The neural mechanisms of top-down attentional control

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Selective visual attention involves dynamic interplay between attentional control systems and sensory brain structures. We used event-related functional magnetic resonance imaging (fMRI) during a cued spatial-attention task to dissociate brain activity related to attentional control from that related to selective processing of target stimuli. Distinct networks were engaged by attention-directing cues versus subsequent targets. Superior frontal, inferior parietal and superior temporal cortex were selectively activated by cues, indicating that these structures are part of a network for voluntary attentional control. This control biased activity in multiple visual cortical areas, resulting in selective sensory processing of relevant visual targets.

Selective attention enables us to focus awareness on objects and events that are relevant to our immediate goals. Spatial attention, the selective direction of visual attention toward a location, can occur covertly, without overt movements of the head or eyes. Theoretically, mechanisms of covert, voluntary spatial attention can be decomposed into elementary mental operations: disengaging attention from the current focus, orienting attention to a new locus and selectively modulating new stimulus inputs are three stages proposed in current models[1,2]. Attentional disengagement and voluntary orienting can be considered aspects of top-down attentional control, whereas subsequent selective modulation of sensory inputs reflects the result of this top-down control on sensory information processing.

Studies in neurological patients and physiological studies in humans and animals implicate a network of cortical and subcortical regions that support visual selective attention[3–6]. Neuroimaging studies identify areas involved in spatial attention in the frontal, parietal, temporal and occipital lobes as well as in subcortical structures[7–11]. However, although neuroimaging studies implicate various brain regions in selective attention, inherent limitations of classical neuroimaging analysis impair efforts to relate neural structures/networks to specific attentional operations. Specifically, such methodologies use averaging of hemodynamic responses over seconds or minutes, a time course that is too long to permit direct viewing of brain activity related to the subcomponents of task performance. As a result, human neuroimaging studies to date are only partly successful in distinguishing between neural activity related to top-down attentional-control processes and activity related to selective sensory and motor processing.

Recordings of event-related neuroelectric potentials (ERPs) allow the selective averaging of responses to different classes of events and, thus, serve to index mechanisms of attentional control separately from selective stimulus processing during spatial attention[12]. However, although ERPs provide information about the timing of neural processes, the limited spatial resolution of this approach hinders identification of the neural structures involved in attentional control. Advances in functional magnetic resonance imaging (fMRI)

analysis[13,14] allowed us to combine the spatial resolution necessary for localization of neural activity, which this technique provides, with neuroimaging methods that selectively extract components of hemodynamic activity[15] correlated with distinct aspects of complex-task performance.

Here we used event-related fMRI methods to determine which brain regions were involved in attentional-control processes and to distinguish these from areas involved in subsequent selective processing of target stimuli. This was accomplished by separately convolving the onsets of the cue and target stimuli with synthetic hemodynamic response functions. Subjects oriented attention covertly (without moving their eyes) to spatial locations based on instructive cues shown at fixation (**Fig. 1**). Subsequently, reversing checkerboard stimuli were presented at both sides of the visual field, and subjects were required to discriminate whether the checkerboard at the cued location contained some gray checks or only black and white checks and to respond accordingly. All stimuli in the opposite (uncued) hemifield were to be ignored.

Based on previous studies implicating various brain regions in attentional control[5,7,8,11], we hypothesized that attentional-control processes in response to an instructive cue directing spatial attention would activate a network of regions in frontal and parietal cortex. Additionally, based on ERP studies in humans[12], regions of occipital cortex corresponding to portions of visual space indicated by the cue should show spatially specific changes in activity in anticipation of selective processing of target stimuli. We also expected lateralized changes in activity of occipitotemporal regions in response to the bilateral target stimuli to reflect spatial attention[7–11]. In line with these predictions, we found distinct patterns of neural activation for attention-directing cues as compared with those for subsequent target stimuli, thereby distinguishing top-down attentional control from selective modulations of target processing in sensory structures.

RESULTS
Subjects discriminated black and white checkerboards from those containing some gray checks at the cued location with a mean

Fig. 1. Stimuli and timing. For simplicity, we show here the inverse black/white contrast of the actual stimulus screen; subjects saw a black background with white outline boxes and fixation cross, and the cues were overlapping isoluminant yellow and blue arrows (pointing in opposite directions). Subjects were told which color arrow to attend for the entire session and were required to covertly orient their attention to the visual field location indicated by that arrow. After a variable interstimulus interval (1000 or 8160 ms), the target checkerboards appeared bilaterally, and subjects were required to perform a discrimination of the checkerboard stimuli at the attended location only.
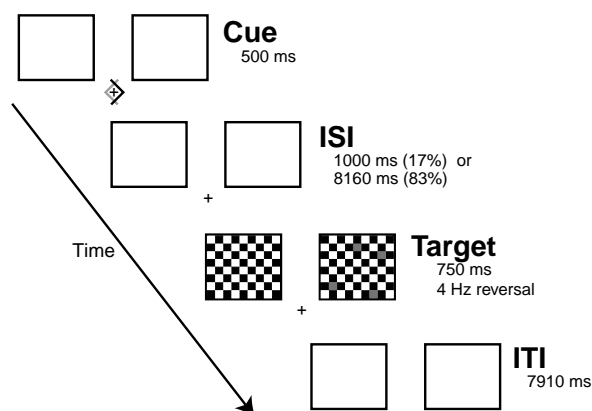
accuracy of 83.9% correct responses. This corresponded to a mean *d′* score of 2.99.

We investigated circuitry involved in attentional control by identifying regions activated in response to the cue. Multiple cortical areas were activated following cue presentation, but before target presentation (**Fig. 2**; **Table 1**). These regions were activated regardless of the cue direction: brain regions activated by rightward- and leftward-pointing cues were highly similar (with the exception of the extrastriate cortex; see below). Regions of the inferior parietal lobule (in the lateral intraparietal sulcus, or IPS), the superior parietal lobule (SPL) and the posterior cingulate cortex (PC) in both hemispheres were activated in response to the instructive cues. Regions of the lateral and medial superior frontal lobes, including the frontal eye fields (FEF), were also activated bilaterally. These

frontal activations tended to be larger in the left hemisphere, regardless of cue direction. In addition, cue stimuli generated activity along the superior temporal sulcus (STS). With the exception of the superior parietal lobule, none of these regions were activated in separate sensory control scans in which cues were viewed passively or were irrelevant to the task (and, therefore, did not instruct the subjects to direct attention to a single location). Posterior occipital regions of cortex were activated in response to the cues, but these regions were also activated by cues in the sensory-control scans, indicating that they represented simple sensory processing of the cues. Additionally, the cues produced bilateral activations in the region of the insula near the putamen.

