The Brain Network Underlying Serial Visual Search: Comparing Overt and Covert Spatial Orienting, for Activations and for Effective Connectivity

S.L. Fairhall[1], I. Indovina[1,2], J. Driver[3] and E. Macaluso[1]

[1]Neuroimaging Laboratory, Santa Lucia Foundation, 00179 Rome, Italy, [2]Behavioral and Clinical Neuroscience Institute, University of Cambridge, Cambridge CB2 3EB, UK and [3]UCL Institute of Cognitive Neuroscience, University College London, London WC1N 3AR, UK

We used functional magnetic resonance imaging (fMRI) to investigate the brain basis of overt and covert forms of attention during search, while employing stringent control of both eye movements and attentional shifts. A factorial design compared overt and covert forms of goal-directed serial search versus stimulus-driven tracking. To match ocular changes and the number and magnitude of attention shifts across cells in the design, stimulus-driven tracking involved trial-specific "replay" of previous goal-directed eye movements. We found that, in terms of cortical activations, engagement of the dorsal fronto-parietal network by goal-directed attention did not depend on oculomotor requirements, being found similarly for covert attention, in accord with other work. However, analyses of effective connectivity (or "functional coupling") revealed that information flow within this network changed significantly as a function of both the task (goal-directed or stimulus-driven) and the overt versus covert form of attention. Additionally, we observed a distinct set of subcortical regions (pulvinar and caudate nucleus) engaged primarily during the covert form of goal-directed search. We conclude that dynamics within the dorsal fronto-parietal attentional system flexibly reorganize to integrate task demands and oculomotor requirements.

Keywords: attention, conjunction search, dynamic causal modeling, fMRI, oculomotor

The capacity to shift visual attention dynamically toward relevant sensory events allows us to actively shape our perceptual processes, adapting them to current needs and goals. A distributed network of dorsal fronto-parietal regions is believed to underlie such attentional control (cf. Corbetta et al. 1998; Corbetta and Shulman 2002). This network activates consistently across a variety of tasks that require the dynamic allocation of spatial attention (Corbetta et al. 1993, 1995, 1998; Nobre et al. 1997; Gitelman et al. 1999; Yantis et al. 2002; Bisley and Goldberg 2003). In humans, this fronto-parietal system encompasses regions of the intraparietal sulcus (IPS), the human "frontal eye fields" (FEF), and medially, the supplementary motor area (SMA). The localization of these regions appears broadly consistent with attention-related neural responses recorded in nonhuman primates (e.g., for the FEF, supplementary eye fields and the lateral IPS, see Bruce and Goldberg 1985; Schlag and Schlag-Rey 1987; Gottlieb et al. 1998; Moore and Fallah 2004; Thompson et al. 2005).

In the visual modality, dynamic shifts of attention may arise in either an overt mode, through ocular targeting with saccades leading to foveation of the attended stimuli; or in a covert mode, through the spatial shifting of attention independently of the line of gaze (James 1890; Posner et al. 1980). The relationship between covert shifts of attention and overt saccades appears to be closely related. For instance, the premotor theory of attention proposes that the capacity to shift attention covertly is in fact derived from the system for oculomotor control, with covert shifts of attention reflecting a latent unexecuted saccade (Rizzolatti et al. 1987). This has gained apparent support from numerous studies demonstrating overlapping neural substrates for overt and covert shifts of attention, both from electrophysiological recordings in non-human primates (e.g., Moore et al. 2003; Moore and Fallah 2004) and from imaging studies in humans (e.g., Corbetta et al. 1998; Nobre et al. 2000; Perry and Zeki 2000; Gitelman et al. 2002; de Haan et al. 2008). However, although this overlap in activated loci appears broadly consistent with premotor theory, recruitment of common cortical regions need not entail a strictly common mechanism. Indeed, recent single-unit recordings have shown some interdigitated yet distinct neural populations within the FEF, which may separately be more involved in attentional processes or in saccade control (Sato and Schall 2003; Thompson et al. 2005). The exact relationship between oculomotor control and shifting of spatial attention remains under active debate (Colby and Goldberg 1999; Snyder et al. 2000a, 2000b; Gottlieb 2007).

Several previous human imaging studies have sought to address this, but typically were restricted to simple left-right saccade tasks, and/or were arguably limited by lack of appropriate control conditions (e.g., Corbetta et al. 1998; Nobre et al. 2000; Perry and Zeki 2000; Beauchamp et al. 2001; Astafiev et al. 2003; Himmelbach et al. 2006). In a pioneering imaging study, Corbetta et al. (1998) investigated overt and covert orienting along the horizontal axis. Covert attention or eye movements were guided by the changing position of a target that shifted predictably along this axis. The overt and covert shifting tasks were compared with mere maintenance of central fixation and revealed overlapping activation within a dorsal fronto-parietal network. These results may be interpreted as evidence for a common neural substrate for eye-movement control and covert shifts of spatial attention. However, an alternative possibility is that the 2 active tasks simply shared other nonspecific task demands that were not required during simple fixation (e.g., maintenance of a task set, target detection, overall alertness, etc.). In the same study, the direct comparison between the 2 shifting tasks showed that the fronto-parietal network was more active during covert than overt shifting. But it should be noted that during the overt task, the target was always presented at the fovea, whereas in the covert task, target detection occurred in the peripheral visual field. Accordingly, the differential activation might potentially relate to peripheral versus foveal target discrimination processes, rather than control of covert spatial attention per se.

Similar arguments can be advanced for most studies that reported overlapping activation for overt and covert orienting when using low-level baselines that required neither eye movements nor shifts of attention (e.g., Nobre et al. 2000; Perry and Zeki 2000; Ohlendorf et al. 2007). Beauchamp et al. (2001) avoided the issue of low-level baselines by using a parametric manipulation of shifting rate, with or without eye movements. This revealed an increase of activity in precentral and intraparietal regions with higher shift rate, during both overt and covert shifting modes. This approach does indeed prevent any trivial overlap resulting from utilization of low-level baseline conditions, but it cannot rule out that the common activations potentially reflect covert shifts of attention that might often co-occur with eye movements (but not necessarily be due to the saccade plans per se, unlike premotor theory). Moreover, such an approach does not provide any control for the sensory consequences of performing eye movements. Those alone might potentially account for the greater fronto-parietal activation for overt than covert shifts that was found in the Beauchamp et al. study (but see Perry and Zeki 2000).

Here we introduce a new paradigm to investigate the interplay between goal-directed shifts of attention and eye movements during visual search, while now including stringent controls for eye movements per se and shifts of attention per se. To achieve this, we implemented a fully factorial design where goal-directed shifts of attention (present or absent) and orienting mode (overt or covert) were manipulated in an orthogonal manner (see Fig. 1A). To trigger goal-directed attention, we employed a specific conjunction visual-search task that is well known to require voluntary, goal-directed shifts of spatial attention (Treisman and Gelade 1980; Wolfe 1994). Similarly to simpler forms of left-right attentional orienting (e.g., Corbetta et al. 1998; Nobre et al. 2000), serial visual search has also been found to activate the dorsal fronto-parietal attentional network (Corbetta et al. 1995; Donner et al. 2000, 2002; Leonards and Singer 2000; Nobre et al. 2003; Anderson et al. 2007). Moreover, it has been suggested that recruitment of IPS and FEF during serial search may specifically reflect the task demand for shifts of goal-driven spatial attention (Yantis et al. 2002).

Two previous studies have employed a serial-search paradigm to investigate potential relations between attention shifting and eye movements for functional magnetic resonance imaging (fMRI) activations. In these studies, exploratory saccades performed during serial visual search were compared with simple saccades between 2 points (Gitelman et al. 2002) or evenly spaced points on a cross (Himmelbach et al. 2006). The results showed increased activation in the fronto-parietal attention networks, but again the relative complexity and diversity of saccadic movements between tasks were unmatched. Here we addressed this potential confound directly by introducing a tracking or "replay" control condition. We recorded subject-specific, trial-by-trial search behavior during overt serial search, and we replayed this to the subject online during the tracking condition (where they now had to follow their previous voluntary search path, either covertly or with their eyes). Thus, the tracking task did not require purely voluntary goal-directed attention shifting, but it did involve shifts of attention (and of eye movements in the overt tracking condition) around the entire visual display, in a spatially comparable manner to the voluntary search conditions. In this way, the number and magnitude of
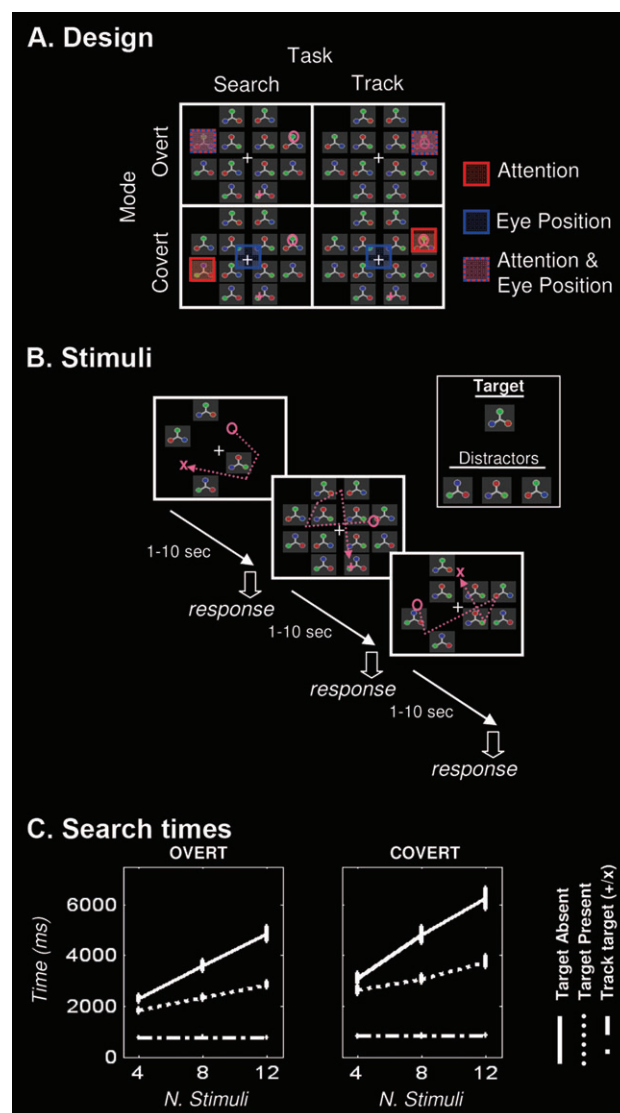

