showed that reference frame effects in neglect could vary as a function of target expectancies and task demands. In this study, patients with unilateral (left) spatial neglect subsequent to right parietal damage were given a target detection task using locations that were defined in either viewer- or object-centered space. On different experimental runs, target probabilities were altered such that 80% of targets appeared in either viewer-centered or object-centered locations. When targets were more likely to appear in viewer-centered locations, the neglected hemifield was defined within a viewer-centered frame of reference. Conversely, when targets were more likely to appear in object-centered locations, the neglected hemifield was defined within an object-centered frame of reference. This hypothesis is bolstered by recent computational simulations of spatial representations in the parietal lobe (Pouget and Sejnowski, 1997, 2001; Pouget et al., 1999) in which damage produces simultaneous deficits in multiple visual frames of reference.

Given the findings reviewed in the foregoing, there are at least two possibilities, therefore, concerning the neural systems involved in orienting attention in different visual frames of reference. One hypothesis is that some degree of functional segregation underlies our ability to orient in different frames of reference (Fink et al., 1997a; Marois et al., 1998), with left posterior parietal regions (Egly et al., 1994a) being relatively specialized for shifting attention in object-centered space. Alternatively, attentional orienting systems in the brain may have access to multiple frames of reference and are therefore similarly activated while shifting

attention within multiple frames of reference (Behrmann and Tipper, 1999; Pouget and Sejnowski, 1997, 2001; Pouget et al., 1999). In the present study, we attempt to distinguish between these two competing alternatives using functional magnetic resonance imaging (fMRI).

Advances in functional neuroimaging have enabled researchers to examine the neural basis of spatial attention in the intact human brain with relatively high spatial resolution. Studies have shown that a network of brain areas, including portions of the superior frontal, superior and inferior parietal, and superior temporal cortices, play an important role in the control of voluntary attention (Corbetta et al., 1993, 1995, 2000; Gitelman et al., 1999; Heinze et al., 1994; Hopfinger et al., 2000; Kastner et al., 1999; Mangun et al., 1998; Martinez et al., 1999; Nobre et al., 1997). Recently, studies employing event-related fMRI techniques have begun to disentangle top-down or "executive" aspects of attentional control from other aspects of selective attention such as the consequential effects of attention on target processing systems. Hopfinger et al. (2000) and Corbetta et al. (2000; see also Giesbrecht et al., 2003; Weissman et al., 2002) showed that top-down attentional control involves a network of brain regions including inferior and superior parietal, as well as superior frontal cortices. These studies used a spatial cueing paradigm and an event-related fMRI approach that permitted the attentional control network to be distinguished from subsequent attentional effects on early visual processing of target stimuli or motor processes. Corbetta et al. (2000) also reported a dissociation between regions that responded to voluntary shifts of attention and those that responded to subsequent target detection, with cortical regions in and around the intraparietal sulcus being particularly important during top-down or voluntary shifts of attention (see also Giesbrecht et al., 2003; Kastner et al., 1999; Weissman et al., 2002; Woldorff et al., 2004).

Although these neuroimaging studies suggest that voluntary shifts of attention involve a fronto-parietal network, the reference frame in which these control mechanisms operate remains unclear. The goal of the current project was therefore to investigate directly the neural mechanisms involved in shifting attention within different frames of reference. The present study employs a rapid, event-related paradigm that has been used in a number of recent neuroimaging studies of attentional control (e.g., Weissman et al., 2002; Woldorff et al., 2004), while at the same time dissociating visual reference frames using techniques commonly employed in behavioral and neuropsychological settings. If there is hemispheric specialization within the attentional control network (Egly et al., 1994a), then activity in left parietal cortex should be particularly strong relative to the right parietal cortex during shifts of attention within an object-centered frame of reference. If, however, attentional control systems have equal access to both viewer- and object-based coordinate systems, consistent with the multiple frames hypothesis (Behrmann and Tipper, 1999), then voluntary shifts of attention in object- and viewer-centered space should engage attentional control circuits in the left and right parietal cortices to a similar degree.

## Materials and methods

### Participants

Sixteen young (mean age, 23y; range, 18–33y) volunteers from the Duke University community (eight male) were financially

compensated for their participation in this study. All participants gave informed consent in accordance with the requirements of the local human participants protection committee prior to testing. All participants were right-handed, native English speaking, neurologically intact individuals with normal or corrected-to-normal vision. In addition, all participants were naive concerning the hypotheses of the study.

### Apparatus

A commercial software package (Presentation; Neurobehavioral Systems; San Francisco, CA) was used to control stimulus presentation and response collection. Participants viewed all displays using VisuaStim XGA goggles (Resonance Technology, Inc.; Los Angeles, CA) within the MRI environment (FOV = $30°$, resolution = $640 \times 480$). All responses were recorded using a custom-built MR-compatible button box.

### Cueing paradigm

Participants performed a shape discrimination task based on the Posner cueing paradigm (Posner, 1980), illustrated in Fig. 1. Potential target locations were outlined at the beginning of each experimental run using one rectangular and two square markers. Square placeholders measured $3.75°$ in each direction, rectangular placeholders measured $3.75°$ vertically and $12.2°$ horizontally. The location of the placeholders was constrained in the following ways. First, the two square placeholders were always in opposite hemifields, and were equally likely to appear at any of four possible locations (upper or lower visual field centered at either $4.2°$ or $12.7°$ left or right of the vertical meridian, centered $5.6°$ above or below the horizontal meridian). Second, the rectangular placeholder was always positioned in the opposite horizontal hemifield (upper or lower) relative to the square placeholders, and was equally like to appear centered $8.5°$ to the left or right of the vertical meridian. This produced a total of eight combinations of square and rectangular placeholders, each of which was used in random order over the course of a single MRI acquisition (Fig. 1C). Target placeholders remained stationary for sequences of twelve trials (54 s) before being moved to different locations on the screen.

Participants were instructed to foveate a centrally presented fixation point (measuring $0.8°$) that was visible throughout each experimental run. At the beginning of each trial, instructive (100% valid[1]) cues were presented at fixation (duration = 250 ms) requiring participants to attend covertly (i.e., without explicit eye movements) to one of the outlined regions. Each cue consisted of a single colored letter (measuring $1.25° \times 1.25°$). The identity of the letter indicated the side of space to attend for that trial ("L" = left; "R" = right). The color of the letter (blue or yellow) indicated the appropriate reference frame for that trial. Letters presented in one color (e.g., yellow) indicated that the participant should attend to the square outlined region on their left or their right (i.e., "left" or "right" in viewer-centered space). Letters presented in the other color (e.g., blue) indicated that they should attend to the left or

right side of the rectangular outlined region, wherever it appears on the screen (i.e., "left" or "right" in object-centered space). The color of the letters and their instructional meanings were counterbalanced across participants.

After a short delay (stimulus onset asynchrony, SOA, of 1, 2, or 3 s presented equiprobably–total trial duration was 4.5 s in all cases), visual stimuli were presented briefly (100 ms) at all four locations on the screen. Participants were required to discriminate the shape of the target ("plus" or "asterisk", each measuring $2.8° \times 2.8°$) presented at the cued location, and to ignore the stimuli presented at the other three locations. Target and distracter stimuli were followed by a variable length delay (interstimulus interval, ISI, of 1150, 2150, or 3150 ms, presented equiprobably). The two possible target shapes ("plus" and "asterisk") were presented equally often at the cued location. In addition, "plus" and "asterisk" stimuli appeared with equal probability at each of the three uncued locations and therefore did not reliably predict the correct response on any trial. All target and distracter stimuli were embedded within noise patterns that consisted of black and grey checkerboards ($3.7° \times 3.7°$, composed of $0.2°$ squares).

Participants made responses using a MR-compatible button box with the index and middle fingers of their right hand (response mapping counterbalanced across participant) and were encouraged to respond as quickly and as accurately as possible. All trials had a total duration of 4.5 s.

### Event-related fMRI paradigm

The cueing paradigm described above was implemented within the context of a rapid event-related paradigm, developed by Woldorff et al. (2004). An important advantage of this technique over various previous event-related fMRI designs is that the temporal structure of experimental trials is more closely matched to those reported in most behavioral and electrophysiological studies of cognition (i.e., relatively short cue-target intervals and overall trial durations). One concern with this approach, however, is that it produces significant overlap of hemodynamic responses from different events within an experimental trial (e.g., cues and targets), as well as from adjacent trials. To deal with this issue, two techniques were employed to isolate hemodynamic activity associated with specific cognitive processes of interest both within and across trials: hierarchical trial structuring and first-order trial counterbalancing.