In contrast, the target stimuli evoked neural activity in brain areas that were largely distinct from those activated by the attention-directing cues (**Fig. 3**; **Table 2**). Bilateral activations in the supplementary motor area (SMA) extending into regions of the midcingulate gyrus and activations surrounding the central sulcus were found in response to targets whether attention was directed to the right or left. Ventrolateral prefrontal areas were also bilaterally activated by the targets. None of these regions were activated by the cues. Only the superior parietal lobule was found to
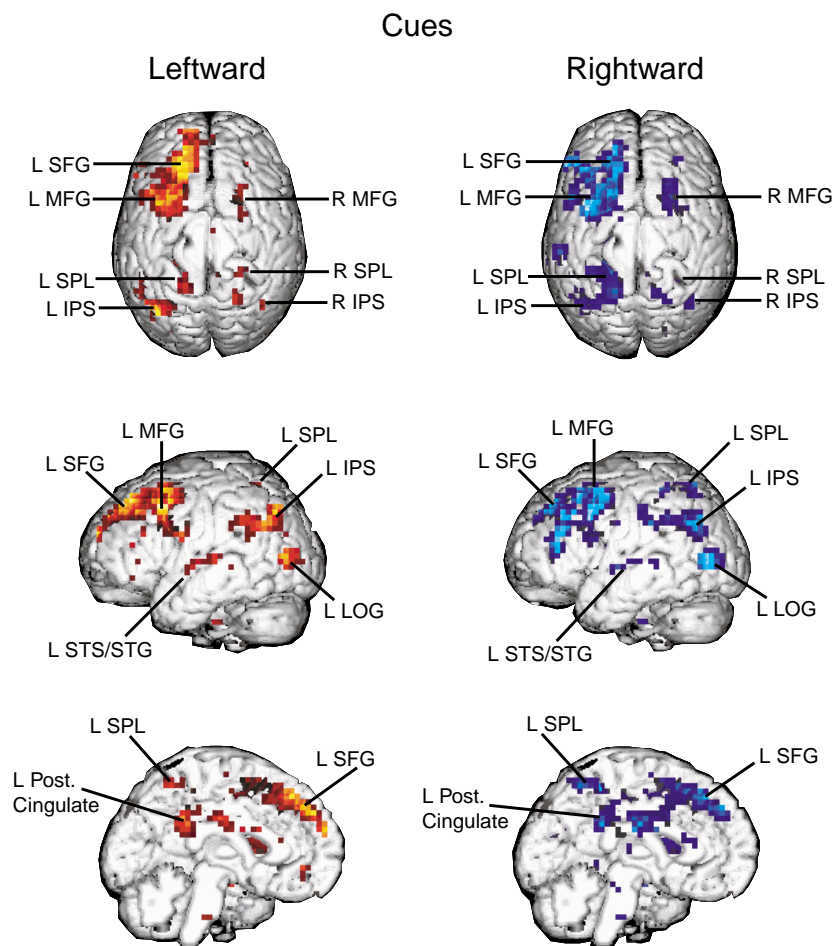

Fig. 2. Activity related to attentional control. Data for brain regions significantly activated in response to the cue stimuli were overlaid onto a brain rendered in 3D. Left column, activations to cues instructing subjects to orient attention to the left visual field location. Right column, activations to cues instructing subjects to attend the right visual field location. Top panels, dorsal view of the brain (frontal pole at top); middle and bottom panels, lateral and medial views, respectively, of the left hemisphere. Labels indicate the brain regions referred to in Table 1. The *Z*-values and stereotactic coordinates for the regional maxima are given in Table 1. SFG, superior frontal gyrus; MFG, middle frontal gyrus; SPL, superior parietal lobule; IPS, intraparietal sulcus; STS, superior temporal sulcus; STG, superior temporal gyrus; LOG, lateral occipital gyrus.

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be activated in response to both targets and cues. Additionally, bilateral targets activated several regions of the ventral and dorsal occipital cortex of both hemispheres. Cue and target responses were directly statistically compared (**Tables 1** and **2; Fig. 4**).

To investigate the consequences of lateralized spatial attention on stimulus processing, the event-related neural activity evoked by the bilateral target stimuli was evaluated for attention to the left versus right. In line with previous neuroimaging studies in humans[9,10,16–19] and related findings in animals[3], attending to the left visual field increased activity in the right ventral occipital cortex, whereas attending to the right increased activity in the left occipital cortex (**Fig. 5a**). In addition, activity in a more dorsal region of visual cortex was also modulated by spatial attention.

To relate these attention-related activations to specific visual-field areas, the vertical and horizontal meridian were mapped in two subjects to identify the borders of the early cortical visual areas[20,21]. Although the spatial smoothing used in the present analysis tended to blend together the attention-related activations in adjacent visual cortical areas, the contralateral attention-related activations in occipital cortex can be seen to cross multiple visual area borders from V2 through V4 (**Fig. 5b**), an observation in line with other reports[10,18,22].

Models of spatial attention propose that attention effects on target processing result from a gain-control mechanism that enhances the excitability of extrastriate neurons coding attended regions of visual space[4,9,23]. To investigate this possibility, we further examined extrastriate cortex for evidence of spatially

selective attentional activations in response to the direction of the instructive cue, but before target presentation, using the attention-related activations to targets as regions of interest. Direct statistical evaluation of the cue-left versus cue-right effects revealed relative increases of activity in extrastriate cortex contralateral to the direction of attention. These contralateral cue-related activations overlapped closely with the extrastriate regions showing attentional modulations in response to the subsequent targets (**Fig. 6**). That is, there was a relative increase in activity in the visual cortical regions representing the spatial locations of the expected target stimuli before the target stimuli were actually presented. These differential activations were not related to inherent sensory features of the cues that activated separate cortical regions in control sessions.