Figure 1. Experimental design, stimuli and search times. Panel (A) illustrates schematically the 2 × 2 factorial design of the experiment, with the orthogonal factors of Task (search or track) and Mode (overt or covert) fully crossed. Panel (B) depicts the visual displays for 3 successive trials (diagonal timeline shown), and at top right the different item types (target or distractors) were used for the Search task. In the overt and CS conditions (OS and CS), the task of the subject was to search for the target stimulus (randomly present on 50% of the trials) among a variable number of distracters (set size = 4, 8, or 12). The trial terminated when the subject responded with a keypress (target present/absent), or after 10 s. In the Track conditions, the task was to follow either overtly (OT) or covertly (CT) a purple circle that was flashed throughout the display, replaying the sequence of fixations recorded during previous OS-trials. After an unpredictable delay, this tracking cue turned into a + or an x, and the subject performed a 2-alternative forced choice (2-AFC). The purple circle was presented also in the Search trials, but the subject was asked to ignore it. Panel (C) shows the mean search times (±SEM) for OS and CS, separately for target present (dotted function) and target-absent (solid function) trials; plus the reaction times for the 2-AFC Task in Track conditions (dashed functions). The Search times increased linearly with set size, demonstrating the highly serial nature of the Search task, for which that target was distinguished from distractors only by its fine conjunction of color and spatial layout.

attentional shifts, their eccentricity, and any low-level sensori-motor activations due to such factors could now be matched across the experimental conditions on a trial-by-trial basis.

In addition to refining the experimental paradigm, we sought also to expand on previous work, by taking the study of the

dorsal fronto-parietal network beyond the domain of mere voxel-level activation of this network, toward a network-dynamics approach. Accordingly, we employed measures of effective connectivity or of "functional coupling" between areas (in terms of dynamic causal modeling; DCM, cf. Friston et al. 2003) to investigate the effects of attention and of oculomotor control on connectivity between the well-established nodes of the dorsal fronto-parietal network.

Thus, our current investigation aimed 1) to test the relative contribution of goal-directed attention and oculomotor control in the activation of the dorsal fronto-parietal network (IPS, FEF, and SMA), while now controlling for the lower-level sensory and motor processes that may have confounded previous studies; 2) to assess possible "interactions" between attention and oculomotor control during performance of a serial search task, with our fully factorial design allowing formal tests of any such interactions for the first time; and 3) to investigate for the first time whether overt and covert orienting produce differential patterns of effective connectivity among nodes within the fronto-parietal network.

Materials and Methods

Participants
Twelve right-handed healthy volunteers (aged 18–35, 8 females) participated. After receiving an explanation of procedures, all gave written informed consent. The study was approved by the independent Ethics Committee of the Santa Lucia Foundation (Scientific Institute for Research Hospitalization and Health Care).

Paradigm
The aim of the study was to investigate the neural substrates of serial visual search and the relationship with oculomotor control. To address this, we manipulated 2 experimental factors orthogonally: "Task" (goal-directed Search for a target, or stimulus-driven Tracking of a moving cue) and "Mode" (Overt eye movements, or Covert attention while maintaining central fixation). Accordingly, during fMRI acquisition, subjects either searched for a target by moving their eyes (Overt Search, OS) or without eye movements (Covert Search, CS), or they tracked a moving cue with their eyes (Overt Track, OT) or without eye movements (Covert Track, CT); see Figure 1A. Critically, on OT-trials, the movement of the tracked item was dictated by the sequence of fixation acquired on previous OS-trials, allowing us to reproduce comparable sequences of actual saccades in the OS and OT conditions.

To ensure a highly serial search during the Search conditions, we minimized the saliency of individual stimulus features that were distributed homogenously across the search field, employing a well-established conjunction-search task (Wolfe 1994; Huang and Pashler 2007). We confirmed the seriality of the search process by manipulating the number of search items (set size = 4, 8, or 12 items) and measuring whether the search times increased linearly with increasing set size.

Stimuli and Tasks
In each trial, the search items were presented on an octagonal grid spanning ~13 deg in the horizontal and the vertical dimensions, plus a white central fixation cross (see Fig. 1A,B). Each item comprised 3 different small colored circles (blue, green, and red) arranged at the vertices of a triangle. The target was defined by a specific combination of colors and their spatial layout (i.e., a complex conjunction of features), whereas the 3 other possible local configurations defined the nonrelevant distractors (see Fig. 1B, panel on the right). The target was present in 50% of the trials (randomly determined). The 4 experimental conditions (OS, CS, OT, and CT) were presented in blocks of 6 consecutive trials, with 2 repetitions for each set size. Written instructions about the upcoming condition were presented for 3 s at

the start of each 6-trials block. Stimuli presentation (including eye-movement detection/replay) using Cogent 2000 software (Cogent 2000, Functional Imaging Laboratory, Wellcome Department of Imaging Neuroscience, UCL, London) within the matlab environment. Fixations were detected using in-house software (see "Eye tracking" below).

Overt and Covert Search
In these 2 conditions, subjects searched for the target and responded once the target was found, or as soon as they determined that the target was not present in the display. In the overt search condition (OS), participants were allowed to move the eyes throughout the search display (and their eye position was recorded, contributing to later "replay" in the overt-tracking condition, see below). In the covert condition (CS), subjects were instructed to search for the target while maintaining central fixation (as also confirmed by eye tracking throughout scanning, see below), thus searching via covert shifts of goal-directed spatial attention. Each trial was terminated by the button press or after 10 s in the rare (less than 1%) cases of no response. Button presses with the index or middle finger of the right hand were used to indicate target present or target absent, respectively.

Overt and Covert Tracking
In the 2 tracking conditions, the sequence of fixations recorded during the overt search (OS-trials) were "replayed" to participants. Each new fixation was triggered by a purple circle briefly appearing at a different position. To prevent foveation of that purple circle while it was still visibly present, the purple cross appeared at each new position for only 150 ms, and so had been extinguished by the time that position was fixated in the over track (OT) condition. The temporal interval between successive presentations of the circle matched the fixation duration recorded in OS-trials; hence, the time that the eye dwelt at particular positions was well matched between OT and OS conditions (see Fig. 2A,B). For both tracking conditions, participants now had to ignore the array of search items and focus on the flashing circle instead. Thus, in these tracking conditions, spatial attention was again shifted around the visual display, but now in a stimulus-driven manner (by the circle) rather than a strictly goal-driven manner as in the search task. During the overt tracking condition (OT), participants were instructed to follow the stimulus with their gaze, and this was monitored with eye tracking. During the covert condition (CT), subjects were instructed to maintain central fixation (as confirmed by the eye tracker) and to track the circle only covertly. To ensure continued vigilance in both cases, at the (unpredictable) end of its path the flashing circle changed and participants had to indicate whether it turned into a "+" or an "x" by pressing a left or right button with right index or middle finger, respectively. To make the overall visual stimulation comparable, this flashing circle was also present in the 2 Search conditions (OS and CS), but in those conditions, participants simply ignored the stimulus, attending to the concurrent search display instead.

The duration of each trial was variable, depending on the participant's search times (max. 10 s). Irrespective of condition, the intertrial interval was 3–4 s. For each condition, a 6-trial block was repeated 3 times in each run of continuous MRI acquisition (72 trials per run). The 3 repetitions were grouped so that first there was always an OS 6-trial block (for sequence of fixations recording; see below), followed by the CS/OT/CT-blocks in a randomized order. We acquired 3 runs per participant, for a total of 54 repetitions of each trial-type (OS, CS, OT, and CT).

