Maintaining and Shifting Attention within Left or Right Hemifield

Rik Vandenberghe, John Duncan[1], Karen M. Arnell[1], Sonia J. Bishop[1], Nicholas J. Herrod[2], Adrian M. Owen[1], Pawanjit S. Minhas[2], Patrick Dupont[3], John D. Pickard[2] and Guy A. Orban

Laboratorium voor Neuro- en Psychofysiologie, Katholieke Universiteit Leuven, Belgium, [1]MRC Cognition and Brain Sciences Unit, University of Cambridge, Cambridge, [2]Wolfson Brain Imaging Centre, Cambridge, UK and [3]Department of Nuclear Medicine, University Hospital Gasthuisberg, Leuven, Belgium

Positron emission tomography (PET) was used to examine two questions: (i) which structures of the intact human brain change their activity with the direction of attention to left or right visual field; and (ii) how does activity in these structures, and in parietal cortex in particular, depend on the frequency of attentional shifts? Subjects were required to discriminate the orientation of peripheral gratings. The two main experimental variables were the attended hemifield (left or right) and the proportion of trials requiring a shift within that hemifield (20% or 80%). A detection control condition was also included. Behaviourally, subjects were less accurate and significantly slower when a trial required a shift than when it did not. Ventral and lateral occipital areas showed significantly higher blood flow levels contralateral to the direction of attention. Replicating previous work, there was also a significant main effect of the direction of attention in left lateral prefrontal cortex: blood flow levels were higher during leftward attention in comparison both to baseline and to rightward attention. This left frontal effect reached significance in single subjects in whom several activation sites could be distinguished within left middle and inferior frontal gyrus. Right and left parietal cortex were activated during both left- and right-field attention conditions, with a tendency for higher activity levels when attention was directed contralaterally. Contrary to the experimental hypothesis, however, parietal regions were not activated differentially by high versus low numbers of attentional shifts. The current experiment confirms that left frontal convexity is sensitive to manipulations of the direction of visuospatial attention. The results do not indicate a specific role of parietal cortex in attentional shifting.

Introduction

Functional imaging studies of the intact human brain have revealed distributed changes in brain activity with variations of the direction of visual attention to left or right visual field. Effects have been most robust and replicable in extrastriate cortex: when attention is directed to the right, activity on the left increases, and vice versa (Corbetta *et al.*, 1993; Heinze *et al.*, 1994; Mangun *et al.*, 1997; Vandenberghe *et al.*, 1997; Woldorff *et al.*, 1997; Tootell *et al.*, 1998; Brefczynski and DeYoe, 1999; Martinez *et al.*, 1999). In higher-order brain regions, effects of the direction of attention have been less consistent. In some (Corbetta *et al.*, 1993; Nobre *et al.*, 1997; Martinez *et al.*, 1999) but not all (Vandenberghe *et al.*, 1997; Tootell *et al.*, 1998) studies, parietal effects have been reported, predominantly on the right side. In right parietal cortex two separate foci have been distinguished which were activated during leftward or rightward orienting respectively (Corbetta *et al.*, 1993; Nobre *et al.*, 1997). In left parietal cortex, activity has been shown to increase during rightward in comparison to leftward orienting (Corbetta *et al.*, 1993; Nobre *et al.*, 1997). This is in agreement with neuropsychological evidence for a lateralized role of parietal cortex in unilateral attention (Weintraub and Mesulam, 1987). Other experiments yielded significant lateral frontal effects (Vandenberghe *et al.*, 1997), most prominent in the left

frontal convexity. Surprisingly, frontal activity was increased ipsilateral to the direction of attention (Vandenberghe *et al.*, 1997).

In this study we examined whether either parietal or frontal activity is dependent on the frequency of spatial-attentional shifts within one hemifield. We hypothesized that parietal cortex is particularly sensitive to the direction of attention when spatial attentional shifts are required, as in the experiments reported by Corbetta *et al.* (Corbetta *et al.*, 1993) and by Nobre *et al.* (Nobre *et al.*, 1997). This would fit with neuropsychological data indicating that parietal neglect patients are particularly deficient on tasks requiring shifts to or within the neglected hemifield (Baynes *et al.*, 1986; Posner *et al.*, 1987).