DISCUSSION
This study used event-related fMRI methods to distinguish between neural networks involved in top-down attentional-control processes and those participating in the subsequent spatially selective attentional processing of target stimuli. A network of cortical areas including superior frontal, inferior parietal and superior temporal brain regions were implicated in top-down attentional control because they were found to be active only in response to instructive cues. In contrast, other regions of the cortex, including the ventrolateral prefrontal cortex, anterior cingulate and supplementary motor area, were found to be selectively activated by the target stimuli, suggesting that these

Table 1. Event-related activations to cue stimuli and statistical contrasts.

| | Leftward-directing cue | | | | Rightward-directing cue | | | | Cues > targets | | | | |
| | Coordinates | | | Z-score | Coordinates | | | Z-score | Coordinates | | | Z-score | *p* |
	x	y	z		x	y	z		x	y	z		(corrected)
Frontal													
Left SFG*	−16	48	36	4.56	−16	48	36	4.10	−16	48	36	7.10	*p* < 0.001
Left SFG (lateral)*	−44	36	16	2.96	−44	36	16	4.30	−52	32	16	6.93	*p* < 0.001
Left MFG*	−20	−4	52	4.36	−20	0	48	5.53	−32	16	48	7.67	*p* < 0.001
Right MFG*	24	0	56	3.96	24	4	52	4.37	20	8	48	4.95	*p* < 0.01
Parietal													
Left SPL*	−16	−52	56	3.27	−16	−56	56	4.21	−12	−56	56	4.41	*p* > 0.05
Right SPL*	24	−40	56	3.84	20	−40	52	2.76	8	−40	56	4.27	*p* > 0.05
Left IPS*	−44	−64	32	3.79	−40	−64	28	4.06	−44	−64	32	7.01	*p* < 0.001
	−44	−48	36	3.29	−40	−48	32	3.88	−44	−48	32	7.29	*p* < 0.001
Right IPS*	40	−68	28	4.23	40	−64	32	3.83	44	−60	36	6.63	*p* < 0.001
	36	−48	36	3.46	32	−48	32	4.23	36	−44	32	7.22	*p* < 0.001
L cingulate (posterior)*	−12	−44	28	3.53	−8	−44	32	2.91	0	−40	44	7.64	*p* < 0.001
R cingulate (posterior)	8	−36	28	2.94	4	−40	28	3.48	4	−44	32	7.63	*p* < 0.001
Temporal													
Left STS/STG*	−60	−24	8	3.53	−56	−24	8	2.39	−56	−24	8	6.71	*p* < 0.001
Right STS/STG	48	−12	8	1.85	48	−12	8	1.76	48	−12	8	5.28	*p* < 0.005
Occipital													
Left LOG*	−36	−76	8	4.05	−36	−76	4	4.42	−36	−76	4	8.12	*p* < 0.001
Right LOG	32	−80	8	2.82	24	−84	8	5.77	28	−80	0	8.58	*p* < 0.001
Other regions													
L insula/putamen	−28	−4	12	4.17	−28	−8	16	4.56	−28	−8	20	5.53	*p* < 0.001
R insula/putamen	28	−8	16	2.77	24	0	16	3.96	24	−8	12	5.28	*p* < 0.005

SFG, superior frontal gyrus; MFG, middle frontal gyrus; SPL, superior parietal lobule; IPS, intra-parietal sulcus; STS, superior temporal sulcus; STG, superior temporal gyrus; LOG, lateral occipital gyrus. Coordinates: *x*, left/right; *y*, anterior/posterior; *z*, inferior/superior in the reference frame of the MNI brain in SPM97. *Activity represented in Figs. 2 and 4.

areas may be more involved in selective stimulus processing and/or response mechanisms.

The activation in the inferior parietal lobule (specifically, IPS) in response to the cues, but not targets, suggests that this region of parietal cortex is involved in attentional-control processes. This finding supports prior evidence from blocked-design imaging studies, which inferred the role of inferior parietal cortex based on activity averaged across blocks of trials[8,11,24,25], as well as work in animals[26], but provides the first direct evidence that these regions of the inferior parietal lobule are specifically linked to attentional control in humans. The present findings in inferior parietal cortex suggest a role for this brain region in attentional control mechanisms, which may include shifting attention[7,24], or working memory processes engaged to support task performance[27].

In contrast, regions in superior parietal cortex, also proposed to be involved in attentional orienting[7], were not only activated by the cue stimuli, but were also (and to a greater extent) activated in response to the target stimuli. This finding agrees with neuroimaging studies reporting that regions of SPL are active both during shifts of attention in the visual periphery and when attention is focused on target stimuli but no attentional shifts are required[28]. These findings fit well with neurological lesion studies finding that inferior regions of parietal cortex (extending into the temporoparietal junction) are more critical than superior parietal regions for normal performance in spatial cueing tasks[29].
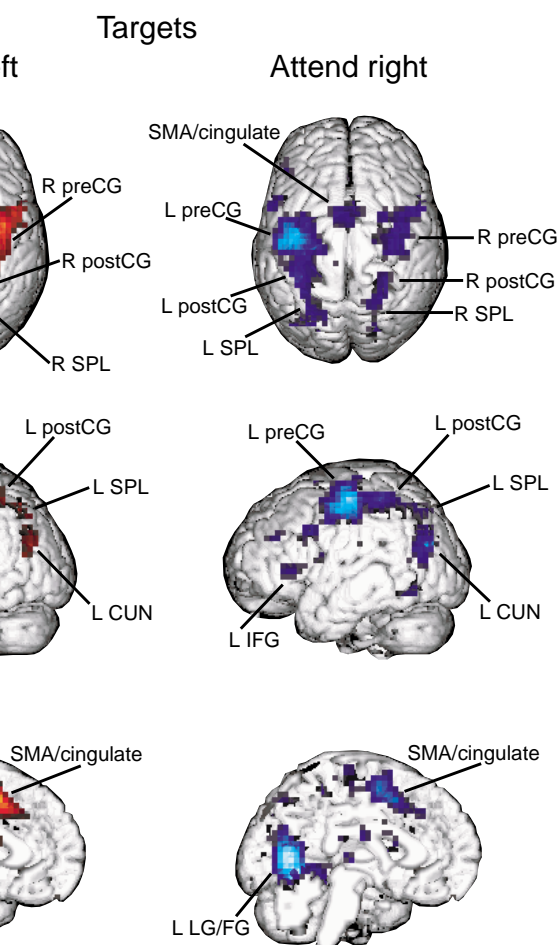

Fig. 3. Activity related to target processing. Brain regions significantly activated in response to the target stimuli, overlaid onto a 3D rendering of a brain, as in Fig. 2. Left column, activations to target stimuli when attention was focused on the left visual field location. Right column, shows activations to target stimuli when attention was focused on the right visual field location. The labels indicate the brain regions referred to in Table 2. The Z-values and stereotactic coordinates for the regional maxima are listed in Table 2. SMA, supplementary motor area; preCG, pre-central gyrus; postCG, post-central gyrus; IFG, inferior frontal gyrus; MFG, middle frontal gyrus; SPL, superior parietal lobule; CUN, cuneus; LG, lingual gyrus; FG, fusiform gyrus.

Neuroimaging studies in humans reveal activations in the posterior STS during the performance of attentional tasks, suggesting that the STS may be involved in attentional processing in humans[11,24], a role supported by induction of attentional neglect in lesions of the STS in monkeys[30]. However, it has remained unclear whether the STS is involved in attentional control circuitry, or instead is involved in attention-related processing of relevant target stimuli. We demonstrated that a region of the STS anterior to the temporal-parietal junction was selectively activated by the attention-directing cues, suggesting a role in attentional control circuitry.