Magnetic Resonance Imaging
Participants lay in the scanner and viewed the visual stimuli through a mirror system. A Siemens Allegra (Siemens Medical Systems, Erlangen, Germany) operating at 3 T and equipped for echo-planar imaging acquired functional MR images. A quadrature volume head coil was used for radio frequency transmission and reception. Head movement was minimized by mild restraint and cushioning. Thirty-two axial slices of functional MR images were acquired using blood-oxygenation-level-dependent imaging (3×3 mm, 2.5 mm thick, 50% distance factor, TR = 2.08 s, TE = 30 ms), covering the entire cortex.
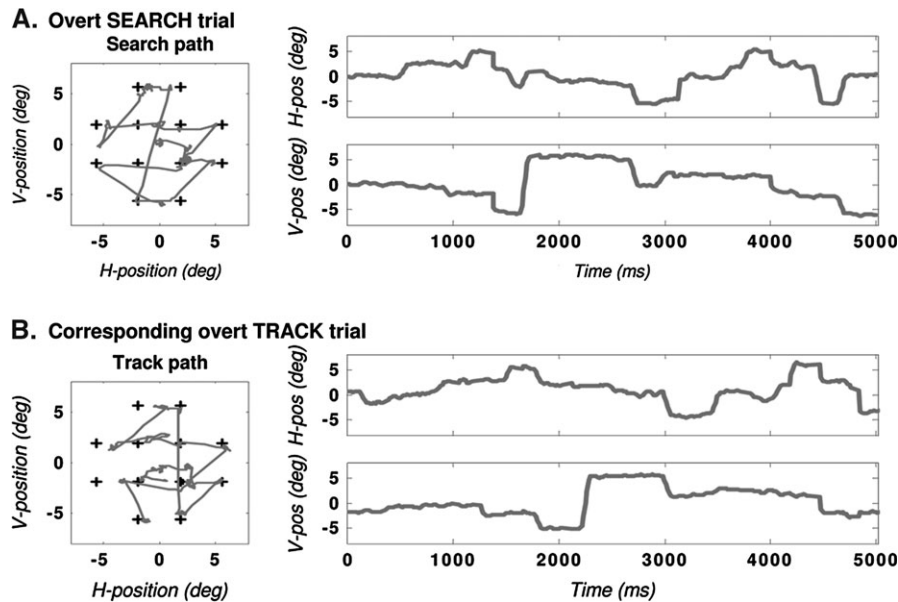
Figure 2. An example of eye-movement recording and replay. (*A*) Search path recorded during a single OS-trial. In this trial, the target was absent and the subject explored all 12 distractor items (see panel on the left). The 2 graphs on the right side show the vertical and the horizontal eye position as a function of time for this OS-trial. Panel (*B*) shows the corresponding OT-trial, when the subject performed a sequence of saccades toward the tracking cue that followed a path derived from the earlier OS-trial (cf. panel *A*). Although some of the saccades in the OT-trial had a slightly smaller amplitude than the original OS-trial (note that the tracking cue was flashed for 150 ms only), the track paths of the 2 trials were highly similar and correlated (see main text). The 2 graphs on the right display vertical and horizontal gaze positions as a function of time, showing the expected tracking delay between OT-trial and OS-trial (416 ms, for this specific trial; see also main text for how tracking delays were computed).

Eye Tracking

Eye position was monitored throughout using an ASL Eye-Tracking System with remote optics, custom-adapted for use in the scanner (Applied Science Laboratories, Bedford, United States; Model 504, sampling rate = 60 Hz). For each subject, the eye-tracking system was calibrated before fMRI scanning. The subject performed a series of eye movements, making 9 sequential saccades to the nodes of a 3 × 3 grid. The sequence started from the top-left of the grid (horizontal position: –5.6 deg; vertical position: +5.6 deg) and ended at the bottom-right (H-pos = +5.6 deg; V-pos = –5.6 deg).

A key novel aspect of the current study was that eye movements were recorded, processed, and replayed to the subject (for the tracking conditions) using an interactive, online procedure. This involved recording of the sequence of fixations during 6 OS-trials and replaying these sequences (purple circle briefly flashed at each fixation) in the 4 subsequent 6-trial blocks (CS, OT, CT, plus the next OS-block; the [irrelevant] sequence for the first OS-block was attained from the data of a pilot subject). This allowed us to obtain subject-specific "control-trials" (OT condition) for each OS-trial, with comparable patterns of eye movements (see Figs. 2 and 3). We also "replayed" (via the purple circle) the recorded sequence of fixations from OS-trials for the CS and CT conditions, but only in the CT conditions did subjects have to covertly track the purple circle.

In the OS-trials, spontaneous changes of fixation during voluntary search with exploratory saccades were detected using a velocity criterion (threshold = 25 deg/s, along the horizontal or the vertical axis). The coordinates of each new fixation following an identified saccade were computed as the horizontal and vertical eye position 67 ms after the eye trace exceeded the velocity threshold, thus identifying the subsequent locus of the new postsaccade fixation point. The sequences of fixation from the 6 OS-trials were then randomly assigned to the next 4 6-trials blocks. It should be noted that because, on average, CS times (to self-terminated trial-end) were somewhat longer than OS times (see also plots in Fig 1*B*), the sequence of OS-fixations could be repeated more than once during a CS-trial (although recall that the flashing circle was task irrelevant during CS). The duration of the OT-trials, for which the purple circle served as the saccade target, was matched to the duration of OS-trials, replaying the OS-fixation sequence exactly once. On the other hand, the duration of the CT-trials was matched to the CS-trials and typically required replaying the OS-fixations sequence more than once. Display duration was determined by search performance, with corresponding durations in the Track conditions, leading to an average presentation time of 3.49 s.

Data Analysis

Analysis was performed in SPM2 and SPM5 (Wellcome Department of Cognitive Neurology) as implemented in MATLAB 6.5 (The MathWorks Inc., Natick, MA). After discarding the first 4 volumes of each run, all images were corrected for head movement. Slice-acquisition delays were corrected using the middle slice as reference. All images were normalized to the standard SPM2 EPI template, resampled to a 2 mm isotropic voxel size, and spatially smoothed using an isotropic gaussian kernel of 8 mm full-width half-maximum. The time series at each voxel for each participant were high pass filtered at 360 s and prewhitened by means of an autoregressive model AR(1).

Statistical inference was based on a random effects approach (Penny and Holmes, 2003). This comprised 2 steps. First, for each subject the data were best fitted at every voxel using a combination of effects of interest. These were box functions representing the duration of the 4 conditions for each trial, convolved with the SPM2 hemodynamic response function (HRF). It should be noted that by modeling the variable duration of each trial, we implicitly accounted for the effect of the set size (4, 8, or 12 items), in the Search conditions. This is because larger set sizes lead to longer search times (see below) that after convolution with the HRF result in greater than expected blood-oxygen-level dependent (BOLD) response. We also modeled the instructions and the onsets of button-press response as delta functions. Parameters of motion were included in the design matrix as covariates of no interest. Linear contrasts were used to determine responses for the 4 conditions of interest (CS, OS, CT, and OT), averaging across fMRI runs. This resulted in 4 contrast images per subject. The contrast images then underwent the second step, comprising a within-subject analysis of variance (ANOVA; implemented in SPM5) that modeled the effect of the 4 conditions in a 2 × 2 factorial design. Finally, linear compounds were used to compare the condition effects, now using between-subjects variance (rather than between scans) in a random-effects approach across subjects. Correction for nonsphericity was

A. Fixation-position (single subject)
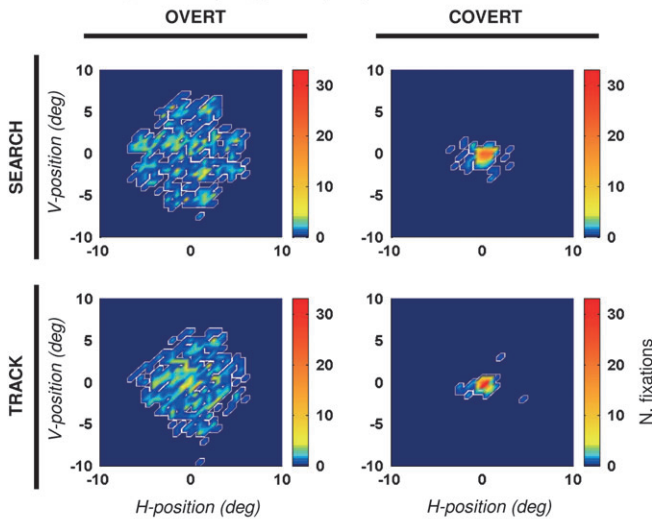
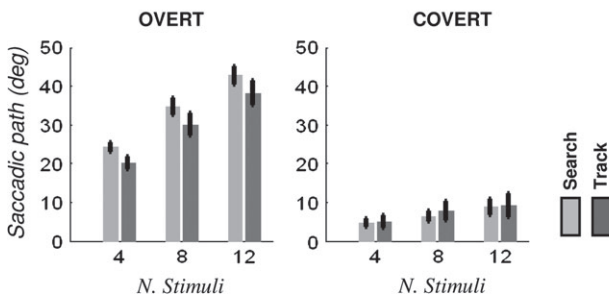## B. Cumulative saccadic path-length (group)

Figure 3. Fixation position and cumulative saccadic path length in the 4 experimental conditions. (*A*) Number of fixations in the search display as a function of condition, for an illustrative single subject. The plots show that during the OS and OT, the subject explored the relevant regions of the visual display, whereas in the covert conditions (CS and CT), they maintained central fixation. Plots depict a 2D histogram of fixation frequency following sorting into 0.5-deg bins with intervening points bilinearly interpolated. (*B*) Average length of the cumulative saccade paths (±SEM) in the group. As expected, the average cumulative saccade path was much longer in the overt conditions (plot on the left) than in the covert conditions (plot on the right). The cumulative path length increased with set size, because of the corresponding increase of trial duration (cf. Fig. 1*C*). As also shown in Figure 2 for a single trial, the cumulative saccade paths tended to be slightly shorter in OT-trials than OS-trials (left panel, compare light vs. dark bars), because subjects slightly underestimated the tracking-target position. Nonetheless, overall the pattern of eye movements was highly similar and correlated for the 2 levels of Task (search and track), but it was different for the 2 levels of Mode (overt and covert).

used to account for possible differences in error variance across conditions and any nonindependent error terms for the repeated measures.