Materials and Methods

Subjects

Ten men between 40 and 65 years of age participated. All were strictly right-handed, free of psychotropic or vasoactive medication, had no neurological or psychiatric history, and had a normal brain magnetic resonance image. They gave their written informed consent in accordance with the Declaration of Helsinki. The experiment was approved by the Cambridge Local Research Ethics Committee.
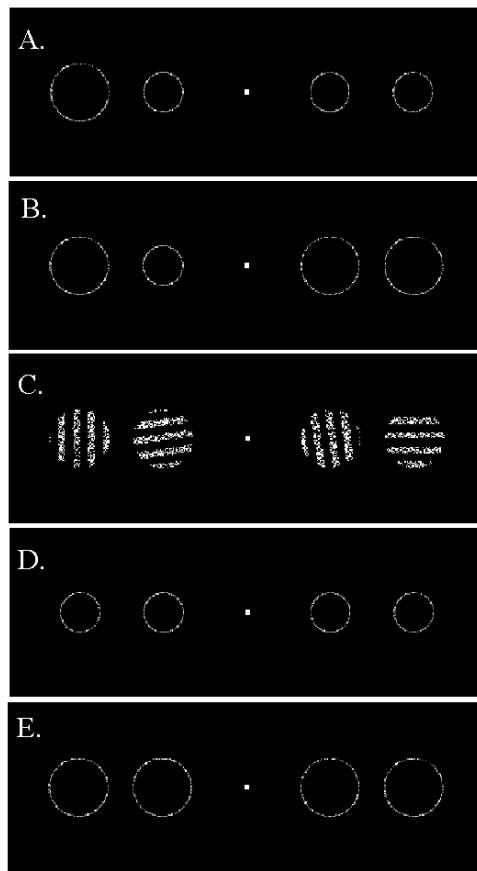
Discrimination Conditions

Stimuli were displayed using a 20 in. Microtouch monitor at a viewing distance of 78 cm and mounted approximately perpendicular to the line of sight.

The experiment was run in blocks of 96 trials, trials within a block following one another in an uninterrupted series of ~144 s. Each trial had two parts: a cue display (Fig. 1*A,B*), indicating which of four display locations was to be attended on this trial, followed by a grating display (Fig. 1*C*). The cue display lasted for 1000 ms (± random variation of 250 ms), and the grating display for 500 ms. The subject's task was to identify the orientation of the cued grating, making no response if it was horizontal or vertical (no go; 50% of trials), or pressing a key simultaneously with both thumbs if it was oblique (go; 50% of trials). The response window for any given trial extended from grating onset on this trial to grating onset on the following trial.

Cue displays consisted of four rings aligned on the horizontal meridian, two to the left and two to the right of a central fixation point, at an eccentricity of 4.2° (near) and 8.4° (far) respectively. Rings were presented throughout the cueing interval. Three rings had an identical diameter (1.9 or 3.0°), while the fourth was either larger or smaller (3.0 or 1.9° respectively) (Fig. 1*A,B*). This fourth ring indicated where to attend. Near and far locations were cued equally often.

A grating display followed the cue display. It consisted of four phase-randomized square-wave gratings (diameter: 3.0°; spatial frequency: 1 cycle/deg) (Fig. 1*C*). For each grating there were four possible orientations: the two canonical orientations, horizontal and vertical, and an oblique variant of each, rotated counterclockwise from the canonical. In each hemifield, one grating was horizontal or rotated from the horizontal axis and the other vertical or rotated from the vertical axis. The angle of rotation was adapted to each subject's performance during the training session. Between-block variations in location cueing defined the different discrimination conditions. Within one block only two locations

Figure 1. Cue and grating displays. (*A*) Cue display during a left field discrimination condition with large ring among small rings. (*B*) Cue display during a left field discrimination condition with small ring among large rings. (*C*) Grating display. (*D*) Cue display during a detection condition where rings are small. (*E*) Cue display during a detection condition where rings are large.

were ever cued, those in the left (four blocks) or in the right (four blocks) visual field. Within a hemifield, either 20% (4 blocks) or 80% (4 blocks) of trials called for a switch of attended location from the preceding trial. Finally, the cued location could be marked either by a small circle among large circles (four blocks), or a large circle among small circles (four blocks). Complete crossing of these three factors produced eight unique conditions, each scanned once. Averaging across cue variants (small among large or large among small) produced two replications of each of the four main conditions: left field 20% shifts (L sust), left field 80% shifts (L shift), right field 20% shifts (R sust), right field 80% shifts (R shift). Such averaging removed confounding perceptual differences between the cue displays used during leftward or rightward attention conditions.

Before each run subjects were instructed explicitly to attend to either left or right. If the cue consisted of a small among large rings, they were instructed to attend to the small ring, and vice versa. Subjects were not informed about the proportion of shifts within each run.

Detection Control Conditions

During detection subjects responded with both thumbs on every trial, as soon as the grating display appeared. Rings presented in cue displays were all small (1.9°) in half of the detection blocks (Fig. 1*D*) and all large (3.0°) in the other half (Fig. 1*E*). Again, averaging between the two cue variants removed perceptual differences between cue displays used during detection or discrimination conditions.

Eye Movement Control

During training and scanning sessions horizontal eye movements were monitored with contact electrodes placed on the outer ocular canthi and a grounding electrode placed between the eyes. To ensure detection of gaze shifts at the onset or the end of the task, subjects were required to read aloud a digit appearing at the fixation point just before and just after the trial block. Electrooculographical recordings (EOG) were stored on disk. At the start of the experiment the EOG was calibrated for fixation and for horizontal saccades. After the session the EOG record from each trial block was inspected semiquantitatively for saccades or slow gaze drift.