The activations to the attention-directing cues in the vicinity of the frontal eye field in the present study suggest a role for this brain region in attentional control. The FEF is proposed to be involved in attentional processes, specifically as they relate to overt eye movements[5,31]. Imaging studies, however, suggest that FEF may be involved in covert shifts of attention as well[24,32]. In the present study,

the cortex in the vicinity of the FEF was activated by the cues, but not by the target stimuli, suggesting its participation in attentional-control processes in the absence of eye movements. Given that eye movements needed to be suppressed to both cue and target presentations, the present pattern cannot be attributed solely to suppression of oculomotor responses[33].

Regions of the dorsolateral prefrontal cortex (superior frontal gyrus) that were anterior to the FEF activations were also activated to the cues but not the targets. These regions of frontal cortex have been associated with working memory processes in studies of spatial working memory[34–38]. In the present task, such processes may have activated these regions as subjects encoded the to-be-attended location in working memory.

In contrast, although ventrolateral prefrontal regions are sometimes considered to be involved in retention of information in working memory[34,35], in the present study, the strongest ventrolateral prefrontal activations were not observed in response to

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the cue stimuli when one might expect working memory processes to be engaged. Rather, these cortical regions were activated upon presentation of the target stimuli. This finding may be consistent with a role in inhibitory filtering of information from the ignored hemifield when the bilateral targets appeared[36–38].

Previously, the supplementary motor area and the anterior cingulate cortex were hypothesized to be part of attentional control systems[2,8]. The present finding that these areas were activated in response to the target stimuli but not the attention-directing cues, however, suggests a role in either the selective analysis of target features or decisional processes engaged once the relevant stimulus is presented, such as selecting appropriate motor actions based on target features[39,40].

As predicted by the previous literature, target-evoked activity in posterior lingual and fusiform regions was enhanced in the hemisphere contralateral to the direction of attention. This supports the idea that spatial attention-related increases in regional blood flow in extrastriate cortex are related to enhanced processing of target stimuli falling within the attentional spotlight, as suggested by prior ERP[4,41,42] and functional imaging studies [9,10,16–19] in humans and single-unit studies in monkeys[3,43]. In addition, a more dorsal region of visual cortex was also enhanced by the direction of attention. This region may be area V3a, which has an upper visual field representation in dorsal visual cortex[44] and which is activated in response to flashing checkerboard patterns[18].

Priming of visual neurons by top-down attentional control signals is suggested by the finding that regions of visual cortex

coding to-be-attended locations were differentially activated in response to the instruction to orient attention by the cue. Single-unit studies in non-human primates show an increase in background firing rates of neurons coding an attended region of space in the absence of stimuli[45], and proposals based on neuroimaging data suggest that increased background firing rates may mediate attentional facilitation in visual cortex[46,47]. The present data show a precise spatial correspondence between areas of visual cortex activated by top-down processes and those showing subsequent selective modulations of target processing. Moreover, these priming effects in visual cortex were shown to follow the retinotopic mapping of the visual fields onto visual cortex as attention was shifted from left to right locations by the cue instructions.

In summary, a top-down attentional control system was isolated using event-related fMRI methods. This network included the superior frontal cortex, inferior parietal cortex, superior temporal cortex and portions of the posterior cingulate cortex and insula. The present evidence indicates that this top-down control system modulated activity in extrastriate cortex as a function of where spatial attention was directed in the visual field. These spatially selective effects in extrastriate cortex, observed before the presentation of the target stimuli, resulted in modulations in the activity evoked by subsequent target stimuli in precisely corresponding early cortical areas. Hence, it seems that effects of spatial attention in visual cortex before target onset may reflect changes in sensory-neural excitability as a function of top-down control. These findings provide direct evidence for clear distinctions between the neural mech-

Table 2. Event–related activations to target stimuli and statistical contrasts.

	Attended left target				Attended right target				Targets > cues				
	Coordinates			Z-score	Coordinates			Z-score	Coordinates			Z-score	*p*
	x	y	z		x	y	z		x	y	z		(corrected)
Frontal													
SMA/cingulate**	4	8	52	7.04	4	8	52	6.10	0	4	52	8.67	*p* < 0.001
Left preCG**	−40	−16	56	7.26	−36	−16	56	7.43	−36	−16	56	8.51	*p* < 0.001
Right preCG**	32	−16	52	5.64	36	−20	56	4.00	36	−16	60	8.34	*p* < 0.001
	40	−4	52	6.37	36	−4	52	4.04	32	4	60	7.11	*p* < 0.001
Left IFG**	−56	12	32	5.01	−52	12	32	3.97	−56	8	32	6.49	*p* < 0.001
Left insula/IFG**	−36	28	4	5.06	−36	28	4	4.39	−36	24	4	7.30	*p* < 0.001
Right IFG/MFG	44	12	24	4.82	44	12	24	4.73	52	4	40	5.28	*p* < 0.005
Right insula/IFG	32	24	4	4.61	32	24	4	4.87	32	28	0	7.64	*p* < 0.001
Parietal													
Left postCG**	−36	−36	56	4.53	−36	−40	56	5.85	−28	−32	64	6.03	*p* < 0.001
Right post CG**	28	−44	56	6.54	24	−48	56	4.52	28	−48	56	7.29	*p* < 0.001
Left SPL**	−24	−64	48	3.76	−20	−68	44	4.16	−16	−72	48	5.37	*p* < 0.001
Right SPL**	24	−60	60	4.87	20	−60	60	4.11	12	−68	52	5.00	*p* < 0.01
Occipital													
Left CUN**	−28	−68	32	4.24	−28	−68	24	7.48	−28	−72	28	7.77	*p* < 0.001
Left LG/FG**	−12	−64	8	7.42	−12	−68	0	8.13	−8	−64	4	9.31	*p* < 0.001
	−24	−48	0	4.40	−24	−44	−4	5.98	−24	−44	8	5.19	*p* < 0.005
	−28	−60	−4	3.76	−28	−60	−4	7.70	−28	−60	−4	8.36*	*p* < 0.001
Right CUN	24	−76	28	7.81	24	−76	28	3.86	24	−76	28	7.8	*p* < 0.001
	36	−68	16	6.29	36	−64	12	3.03	36	−68	20	6.07	*p* < 0.001
Right LG/FG	12	−60	0	7.75	8	−60	8	6.89	4	−64	8	9.04	*p* < 0.001
	20	−56	4	7.45	24	−64	0	2.05	20	−56	4	7.78*	*p* < 0.001
	28	−48	−8	4.03	24	−40	0	2.29	24	−48	−16	7.86	*p* < 0.001