A hierarchical trial structure was used to implement the task described above. Specifically, three distinct trial types were included in the design in order to isolate cognitive operations involved in different aspects of a single experimental trial, such as processing attention-directing cues, or subsequent visual targets. The first trial type, Cue-Target trials (33% of all trials), consisted of an attention-directing cue followed by a to-be-discriminated visual target at SOAs of 1, 2, or 3 s as described above. The second trial type, Cue-Only trials (33% of all trials), consisted of an attention-directing cue followed by a 4250-ms blank interval, but did not include a visual target. A direct comparison between these two trial types reflects cognitive operations invoked specifically by target processing, such as selective stimulus processing for the to-be discriminated visual target, response selection and preparation, and motor execution. The use of evenly distributed, variable SOAs on Cue-Target trials made it difficult to predict whether or not a target would appear on any given trial, and thus it is unlikely that participants were able to categorize

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[1] Instructive (100% valid) cues were chosen because they are thought to engage focused attention more effectively than the typical predictive (i.e., less than 100% valid) cueing paradigm, since participants are never required to respond to uncued targets and, therefore, are unlikely to divide attentional resources across multiple locations (Bashinski and Bacharach, 1980; Downing, 1988; Hawkins et al., 1990; Mangun and Hillyard, 1991).
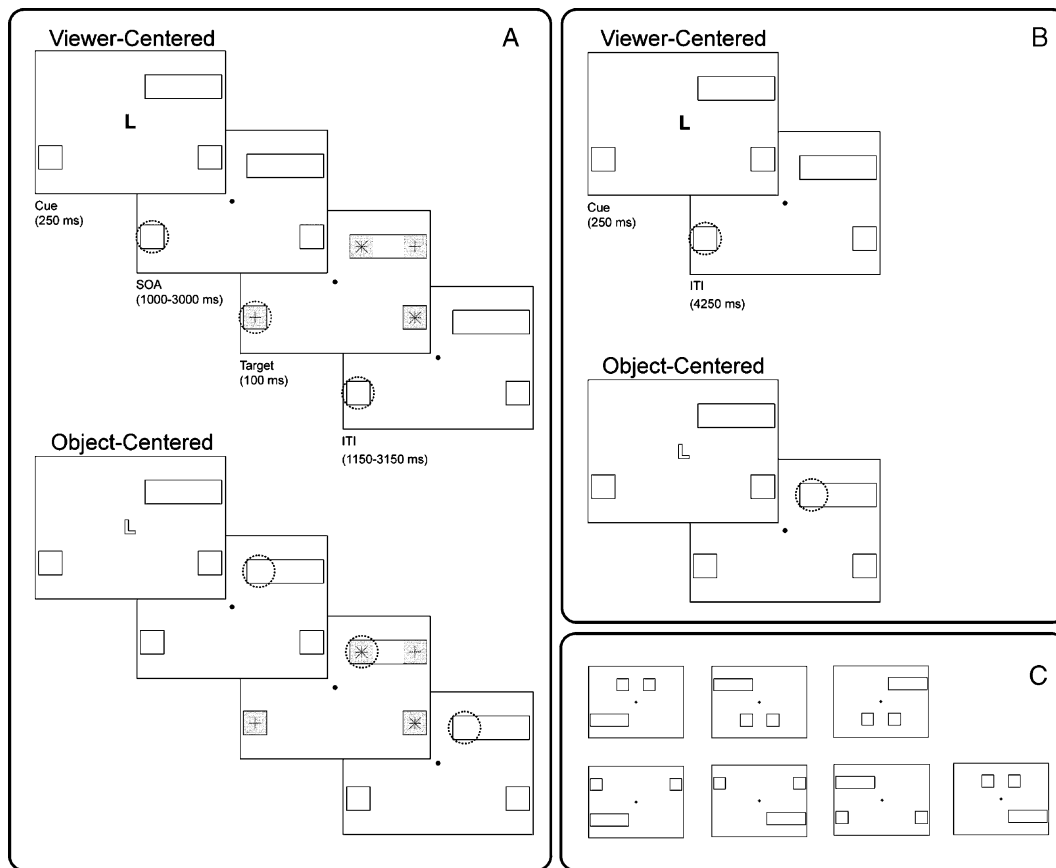
Fig. 1. Stimulus and timing parameters. Displays are shown using reversed contrast here, but appeared to participants as white figures against a black background. (A) Cue-Target trials. Participants were instructed to covertly attend the visual region indicated by the 100% valid cue (indicated here by a dashed circle) and to discriminate the target shape ("plus" or "asterisk") appearing at that location. The central cue was colored blue or yellow to indicate the appropriate reference frame for that trial. After a variable delay (1, 2, or 3 s), targets appeared at all four locations on the screen. (B) Cue-Only trials. Cues were presented at fixation as in the Cue-Target trials but were followed by a 4250-ms inter-trial interval without target presentation. (C) Additional stimulus displays used in this experiment in order to equate target locations across conditions.

Cue-Only trials as such until the trial terminated (4250 ms subsequent to cue presentation). The third trial type, No-Stim trials (33% of all trials), were points in time that were randomized in the sequence with the occurrences of the other trials types but during which no stimuli (neither cues nor targets) were actually presented (Buckner et al., 1998; Burock et al., 1998; Woldorff et al., 2004). No-Stim trials provide a specific estimate of hemody-namic overlap from nearby trials in a sequence and accordingly can be used to distinguish (or subtract off) such overlap from the event-related activity evoked by a given trial. From a regression standpoint, such trials can also be viewed as being functionally equivalent to a variable inter-trial interval separating the other two trial types (Cue-Target and Cue-Only trials), thereby facilitating the deconvolution of the overlapping event-related responses (Ollinger et al., 2001a,b). Comparison of time-locked averages to the Cue-Only and No-Stim trials reflects cognitive processes invoked specifically by the visual cues, including the attentional orienting mechanisms, while comparison between the different Cue-Only trial types (Object-Centered vs. Viewer-Centered) control for lower-level visual stimulation. In all cases, total trial duration was equivalent (4.5 s). Such rapid, event-related paradigms have been used successfully in a number of recent fMRI studies to reveal cortical mechanisms responsible for attentional orienting (Weissman et al., 2002; Woldorff et al., 2004).

The second technique used to overcome hemodynamic overlap from adjacent trials involved first-order trial counterbalancing. Cue-Target, Cue-Only, and No-Stim trials were pseudo-random-ized with a first-order counterbalancing restriction using a 2 × 2 × 2 design with Trial Type (Cue-Target vs. Cue-Only), Reference Frame (Viewer- vs. Object-Centered), and Visual Field (Left vs. Right) as factors, in addition to No-Stim trials, for a total of nine different trial types. The counterbalancing constraint guaranteed that each of the nine trial types was equally often preceded and followed by every other trial type in the design, and thus that hemodynamic overlap between adjacent trials was equivalent for all trial types. This technique therefore ensured that differences in event-related activity for different trial types were not due to differential response overlap. (For alternate approaches, see Ollinger et al., 2001a,b.)

*Training session*

All participants completed a training session outside of the MR facility at least 24 h prior to MRI data acquisition. Participants performed the cueing task as described above, except that error feedback was provided on each trial. Each participant completed four experimental runs, with feedback, during the training session.

Vertical and horizontal electro-oculograms (EOGs) were recorded during the training session using a SynAmps electro-physiological acquisition system (NeuroScan, Inc.). EOG signals were recorded using a digitization sampling rate of 250 Hz. Vertical electrodes were placed inferior and superior to the right eye; horizontal electrodes were located on the outer canthi of the left and right eyes. Off-line, automated artifact rejection was used to eliminate trials during which blinks occurred. EOGs from each condition of interest were then averaged into 1100 ms epochs, starting 100 ms prior to cue onset. After the training session, each participant completed a calibration task that was used to estimate the voltage fluctuation produced by voluntary eye movements of $0.5°$, $1.0°$, $1.5°$, and $2.0°$ of visual angle into both the left and right visual fields.

## MRI data acquisition

Imaging was carried out on a GE 4T whole-body MRI scanner housed at the Duke University Medical Center. A standard radiofrequency head coil was used with foam padding to restrict head motion in a comfortable manner. Thirty-two functional images were obtained from each participant using a spiral imaging sequence sensitive to the blood oxygenation level-dependent (BOLD) contrast, collected parallel to the AC-PC line (repetition time (TR) = 1.5 s; echo time (TE) = 31 ms; field of view (FOV) = 24 cm; image matrix = $64^2$; flip angle = $62°$; slice thickness = 3.75 mm; in-plane resolution = $3.75$ mm$^2$). Prior to the acquisition of functional data, thirty-two structural images were obtained from each participant using high-resolution axial T1-weighted images, collected parallel to the AC-PC line (TR = 450 ms; TE = 20 ms; FOV = 24 cm; image matrix = $256^2$; slice thickness = 3.75 mm; in-plane resolution = $0.9375$ mm$^2$).

Participants completed eight 6-min functional runs over the course of a single 1.5-h experimental scanning session. Two hundred forty brain volumes were collected in each run. Eighteen seconds of gradient and RF pulses were included at the beginning of each run to reach steady-state magnetization, but were not included in the data analyses.

## Data analysis

Images were reconstructed off-line and spatially pre-processed using SPM99. Data were corrected for asynchronous fMRI acquisition and head motion, realigned, normalized to standardized stereotactic (MNI) space, and smoothed spatially with a Gaussian filter (FWHM = 8 mm in the $x$, $y$, and $z$ dimensions).