Training Session

Subjects were trained prior to the scanning session during a 2 h training session. Runs of 100 left-field and right-field discrimination trials as well as detection trials were administered four times each. During discrimination practice runs shifts were required in 50% of trials except for the two last discrimination runs, during which shifts were required in 20% or 80% of trials. During the first half of the training session the cue interval duration was 1500 ms and the orientation difference (rotation from canonical) 12°. In the second half the cue interval was shortened to 1000 ms. Depending on the subject's accuracy the orientation difference was sometimes reduced to 8°. Subjects who could not maintain fixation or who did not reach a fixed accuracy criterion at the end of the practice session were excluded.

Image Acquisition

Measures of regional cerebral blood flow (rCBF) were acquired by use of a GE Advance Scanner operated in three-dimensional mode. The subject's head was immobilized using a canoe helmet and positioned parallel to the canthomeatal line using laser alignment beams. A transmission scan with a germanium–gallium source was obtained to correct for attenuation. It was also used for verifying the correct head position. For each condition 9 mCi ^{15}O-labelled H$_2$O was injected over a period of 20 s. The task was started at the same moment as the infusion; image acquisition began 50 s later. The first 90 s of image acquisition were used for further analysis. The task ended shortly after the end of image acquisition. An interval of at least 12 min separated two successive injections. During this interval subjects received a practice run with the direction of attention and the type of cue display matched to the condition scanned next. During the practice run shifts occurred in 50% of trials. The scan order was approximately counterbalanced between conditions across subjects.

The data were corrected for scatter, randoms and attenuation prior to reconstruction using three-dimensionally filtered back-projection (Kinahan and Rogers, 1989) with a Colsher filter of cut-off frequency 0.12 per mm. The brain tissue radiation count rate was used as a measure of rCBF.

Analysis

All subsequent data analysis was performed using Statistical Parametric Mapping version SPM96 (Wellcome Department of Cognitive Neurology, Institute of Neurology, London). In one subject one detection condition was rejected due to technical failure. The scans from each subject were realigned and stereotactically normalized to the Montreal Neurological Institute PET template in the Talairach space (Talairach and Tournoux, 1988; Friston *et al.*, 1995a). Data were analyzed using a fixed-effects general linear model determining parameters estimates for each condition in each subject with one replication (SPM96 option multi-study design, single subject per study, replications). The replication was provided by studying each of the conditions of interest once with a small and once with a large cue. Differences in cue size between conditions were not modelled. Subject-specific effects as well as interactions between subject and condition were modelled explicitly. This approach allows one to look at individual subject as well as group results. It differs from a classical group analysis where parameter estimates are determined only for each condition but not for each subject. Global brain activity was used as a covariate of no interest fixed at 50ml/dl/min (Friston *et al.*, 1995b). A smoothing filter of $16 \times 16 \times 16$ mm^3 was applied.

First we defined a general network for peripheral orientation discrimination. We subtracted the mean blood flow pattern obtained during detection from the mean across all discrimination conditions [(L sust + L shift + R sust + R shift) – det]. Second, we compared the blood flow patterns during leftward attention conditions to those obtained during rightward attention conditions, in both directions (main effect of

A. Lateral frontal region of interest
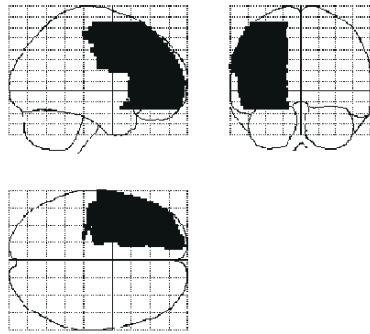
B. Parietal regions of interest
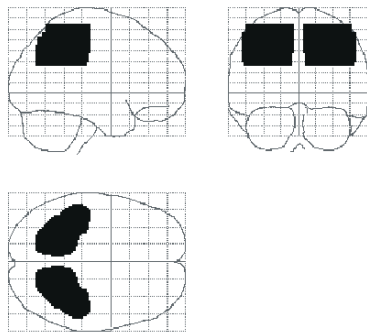
Figure 2. Frontal (*A*) and parietal (*B*) regions of *a priori* interest. The regions are projected on a glass brain view. Although not clear from this projection, the regions are restricted to gray matter only.

direction of attention) [(L sust + L shift) – (R sust + R shift) and the inverse]. Third, we compared the blood flow patterns during the 20% shift conditions to those obtained during the 80% shift conditions, in both directions (main effect of attention shifting) [(L sust + R sust) – (L shift + R shift) and the inverse]. Finally, we also determined the interaction effects between direction and shifting [(L sust – L shift) – (R sust – R shift) and (L shift – L sust) – (R shift – R sust)].