For statistical inference, we first highlighted the entire network of brain areas activated during our tasks, computing the mean activation of the 4 experimental conditions against the intertrial interval. This included occipital visual cortex, dorsal and ventral fronto-parietal areas plus subcortical regions as the superior colliculus and the thalamus (see Table 1). Within this search volume we then assessed main effects and interactions of our 2 × 2 factorial design (search/track Task × overt/covert Mode). The main effects allow the identification of the overall influences of the 2 different tasks or modes of orienting. The interaction contrasts (for Task × Mode) allow tests for any differences between Search and Track that are specific for 1 or the other form of orienting (i.e., Covert or Overt). All reported clusters are significant at P-corr < 0.05, corrected for multiple comparisons at cluster-level (following an initial voxel-level threshold of P-unc. < 0.001) and considering all voxels

Table 1

Mean effect of all conditions assessed against the intertrial interval, with extent, location, and significance of activation

Region	$P_{(corrected)}$	Extent (cm³)	Hemi	Z score	MNI		
					x	y	z
SOG	<0.001	364.2	Left	inf	−12	−102	10
SOG			Right	inf	20	−98	12
FG			Left	5.73	−44	−66	−15
FG			Right	5.23	51	−70	−16
IPS			Left	7.41	−30	−60	62
IPS			Right	6.46	32	−46	46
FEF			Left	7.52	−26	−10	62
FEF			Right	6.86	34	-2	54
SMA			Medial	6.73	−4	−6	58
Pre-SMA			Medial	6.24	4	10	56
MFG			Left	5.55	−26	−6	52
MFG			Right	7.77	42	−2	58
MTG			Left	5.79	−46	−78	10
STS/TPJ			Left	3.57	−50	−40	−12
STS/TPJ			Right	4.09	56	−40	14
IFG			Left	5.88	−54	4	34
IFG	<0.001	9.7	Right	4.65	34	27	1
Thalamus	<0.001	32.0	Left	7.42	−20	−30	−2
Thalamus			Right	6.80	22	−30	−2
SC			Left	4.26	−6	−26	−9
SC			Right	5.35	8	−26	−6

Note: These clusters were used as the volume of interest to assign corrected P values to all comparisons between conditions (see Method section). Abbreviations: FEF, frontal eye fields; FG, fusiform gyrus; IFG, inferior frontal gyrus; IPS, intraparietal sulcus; MFG, middle frontal gyrus; MTG, middle temporal gyrus; SC, superior colliculus; SMA, supplementary motor area, pre-SMA, prefrontal supplementary motor area; SMG, supramarginal gyrus; SPL, superior parietal lobe; SOG, superior occipital gyrus; STS, superior temporal sulcus;. Lower case "a" and "p" indicate anterior and posterior. All reported clusters were significant at $P < 0.05$, cluster-level corrected.

showing an average positive effect (*t*-test) of the experimental conditions (see Table 1) as the volume of interest (Worsley et al. 1996). Masking was accomplished by using this volume of interest as an inclusive mask for the generation of images and as the delineator for a small volume correction for the generation of corrected statistics.

Results

Behavioral Measures

Figure 1*C* shows the mean search times for OS-trials (panel on the left) and for CS-trials (panel on the right), separately for target absent (continuous line) and target present (dotted line). As expected, given the complex conjunction of features (color and spatial configuration) that was required to identify the target among distracters, the search times increased substantially and linearly with increasing set size, providing the classic hallmark of serial visual search (Treisman and Gelade 1980). To assess the linearity of this relationship, for each subject a regression was performed between Set size (4/8/12) and reaction time. Group analyses showed highly significant effects for both OS (slope of 142 ms/item, $F_{(1,11)} = 163$, $P < 0.001$) and CS (slope of 173 ms/item, $F_{(1,11)} = 130$, $P < 0.001$) search. The regression parameters also entered a 2 × 2 within-subject ANOVA with Mode (overt/covert) and Target presence (present/absent) as independent factors. This showed that the linear relationship between RTs and set size was not significantly different for the overt and covert conditions (main effect of Mode was not significant: $F_{(1,11)} = 3.9$, $P = 0.074$, n.s.). Moreover, there was no Mode × Target presence interaction ($F_{(1,11)} = 1.9$, $P = 0.19$, n.s.), again suggesting that similar serial processes were occurring during both types of search, an important aspect of our design. As typically found in serial

search tasks (Wolfe 1998), steeper slopes were found for target absent than target present trials (main effect of Target presence: $F_{(1,11)} = 70.9$, $P < 0.001$). No significant linear trends were observed in either overt or covert tracking conditions ($F < 1$ for both OT and CT), as expected.

A key aspect of the current design concerned the replay of eye-movement paths from the OS condition in the OT condition (see Figs. 2 and 3). We quantified the similarity of these patterns in 2 ways. First, we calculated the average cumulative saccadic path length for the 4 experimental conditions (see Fig. 3B). A within-subject ANOVA with Mode (overt/covert) and Task (search/track) and Set size (4/8/12) as independent factors revealed the expected main effect of Mode (with much longer paths for overt than covert Mode; 31.6 vs. 6.9 deg $F_{(1,11)} = 129.3$ $P < 0.001$) and main effect of Set size ($F_{(1,11)} = 47.4$, $P < 0.001$). The effect of Set size can be readily explained by the systematic increase of trial duration with larger set sizes: Extended eye traces lead to the detection of more changes of fixation and, consequently, to longer cumulative saccadic paths. Inspection of the data revealed that the 6.9 deg of scan path identified in the covert conditions could be attributed to the cumulative detection of non-systematic noise (position shifts < 1 deg) within the eye-tracker setup, by the sensitive saccade-detection algorithm. Cumulative scan-paths were quite closely matched in the 2 overt conditions (33.8 vs. 29.4 deg, for OS and OT). The tendency for slightly longer cumulative saccade paths in Search than Track overt conditions may reflect the eye falling slightly behind the purple circle in OT-trials (see also Fig. 2). But nevertheless, there was very good agreement in the spatial pattern of eye movements for OS and OT conditions, as confirmed further below.

We calculated correlation coefficients between the original OS-trials and the corresponding OT-trials. Because of the inevitable delay between the appearance of the tracking cue (purple circle) at a new location and the saccadic eye movements to this cue in OT-trials, we iteratively shifted the OT-trace back in time (in steps of 16 ms, matching the temporal resolution of the eye-tracking system) computing the OS/OT-correlations for each time point. The time point of maximal correlation was used to estimate the average delay between OS and OT eye traces. This procedure yielded an average delay of 434 ms, and a high average correlation coefficient of 0.833. This confirms the high correspondence between scan paths in OS- and OT-trials (see Figs. 2 and 3).

BOLD Activation Results

Effect of Goal-Driven Search
Figure 4A and Table 2 show the regions demonstrating an enhanced response during goal-directed Search versus stimulus-driven Track conditions ([OS + CS] > [OT + CT]). Increased activation was observed across visual, parietal (anterior and posterior IPS), and frontal regions (FEF, pre-SMA, lateral prefrontal cortex [PFC], frontal operculum). The magnitude of the BOLD response (see bar graphs in Fig. 4A) reveals a similar trend across all regions, with pronounced differences between Search and Track but with little or no modulation by Mode. For the fusiform gyrus (FG) that showed both a main effect of Task (search > track) and a main effect of Mode (overt > covert; see below), the effect of search had a similar size for overt and

covert Modes (compare bar 1–3 and bar 2–4 in the graphs of Fig 4A that show additive effects of Search and Mode in this region). Concordant with these observations, there was no significant Task by Mode interactions for these regions, not even at an uncorrected threshold.

Main Effect of Stimulus-Driven Tracking
Because our control conditions (OT and CT) also entailed a form of visuo-spatial attentional orienting, namely, stimulus-driven orienting, we also tested for the main effect of Track versus Search ([OT + CT] > [OS + CS]). It should be noted that, as in the case of the Search versus Track contrast, any trivial sensory-motor aspects should be well matched across the conditions by virtue of our fully factorial design. The Track conditions revealed bilateral activation of a distinct network of regions of the superior parietal lobe and regions at the temporal–parietal junction (TPJ): the superior temporal sulcus and middle temporal gyrus (STS and MTG) and the supra-marginal gyrus (SMG; see Fig. 4B and Table 2). These regions activated during both overt and covert forms of stimulus-driven tracking. This can be observed in the signal plots of these regions (Fig. 4B), comparing bar 3 versus bar 1 (track vs. search, in the overt mode) and bar 4 versus bar 2 (for the covert conditions). Thus stimulus-driven attentional tracking activated regions around the TPJ (plus the superior parietal lobule), irrespective of oculomotor requirements.

Effect of Overt Mode
The main effect of Overt Mode ([OS + OT] > [CS + CT]) should reveal any brain regions differentially activated due to the demands of overt oculomotor behavior, as well as regions responsive to the altered sensory input resulting from eye movements. We hypothesized that activation within occipital cortex should result largely from the latter, whereas activations elsewhere may be more likely to reflect oculomotor control per se. Increased activation resulting from eye movements was observed contiguously throughout the occipital cortex, including dorsal, lateral, and ventral occipital cortex, peaking in BA17 (see Table 2). Within these regions, there was no interaction between Mode and Task, indicating that this modulation by eye movement did not vary with search (see the signal plot for the FG in Fig. 4 for a representative pattern of activation). But outside the occipital cortex, no significantly increased activation was observed for overt versus covert conditions. Even at a very lenient uncorrected threshold (P-unc. = 0.05), no differentiation was seen within the IPS or FEF (cf. also signal plots, Fig. 4). Thus these dorsal fronto-parietal regions activated strongly during both OS and CS, but they were unaffected by mere eye movement when attentional components are carefully taken into account (n.b. attention shifts around the visual display also occurred in the "control" covert conditions that are subtracted here).