SMA, supplementary motor area; preCG, pre-central gyrus; postCG, post-central gyrus; IFG, inferior frontal gyrus; MFG, middle frontal gyrus; SPL, superior parietal lobule; CUN, cuneus; LG, lingual gyrus; FG, fusiform gyrus. *Not a regional maximum; selected from regional maximum of target-related activations. **Activations shown in Figs. 3 and 4
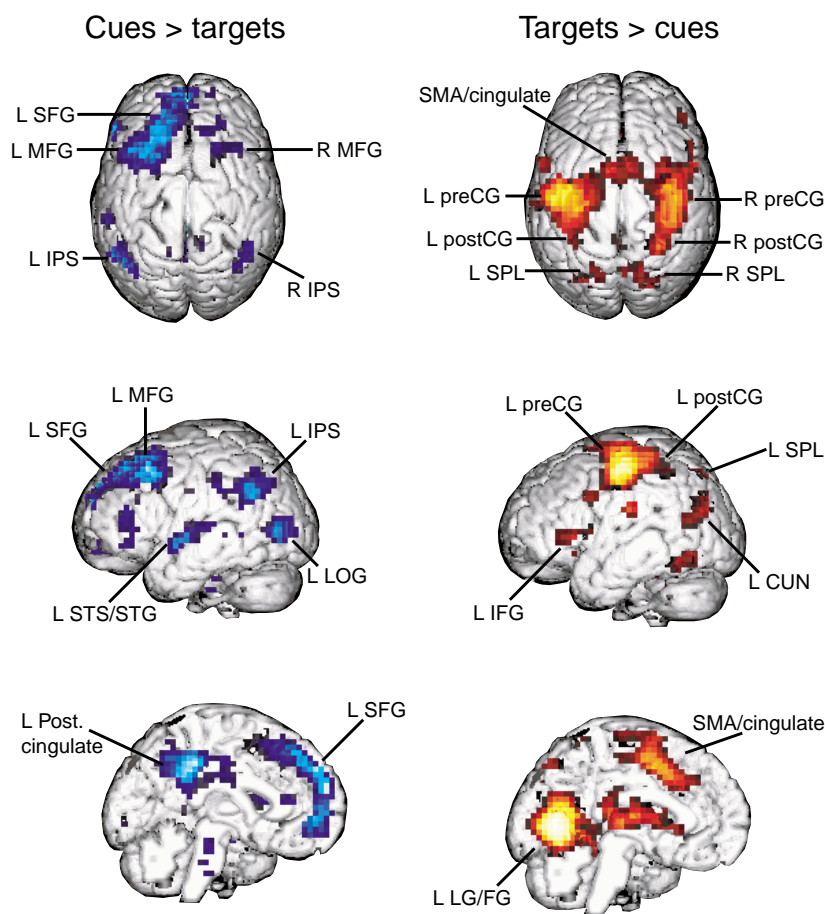
Cues > targets

Targets > cues

Fig. 4. Significant differences between cue and target processing. Areas significantly more active for cues than targets (left column) and those active more for targets than for cues (right column) projected on a 3D-rendered brain. Labels indicate the brain regions referred to in Tables 1 and 2. The Z-values and stereotactic coordinates for the regional maxima are listed in Tables 1 and 2. SFG, superior frontal gyrus; MFG, middle frontal gyrus; SPL, superior parietal lobule; IPS, intra-parietal sulcus; STS, superior temporal sulcus; STG, superior temporal gyrus; LOG, lateral occipital gyrus. SMA, supplementary motor area; preCG, pre-central gyrus; postCG, post-central gyrus; IFG, inferior frontal gyrus; CUN, cuneus; LG, lingual gyrus; FG, fusiform gyrus.

checks) that reversed at 4 Hz over a 750-ms duration (so that each stimulus comprised 3 checkerboards lasting 250 ms each). A random one-half of target stimuli contained between 3 and 9 gray checks (randomly located) in place of white checks during one phase of the reversals (the second 250-ms period). Subjects were required to discriminate the target stimuli at the cued location only, pressing a button with one hand if gray checks were present, or pressing a button with the other hand if there were no gray checks (hand of response was counter-balanced across subjects). On 17% of trials, the target stimuli occurred 1000 ms after the offset of the cue. On the remaining 83% of trials, targets occurred 8160 ms following the cue. In order to distinguish the hemodynamic response to the cues from that to the targets, only the longer ISI data were analyzed and reported. The interval from the offset of the targets to the onset of the next trial cue was 7910 ms. Stimuli were delivered through an MRI-compatible goggle system (Resonance Technology, Northridge, California). Subjects were trained before the MRI session to ensure that the task was clearly understood and that subjects were able to perform the task without eye movements. In the scanner, they were instructed to covertly orient attention at the moment the cue was presented and to diligently maintain fixation throughout all runs; this was verified in control studies in two subjects using signal-averaged electrooculography outside the scanner. Speed of response was not emphasized, in order to minimize head-motion artifacts that might result from requiring a speeded response. Head motion was minimized by using a bite bar attached to the head coil. Six healthy adults (ages 22–34; 4 female) participated and gave written informed consent before all sessions. All procedures were approved by the UC Davis human subjects review committee. Each subject performed 5 runs of the task (396 s per run) while MRI data was acquired.
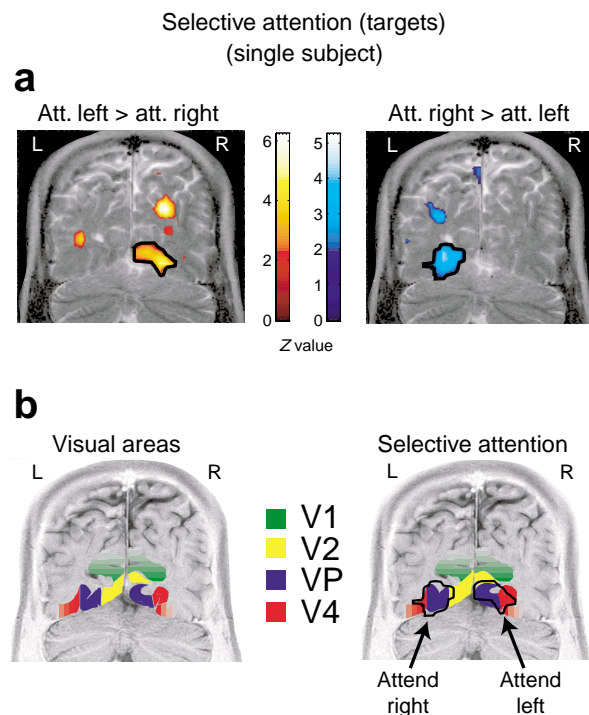
anisms of attentional control and the resulting modulation of sensory signals. The challenge for the future is to relate activity in each of these identified brain regions to the specific neurocomputational operations they subserve during visual spatial attention.