To assess changes occurring anywhere in the brain we used a significance threshold of $P < 0.05$ corrected for the entire search volume. In addition three cortical regions of *a priori* interest — left frontal convexity, left parietal and right parietal convexity (Fig. 2) — were delineated manually by means of ANALYZE (Mayo Clinic Foundation, Rochester, MN) software (Fig. 2) using anatomical features. To assess significance of changes within these regions the significance threshold was set at $P < 0.05$ corrected for the region's size (Worsley *et al.*, 1996) following a procedure that takes into account the region's shape and the study's smoothness estimate (Worsley *et al.*, 1996). This led to a corrected $P < 0.05$ significance threshold corresponding to a Z score of 3.02 in the frontal region, and to a Z score of 3.67 in each of the parietal regions. The corrected significance threshold for the frontal region was calculated separately from that of the parietal regions since the frontal region was used to address a separate question concerning inter-individual differences in left lateral frontal direction-sensitivity (see below). Corrected significance thresholds for the two parietal regions were also calculated separately from one another in order to enhance sensitivity.

For the purpose of anatomical localization a three-dimensional T_1 MR image was acquired in each subject using a 0.5 T Oxford Magnet. For each subject this image was coregistered to the mean of the realigned PET images and stereotactically normalized using the normalization matrix calculated on the basis of the PET images.

Table 1
Behavioural parameters

Condition	Trial type	Accuracy		Reaction times	
		Mean	SE	Mean	SE
L sust	same	0.87	0.03	490	29
	diff	0.82	0.06	517	31
L shift	same	0.85	0.04	499	31
	diff	0.85	0.04	518	23
R sust	same	0.84	0.03	476	19
	diff	0.83	0.04	511	15
R shift	same	0.81	0.04	501	28
	diff	0.73	0.05	530	27

Accuracy (expressed as the sensitivity measure *A′*) and reaction times (in ms). The two blocked variables referred to in the first column correspond to the direction of attention and the proportion of attentional shifts (20% or 80% shifting). The second column refers to whether or not the cued location in a given trial is identical to the location cued in the preceding trial.

Results

Behavioural Data during Scanning

Depending on performance in the training session, the orientation difference in the PET session was set at 8° in eight subjects, and 12° in the remaining subjects. Hits and false alarms from discrimination conditions were converted into the non-parametric sensitivity measure *A′* (Snodgrass and Corwin, 1988) individually for each cell for each participant. *A′* values vary from 0 to 1 where 0.5 is chance and 1.0 indicates perfect performance. A three-way, repeated-measures ANOVA was performed on accuracy as well as reaction time data. Two blocked variables consisted of the proportion of attentional shifts within a condition (20% or 80%) and the attended hemifield (left versus right). A third variable consisted of whether or not an individual trial required a spatial shift. When a trial belonged to a condition containing 80% of shift trials, accuracy was significantly worse than when it belonged to a condition that required shifting only in 20% of trials [$F(1,9) = 15.0$, $P < 0.005$] (Table 1). When attention was to the right, accuracy was significantly worse than when attention was to the left [$F(1,9) = 9.4$, $P < 0.05$] (Table 1). When a trial required a spatial shift, accuracy tended to be worse than when it did not [$F(1,9) = 5.00$, $P = 0.052$] (Table 1). Furthermore, in such trials reaction times were significantly longer than when the trial did not require a shift [$F(1,9) = 8.60$, $P < 0.05$] (Table 1). Finally, accuracy data demonstrated a significant three-way interaction effect between the three variables [$F(1,9) = 6.72$, $P < 0.05$] (Table 1).

EOG traces were inspected for the occurrence of saccades. Only bidirectional saccades were found with a peripheral fixation phase of maximally 500 ms and an amplitude of maximally 2°. A one-way ANOVA revealed a significant difference in the number of saccades between conditions [$F(4,109) = 6.75$, $P < 0.001$] (Table 2). According to a *post hoc* Scheffé test, this was mainly due to a significantly higher number of saccades during right-field shifting in comparison to detection ($P < 0.05$).

PET data

Results of the overall discrimination minus detection contrast are shown in Table 3. Discrimination yielded significantly higher blood flow levels than detection in left fusiform gyrus, in the intraparietal sulci bilaterally, in right middle frontal gyrus, right precentral sulcus, right thalamus and in cerebellar hemispheres bilaterally. This network resembles that described in earlier studies (Corbetta *et al.*, 1993; Coull *et al.*, 1996; Vandenberghe *et al.*, 1996, 1997; Nobre *et al.*, 1997).

Table 2
Average number of saccades per condition

Condition	Mean	SE
L sust	5.1	1.8
L shift	3.4	0.91
R sust	4.4	1.2
R shift	8.6	2.1
det	0.87	0.30

Average number of saccades per condition during the 90 s image acquisition period. Abbreviations: R, right; L, left; sust, 20% shifts; shift, 80% shifts.