Effect of Covert Mode
Next we tested for the main effect of covert Mode, comparing conditions requiring maintenance of central fixation versus conditions with eye movements allowed ([CS + CT] > [OS + OT]). This is expected to identify any regions involved in the uncoupling of the spatial attention control (goal driven for Search and stimulus-driven for Track) from overt oculomotor control. This contrast revealed a network of regions including bilaterally the putamen, anterior thalamus and regions of the
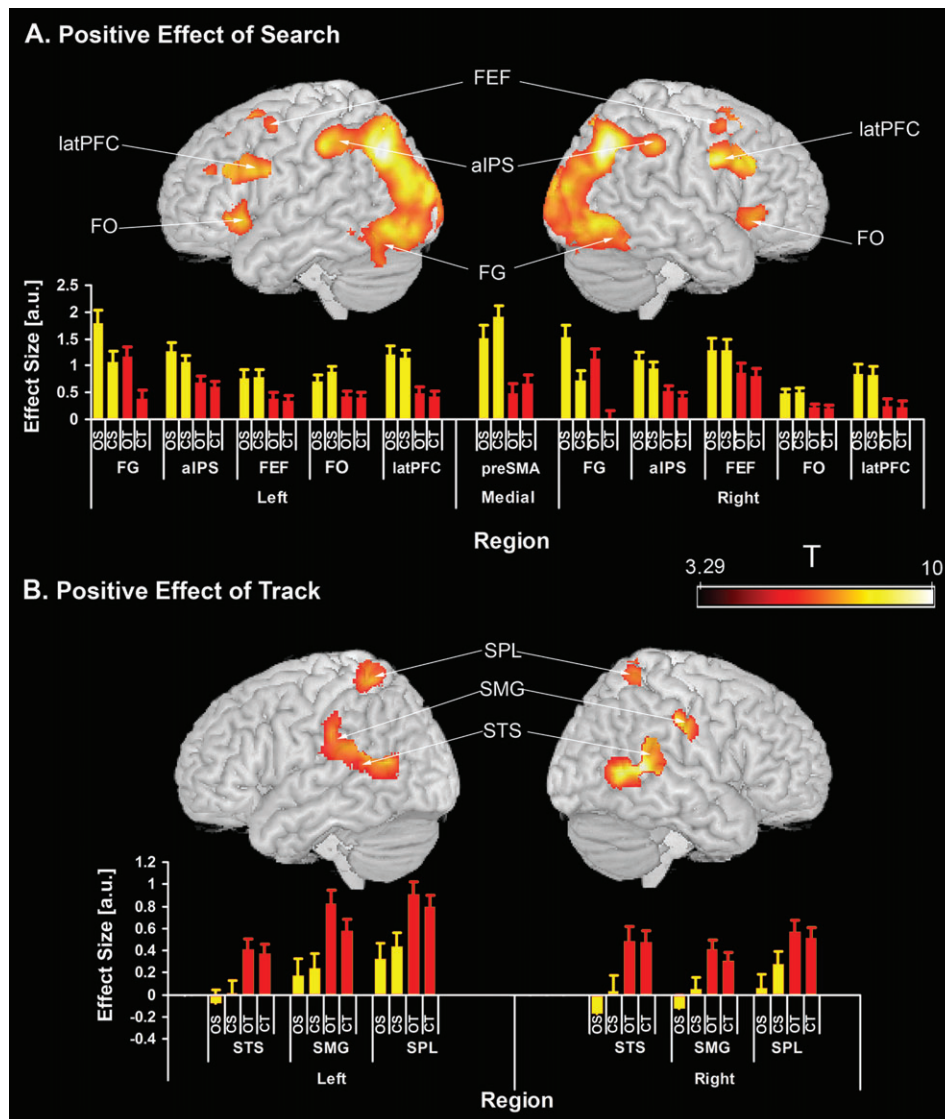
Figure 4. Location, significance, and effect size for the main effect of Search and Track. (*A*). Positive influence of search (i.e., Search > Track conditions), displayed on the lateral surface, revealing activation dorsal parietal regions, dorsal and ventral premotor cortex, plus visual areas. Additionally, regions of the thalamus were found to be modulated by search. Bar graphs depict the estimated activity (in arbitrary units, ±SEM) for each condition at peak voxels within each region; note yellow bars (search) higher than red bars (track). (*B*) Positive influence of track (i.e., Track > Search conditions). This reveals activation of the SPL and STS/SMG, with the latter regions comprising the posterior parts of the putative "ventral" attention network; note red bars (track) higher than yellow bars (search) in these regions.

caudate nucleus, as well as cortical regions in the right insula and medially the SMAs.

Analysis within these regions revealed the critical role of the covert search condition (CS) in particular in the positive main effect of covert mode (cf. signal plots Fig. 5). To reflect this, Figure 5 depicts the interaction between Mode (Covert > Overt) and Task (Search > Track, i.e., [CS–OS] > [CT–OT], at *P*-corr < 0.05, cluster-level correction). The significant influence of this interaction encompasses large sections of the thalamus extending into the pulvinar and inferiorly into regions anatomically consistent with the superior colliculus. We would expect this interaction to detect instances where the difference between CS and CT is greater than that between OS and OT; but it will also detect instances where the difference between OT and OS is greater than the difference between CT and OS. The significant influence of this interaction encompasses large sections of the thalamus extend-

ing into the pulvinar and inferiorly into regions anatomically consistent with the superior colliculus. With the exception of the left pulvinar, this interaction was driven by greater activation during CS. The interaction shows that the increase seen in these regions during CS cannot be explained in terms of common sensory or search demands in general, but that these regions are specifically recruited during covert forms of search. It should be noted that this network was largely distinct from both the dorsal and ventral fronto-parietal networks (see effect of Search and of Track, above).

Functional Coupling in Dorsal Fronto-parietal Regions

A relatively surprising finding, from our voxelwise analyses of fMRI activation was that the pattern of activation for the dorsal fronto-parietal network (including IPS and FEF) could be fully explained by attentional factors (goal-directed orienting) and appeared unaffected by oculomotor factors (no main effect of

Mode, nor any Mode × Search interactions within the dorsal fronto-parietal network). However, intraregional fMRI analyses can only capture local changes in BOLD activity and so are insensitive to any task-induced changes in the degree of coordination or "coupling" between distinct but interconnected brain regions. Such potential dynamic interregional interactions can be captured in terms of effective connectivity, through DCM (Friston et al. 2003; Penny et al. 2004). DCM relies on the construction of neural models that are experiment dependent and requires some a priori specification of the brain

	Region	$P_{(corrected)}$	Extent (cm³)	Hemi	Z score	MNI		
						x	y	z
Search	pIPS	<0.001	135.8	Left	7.25	−28	−68	38
	pIPS			Right	7.55	28	−66	38
	aIPS			Left	5.49	−44	−36	40
	aIPS			Right	6.13	48	−32	42
	FG			Left	4.81	−32	−54	−20
	FG			Right	4.25	32	−52	−18
	Pre-SMA	<0.001	19.9	Medial	6.88	0	18	50
	FEF			Left	4.57	−28	4	54
	FEF	0.041	1.4	Right	4.53	34	0	54
	IFG	<0.001	9.3	Left	6.66	−44	2	32
	MFG			Left	6.00	−50	24	30
	FO	<0.001	3.7	Left	5.09	−28	24	−4
	FO	<0.001	6.7	Right	5.69	26	26	−4
	MFG	<0.001	12.4	Right	5.60	42	30	28
	IFG			Right	5.52	44	4	26
	Thalamus	0.004	2.6	Left	4.39	−16	−6	16
	Thalamus	<0.001	4.6	Right	4.28	20	−10	18
Track	pSTS	<0.001	8.5	Right	7.18	60	−46	8
	pMTG			Right	6.69	60	−60	10
	SMG	0.014	2.4	Right	6.66	66	−22	34
	SPL	<0.001	0.2	Right	4.81	22	−52	66
	pSTS	<0.001	9.9	Left	5.80	−64	−34	26
	pMTG			Left	5.60	−54	−60	12
	SPL	<0.001	6.1	Left	5.34	−24	−50	64

Note: Abbreviations as in Table 1. All reported clusters were significant at $P < 0.05$, cluster-level corrected.

regions involved; concerning the driving input into the model, interregional connectivity (also known as intrinsic coupling) and any extrinsic modulation of this connectivity by experimental conditions (Friston et al. 2003; Stephan et al. 2007).

Here we used DCM to characterize effective connectivity across those nodes in the dorsal fronto-parietal network that we had already found to be activated specifically during goal-directed search (IPS, FEF, and pre-SMA; cf. also Fig. 4A), but to be unaffected (in terms of overall activation) by search Mode (overt/covert). Driving input was modeled as entering the visual cortex (here the FG, cf. Fig. 4). Reciprocal interregional connections were considered to link the FG to elements of the dorsal fronto–parietal network (IPS, FEF, and pre-SMA) through the IPS (see Fig 6C). Each of the 4 experimental conditions was allowed to separately modulate (as extrinsic modulations) the connections within the fronto-parietal network and the descending connections from the IPS to the FG. In addition, the main effect of Search (across both Modes) was included as extrinsic modulation of ascending connection from FG to IPS. It should be noted that allowing extrinsic modulation by all conditions on this connection would be problematic for the analysis, because the strong driving input entering the model in FG could lead to the underestimation of condition-specific effects on the ascending connection from FG to IPS. Importantly, for a within-subject validation of the model, the DCMs were constructed separately for each hemisphere, so that we could then assess whether the patterns observed for each hemisphere would replicate each other, which would allow more confidence (via replication) in the validity of the DCM approach. For each subject and each fMRI run, the DCM parameters were estimated using Bayesian techniques in SPM5. The model parameters were then averaged across fMRI runs using Bayesian averaging (Friston et al. 2003). Connectivity coefficients were analyzed at the group level using traditional parametric statistics.