Functional data from each scan were analyzed using multiple linear regression as implemented in SPM99. Regressors were constructed by convolving onset times for each trial type (e.g., Object-Centered Cue-Only trials) with a canonical hemodynamic response function. Regressors were included for each of eight trial types using a 2 × 2 × 2 design with Trial Type (Cue-Target vs. Cue-Only), Reference Frame (Viewer- vs. Object-Centered), and Cued Visual Field (LVF vs. RVF). No-Stim trials were not modeled explicitly as cognitive events of interest in the SPM99 analyses, but were treated instead as between-trial baseline epochs. In this manner, statistical modeling of each other trial type (e.g., Cue-Target and Cue-Only trials) was automatically contrasted with the No-Stim condition, which constituted an ideal baseline (for a more complete description of these techniques, see Woldorff et al., 2004). Motion regressors, derived during spatial pre-processing,

were also included in the model to accommodate signal variance associated with bulk rotations and translations of the head.

A second-level, random-effects analysis was performed on the individual participant t-maps to assess group-wide activations. These parametric maps were generated using an activation threshold of $P < 0.001$ (uncorrected) combined with an extent threshold of 8 contiguous voxels in order to control for Type I errors (Xiong et al., 1995). These activation and clustering requirements were established on the basis of preliminary data sets using a similar paradigm (Wilson and Mangun, 2002). It is important to note that the resulting maps were not threshold dependent and were both qualitatively and quantitatively similar across a variety of statistical thresholds and clustering requirements.

Regions-of-interest (ROIs) were constructed based on the results of these second-level analyses, using Cue-Only trials collapsed across conditions. Binary masks were created using random-effects SPMs for all Cue-Only trials (see above), and then segmented into discrete clusters for each activated region. Raw MR signal intensities were then extracted separately for each participant from all voxels within each of these ROIs using 24 s epochs, starting 4.5 s prior to cue onset, in order to construct more specific contrasts (e.g., differential responses during Object-Centered and Viewer-Centered Cue-Only trials). These trial-averaged MR intensities were averaged across all voxels within a region, and then converted to percent signal change using condition-specific baseline estimates (i.e., percent signal change relative to the average MR intensity for the 4.5 s prior to cue onset for each trial type, within each region, for each participant). After correcting for hemodynamic overlap between adjacent trials (by subtracting off time-locked averages for the No-Stim condition), peak percent signal change estimates were computed for each trial type by averaging evoked activity amplitude during a time window of 6–9 s subsequent to cue onset.

## Results

### Behavioral results

Behavioral responses were successfully recorded from 15 of 16 participants during fMRI data acquisition. Mean reaction times (RTs) from these 15 participants were analyzed using repeated-measures analysis of variance (ANOVA) with Reference Frame (Object-Centered vs. Viewer-Centered), Visual Field (Left vs. Right), and ISI (Short, Medium, or Long) as within-subject factors (Table 1). The main effects of Visual Field, Reference Frame, and ISI were not statistically significant ($F(1,14) = 1.95$, $P = 0.18$, $F(1,14) = 3.98$, $P = 0.07$, $F(1,14) = 1.77$, and $P = 0.19$, respectively), nor were any of the interactions between these factors ($P > 0.1$ in all cases). Critically, neither the Reference Frame × Visual Field nor the Reference Frame × ISI interactions were significant ($F(1,14) = 0.01$, $P = 0.93$ and $F(2,28) = 0.84$, $P = 0.44$, respectively).[2]

Accuracy measures, expressed as percent correct, were entered into an analogous repeated measure ANOVA (Table 1). Overall, participants responded correctly on 82% of trials. Accuracy did not

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[2] Reaction times were comparable during scanning and training sessions ($F(1,14) = 0.602$, $P = 0.45$). Similarly, pairwise comparisons revealed that reaction times during the training and scanning sessions did not differ for the Object-Centered or Viewer-Centered conditions ($t(14) = -1.355$, $P = 0.20$ and $t(14) = -0.149$, $P = 0.88$, respectively).

Table 1
Behavioral data collected during MRI acquisition as a function of Reference Frame and SOA ($n = 15$)

| SOA | Object-centered | | Viewer-centered | |
|---|---|---|---|---|
| | RT | Accuracy | RT | Accuracy |
| 1 s | 884 (±30) | 78.9 (±3.3) | 876 (±31) | 83.4 (±3.0) |
| 2 s | 870 (±30) | 82.4 (±3.0) | 835 (±29) | 82.3 (±3.1) |
| 3 s | 885 (±25) | 83.3 (±2.6) | 875 (±30) | 83.6 (±2.8) |
| Mean | 880 (±16) | 81.6 (±1.7) | 862 (±17) | 83.1 (±1.7) |

*Note*. SOA, stimulus onset asynchrony between cue and target onsets; RT, mean reaction time expressed in milliseconds; Accuracy, mean response accuracy expressed as percent correct. Standard errors of the mean are listed in parentheses for each condition.

differ significantly for Viewer-Centered (83%) and Object-Centered (82%) trials ($F(1,14) = 1.19$, $P = 0.29$). The analysis did, however, reveal a main effect of Visual Field ($F(1,14) = 6.41$, $P = 0.02$), with higher accuracy on RVF (84%) than on LVF (81%) trials. No other main effects or interactions were significant and error rates were not consistent with a speed-accuracy trade-off in any condition.

*Neuroimaging results*

Cue-Only trials (combining both Object- and Viewer-Centered conditions) activated a distributed, bilateral network of brain regions (Table 2, Fig. 2), including the inferior and superior parietal lobules neighboring the intraparietal sulci, lateral and superior frontal cortices including the frontal eye fields, medial and superior frontal cortices including the supplementary motor and anterior cingulate cortices, and the insular cortices. Similar patterns of activation were observed when Object-Centered and Viewer-Centered Cue-Only trials were considered separately (Fig. 3), revealing a distributed, bilateral fronto-parietal network in each case. Activations were spatially more extensive in the left lateral frontal and intraparietal regions compared to the right, whereas insular and medial frontal regions exhibited a more symmetrical

activation pattern across the two hemispheres. In addition to these bilateral activations, Cue-Only trials evoked activity in left dorsolateral prefrontal cortex and the left inferior occipital gyrus.

Whole-brain direct comparisons did not reveal any statistically significant differences for cue-related activity during Object- and Viewer-Centered trials. We therefore investigated the possibility that the commonly activated top-down control network was differentially engaged by shifts of attention in different frames of reference by comparing activity within each of the regions engaged during Cue-Only trials (see Materials and methods), including the left and right intraparietal sulci (IPS), the left and right frontal eye fields (FEF), the left and right anterior cingulate cortices (ACC), the left and right insular cortices (INS), as well as left dorsolateral prefrontal cortex (PFC) and the left inferior occipital gyrus (IOG). Responses during shifts of attention in object- and viewer-centered frames of references were then compared directly within each of these ROIs (Table 2). The majority of regions activated during Cue-Only trials exhibited greater activity during Object-Centered trials relative to Viewer-Centered trials, including the left and right intraparietal sulci ($t(15) = 4.78$, $P = 0.0002$ and $t(15) = 3.29$, $P = 0.0050$, respectively), the left and right anterior cingulate cortices ($t(15) = 4.35$, $P = 0.0006$ and $t(15) = 4.12$, $P = 0.0009$, respectively), the left and right frontal eye fields ($t(15) = 4.32$, $P = 0.0006$ and $t(15) = 2.70$, $P = 0.02$, respectively), as well as the left dorsolateral prefrontal cortex ($t(15) = 3.23$, $P = 0.0056$). The right insular cortex exhibited a non-significant trend for greater activity during object-centered shifts of attention ($t(15) = 1.87$, $P = 0.08$), while the left inferior occipital gyrus was not differentially activated in the two conditions ($t(15) = 1.25$, $P = 0.23$). Interestingly, no regions were significantly more active during Viewer-Centered Cue-Only trials than during Object-Centered Cue-Only trials.

To test for hemispheric asymmetries with respect to voluntary shifts of attention in object- and viewer-centered space, percent signal change estimates were entered into new repeated-measures ANOVAs for the IPS, FEF, ACC, and INS regions, with Reference Frame (Viewer-Centered vs. Object-Centered) and Hemisphere (Left vs. Right) as within-subject factors. Within the IPS, there was

Table 2
Event-related activations during Cue-Only trials

| | Region | BAs | $x$ | $y$ | $z$ | $T$ | $P$ | OC vs. VC |
|---|---|---|---|---|---|---|---|---|
| *Frontal* | L. FEF | 6/9 | −34 | −4 | 41 | 6.79 | <0.001 | 4.321 (0.0006) |
| | R. FEF | 6/8 | 34 | 0 | 49 | 3.52 | 0.002 | 2.702 (0.0164) |
| | L. SMA/ACC | 6/32 | −8 | 15 | 49 | 5.29 | <0.001 | 4.352 (0.0006) |
| | R. SMA/ACC | 24/32 | 11 | 15 | 45 | 4.39 | <0.001 | 4.120 (0.0009) |
| | L. DLPFC | 45/46 | −41 | 30 | 23 | 4.29 | <0.001 | 3.230 (0.0056) |
| *Parietal* | | | | | | | | |
| | L. IPS | 7/19 | −23 | −68 | 41 | 6.53 | <0.001 | 4.777 (0.0002) |
| | R. IPS | 7 | 30 | −68 | 45 | 3.99 | 0.001 | 3.289 (0.0050) |
| *Occipital* | | | | | | | | |
| | L. IOG | 18/19 | −41 | −98 | 0 | 4.37 | <0.001 | 1.254 (0.2291) |
| *Temporal* | | | | | | | | |
| | L. INS | 47/24 | −26 | 30 | 0 | 5.20 | <0.001 | 2.718 (0.0159) |
| | R. INS | 47/24 | 30 | 26 | −4 | 3.89 | 0.001 | 1.871 (0.0809) |