Table 3
General circuit for peripheral feature discrimination

	x	y	z	L sust	L shift	R sust	R shift	
L fusiform g.	−32	−62	−20	1.23	1.42	3.19	4.27	$Z = 4.98$
R intraparietal s.	24	−62	60	4.38	5.38	3.68	2.24	$Z = 5.98$
L intraparietal s.	−26	−56	52	2.07	3.98	3.41	3.06	$Z = 6.33$
	−18	−68	56	2.02	2.42	3.46	3.48	$Z = 5.19$
R middle frontal g.	42	40	24	3.33	3.33	3.96	3.93	$Z = 5.64$
R precentral s.	44	4	20	2.41	3.16	3.77	2.71	$Z = 5.72$
	36	−4	52	3.15	3.19	4.74	1.20	$Z = 4.79$
R thalamus	12	−12	16	3.67	2.32	2.81	2.98	$Z = 4.96$
	12	−2	0	2.62	2.16	1.74	3.08	$Z = 4.51$
R cerebellum	34	−64	−28	2.51	3.39	1.94	1.82	$Z = 5.26$
L cerebellum	−48	−66	−28	3.22	2.04	3.54	2.74	$Z = 5.27$

Peak activations obtained by subtracting detection from discrimination. Column 1: anatomical name; columns 2–4: Talairach coordinates; columns 5–8: percentage rCBF increase over detection (expressed as a percentage of detection rCBF); column 9: Z score obtained in the subtraction of detection from discrimination. Abbreviations: g,: gyrus; s., sulcus.

Table 4
Effect of the direction of attention

	x	y	z	L sust	L shift	R sust	R shift	
Left-sided minus right-sided attention								
R middle occ. g.	26	−84	12	2.24	2.98	−0.26	−0.43	$Z = 5.33$
R fusiform g.	44	−68	−20	2.50	3.81	0.64	0.17	$Z = 4.81$
L middle frontal g.	−40	42	36	4.00	4.01	0.22	−1.36	$Z = 4.61$
Right-sided minus left-sided attention								
L middle occ. g.	−46	−82	0	−0.50	0.01	3.30	3.20	$Z = 4.45$
L fusiform g.	−18	−60	−16	−0.07	−0.46	2.05	3.02	$Z = 4.97$
	−32	−66	−8	−1.27	−0.21	2.70	3.17	$Z = 4.82$

Peak activations obtained by comparing left-sided and right-sided attention conditions and thresholded at $P < 0.05$ after correction for the entire search volume. Activity levels in each condition are expressed as a percentage of detection rCBF. Abbreviation: occ., occipital.

Table 5
Left frontal effects: group analysis

	x	y	z	L sust	L shift	R sust	R shift	
Left-sided minus right-sided attention								
L middle frontal g.	−40	42	36	4.00	4.01	0.22	−1.36	$Z = 4.61$
L inferior frontal g.	−54	38	−12	3.02	2.29	−1.19	−2.07	$Z = 4.15$
L superior frontal g.	−32	14	64	2.56	3.20	−0.86	−1.17	$Z = 3.78$

Peak activations in left frontal convexity obtained in the group analysis by subtracting right-sided from left-sided attention conditions. All activations are significant at $P < 0.05$ after correction for a volume of interest restricted to the left lateral frontal convexity. Activity levels in each condition expressed as a percentage of detection rCBF.

When attention was directed to the left instead of the right, blood flow levels were higher in right middle occipital gyrus and right fusiform gyrus (Table 4; Fig. 3, foci 1 and 2). In left middle frontal gyrus blood flow levels were also significantly increased, confirming our previous results (Vandenberghe *et al.*, 1997) (Table 4; Fig. 3, focus 3). When the analysis was restricted to the left frontal convexity only, two further significant activations were observed in left inferior and left superior frontal gyrus (Table 5). No significant changes were observed within the right parietal region of interest, although activity in the right intraparietal sulcus tended to be higher during leftward in comparison to rightward attention (Table 7; Fig. 3). We determined the anatomical location of the left lateral frontal effect in single subjects. Activation in left frontal convexity reached a corrected $P < 0.05$ significance threshold in 6/10 subjects. Different activation peaks could be distinguished in left middle frontal gyrus, left inferior frontal sulcus and left inferior frontal gyrus (Table 6). Left middle frontal gyrus was most frequently involved, being activated in 5/10 subjects.

Returning to the group analysis, when attention was directed to the right instead of the left, left middle occipital gyrus and the left fusiform gyrus showed significant activity increases (Table 4; Fig. 4, foci 4–6). This left middle occipital gyrus activation was lateral and inferior to the corresponding focus on the right side revealed during leftward attention. No right lateral frontal differences were observed, even when the threshold was lowered to an uncorrected $P < 0.005$. Within the left parietal region of interest, activity in left superior parietal lobule tended to be higher during rightward attention (Table 7; Fig. 4).