A set of 1-sample t-tests on the intrinsic coupling parameters consistently revealed significant connectivity across all connections and for both hemispheres (all $P < 0.05$). This implies
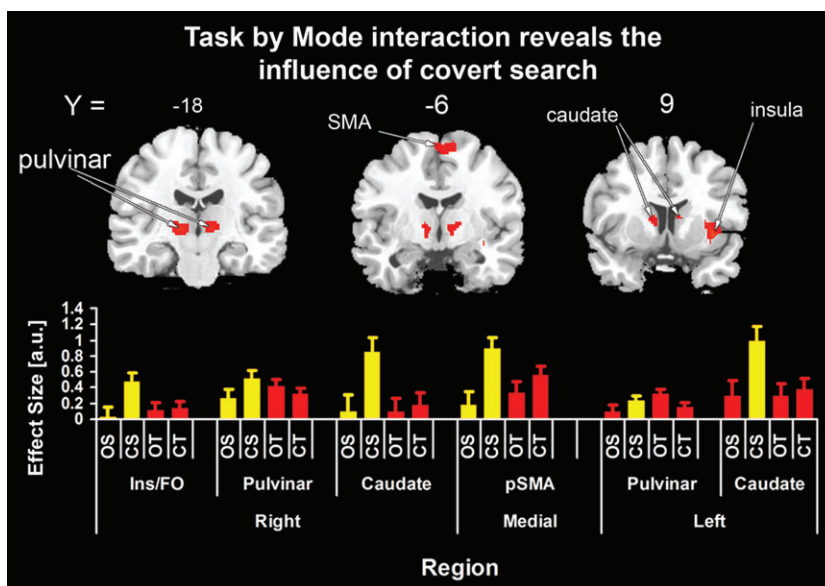

Figure 5. Location and effect sizes for the interaction isolating the positive influence of the CS condition in particular (yellow bars). Activation is observed within a cortical subcortical network during CS, including the thalamus and the caudate, plus the right insula and SMA.
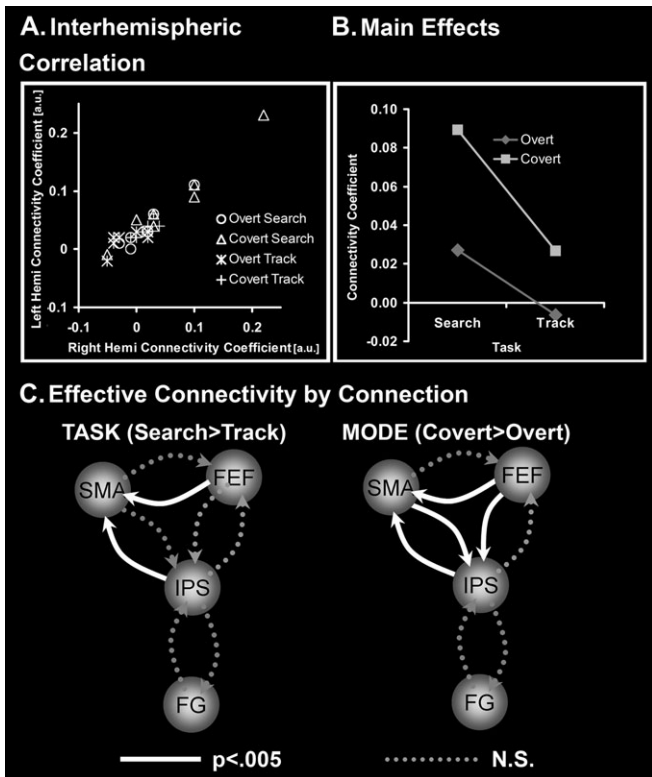
Figure 6. DCM within the fronto-parietal network. Bilinear terms representing all 4 conditions could independently modulate interregional connections. (*A*) High correlation of condition-specific bilinear terms between left and right hemispheres was found across all 4 conditions, thus showing the high replicability of the effective connectivity results across hemispheres. The data points represent the connectivity coefficients for each connection and condition, in arbitrary units (a.u.). (*B*) Summary of the effects of Task and Mode on connectivity averaged across connections of the fronto-parietal network. (*C*). Specific fronto-parietal connection profiles across the 4 conditions, with solid arrows indicating those connections that were significantly enhanced for Task (panel on the left) and Mode (panel on the right).

that the 4 selected regions show some functional connectivity, irrespective of experimental condition. However, the critical model parameters pertain to the condition-specific effects (extrinsic modulations). These were entered into a within-subject ANOVA, with Task, Mode, Connection, and Hemisphere as independent factors. None of the main effects nor interactions involving the factor of hemisphere reached statistical significance (all $P > 0.2$, i.e., the patterns obtained for the 2 hemispheres did not differ). More impressively, the condition-specific extrinsic modulations were highly correlated for the 2 separate hemispheres ($R^2 = 0.92$, see Fig. 6*A*), providing evidence of the high reproducibility of the estimation procedure. Accordingly, the results are henceforth reported as collapsed across hemispheres.

Within the fronto-parietal network, there was a significant main effect of Task ($F_{(1,11)} = 24.7$, $P < 0.001$), with increased effective connectivity during Search compared with Track. This result parallels the main intraregional voxel-level results, showing that within the dorsal fronto-parietal network both intraregional activation and interregional connectivity increase during goal-driven Search. However, unlike the intraregional analyses, the connectivity analyses further demonstrated a significant main effect of Mode ($F_{(1,11)}=30.3$, $P < 0.001$), with higher effective connectivity during Covert than Overt spatial

orienting (see Fig. 6*B*). Overall, there was no interaction between Task and Mode suggesting that, although these 2 factors jointly modulated interregional coupling, they did so in an independent, additive manner.

Significant interactions for Connection by Task ($F_{(1,11)} = 13.2$, $P < 0.01$), and Connection by Mode ($F_{(1,11)}=8.8$, $P < 0.01$) indicate that the effects of Task and Mode were differentially present across the connections of the fronto-parietal network (see Fig. 6*C*). Posthoc testing revealed that Task (search > track) and Mode (covert > overt) modulated connections from IPS and FEF to pre-SMA; and that Mode additionally influenced connections back from pre-SMA to IPS and from FEF to IPS (all $P < 0.005$). Thus, this additional DCM analysis revealed that Mode (covert > overt) can affect the dorsal fronto-parietal network, in terms of interregional coupling rather than voxel level activation (which has not been affected by Mode for the dorsal fronto-parietal network, see earlier sections above).

No significant main effects of Task and Mode were present in the top-down connections from IPS to visual cortex ($F < 1$).

Discussion

Our fMRI study of visual search tested for any commonalities and differences in brain activations (and in effective connectivity), in situations of either overt forms (with eye movements allowed) or covert forms (with central fixation) of goal-directed search or tracking. An important and novel aspect of our protocol was that we "replayed" sequence of fixations from previous OS trials to dictate a corresponding series of saccades on overt tracking trials. This allowed better control over saccadic (and related sensory) aspects than in many previous fMRI studies of search. We were also able to control attention-shifting requirements across other cells in our fully factorial design.

Our standard voxelwise analyses revealed that goal-directed serial search activates a distinct network of dorsal fronto-parietal cortical areas plus subcortical regions. Overt or covert mode of voluntary goal-directed search did not reveal any distinct activation within this fronto-parietal network (although the pulvinar and the caudate were selectively activated during covert goal-directed search in particular). Although these equivalent activation levels were observed in the fronto-parietal network, importantly the dynamic coupling (or effective connectivity) between these cortical regions in the fronto-parietal network was seen to increase during CS. Thus, dynamic changes in coupling between nodes in the attention network may distinguish CS and OS, in a way that is missed by studies that only considered overall activation levels, rather than potential changes in interregional influences. Our results for the latter aspect of the fronto-parietal attention network were closely replicated across different hemispheres here, providing some cross-validation of the DCM approach to changes in effective connectivity due to task demand.

The neural substrates of spatial attention have often been addressed in neuroimaging studies by variants on the attentional-precuing paradigm popularized by Posner and others (e.g., Corbetta et al. 1998; Nobre et al. 2000; Perry and Zeki 2000; Beauchamp et al. 2001; Astafiev et al. 2003). The use of a serial search paradigm instead affords the opportunity to investigate attentional control under a different set of

conditions that might arguably better represent more natural cases of directing attention voluntarily around a scene in search of a particular object (see also Himmelbach et al. 2006). To perform the present conjunction-search task, subjects shifted attention to particular locations in succession in a goal-directed fashion. Our results accord with others in confirming that the dorsal fronto-parietal attentional network is activated during serial search (Corbetta et al. 1995; Donner et al. 2000, 2002; Leonards and Singer 2000; Nobre et al. 2003; Anderson et al. 2007). But here we brought something new to this literature by using tightly controlled, trial-specific tracking conditions to allow close comparisons of OS and CS against stimulus-driven tracking conditions that could closely approximate saccadic (or fixation) factors per se, across the critical comparisons.

Although several previous studies had reported overlapping fronto-parietal activations for overt and covert orienting (e.g., Corbetta et al. 1998; Nobre et al. 2000; Perry and Zeki, 2000; Gitelman et al. 2002; de Haan et al. 2008), that outcome might sometimes have been attributed to the use of very low-level or passive baselines. This is unlikely as an explanation for our present findings, given the use of well-matched control conditions in a fully factorial design here. Conversely, although some prior studies have reported occasional differences in activation for overt or covert orienting conditions (Nobre et al. 2000; Perry and Zeki 2000; Beauchamp et al. 2001), such differences might potentially have related to a lack of control over saccadic or sensory differences between overt and covert conditions in some cases. Here we demonstrate that, once such aspects are well accounted for (e.g., by imposing a similar sequence of fixations in the overt tracking condition as for the over search condition), overlapping regions of the fronto-parietal networks are implicated for goal-directed search regardless of overt or covert mode (see Fig. 4).

In addition to the expected involvement of the dorsal fronto-parietal network, the search task also activated some subcortical regions. Unlike the dorsal fronto-parietal network, intraregional subcortical activations including the right pulvinar nucleus of the thalamus and the caudate nucleus were maximally activated in the "Covert" Search condition (see Fig. 5).