*Note*. L, Left; R, Right; FEF, frontal eye fields; SMA, supplementary motor area; ACC, anterior cingulate cortex; IPS, Intraparietal sulcus; INS, Insular cortex; DLPFC, dorsolateral prefrontal cortex; IOG, inferior occipital gyrus; BAs, Brodmann areas; coordinates: $x$, left/right; $y$, anterior/posterior; $z$, inferior/superior in the reference frame of the MNI brain in SPM99; $T$, peak voxel $t$ score within a region; $P$, $P$ value of peak voxel $t$ score; OC vs. VC, paired $t$ test for activation during object-centered and viewer-centered trials within each region of interest ($P$ values in parentheses).
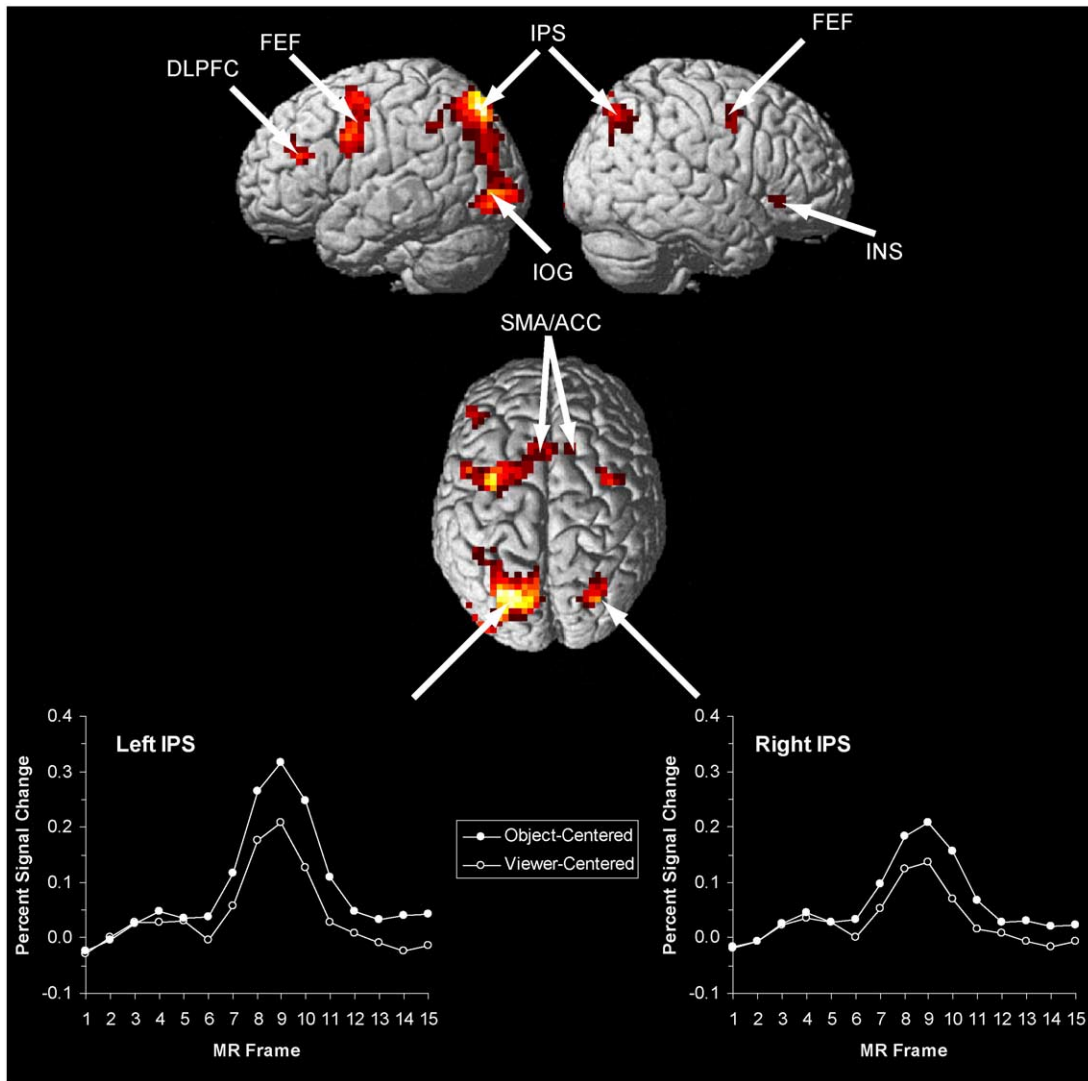
Fig. 2. Activity related to attentional control. BOLD responses to Cue-Only trials, collapsed across conditions, are overlaid onto the SPM99 3D-rendered brain. The top row depicts left and right lateral views; the middle row depicts a dorsal view. Activations are as described in Table 2 and in the text. The bottom row depicts BOLD averaged timecourses extracted from the left and right intraparietal ROIs, respectively, during Object- and Viewer-Centered Cue-Only trials, expressed as percent signal change, and after removing overlap by subtracting off the responses to the No-Stim trials. MR frames were 1.5 s in duration and cue onset occurred at frame 4. DLPFC, dorsolateral prefrontal cortex; FEF, frontal eye fields; IPS, intraparietal sulcus; IOG, inferior occipital gyrus; INS, insular cortex; SMA, supplementary motor cortex; ACC, anterior cingulate cortex.

a significant main effect of Reference Frame ($F(1,15) = 18.018$, $P = 0.0007$), with greater activity during shift of attention in object- versus viewer-centered space in both hemispheres. In addition, there was a significant main effect of Hemisphere ($F(1,15) = 21.57$, $P = 0.0003$), with greater activity in the left relative to the right IPS region for both cue types. Critically, there was a significant interaction between Reference Frame and Hemisphere ($F(1,15) = 6.18$, $P = 0.03$), as shown in Fig. 4. Hemispheric differences were larger during Object-Centered (0.276% and 0.182% for the left and right hemisphere, respectively) relative to Viewer-Centered trials (0.170% and 0.110% for the left and right hemisphere, respectively), with the single largest cue-related activity being in the left IPS in response to object-centered cues.

The left intraparietal sulcus was significantly more active than the right intraparietal sulcus in response to attention-directing cues, even during viewer-centered shifts of attention. This lateralization

pattern is consistent with other recent investigations of top-down attentional control networks (Giesbrecht et al., 2003; Hopfinger et al., 2000; Weissman et al., 2002), but must be considered when interpreting the significant interaction between Reference Frame and Hemisphere observed in the posterior parietal cortex in the present study. It is interesting to note, therefore, that while the hemispheric asymmetry in inferior parietal cortex was larger for object-centered shifts of attention relative to viewer-centered shifts of attention, normalized estimates of these hemispheric effects (e.g., Peak$_{Left}$/Peak$_{Right}$) did not differ significantly in the two conditions ($t(15) = 0.11$, $P = 0.91$). The implications of this normalization will be addressed in Discussion.

Percent signal change estimates were entered into analogous repeated-measures ANOVA for the anterior cingulate cortex. Once again, the main effect of Reference Frame was significant ($F(1,15) = 18.44$, $P = 0.0006$), with greater activity in the ACC during shifts of attention in object- relative to viewer-centered
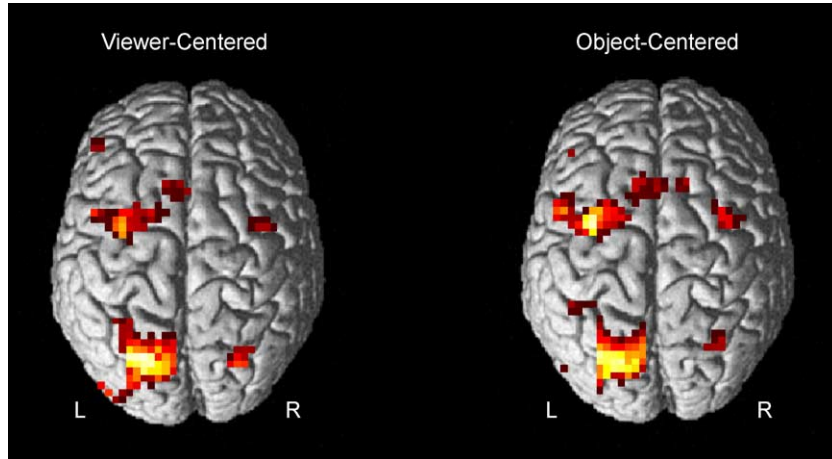
Fig. 3. Group-averaged activity related to attentional control for Viewer-Centered Cue-Only trials (left) and Object-Centered Cue-Only trials (right), overlaid onto the SPM99 3D-rendered brain. Conventions are as described in Fig. 2. Largely overlapping patterns of activation were observed, bilaterally, in regions of the intraparietal sulcus, the frontal eye fields, the supplementary motor and anterior cingulate cortices, as well as the left dorsolateral prefrontal cortex.