Surprisingly, no significant blood flow differences were found when 20% and 80% shifting conditions were compared at a corrected $P < 0.05$. Likewise, no significant interaction effects were observed at $P < 0.05$. It is, however, worth noting that a subthreshold interaction effect occurred in the posterior third of the right intraparietal sulcus (Table 7). In this region blood flow was increased during left-field shifting in comparison to right-field shifting ($Z = 3.35$) while no difference was observed between left-field and right-field sustaining of attention (uncorrected $P > 0.05$). Blood flow was also increased during left-field shifting in comparison to left-field sustaining of attention ($Z = 2.48$) and during right-field sustaining in comparison to right-field shifting of attention ($Z = 2.23$). No main effect of direction of attention was observed in this focus ($Z = 1.73$). Unexpectedly, a comparable effect was seen in the depth of the *left* intraparietal sulcus anterior to the corresponding right parietal focus. Again, the interaction effect resulted from both an increase during left-field shifting in comparison to left-field sustaining of attention ($Z = 2.58$) and from an increase during right-field sustaining in comparison to right-field shifting of attention ($Z = 2.08$) (Table 7).

Discussion

The current results are consistent with previous studies (Corbetta *et al.*, 1993; Heinze *et al.*, 1994; Woldorff *et al.*, 1995; Mangun *et al.*, 1997; Nobre *et al.*, 1997; Vandenberghe *et al.*, 1997; Tootell *et al.*, 1998; Brefczynski and DeYoe, 1999; Martinez *et al.*, 1999) demonstrating that changing the direction of attention to left or right visual field elicits occipital, parietal and frontal blood flow changes. Both lateral and ventral occipital activity increases were found contralaterally to the direction of attention (Corbetta *et al.*, 1993; Heinze *et al.*, 1994; Woldorff *et al.*, 1995; Mangun *et al.*, 1997; Vandenberghe *et al.*, 1997; Tootell *et al.*, 1998; Brefczynski and DeYoe, 1999; Martinez *et al.*, 1999). The anatomical location of these changes differed slightly between left and right hemispheres, in particular on the lateral surface. Identical or nearby occipital effects contralateral
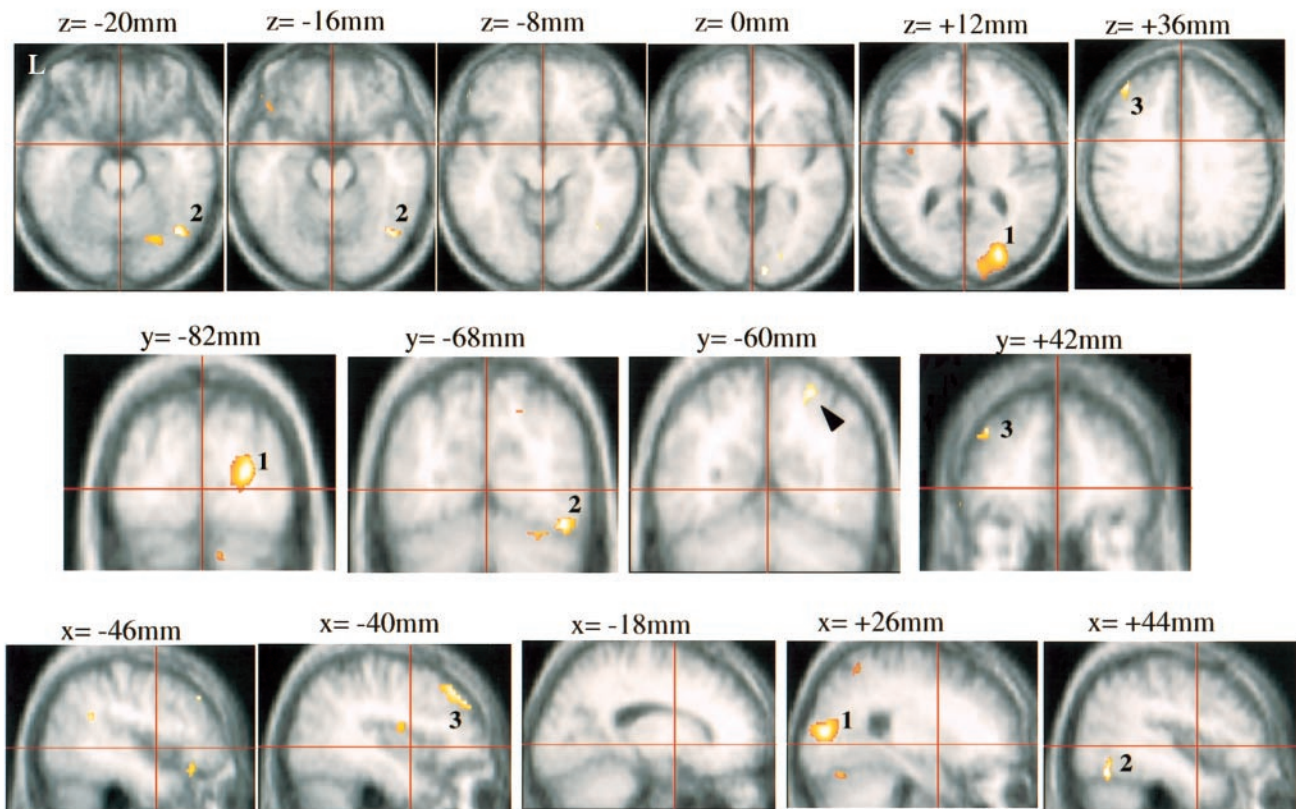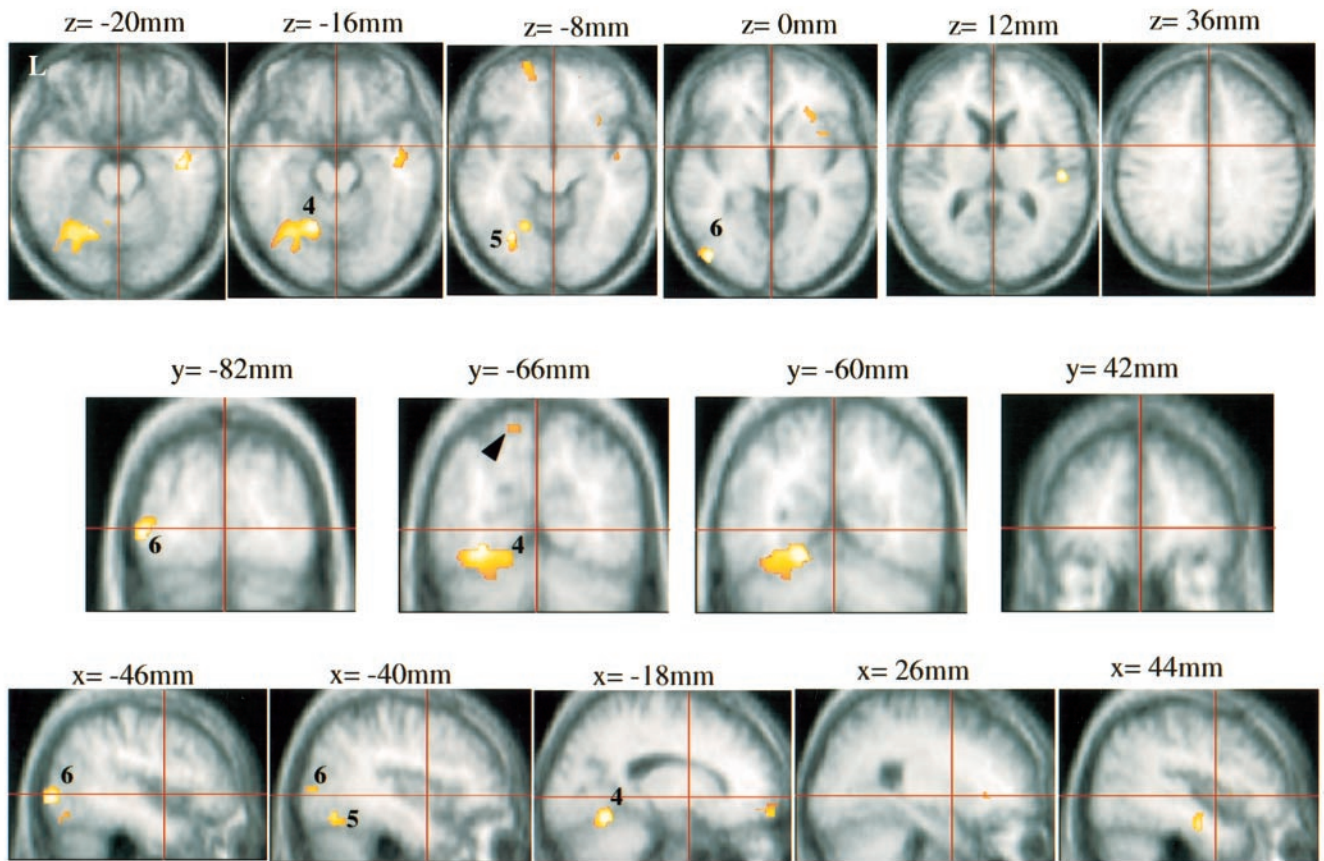
Figure 3. *Z* map obtained by subtracting right-field from left-field attention conditions, thresholded at an uncorrected $P < 0.005$. Activations at a corrected $P < 0.05$ significance threshold are numbered. (1) R middle occipital gyrus. (2) R fusiform gyrus. (3) L middle frontal gyrus. The activation in R intraparietal sulcus is marked with an arrow. The *Z* map is projected upon the group-averaged brain MRI.