The putamen was also affected by Mode showing a main effect of covert versus overt Mode, but here irrespective of task (i.e., activating similarly for covert searching and covert tracking; see Table 3). Although outside the classical fronto-parietal attention network, these subcortical regions of the basal ganglia and thalamus have long been associated with attentional control. Neuroimaging in healthy subjects, as here, has suggested this previously (Nobre et al. 1997; Gitelman et al. 1999; Kim et al. 1999). Lesion studies of patients have also implicated similar regions in disorders of spatial attention (e.g., Posner and Petersen 1990; Karnath et al. 2002, 2005) as have animal lesion studies (e.g., Petersen et al. 1987). Invasive recordings in monkeys have shown that pulvinar and caudate neurons increase discharge rate during spatial orienting (Petersen et al. 1987; Hikosaka et al. 1989). The exact role of the caudate nucleus in attentional search is uncertain, but may reflect the focusing of attention (Gitelman et al. 1999). This may explain the enhanced activation of this region found here during CS, when attention must be maintained and redirected away from the fovea. The pulvinar has already been shown to be more active when there is a greater need to filter out irrelevant information (LaBerge and Buchsbaum 1990), as may arise particularly for CS when (unlike OS) the currently selected item cannot be foveated.

Our experimental design also allowed us to test for any areas that activated more during stimulus-driven tracking than during goal-directed shifts of attention, for both overt and covert situations in our factorial design. This revealed activation of the TPJ and SPL for stimulus-driven tracking, irrespective of the overt or covert mode. This aspect of our findings seems particularly notable, as in many respects Search might be considered the more demanding or effortful of the 2 tasks, yet our results still doubly dissociated the Search and Track tasks (rather than finding distinct activations only for Search). Although our tracking and search tasks were closely matched for sensory-motor requirements and visual presentation, those tasks still differ in several potential cognitive aspects. For instance, the Serial Search task requires endogenously generated, goal-directed (noncued) shifts of attention,

Table 3

Main effect of mode (positive effects of Overt > Covert, or vice versa) and Task × Mode Interaction

	Region	Positive main effects of mode							Task × mode interaction					
		$P_{(corrected)}$	Extent (cm³)	Hemi	Z score	MNI			$P_{(corrected)}$	Extent (cm³)	Z score	MNI		
						x	y	z				x	y	z
Covert	Caudate	0.008	2.7	Left	4.19	−8	0	8	<0.001	10.1	3.89	−8	4	6
	Thalamus			Left	4.42	−22	−12	16			4.28	−6	−10	−2
	Putamen			Left	4.85	−26	−12	10						
	Caudate	<0.001	9.0	Right	3.96	18	−6	16			3.92	6	4	8
	Thalamus			Right	3.96	18	−6	16			4.20	8	−10	−4
	Putamen			Right	5.04	28	−18	6						
	Pulvinar										4.15	−12	−18	−2
	Pulvinar										4.06	12	−20	0
	Insula			Right	4.49	56	2	6			4.40	38	10	−8
	SMA	0.002	3.13	Medial	4.75	4	−6	62	0.029	1.6	3.81	−4	−6	64
Overt	Calcarine	<0.001	212.0	Medial	Inf	−2	−82	8						
	SOG			Left	7.19	−10	−100	16						
	SOG			Right	14.71	12	−96	20						
	MOG			Left	Inf	−28	−92	12						
	MOG			Right	Inf	24	−96	6						
	IOG			Left	7.55	−40	−88	−10						
	IOG			Right	Inf	22	−94	−4						

Note: IOG, inferior occipital gyrus; MOG, middle occipital gyrus; SMA, supplementary motor area, SOG, superior occipital gyrus. All reported clusters were significant at $P < 0.05$, cluster-level corrected.

presumably along with maintenance of a template for the target being searched for in some form of working memory, and some comparison of this template with the currently attended stimulus. On the other hand, the tracking task requires stimulus-driven shifts of attention toward a salient and task-relevant stimulus (i.e., the purple circle, requiring discrimination when changing to an "x" or "+") presented at unpredictable locations. Activation of TPJ for stimulus-driven shifts toward task-relevant stimuli is consistent with the ventral attentional network suggested by Corbetta and Shulman (2002), but there were 2 further novel aspects to the pattern found here. First, the TPJ was found to be coactivated (for Track > Search, regardless of overt/covert mode) with a region in the superior parietal lobule (SPL). This parietal region appeared to be more superior and anterior compared with activations typically reported during previous tasks of attentional control and attentional shifting (e.g., Corbetta and Shulman 2002; Kelley et al. 2008). Dissociations between IPS and SPL have been reported previously. The IPS has been found to be responsive to both stimulus novelty (so-called "oddball" effects) and spatial reorienting, whereas SPL and TPJ are responsive only to the latter (Vossel et al. 2009). Furthermore, the IPS is observed to be preferentially activated during endogenous shifts of spatial attention compared with exogenous attention, whereas SPL is activated equally during both exogenous and endogenous shifts of attention (Molenberghs et al. 2007). Here we show differential effects for endogenous and exogenous attention in TPJ and SPL, with greater activation in these regions when shifts are cued by an external stimulus (tracking conditions) compared with shifts that are internally generated in a goal-directed fashion (search conditions, albeit SPL activated are also above baseline during search). Second, there was a dissociative pattern for posterior (TPJ) and anterior (ventral premotor) components of the proposed ventral attention network (e.g., Corbetta and Shulman 2002; Kelley et al. 2008). Although TPJ activated during tracking but not during search (see Fig. 4B), ventral premotor regions were more active during search than during tracking (see Fig. 4A). Some dissociation between parietal and frontal regions has already been reported in the context of overt orienting. Mort et al. (2003) found increased activity in posterior regions without significant differences in ventral premotor regions (as here), while frontal regions activated for both types of overt orienting tasks. The segregation between anterior and posterior regions may reflect differential roles in more perceptual (parietal) or more top-down (frontal) control of spatial attention (Corbetta et al. 2008).

Task-Dependent Changes in Effective Connectivity within the Fronto-Parietal-Visual Network

A major goal of this project was to understand how the dorsal frontal–parietal network controlled overt and covert variants of attentional shifts. Although at the voxelwise level the dorsal attention network was found to be activated equivalently by both covert and overt goal-directed search (relative to the corresponding tracking controls), in contrast we found that effective connectivity within the network, as assessed by the DCM approach, did differ significantly for covert versus overt orienting. Moreover, this changed pattern of effective connectivity was highly replicable across hemispheres. DCM revealed that effective connectivity increased during goal-directed

Search compared with stimulus-driven Track. This may reflect the greater need to coordinate information between the regions of the dorsal–frontal–parietal network during active search. But importantly, the mode of goal-directed search also affected interregional coupling. CS led to higher interregional coupling across the modeled elements of the fronto-parietal network.

Examination of each single connection revealed specific and directional influences between the fronto-parietal areas. Goal-directed Search resulted in an increased influence of both IPS and FEF on pre-SMA. This may accord with the notion that IPS and FEF may contain saliency maps of the search field (Shipp 2004) that is fed to pre-SMA when endogenous planning is required (Halsband et al. 1994). Accordingly, goal-directed search would presumably require more information (when compared with stimulus-driven orienting) about the search field, for the planning and execution of shifts of attention. CS led to greater increases in functional coupling than OS, notably for the connections back from the pre-SMA and FEF to the IPS were also seen to be potentiated. Strengthening of these "top-down" influences may arise when pre-SMA is required not only to plan a search sequence in the form of saccades, but also to plan a serial search that requires attention to be directed away from the fovea, without any actual eye movement. Although the exact nature of the observed task-dependent changes in effective connectivity within the dorsal–frontal–parietal network may be uncertain, a key finding of our present study is that CS versus OS leads to changes of interregional coordination, changes that would be entirely missed if only overall activation levels were examined.

The importance of interregional influences within the dorsal fronto-parietal network has also recently been emphasized by He et al. (2007). When assessing functional connectivity in a group of brain-damaged patients suffering from the unilateral neglect syndrome, a breakdown in functional coupling between left and right parietal regions was correlated with performance in a spatial cuing attentional task, and also with chronic clinical recovery. As with the present data set from neurologically healthy individuals, that patient study found a critical pattern of functional connectivity that would have been entirely missed (along with the relation to performance and recovery) if considering only overall levels of intraregional activation, rather than of interregional coupling.

In summary, we found that goal-directed visual search engages a network of dorsal fronto-parietal areas. For the first time, we used trial-by-trial matched fixation sequence to show that intraregional activity level within these areas does not depend on oculomotor requirements, but rather on the requirement for goal-directed search rather than stimulus-driven tracking. On the other hand, analyses of interregional effective connectivity revealed that the information flow within this network changes as a function of both task condition (search or track) and of overt/covert mode. In particular, covert orienting entailed increased connectivity between FEF, IPS, and pre-SMA. In addition, we found that a distinct set of subcortical regions (pulvinar and caudate nucleus) engages primarily during covert forms of goal-directed search. We conclude that the dorsal fronto-parietal attentional system can flexibly reorganize dynamically to integrate task demands and oculomotor requirements.

References

Anderson EJ, Mannan SK, Husain M, Rees G, Sumner P, Mort DJ, McRobbie D, Kennard C. 2007. Involvement of prefrontal cortex in visual search. Exp Brain Res. 180:289-302.

Astafiev SV, Shulman GL, Stanley CM, Snyder AZ, Van Essen DC, Corbetta M. 2003. Functional organization of human intraparietal and frontal cortex for attending, looking, and pointing. J Neurosci. 23:4689-4699.

Beauchamp MS, Petit L, Ellmore TM, Ingeholm J, Haxby JV. 2001. A parametric fMRI study of overt and covert shifts of visuospatial attention. Neuroimage. 14:310-321.