space. The main effect of Hemisphere, however, was not statistically significant ($F(1,15) = 0.03$, $P = 0.87$). There was a non-significant trend towards an interaction between Hemisphere and Reference Frame ($F(1,15) = 4.09$, $P = 0.06$), suggesting that object-centered cues produced greater activity in the right ACC, while viewer-centered cues produced greater activity in the left ACC. Simple comparisons revealed, however, that responses to object-centered cues were comparable in the left and right ACC ($t(15) = -0.92$, $P = 0.37$), as were responses to viewer-centered cues in the left and right ACC ($t(15) = 0.85$, $P = 0.41$). Moreover, neither the left nor the right anterior cingulate responded significantly above baseline during viewer-
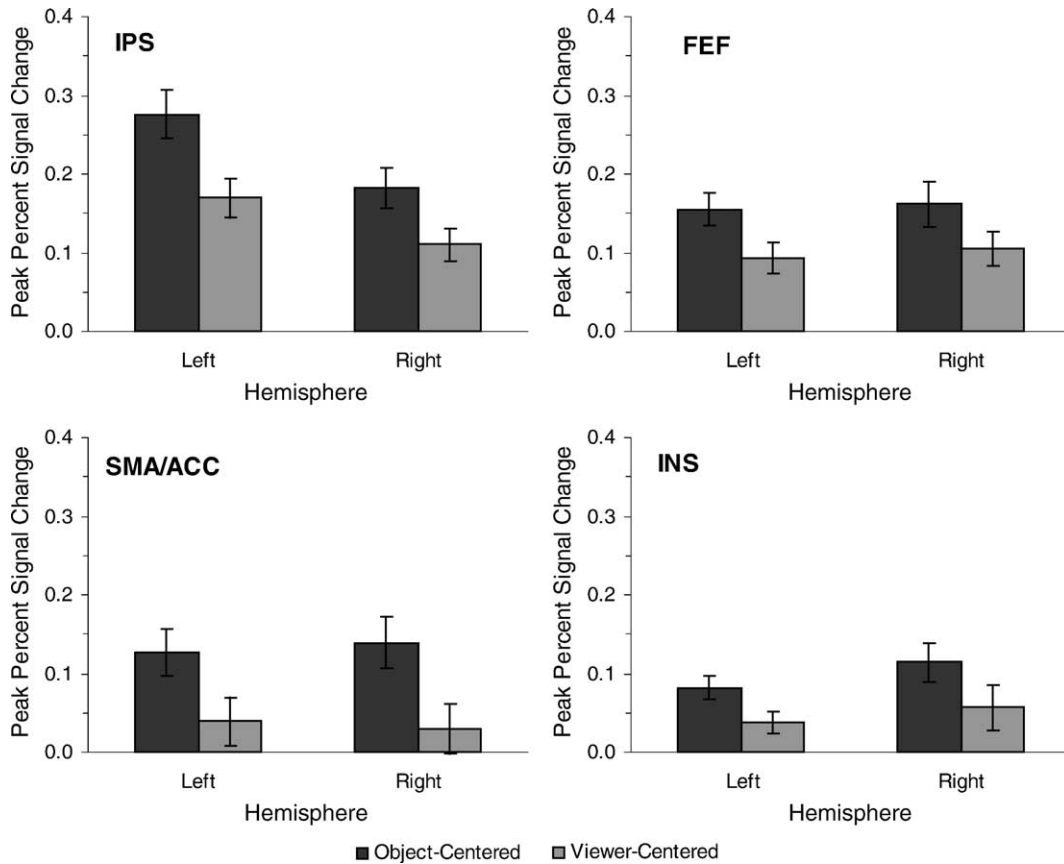


Fig. 4. Activation related to covert orienting as a function of Reference Frame and Cerebral Hemisphere for four regions of interest. Peak BOLD responses during Cue-Only trials (averages of MR frames 8–10; 6–9 s post-cue) were extracted within each region and converted to percent signal change. The Reference Frame x Hemisphere interaction was only significant in the intraparietal sulcus. IPS, intraparietal sulcus; FEF, frontal eye fields; SMA, supplementary motor cortex; ACC, anterior cingulate cortex; INS, insular cortex.

centered shifts of attention ($t(15) = 1.28$, $P = 0.22$ and $t(15) = 0.93$, $P = 0.37$, respectively). The trend towards a significant interaction between Hemisphere and Reference Frame is therefore unlikely to reflect a substantive hemispheric asymmetry within this region for deploying attention in different spatial frames of reference.

Within both the FEF and INS regions, the main effect of Reference Frame was significant ($F(1,15) = 15.60$, $P = 0.0013$ and $F(1,15) = 5.00$, $P = 0.04$, respectively), with greater activity for object-centered relative to viewer-centered shifts of attention. In each case, however, neither the main effect of Hemisphere nor the interaction between Reference Frame and Hemisphere was significant ($P < 0.20$ in all cases).

In line with previous neuroimaging studies of selective attention (Heinze et al., 1994; Hopfinger et al., 2000; Martinez et al., 1999), activity in contralateral regions of extrastriate cortex was enhanced by the direction of attention (Fig. 5). Importantly, these spatially selective attention effects occurred not only on Cue-Target trials, but also on Cue-Only trials, consistent with a gain-modulation mechanism in which visual cortical activity is amplified prior to the presentation of an expected, behaviorally relevant target (Hopfinger et al., 2000; Kastner et al., 1999). These lateralized effects of spatial attention confirm that our attention manipulation was successful and that participants complied with task instructions to deploy their attentional resources covertly to the cued location. Moreover, the similarity between lateralized attention effects during Cue-Only and Cue-Target trials suggests that attentional resources were deployed similarly during both types of trials.

The interaction between Reference Frame and Hemisphere within the intraparietal ROI suggests a greater degree of hemispheric specialization for object-centered shifts of attention. One concern, however, is that the left intraparietal ROI encompassed a larger region of cortex than the right intraparietal ROI (348 vs. 83 voxels, respectively), and therefore that any differential response

within the left IPS may have resulted from a larger sampling area. We controlled for this possibility by flipping the left intraparietal ROI along the interhemispheric commissure and then comparing symmetrical regions of the left and right IPS. Statistical analyses again revealed significant main effects of Hemisphere ($F(1,15) = 60.79$, $P = 0.0001$) and Reference Frame ($F(1,15) = 16.82$, $P = 0.0009$). More importantly, there was again a significant interaction between Reference Frame and Hemisphere ($F(1,15) = 5.16$, $P = 0.03$), confirming that the relative specialization of left IPS for shifts of attention within object-centered space did not result from comparing cortical regions of different size.

Cue-related activity was greater for object-centered relative to viewer-centered shifts of attention throughout the fronto-parietal attentional control network. Although there were no significant behavioral differences between the two conditions, we did observe a non-significant trend for greater response times during object-centered (880 ms) relative to viewer-centered (862 ms) trials. This pattern of results might suggest that the Object-Centered condition was simply more difficult than the Viewer-Centered condition, and that our reference frame effects were the result of differences in task difficulty. To rule out this possibility, we correlated brain activity with response times throughout the attentional control network, including the left and right intraparietal ROIs (Fig. 6A). Response times differences did not correlate significantly with percent signal change differences in any cue-related regions, particularly in the left and right IPS ($r(15) = 0.076$, $P = 0.7927$ and $r(15) = 0.180$, $P = 0.5279$, respectively). This result bolsters the claim that increased brain activity during object-centered shifts of attention was not strictly the result of greater task difficulty or arousal.

Although attention was deployed to potential target locations that were identical in size and at the same retinal eccentricities across both object- and viewer-centered conditions, there was one important difference between these two trial types concerning the
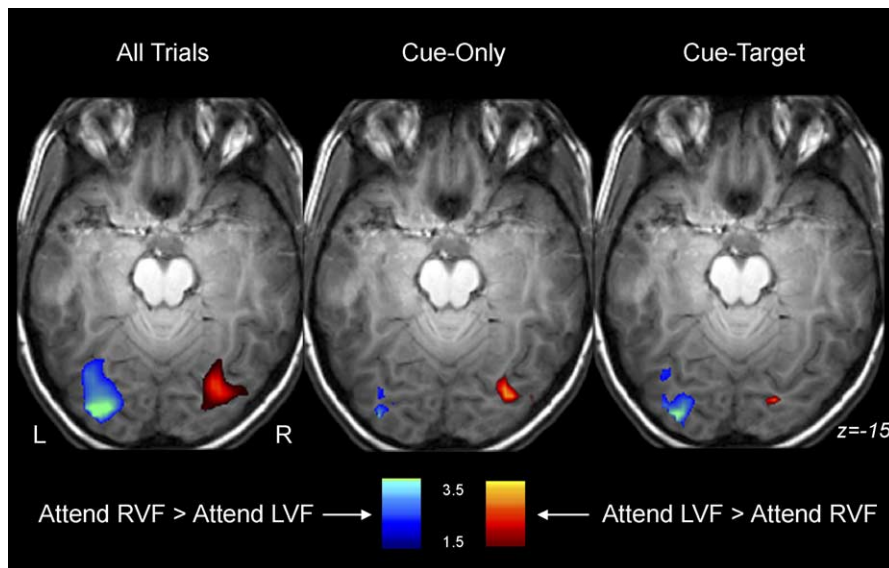