METHODS

Stimuli and task parameters: cueing study. Each trial began with a cue that consisted of two overlapping isoluminant arrows presented at fixation (one blue and one yellow, pointing in opposite directions, each 1.9° tall × 0.96° wide; duration, 500 ms). To eliminate differential activations based on the physical differences in right versus left cues, half the subjects were instructed to orient attention based on the direction of the blue arrow, and the other half were required to use the yellow arrow. The relevant arrow pointed randomly to the left or right. Target locations were demarcated by white outline rectangles (8.1° wide × 7.2° tall, centered 5.6° above the horizontal meridian and 7.7° lateral to the vertical meridian) that remained on the screen throughout all runs.

Target stimuli appeared within the white outline rectangles and consisted of black and white checkerboards (8.1° × 7.2°, composed of 0.9° square

Stimuli and parameters: stimulation of meridia and control sessions. In two of the subjects, visual field mapping and cue control sessions were performed. Meridian stimuli for visual area mapping were 9.0° × 2.7° checkerboard patterns aligned on the vertical or horizontal meridia and composed of alternating 0.9° square black and white checks, reversing at 15 Hz. Stimuli were presented in alternating 22-s blocks of right versus left meridia and in a separate run, upper versus lower meridia. The alternating pattern of vertical and horizontal meridia activations in visual cortex were used to identify the borders between V1, V2, VP and V4 (refs. 44, 47). For the cue sensory-control session, the cues used in the main experiment were flashed every 750 ms (duration, 500 ms) for 22 s alternating with 22-s no-stimulus blocks. A synthetic hemodynamic response function was convolved with the box-car function that represented the periodic alternation in the experimental conditions to yield the model response function that included a temporal derivative. Low-frequency drifts were modeled and filtered with a high-pass filter cutoff of 88 s, and the data were temporally smoothed by convolving the time series with a 4-s full width at half maximum (FWHM) Gaussian kernel. In another cue control, the cue and target stimuli were identical to that used in the main attention study except that the cues were not instructive as to where to orient attention. (Subjects had to

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Fig. 5. Selective processing of target stimuli and retinotopy (single subject). (**a**) A T2-weighted coronal slice ($y = -72$) showing the activations due to selective visual attention on target processing for one subject. The left column shows the regions showing greater activity when attention was focused on the left visual field. The right column shows those areas showing greater activity when attention was focused on the right. Attention-related activations in the contralateral fusiform and lingual gyri are outlined in black (coordinates of left hemisphere maximum, −32, −60, −8; $Z = 5.26$; right hemisphere maximum, 20, −68, −8; $Z = 5.39$). A more dorsal region in the cuneus (not outlined in black) also showed enhanced activity contralateral to the direction of attention (left hemisphere maximum = −32, −64, 28, $Z = 4.02$; right hemisphere maximum = 24, −72, 28, $Z = 6.27$). (**b**) Left panel, ventral visual areas for the same subject shown at top, determined using the meridia scans (see Methods) and traced onto contrast-inverted, T2-weighted MRI scans ($y = -72$). Right panel, effect of attention to target stimuli on responses in lingual and fusiform gyri (shown as thick black outlines) overlaid onto the subject's retinotopically mapped visual areas. Attention-related target processing extends from V2 through V4 in the ventral visual-processing stream.

detect gray checks in both hemifields). During these sessions, target stimuli (250 ms) were presented on only 22% of trials with an ISI of 300 ms, whereas the other 78% of trials (catch trials) consisted only of the cue stimuli; only these catch trials were analyzed, using event-related methods (see below).

Scanning procedures. Functional images were acquired with a Signa Advantage 1.5 Tesla whole-body MRI system (General Electric, Waukesha, Wisconsin), with an elliptical end-capped quadrature radio frequency and local gradient head coil (Medical Advances, Milwaukee, Wisconsin). Images were acquired using T2*-weighted gradient-recalled echo, echo planar imaging (EPI) in the coronal plane with a repetition time (TR) of 2.75 seconds, an effective echo time (TE) of 40 ms and a flip angle (FA) of 90°. Twenty-two interleaved slices were collected with a 22-cm field of view (FOV), 64 × 64 matrix, slice thickness of 6 mm and an interslice gap of 2 mm, yielding a voxel size of 3.43 × 3.43 × 6.00 mm³.

Fourier image reconstruction included N/2 ghost correction using image phase correction[48]. Neural activation was detected via the blood oxygenation level dependent (BOLD) contrast mechanism[15], which provided differences in signal intensity based upon differences in tissue T2* and perfusion. High-

Selective attention (targets)
(single subject)

a

Att. left > att. right   Att. right > att. left

Z value

b

Visual areas   Selective attention

- ■ V1
- ■ V2
- ■ VP
- ■ V4

Attend right   Attend left

resolution proton density and T2-weighted fast spin echo (FSE) images were also obtained in the coronal plane during the same scanning session. The anatomical scans were acquired with the following parameters: TR = 4.2 s; TE = 17 and 136 ms; echo train = 8; FOV = 22 cm, matrix = 512 × 256 (interpolated to 512 × 512 for display), slice thickness of 6 mm, with an interslice gap of 2 mm. In each EPI acquisition, 144 images were acquired at each of the 22 slice locations, for a total acquisition time of 396 s (6 min, 36 s).

Image processing. The first 16 images at each slice location (initial 44 s of acquisition) were discarded from the analysis. The remaining 128 images at each slice were used for the time-series analyses. Images were realigned and corrected for movement artifacts. The anatomical T2 images were coregistered with the proton density images and the functional images for each subject. Each subject's T2 (and coregistered proton density scans) were then
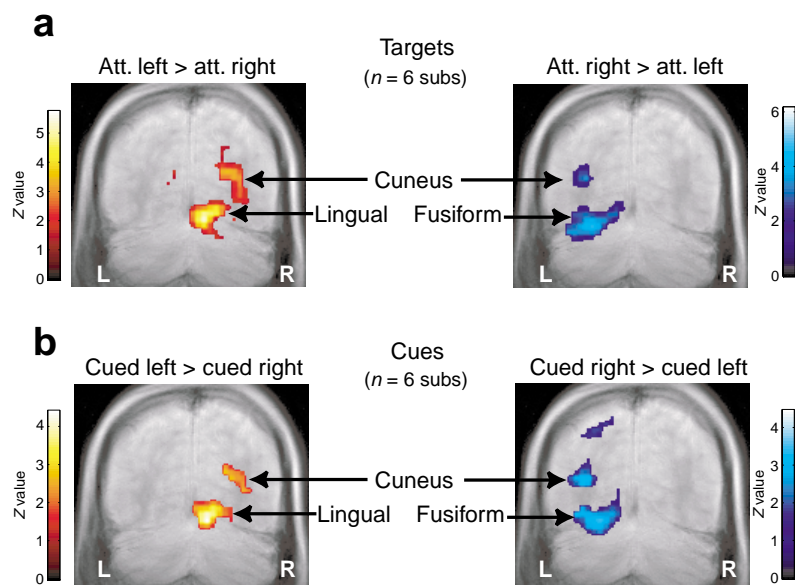

a   Targets
                      (*n* = 6 subs)