Bisley JW, Goldberg ME. 2003. Neuronal activity in the lateral intraparietal area and spatial attention. Science. 299:81-86.

Bruce CJ, Goldberg ME. 1985. Primate frontal eye fields. I. Single neurons discharging before saccades. J Neurophysiol. 53:603-635.

Colby CL, Goldberg ME. 1999. Space and attention in parietal cortex. Annu Rev Neurosci. 22:319-349.

Corbetta M, Akbudak E, Conturo TE, Snyder AZ, Ollinger JM, Drury HA, Linenweber MR, Petersen SE, Raichle ME, Van Essen DC, et al. 1998. A common network of functional areas for attention and eye movements. Neuron. 21:761-773.

Corbetta M, Miezin FM, Shulman GL, Petersen SE. 1993. A PET study of visuospatial attention. J Neurosci. 13:1202-1226.

Corbetta M, Patel G, Shulman GL. 2008. The reorienting system of the human brain: from environment to theory of mind. Neuron. 58:306-324.

Corbetta M, Shulman GL. 2002. Control of goal directed and stimulus-driven attention in the brain. Nat Rev Neurosci. 3:215-229.

Corbetta M, Shulman GL, Miezin FM, Petersen SE. 1995. Superior parietal cortex activation during spatial attention shifts and visual feature conjunction. Science. 270:802-805.

de Haan B, Morgan PS, Rorden C. 2008. Covert orienting of attention and overt eye movements activate identical brain regions. Brain Res. 1204:102-111.

Donner T, Kettermann A, Diesch E, Ostendorf F, Villringer A, Brandt SA. 2000. Involvement of the human frontal eye field and multiple parietal areas in covert visual selection during conjunction search. Eur J Neurosci. 12:3407-3414.

Donner TH, Kettermann A, Diesch E, Ostendorf F, Villringer A, Brandt SA. 2002. Visual feature and conjunction searches of equal difficulty engage only partially overlapping frontoparietal networks. Neuroimage. 15:16-25.

Friston KJ, Harrison L, Penny W. 2003. Dynamic causal modelling. Neuroimage. 19:1273-1302.

Gitelman DR, Nobre AC, Parrish TB, LaBar KS, Kim YH, Meyer JR, Mesulam M. 1999. A large-scale distributed network for covert spatial attention: further anatomical delineation based on stringent behavioural and cognitive controls. Brain. 122(Pt 6):1093-1106.

Gitelman DR, Parrish TB, Friston KJ, Mesulam MM. 2002. Functional anatomy of visual search: regional segregations within the frontal eye fields and effective connectivity of the superior colliculus. Neuroimage. 15:970-982.

Gottlieb J. 2007. From thought to action: the parietal cortex as a bridge between perception, action, and cognition. Neuron. 53:9-16.

Gottlieb JP, Kusunoki M, Goldberg ME. 1998. The representation of visual salience in monkey parietal cortex. Nature. 391:481-484.

Halsband U, Matsuzaka Y, Tanji J. 1994. Neuronal activity in the primate supplementary, pre-supplementary and premotor cortex during externally and internally instructed sequential movements. Neurosci Res. 20:149-155.

He BJ, Snyder AZ, Vincent JL, Epstein A, Shulman GL, Corbetta M. 2007. Breakdown of functional connectivity in frontoparietal networks underlies behavioral deficits in spatial neglect. Neuron. 53:905-918.

Hikosaka O, Sakamoto M, Usui S. 1989. Functional properties of monkey caudate neurons. III. Activities related to expectation of target and reward. J Neurophysiol. 61:814-832.

Himmelbach M, Erb M, Karnath HO. 2006. Exploring the visual world: the neural substrate of spatial orienting. Neuroimage. 32:1747-1759.

Huang L, Pashler H. 2007. A Boolean map theory of visual attention. Psychol Rev. 114:599-631.

James W. 1890. Principles of psychology. New York: Henry-Holt & Co.

Karnath HO, Himmelbach M, Rorden C. 2002. The subcortical anatomy of human spatial neglect: putamen, caudate nucleus and pulvinar. Brain. 125:350-360.

Karnath HO, Zopf R, Johannsen L, Fruhmann Berger M, Nagele T, Klose U. 2005. Normalized perfusion MRI to identify common areas of dysfunction: patients with basal ganglia neglect. Brain. 128:2462-2469.

Kelley TA, Serences JT, Giesbrecht B, Yantis S. 2008. Cortical mechanisms for shifting and holding visuospatial attention. Cereb Cortex. 18:114-125.

Kim YH, Gitelman DR, Nobre AC, Parrish TB, LaBar KS, Mesulam MM. 1999. The large-scale neural network for spatial attention displays multifunctional overlap but differential asymmetry. Neuroimage. 9:269-277.

LaBerge D, Buchsbaum MS. 1990. Positron emission tomographic measurements of pulvinar activity during an attention task. J Neurosci. 10:613-619.

Leonards U, Singer W. 2000. Conjunctions of colour, luminance and orientation: the role of colour and luminance contrast on saliency and proximity grouping in texture segregation. Spat Vis. 13:87-105.

Molenberghs P, Mesulam MM, Peeters R, Vandenberghe RR. 2007. Remapping attentional priorities: differential contribution of superior parietal lobule and intraparietal sulcus. Cereb Cortex. 17:2703-2712.

Moore T, Armstrong KM, Fallah M. 2003. Visuomotor origins of covert spatial attention. Neuron. 40:671-683.

Moore T, Fallah M. 2004. Microstimulation of the frontal eye field and its effects on covert spatial attention. J Neurophysiol. 91:152-162.

Mort DJ, Perry RJ, Mannan SK, Hodgson TL, Anderson E, Quest R, McRobbie D, McBride A, Husain M, Kennard C. 2003. Differential cortical activation during voluntary and reflexive saccades in man. Neuroimage. 18:231-246.

Nobre AC, Coull JT, Walsh V, Frith CD. 2003. Brain activations during visual search: contributions of search efficiency versus feature binding. Neuroimage. 18:91-103.

Nobre AC, Gitelman DR, Dias EC, Mesulam MM. 2000. Covert visual spatial orienting and saccades: overlapping neural systems. Neuroimage. 11:210-216.

Nobre AC, Sebestyen GN, Gitelman DR, Mesulam MM, Frackowiak RS, Frith CD. 1997. Functional localization of the system for visuospatial attention using positron emission tomography. Brain. 120(Pt 3):515-533.

Ohlendorf S, Kimmig H, Glauche V, Haller S. 2007. Gaze pursuit, 'attention pursuit' and their effects on cortical activations. Eur J Neurosci. 26:2096-2108.

Penny WD, Holmes AP. 2003. Random effects analysis. In: Frackowiak RS, Friston KJ, Frith CD, Dolan RJ, Price CJ, Ashbumer J, Zeki S, editors. Human brain function. Academic Press.

Penny WD, Stephan KE, Mechelli A, Friston KJ. 2004. Comparing dynamic causal models. Neuroimage. 22:1157-1172.

Perry RJ, Zeki S. 2000. The neurology of saccades and covert shifts in spatial attention: an event-related fMRI study. Brain. 123(Pt 11): 2273-2288.

Petersen SE, Robinson DL, Morris JD. 1987. Contributions of the pulvinar to visual spatial attention. Neuropsychologia. 25:97-105.

Posner MI, Petersen SE. 1990. The attention system of the human brain. Annu Rev Neurosci. 13:25-42.

Posner MI, Snyder CR, Davidson BJ. 1980. Attention and the detection of signals. J Exp Psychol. 109:160-174.

Rizzolatti G, Riggio L, Dascola I, Umilta C. 1987. Reorienting attention across the horizontal and vertical meridians: evidence in favor of a premotor theory of attention. Neuropsychologia. 25:31-40.

Sato TR, Schall JD. 2003. Effects of stimulus-response compatibility on neural selection in frontal eye field. Neuron. 38:637-648.

Schlag J, Schlag-Rey M. 1987. Evidence for a supplementary eye field. J Neurophysiol. 57:179-200.

Shipp S. 2004. The brain circuitry of attention. Trends Cogn Sci. 8:223-230.

Snyder LH, Batista AP, Andersen RA. 2000a. Intention-related activity in the posterior parietal cortex: a review. Vision Res. 40:1433-1441.

Snyder LH, Batista AP, Andersen RA. 2000b. Saccade-related activity in the parietal reach region. J Neurophysiol. 83:1099-1102.

Stephan KE, Harrison LM, Kiebel SJ, David O, Penny WD, Friston KJ. 2007. Dynamic causal models of neural system dynamics: current state and future extensions. J Biosci. 32:129-144.

Thompson KG, Biscoe KL, Sato TR. 2005. Neuronal basis of covert spatial attention in the frontal eye field. J Neurosci. 25:9479-9487.

Treisman AM, Gelade G. 1980. A feature-integration theory of attention. Cognit Psychol. 12:97-136.

Vossel S, Weidner R, Thiel CM, Fink GR. 2009. What is "Odd" in Posner's location-cueing paradigm? Neural responses to unexpected location and feature changes compared. J Cogn Neurosci. 21:1-12.

Wolfe JM. 1994. Guided search 2. 0. A revised model of visual search. Psychon Bull Rev. 1:202-238.

Wolfe JM. 1998. What can 1 million trials tell us about visual search? Psychol Sci. 9:33-39.

Worsley KJ, Marrett S, Neelin P, Vandal AC, Friston KJ, Evans AC. 1996. A unified statistical approach for determining significant signals in images of cerebral activation. Hum Brain Mapp. 458:73.

Yantis S, Schwarzbach J, Serences JT, Carlson RL, Steinmetz MA, Pekar JJ, Courtney SM. 2002. Transient neural activity in human parietal cortex during spatial attention shifts. Nat Neurosci. 5:995-1002.