Fig. 5. Modulations of activity in extrastriate cortical regions with the direction of attention during all trial types (left), Cue-Only trials (middle), and Cue-Target trials (right). Areas in blue indicate brain regions more active in response to right visual field cues than to left visual field cues, while areas in red indicate brain regions more active in response to left visual field cues than to right visual field cues. Group-averaged data are overlaid onto a single anatomical image obtained from one participant ($z = -15$ mm in all three slices). Activated regions survived a direct comparison between cues that indicated locations in the left versus right visual fields with a $P < 0.05$, uncorrected, threshold using anatomically defined a priori regions of interest (BAs 18 and 19). MNI coordinates of local maxima ($x, y, z$ mm): Right Visual Field (RVF) Cue > Left Visual Field (LVF) Cue, $-30, -90, -18.75$; LVF Cue > RVF Cue, $26.25, -82.5, -15$.
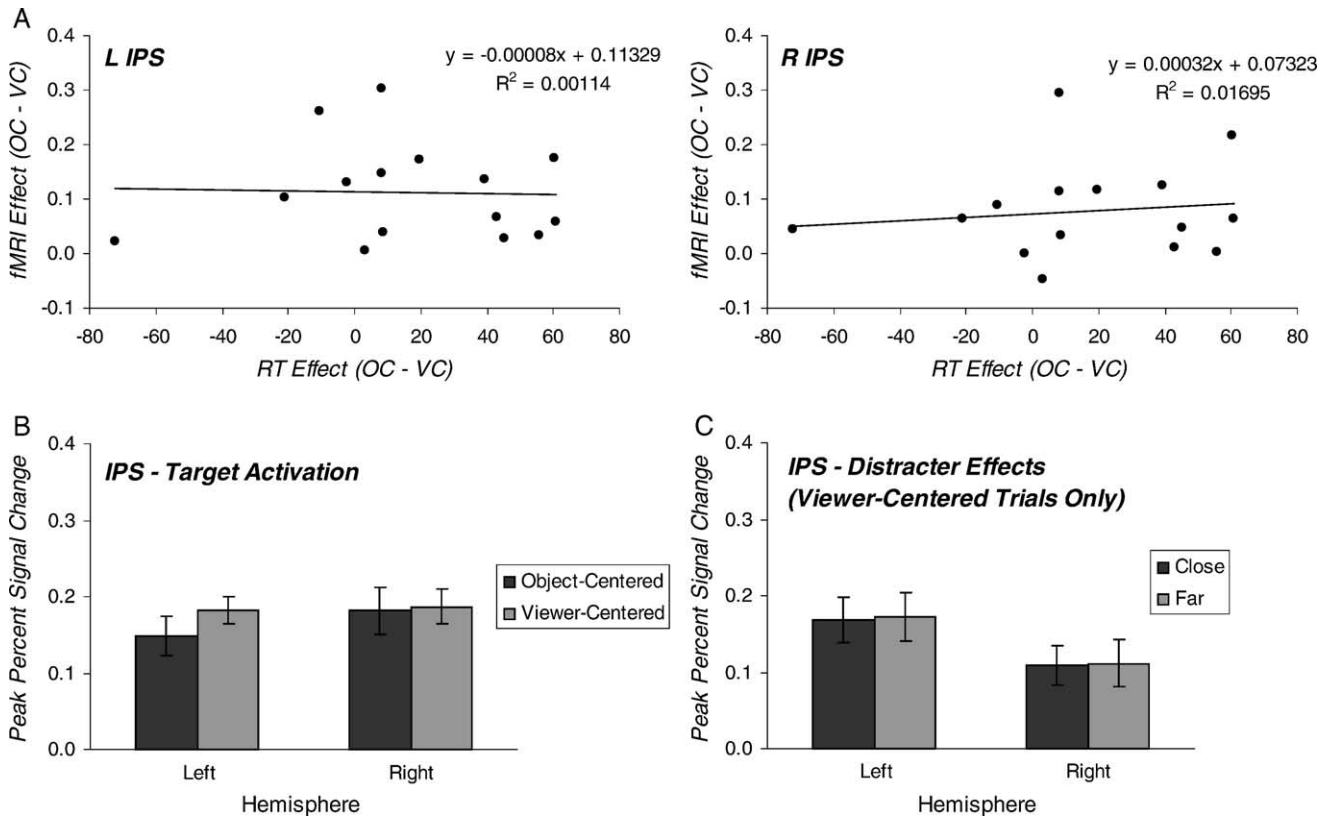
Fig. 6. (A) Relationship between behavioral performance (reaction times) and neuronal activity (BOLD signal) during Cue-Only trials in the left and right intraparietal ROI. Reference frame effects were computed for percent signal change and reaction times for each participant individually and then entered into a group analysis. Reaction time differences did not correlate with BOLD signal intensity within the intraparietal ROIs, or in any of the other cue-related brain regions. (B) BOLD activation associated with target processing (Cue-Target minus Cue-Only) did not differ as a function of Reference Frame in either the left or right IPS. (C) BOLD activation also did not differ as a function of distracter distance ("close" versus "far") on Viewer-Centered Cue-Only trials within the IPS.

spacing of distracter stimuli. Although the same number of distracter stimuli was present on all trials (three in all cases), the spacing between targets and distracters was not equivalent in each case. On Object-Centered trials, for example, the closest distracter occurred at the opposite end of the rectangular placeholder and was always positioned 8.5° from the center of the target. On Viewer-Centered trials, however, the distracter stimuli occurring at the opposing square placeholder was equally often positioned 8.5° and 25.3° from the center of the target. The influence of distracter stimuli may have therefore been smaller, on average, in the Viewer-Centered condition because of the trials during which square placeholders were positioned at the more lateral eccentricities. It is therefore possible that greater neuronal activity observed during Object-Centered trials simply resulted from higher levels of target-distracter interference for those trials.

To control for this possibility, we compared neuronal activity during Viewer-Centered trials in which the square placeholders occurred at the medial (3.75°) versus lateral (12.7°) eccentricities within each of the regions significantly activated by Cue-Only trials. Evoked activity was comparable within each ROI (particularly the IPS, Fig. 6B) during shifts of attention in viewer-centered space, regardless of the eccentricity of the distracter stimuli ($P > 0.1$ in all cases). Similarly, a significant interaction between Reference Frame and Hemisphere was observed when Object-Centered trials were compared to Viewer-Centered trials using only the more proximal stimulus locations ($F(1,15) = 5.55$, $P = 0.03$), with hemispheric differences in parietal cortex again being larger during Object-

Centered trials relative to Viewer-Centered trials (0.168% and 0.109% for the left and right hemisphere, respectively for proximal location Viewer-Centered Cue-Only trials). These results rule out alternative hypotheses involving differential levels of target-distracter interference between Viewer- and Object-Centered conditions. Future studies could address this issue more directly by including equivalently space distracters across both Object- and Viewer-Centered conditions.

Within the fronto-parietal control network, differences in neuronal activity between Viewer- and Object-Centered trials were relatively specific to the initial processing of attention-directing cues, with little differences occurring during target processing. More specifically, target-related activity was not significantly different during Viewer- and Object-Centered Cue-Target trials in the majority of the attentional control regions, including the left and right IPS ($t(15) = -1.25$, $P = 0.23$ and $t(15) = -0.19$, $P = 0.86$, respectively; Fig. 6C), the left and right FEF ($t(15) = -1.57$, $P = 0.14$ and $t(15) = -0.02$, $P = 0.35$, respectively), the left ACC ($t(15) = -1.53$, $P = 0.15$), and the left INS ($t(15) = -1.27$, $P = 0.22$). There were marginally significant differences in left DLPFC ($t(15) = -1.97$, $P = 0.07$) and right INS ($t(15) = -2.21$, $P = 0.04$), with slightly greater activity during Viewer-Centered trials relative to Object-Centered Cue-Target trials in both cases. Taken together, these results suggest that the reference frame effects observed during Cue-Only trials reflect differential neuronal responses associated specifically with the initial deployment of attention, prior to the onset of to-be-discriminated visual stimuli.