Att. left > att. right   Att. right > att. left

Cuneus

Lingual   Fusiform

b   Cues
                      (*n* = 6 subs)

Cued left > cued right   Cued right > cued left

Cuneus

Lingual   Fusiform

Fig. 6. Selective attention-related activations to targets and cues (group data). Results of group analysis showing regions with differential activity due to the direction of attention, overlaid onto averaged (6 subject) proton density MRI scans (slice at $y = -64$). (**a**) Target processing was enhanced in regions of visual cortex contralateral to the attended hemifield. These significant (all $p < 0.001$ corrected) attention-related activations were observed in the lingual and fusiform gyri in the right (12, −64, −4; $Z = 5.86$) and left (−28, −60, −8; $Z = 6.15$) hemispheres, and also in dorsal regions of the cuneus in the right (24, −72, 28; $Z = 6.04$) and left (−28, −68, 24; $Z = 5.30$) hemispheres. (**b**) Contralateral to the direction of attention, multiple regions of extrastriate cortex showed responses to the cue stimuli that differed based on the direction of attention, including the lingual and fusiform gyri (12, −64, −4, $Z = 4.51$; −20, −64, −4, $Z = 4.25$) as well as a more dorsal region of the cuneus (24, −68, 28, $Z = 3.87$; −28, −68, 24, $Z = 4.61$). The maxima of these activations were 0–1 cm from those in response to targets and were all significant at $p < 0.001$, uncorrected. (Because regions of interest analyzed for cue responses were specified *a priori* by analyses for attention effects on target responses, we give uncorrected p values for cue responses.)

spatially normalized to a standard stereotactic space[49] (using, however, the canonical Montreal Neurological Institute template in the SPM97 package), with the origin at the anterior commisure and the *x–y* plane extending through the anterior and posterior commisures. The functional images were then spatially normalized into stereotactic space, resampled to $4 \times 4 \times 4$ mm³ voxels and spatially smoothed with an 8-mm isotropic Gaussian kernel.

Event-related analyses. The responses of interest in the event-related design were modeled by convolving a vector containing the onset times of the cues and targets with a synthetic hemodynamic response function composed of the sum of two gamma functions and its temporal derivative (accounting for the hemodynamic response and subsequent undershoot and for slight variations in timing)[50]. As a result, the present analysis emphasizes transient hemodynamic activity temporally adjacent to the cue and target events. Multiple linear regression (using a least-squares approach to estimate the parameters), as implemented in SPM97, was used to model the effects of interest and other confounding factors (such as session effects and low-frequency drifts of signal intensity) at every voxel simultaneously. Data from different sessions were proportionally scaled to a grand mean of 100 arbitrary units to account for overall differences in the intensity of whole brain volumes across the time series. Temporal smoothing was accomplished by convolving the data with a 4-s FWHM Gaussian filter (to account for temporal autocorrelations in the time series). An omnibus voxel-wise analysis provided an SPM(*F*), and those voxels with significant *F*-ratios ($p < 0.001$ uncorrected) were retained for further specific statistical tests. Specific hypotheses were then tested with *t*-tests at those voxels, and the resulting SPM{*t*} was transformed to the unit normal distribution resulting in the *Z*-scores and SPM(*Z*) maps in the figures and tables.