*EOG results*

Electro-oculograms (EOG), recorded from eleven participants during the training sessions, revealed that participants were able to maintain fixation while performing this task (Fig. 7). Pairwise comparisons revealed that mean horizontal EOG (HEOG) amplitudes did not differ significantly between any two conditions ($P > 0.1$ in all cases). HEOG amplitudes were also not significantly greater than zero for any experimental condition ($P > 0.1$ in all cases). The HEOG traces obtained during task performance were also compared to those recorded while participants were explicitly required to make systematic saccadic eye movements of varying distances. HEOG amplitudes recorded during task execution were significantly smaller than those associated with even the smallest explicit saccade of $0.5°$ during the calibration task (Object-Centered LVF trials $t(10) = 3.72$, $P = 0.0040$; Object-Centered RVF trials $t(10) = -3.88$, $P = 0.0031$; Viewer-Centered LVF trials $t(10) = 4.03$, $P = 0.0024$; Viewer-Centered RVF trials $t(10) = 3.59$, $P = 0.0040$). Thus, our measure was sensitive to deviations of eye position of as little as $0.5°$ into both the left and right visual fields (note that the closest target eccentricities in our study were $4.2°$) and any differences in brain activity or behavioral performance between Object- and Viewer-Centered trials are therefore very unlikely to be attributable to differential eye movements between conditions.[3]

## Discussion

This study used a rapid, event-related fMRI paradigm to distinguish between two hypotheses concerning the neuronal networks involved in voluntarily deploying attention in different visual frames of reference. A distributed network of brain regions was shown to be involved specifically with top-down attentional control, including inferior and superior parietal, lateral and medial frontal, and insular cortices. This fronto-parietal control network has been revealed in a growing number of recent studies using both "slow" and "rapid" event-related functional MRI (e.g., Corbetta et al., 2000; Hopfinger et al., 2000; Kastner et al., 1999). These regions were activated by attention-directing cues in the absence of visual targets, and thus reflect cognitive processes associated with the initial orienting of attention. Importantly, this attentional control network was differentially activated when attention was deployed in object- versus viewer-centered coordinate systems. Specifically, when attention was deployed in object-centered space, activity was greater in bilateral portions of the posterior parietal cortex in the vicinity of the intraparietal sulcus, in lateral superior frontal cortex in the vicinity of the frontal eye fields, in medial superior frontal regions including supplementary motor and anterior cingulate cortices, and in the left dorsolateral and insular

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[3] Since eye movements were not recorded during fMRI data acquisition, we cannot entirely rule out the possibility that participants moved their eyes more in the Object-Centered condition than in the Viewer-Centered condition during fMRI data acquisition. However, participants were able to maintain fixation equally well during Object-Centered and Viewer-Centered trials during the training session, and behavioral performance was comparable during the scanning and training sessions. Moreover, participants were well trained and highly motivated, and none reported difficulty in complying with task instructions involving the maintenance of fixation during either the training or fMRI data acquisition sessions.
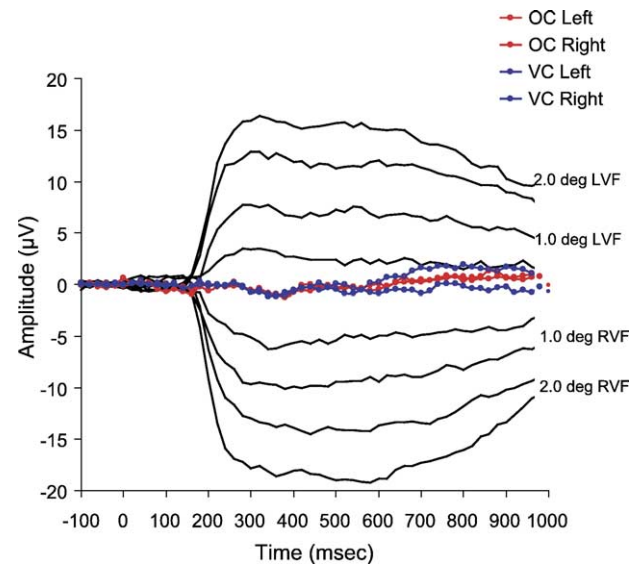


Fig. 7. Eye movements associated with Cue-Only trials, recorded during training, as a function of Reference Frame and Cued Visual Field. Traces are overlaid onto horizontal electro-oculograms collected during a saccade calibration task that was completed at the end of training (see Materials and methods). OC, Object-Centered; VC, Viewer-Centered; μV, microvolt; LVF, left visual field; RVF, right visual field.

cortices. Finally, a significant interaction was observed between Reference Frame and Hemisphere in the intraparietal sulcus such that the left hemisphere advantage was greater during object-centered relative to viewer-centered shifts of attention. These findings support the hemispheric specialization hypothesis (Egly et al., 1994a), which suggests that the left posterior parietal cortex is particularly important for shifting attention in object-based coordinate systems (c.f. Giesbrecht et al., 2003).

*Top-down attentional control*

We observed significant activity in and around the intraparietal sulci of both the left and right hemispheres in response to attention-directing cues, during shifts of attention in both viewer- and object-centered reference frames. Converging evidence from neuroimaging studies (Corbetta et al., 1993; Gitelman et al., 1999; Nobre et al., 1997), behavioral analysis in neurological patients with focal cortical lesions (Friedrich et al., 1998; Lynch and McLaren, 1989; Posner et al., 1984; Watson et al., 1994), and neurophysiological recordings in non-human primates (Bisley and Goldberg, 2003; Bushnell et al., 1981; Colby and Goldberg, 1999; Colby et al., 1996; Robinson et al., 1991; Steinmetz, 1998), implicate inferior and superior parietal regions neighboring the intraparietal sulcus in the voluntary allocation of visuospatial attention. Moreover, our findings fit well with a number of recent fMRI studies that have demonstrated left hemispheric lateralization for top-down attentional control processes (Corbetta et al., 2000; Hopfinger et al., 2000), although the degree to which such processes are lateralized to the left hemisphere is still a matter of some debate (Gitelman et al., 1999). Nevertheless, our data are consistent with a large body of research demonstrating a critical role for intraparietal regions (and perhaps the left intraparietal regions in particular) during voluntary shifts of spatial attention.

Attention-directing cues recruited lateral portions of the frontal lobes in and around the frontal eye fields, bilaterally. These

activations are consistent with the known role of FEF in executing covert shifts of attention in the absence of explicit eye movements (Henik et al., 1994; Mesulam, 1981; Thompson et al., 1997). Medial superior frontal regions, including the supplementary motor and anterior cingulate cortex were also activated by attention-directing cues, on trials during which target stimuli were not presented and no overt response was required, consistent with a number of recent studies that have implicated this region as part of the attentional orienting network (Gitelman et al., 1999; Mangun and Hillyard, 1991; Mesulam, 1981; Moran and Desimone, 1985; Posner and Petersen, 1990; Posner et al., 1984; Woldorff et al., 1999).

Other regions, including bilateral portions of the insular cortex and the left dorsolateral prefrontal cortex, were also significantly activated by attention-directing cues in both object- and viewer-centered conditions. The insulae have been linked to a range of cognitive functions including both voluntary (endogenous) and involuntary (exogenous) shifts of attention (Corbetta et al., 1991; Kim et al., 1999; LaBar et al., 1999; Perry and Zeki, 2000) as well selective processing of novel and task-relevant stimuli (Downar et al., 2001, 2002; Hopfinger et al., 2000). Dorsolateral prefrontal cortex has been linked to working memory in numerous functional neuroimaging studies (Braver et al., 1997; D'Esposito et al., 1998; Jonides et al., 1993, 1998; Kojima and Goldman-Rakic, 1982; Smith and Jonides, 1998). It is possible that dorsolateral prefrontal activity resulted from the recruitment of general working memory processes such as remembering the color mapping between cue letters and reference frames, or the response mappings for each target shape. Note, however, that cues and targets were separated by relatively short SOAs in the present study (on the order of 1 s), in contrast to a number of previous neuroimaging studies of top-down attentional control that used significantly longer cue-target intervals (on the order of 8 s, e.g., Giesbrecht et al., 2003; Hopfinger et al., 2000).

*Reference frame effects*

Differences were observed within the fronto-parietal attentional control network depending on whether attention was allocated within an object- or viewer-centered frame of reference. The majority of regions within this network were more heavily recruited when attention was deployed in object- relative to viewer-centered space, with the exception of the inferior occipital gyrus and the right insular cortex. Interestingly, no cortical areas were more active in response to attention-directing cues in viewer-centered space relative to object-centered space. This asymmetry suggests that orienting attention in an object-centered coordinate system involves recruitment of additional processing resources, above and beyond those used when orienting attention in the more commonly employed viewer-centered reference frame (Arrington et al., 2000).

A number of hypotheses may help to explain the fact that object-based shifts of attention produced greater activity throughout the attention control network, particularly within the parietal cortex. For instance, recent studies have suggested that one characteristic of object-based attentional selection is that attention automatically spreads to multiple parts of an attended object (Avrahami, 1999; Moore et al., 1998; Neely et al., 1998; Saiki, 1997; Shomstein and Yantis, 2002). This phenomenon could help to explain why activity in the fronto-parietal network was greater during object-centered shifts of attention since participants were

required to focus selectively on one part of a visual object in this condition (e.g., the left side of a rectangle), but not in the viewer-centered condition (e.g., the square on the left or right side). Greater involvement of the attentional orienting network may have therefore been required as participants more selectively focused attentional resources in order to overcome the tendency for attention to spread across the entire rectangle in the object-centered condition. Note that such compensatory mechanisms would not have been necessary during viewer-centered trials, since an entire square was selected for attention, and therefore such effects would be more pronounced in our object-centered condition.[4]

Another hypothesis that may help to explain greater parietal activation during object-centered attentional shifts is that this region transforms spatial representations into a common frame of reference, most likely centered on the viewer, in order to coordinate information from sensory input and response output systems (Andersen, 1995, 1997; Andersen and Buneo, 2002; Andersen et al., 1998; Batista et al., 1999; Cohen and Andersen, 2002; Scherberger et al., 2003). The observed differences in IPS activity are consistent with this proposal, particularly if the viewer-centered target locations are more closely aligned with the common coordinate system employed by these posterior parietal regions.

Activity within portions of the medial superior frontal cortex was also greater during shifts of attention in object- relative to viewer-centered space. Although our activations appeared to be inferior to the proposed homologue of the macaque supplementary eye field (SEF), it is possible that this region was also engaged in the present study. Neurophysiological recordings have consistently demonstrated reference frame effects in the macaque SEF (Olson and Gettner, 1995, 1996, 1999; Olson and Tremblay, 2000; Tremblay et al., 2002). Specifically, when monkeys prepare to make a saccade to either the left or right side of an object, regardless of where the object appears on the screen, a significantly greater number of SEF neurons exhibit object- as opposed to viewer-centered directional sensitivity. It is possible that our medial frontal regions encompassed the human homologue of SEF, and our results are therefore consistent with the proposed role of this medial frontal region in object-based spatial awareness.

It is important to stress that increased activity during object-centered shifts of attention within the intraparietal sulci, the frontal eye fields, the anterior cingulate, and the insular cortices cannot be attributed to confounds involving differential eye movements, longer response times, lower accuracy rates, or greater levels of distracter interference because none of these factors differed significantly between conditions. Similarly, these effects cannot be attributed to differential working memory demands in the two conditions, since the attention-directing cue conveyed the same amount of to-be-maintained information in both conditions (i.e., the relevant reference frame, and the side of space within that

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[4] One interpretation of this hypothesis is that the Object-Centered condition was more effortful, and therefore more difficult, than the Viewer-Centered condition. Although our results show that reaction time effects were not correlated with brain activity, and other studies have also found increased parietal activity during object-based attention in the absence of behavioral differences (Arrington et al., 2000), there was nevertheless a trend towards slower reaction times in the Object-Centered condition in the current study, consistent with this interpretation. Future experiments, in which participants are required to attend to single regions of a multi-part object in both the Viewer- and Object-Centered conditions, could address the issue more directly.

reference frame, to be attended). Further, reference frame effects in these regions were observed specifically in response to attention-directing cues and were not observed in response to subsequent visual targets, suggesting that reference frame effects can be manifested differently at multiple neuronal stages of covert attention.

The reference frame effects observed in the present study are largely different from the results reported by Fink et al. (1997a). Using PET, they showed that left striate and prestriate cortex were more active when participants were required to decide whether a square appeared on the left or right side of a line segment (their "object-based" condition) than when they were required to decide whether the line segment fell within their left or right visual field (the "space-based" condition). In contrast, regions of the right inferior temporal cortex and dorsolateral prefrontal cortex were more active during the space-based condition relative to the object-based condition.

Direct comparisons between the results of Fink et al. (1997a) and the present study are complicated by a number of important differences between the two studies concerning the imaging paradigm, the experimental task, and eye movements. One critical difference concerns the fact that largely distinct aspects of attention were investigated in the two. In the present study, we assessed the neural systems involved specifically with making voluntary shifts of spatial attention to locations defined within different spatial frames of reference. In contrast, Fink et al. investigated the neural systems involved in making spatial discriminations within different spatial frames of reference. While both studies explored the influences of reference frames on various aspects of spatial cognition, the attentional systems being investigated were largely distinct in the two cases, and thus any direct comparisons are difficult at best. Our results do, however, fit well with the fact that Fink et al. found that medial parietal cortices, bilaterally, as well as the left inferior parietal cortex, were involved in both object- and space-based attention.

*Hemispheric asymmetries*

Hemispheric asymmetries were observed in the vicinity of the intraparietal sulcus during voluntary shifts of spatial attention. Critically, hemispheric differences were greater within the intraparietal region in response to object-centered relative to viewer-centered attentional shifts. The interaction between Reference Frame and Hemisphere within IPS is consistent with previous studies involving split-brain patients (Egly et al., 1994b), patients with focal, unilateral parietal lesions (Egly et al., 1994a), and Alzheimer's disease patients (Buck et al., 1997). The data are also in agreement with a recent fMRI study showing that the left inferior parietal lobule was significantly more active on blocks of trials during which participants attended to bound (object-based) as opposed to unbound (space-based) regions of space (Arrington et al., 2000). The present study is the first, however, to look specifically at the top-down deployment of visual attention in different visual frames of reference and therefore represents a novel test of the hemispheric specialization hypothesis.

Within the parietal cortex, hemispheric differences in cue-related activity were greater for object-centered shifts of attention relative to viewer-centered shifts of attention, consistent with the hypothesis that the left hemisphere plays a privileged role during object-based shifts of attention. We noted, however, that normalized estimates of this left hemisphere advantage were not

statistically different for the object-centered and viewer-centered conditions. Although this result could be used to suggest that the relative contributions of the left and right posterior parietal regions were comparable for object- and viewer-centered shifts of attention, the data are nevertheless consistent with the hypothesis that the left posterior parietal cortex plays a privileged role in orchestrating voluntary shifts of attention in object-centered coordinates. This is especially true when considered in light of the fact that voluntary shifts of attention, overall, resulted in greater activity in the left parietal cortex than in the right parietal cortex and that object-centered shifts of attention, in particular, resulted in greater activity throughout the attentional control network. The fact that activation was greater in the left parietal region during object-based shifts of attention than in any other region during shifts of attention into either reference frame suggests that damage to the left hemisphere would more severely impair object-centered shifts of attention than damage to the right hemisphere, in line with the predictions of the hemispheric specialization hypothesis. It is also important to recognize that the strong version of the hemispheric specialization hypothesis (Egly et al., 1994a), in which the left parietal cortex is *uniquely* involved in orchestrating shifts of attention in object-based coordinates, derives from a somewhat different paradigm involving the re-allocation of attention in response to invalid, *exogenous* cues, whereas the present study investigated the initial allocation of attention in response to valid, *endogenous* cues. Given that the brain systems involved in the top-down deployment of attention are largely separate from those involved in reorienting attention in response to invalid cues (Corbetta et al., 2000), it is not clear that the same predictions should be made concerning reference-frame effects during top-down and bottom-up shifts of attention. In this sense, our findings represent a novel demonstration of hemispheric asymmetries in parietal cortex during object-based attentional selection without contradicting their role in object-based attentional reorienting.

The basis of this parietal lobe asymmetry during voluntary orienting is not entirely clear, although several models have been proposed concerning functional specialization within parietal cortex that may give rise to the privileged role of the left hemisphere during object-centered shifts of attention. For instance, previous studies suggest that left and right parietal regions are more responsive to the local and global aspects, respectively, of a visual object or scene (Fink et al., 1996, 1997b,c, 1999; Heinze et al., 1998). Still, others have argued that the left hemisphere is more involved in encoding and representing relatively abstract aspects of visual stimuli while the right hemisphere is more involved in encoding and representing relatively concrete or form-specific information (Burgund and Marsolek, 1997; Kosslyn et al., 1992; Marsolek, 1995; Marsolek et al., 1996, 2002). Orienting to a location defined with respect to an object in the visual scene may require attending to relatively more local aspects of the visual display, which would arguably require greater left hemisphere involvement. Similarly, encoding and representing locations in an object-centered coordinate system may require a relatively more abstract level of representation and therefore engage the left hemisphere to a greater extent. The present results are therefore consistent with both of these possibilities.

Another dichotomy has been proposed between the representation of high and low spatial frequency information in the left and right parietal cortices, respectively (Grabowska and Nowicka, 1996; Martinez et al., 2001; Sergent, 1982). In the present study,

however, spatial frequency content of the relevant visual information was equivalent in the Object- and Viewer-Centered conditions. Although targets and distracters were on average closer to one another in the Object-Centered condition than in the Viewer-Centered condition (i.e., occurring at higher spatial frequencies), parietal cortex activity did not vary as a function of distracter distance during Viewer-Centered trials. Thus, the hemispheric asymmetries observed in the present study cannot be reduced to attending to differential spatial frequencies in the two conditions of interest.

In summary, we tested two distinct hypotheses concerning the neural mechanisms that underlie covert attentional orienting in object- and viewer-centered frames of reference using an event-related fMRI paradigm with rapid stimulus presentation rates. We found that attention-directing cues, in the absence of subsequent visual targets, engaged bilateral portions of the intraparietal sulcus, the lateral and medial superior frontal cortices, the insular cortices, as well as the left dorsolateral prefrontal cortex. This attentional control network was significantly more active when attention was deployed in object-centered space, particularly in the cortex surrounding the intraparietal sulci, the frontal eye fields, the supplementary motor cortices, and the anterior cingulate gyri. Finally, we found an asymmetry within the intraparietal sulcus such that the left hemisphere advantage was greater during object-centered shifts of attention than during viewer-centered shifts of attention. These results agree with previous demonstrations of a fronto-parietal attentional control network (Corbetta et al., 2000; Hopfinger et al., 2000) and support the hypothesis that the left parietal cortex plays a specialized role for implementing covert shifts of spatial attention in an object-centered coordinate system (Egly et al., 1994a).

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