1. Pashler, H. *The Psychology of Attention* (MIT Press, Cambridge, Massachusetts, 1999).
2. Posner, M. I. & Petersen, S. E. The attention system of the human brain. *Annu. Rev. Neurosci.* **13**, 25–42 (1990).
3. Moran, J. & Desimone, R. Selective attention gates visual processing in the extrastriate cortex. *Science* **229**, 782–784 (1985).
4. Mangun, G. R. & Hillyard, S. A. Modulation of sensory-evoked brain potentials provide evidence for changes in perceptual processing during visual-spatial priming. *J. Exp. Psychol. Hum. Percept. Perform.* **17**, 1057–1074 (1991).
5. Mesulam, M.-M. A cortical network for directed attention and unilateral neglect. *Ann. Neurol.* **10**, 309–325 (1981).
6. Posner, M. I., Walker, J. A., Friedrich, F. A. & Rafal, R. D. Effects of parietal injury on covert orienting of attention. *J. Neurosci.* **4**, 1863–1874 (1984).
7. Corbetta, M., Miezin, F., Shulman, G. & Petersen, S. A PET study of visuospatial attention. *J. Neurosci.* **13**, 1202–1226 (1993).
8. Gitelman, D. R. *et al.* A large-scale distributed network for covert spatial attention. *Brain* **122**, 1093–1106 (1999).
9. Heinze, H. J. *et al.* Combined spatial and temporal imaging of spatial selective attention in humans. *Nature* **392**, 543–546 (1994).
10. Martinez, A. *et al.* Involvement of striate and extrastriate visual cortical areas in spatial attention. *Nat. Neurosci.* **2**, 364–369 (1999).
11. Nobre, A. C. *et al.* Functional localization of the system for visuospatial attention using positron emission tomography. *Brain* **120**, 515–533 (1997).
12. Harter, M. R., Miller, S. L., Price, N. J., LaLonde, M. E. & Keyes, A. L. Neural processes involved in directing attention. *J. Cogn. Neurosci.* **1**, 223–237 (1989).
13. Buckner, R. *et al.* Detection of cortical activation during averaged single trials of a cognitive task using functional magnetic resonance imaging. *Proc. Natl. Acad. Sci. USA* **93**, 14302–14303 (1996).
14. McCarthy, G., Luby, M., Gore, J. & Goldman-Rakic, P. Infrequent events transiently activate human prefrontal and parietal cortex as measured by functional MRI. *J. Neurophysiol.* **77**, 1630–1634 (1997).
15. Ogawa, S. *et al.* Intrinsic signal changes accompanying sensory stimulation: functional brain mapping with magnetic resonance imaging. *Proc. Natl. Acad. Sci. USA* **89**, 5951–5955 (1992).
16. Mangun, G. R., Hopfinger, J., Kussmaul, C., Fletcher, E. & Heinze, H. J. Covariations in ERP and PET measures of spatial selective attention in human extrastriate cortex. *Hum. Brain Mapp.* **5**, 273–279 (1997).
17. Mangun, G. R., Buonocore, M., Girelli, M. & Jha, A. ERP and fMRI measures of visual spatial selective attention. *Hum. Brain Mapp.* **6**, 383–389 (1998).
18. Tootell, R. B. *et al.* The retinotopy of visual spatial attention. *Neuron* **21**, 1409–1422 (1998).
19. Brefczynski, J. A. & DeYoe, E. A. A physiological correlate of the spotlight of visual attention. *Nat. Neurosci.* **2**, 370–374 (1999).
20. Engel, S. A., Glover, G. H. & Wandell, B. A. Retinotopic organization in human visual cortex and the spatial precision of functional MRI. *Cereb. Cortex* **7**, 181–192 (1997).
21. Sereno, M. I. *et al.* Borders of multiple visual areas in humans revealed by functional magnetic resonance imaging. *Science* **268**, 889–893 (1995).
22. Woldorff, M. *et al.* Retinotopic organization of early visual spatial attention effects as revealed by PET and ERPs. *Hum. Brain Mapp.* **5**, 280–286 (1997).
23. Treue, S. & Maunsell, J. H. R. Attentional modulation of visual motion processing in cortical areas MT and MST. *Nature* **382**, 539–541 (1996).
24. Corbetta, M. *et al.* A common network of functional areas for attention and eye movements. *Neuron*, **21**, 761–773 (1998).
25. Coull, J. T. & Nobre, A. C. Where and when to pay attention: The neural systems for directing attention to spatial locations and to time intervals as revealed by both PET and fMRI. *J. Neurosci.* **18**, 7426–7435 (1998).
26. Bushnell, M. C., Goldberg, M. E. & Robinson, D. L. Behavioral enhancement of visual responses in monkey cerebral cortex. I. Modulation in posterior parietal cortex related to selective visual attention. *J. Neurophysiol.* **46**, 755–772 (1981).
27. LaBar, K. S., Gitelman, D. R., Parrish, T. B. & Mesulam, M. -M. Neuroanatomic overlap of working memory and spatial attention networks: A functional MRI comparison within subjects. *Neuroimage* **10**, 695–704 (1999).
28. Corbetta, M. Frontoparietal cortical networks for directing attention and the eye to visual locations: Identical, independent, or overlapping neural systems? *Proc. Natl. Acad. Sci. USA* **95**, 831–838 (1998).
29. Friedrich, F. J., Egly, R., Rafal, R. & Beck, D. Spatial attention deficits in humans: a comparison of superior parietal and temporal-parietal junction lesions. *Neuropsychology* **12**, 193–207 (1998).
30. Watson, R. T., Valenstein, E., Day, A. & Heilman, K. M. Posterior neocortical systems subserving awareness and neglect. *Arch. Neurol.* **51**, 1014–1021 (1994).
31. Henik, A., Rafal, R. & Rhodes, D. Endogenously generated and visually guided saccades after lesions of the human frontal eye fields. *J. Cogn. Neurosci.* **6**, 400–411 (1984).
32. Rosen, A. C. *et al.* Neural basis of endogenous and exogenous spatial orienting: a functional MRI study. *J. Cogn. Neurosci.* **11**, 135–152 (1999).
33. Petit, L. *et al.* PET study of the human foveal fixation system. *Hum. Brain. Mapp.* **8**, 28–43 (1999).
34. Jonides, J. *et al.* Spatial working memory in humans as revealed by PET. *Nature* **363**, 623–625 (1993).
35. Kojima, S. & Goldman-Rakic, P. S. Delay-related activity of prefrontal neurons in rhesus monkeys performing delayed response. *Brain Res.* **248**, 43–50 (1982).
36. D'Esposito, M., Ballard, D., Aguirre, G. K. & Zarahn, E. Human prefrontal cortex is not specific for working memory: a functional MRI study. *Neuroimage* **8**, 274–282 (1998).
37. Jonides, J., Smith, E. E., Marshuetz, C., Koeppe, R. A. & Reuter-Lorenz, P. A. Inhibition in verbal working memory revealed by brain activation. *Proc. Natl. Acad. Sci. USA* **95**, 8410–8413 (1998).
38. Smith, E. E. & Jonides, J. Neuroimaging analyses of human working memory. *Proc. Natl. Acad. Sci. USA* **95**, 12061–12068 (1998).
39. Corbetta, M. in *The Attentive Brain* (ed. Parasuraman, R.) 95–122 (MIT Press, Cambridge, Massachusetts, 1998).
40. Posner, M. I. & DiGirolamo, G. J. in *The Attentive Brain* (ed. Parasuraman, R.) 401–423 (MIT Press, Cambridge, Massachusetts, 1998).
41. Luck, S. J. *et al.* Effects of spatial cuing on luminance detectability: Psychophysical and electrophysiological evidence for early selection. *J. Exp. Psychol. Hum. Percept. Perform.* **20**, 887–904 (1994).
42. Van Voorhis, S. T. & Hillyard, S. A. Visual evoked potentials and selective attention to points in space. *Percept. Psychophys.* **22**, 54–62 (1977).
43. McAdams, C. J. & Maunsell, J. H. R. Effects of attention on orientation-tuning functions of single neurons in macaque cortical area V4. *J. Neurosci.* **19**, 431–441 (1999).
44. Tootell, R. *et al.* Functional analysis of human MT and related visual cortical areas using magnetic resonance imaging. *J. Neurosci.* **15**, 3215–3230 (1995).
45. Luck, S. J., Chelazzi, L. Hillyard, S. A. & Desimone, R. Neural mechanisms of spatial selective attention in areas V1, V2 and V4 of macaque visual cortex. *J. Neurophysiol.* **77**, 24–42 (1997).
46. Chawla, D., Rees, G. & Friston, K. J. The physiological basis of attentional modulation in extrastriate visual areas. *Nat. Neurosci.* **7**, 671–676 (1999).
47. Kastner, S., Pinsk, M. A., De Weerd, P., Desimone, R. & Ungerleider, L. G. Increased activity in human cerebral cortex during directed attention in the absence of visual stimulation. *Neuron* **22**, 751–761 (1999).
48. Buonocore, M. H. & Gao, L. Ghost artifact reduction for echo planar imaging using image phase correction. *Magn. Reson. Med.* **38**, 89–100 (1997).
49. Talairach, J. & Tournoux, P. *Co-Planar Stereotaxic Atlas of the Human Brain* (Thieme, New York, 1988).
50. Friston, K. J. *et al.* Event-related fMRI: Characterizing differential responses. *Neuroimage* **7**, 30–40 (1998).