to the direction of attention have been reported in paradigms requiring shape (Heinze *et al.*, 1994; Mangun *et al.*, 1997) or displacement (Vandenberghe *et al.*, 1997) discrimination, as well as simple detection of dots (Mangun *et al.*, 1997; Woldorff *et al.*, 1997). Previous studies suggest that the posterior ventral and dorsal occipital regions are probably retinotopically organized, while this is probably not the case for the more anterior ventral occipital regions (Woldorff *et al.*, 1997; Tootell *et al.*, 1998). The right and left fusiform region have also been previously activated during central orientation discrimination in comparison to detection tasks (Vandenberghe *et al.*, 1996; Schiltz *et al.*, 1999). In parietal cortex we found relatively weak increases contralateral to the direction of attention (Corbetta *et al.*, 1993; Nobre *et al.*, 1997). In contrast with our *a priori* hypothesis (Baynes *et al.*, 1986; Posner *et al.*, 1987; Posner and Petersen, 1990) no significant effects of the frequency of visuospatial shifts nor any interaction effects between direction of attention and shifting were observed.

The current experiment confirmed our earlier findings that left lateral frontal activity changed significantly with the direction of spatial attention (Vandenberghe *et al.*, 1997). The current study differs in several aspects from our previous experiments revealing frontal direction-sensitivity. These modifications were introduced with the purpose of determining the generality of our previous results. Subjects responded manually instead of verbally, the response rule was go–no go instead of conditional-associative, stimuli were shown on the horizontal meridian and not on the diagonal. The experiment was also carried out using a different PET scanner at a different

site and subjects were older than in earlier studies. Orientation was the discriminandum in the current experiment but both orientation and displacement have been studied previously (Vandenberghe *et al.*, 1997). None of these modifications significantly altered the basic findings. When attention is directed to the left, blood flow levels in left frontal convexity are significantly higher than when it is to the right. The current data also prove that the left frontal direction-sensitive effect is not limited to paradigms where relevant events occur at one fixed peripheral location. In contrast to the left side, the right lateral frontal cortex did not demonstrate an effect of the direction of attention, though a weak effect of this sort appeared in our previous work (Vandenberghe *et al.*, 1997). Most probably the present negative result can be explained by a general involvement of right prefrontal cortex in our tasks, regardless of the direction of attention (Table 3). This general effect may be so strong that any further modulatory effects elicited by varying the direction of attention are no longer detectable.

At present, we can only speculate about the processes reflected by the left lateral frontal blood flow changes. Since subjects performed fine perceptual discriminations of peripheral stimuli while fixating the center of the screen, one possibility is active suppression of saccades towards the relevant stimuli. Left frontal activity could reflect suppression of saccades to the left visual field. This, however, seems unlikely: although frontal lesions can disinhibit reflexive saccades (Butter *et al.*, 1988; Paus *et al.*, 1991), it is saccades into the contralateral, not the ipsilateral field that are affected. There is no apparent reason why leftward covert attention would require more inhibition of

Figure 4. *Z* map obtained by subtracting left-field attention conditions from right-field attention conditions, thresholded at an uncorrected *P* < 0.005. Activations that reach a corrected *P* < 0.05 significance threshold are numbered. (4,5) L fusiform gyrus. (6) R middle occipital gyrus. The activation in L superior parietal lobule is marked with an arrow.

Table 6
Left frontal effects: individual subject analysis

	x	*y*	*z*		
L middle frontal g.	−40	36	40	*Z* = 3.61	s2
	−42	26	48	*Z* = 3.57	s6
	−40	42	36	*Z* = 3.28	s9
	−30	48	20	*Z* =3.53	s4
	−32	36	24	*Z* = 3.81	s7
L inferior frontal s.	−30	38	8	*Z* = 4.27	s7
L inferior frontal g.	−54	42	−8	*Z* = 3.98	s4
	−48	28	−16	*Z* = 3.68	s5

Single subject peak activations obtained by subtracting right-sided attention from left-sided attention conditions. Column 1: anatomical name; columns 2–4: Talairach coordinates; column 5: *Z* score obtained in the subtraction of right-sided attention from left-sided attention conditions; column 6: identification of the subjects who demonstrate the effect. Abbreviation: s, subject.

Table 7
Parietal effects: group analysis

	x	*y*	*z*	L sust	L shift	R sust	R shift	
		(L shift + L sust) − (R shift + R sust)						
R intraparietal s.	26	−60	60	4.75	5.44	3.49	2.27	*Z* = 3.09
		(R shift + R sust) − (L shift + L sust)						
L superior parietal l.	−12	−68	64	1.45	1.16	4.54	2.86	*Z* = 3.22
		(L shift − L sust) − (R shift − R sust)						
R intraparietal s.	22	−60	68	2.47	4.66	3.49	1.33	*Z* = 3.24
L intraparietal s.	−32	−40	40	0.52	2.78	1.49	−0.47	*Z* = 3.26

Peak activations within the left and right parietal regions of interest. None of the effects reached significance. Activity levels in each condition expressed as a percentage of detection rCBF. Abbreviation: l., lobule.

rightward saccades than of leftward saccades. Alternatively, frontal activation could potentially relate to suppression of perceptual signals arising from the ignored contralateral hemi-field. Bilateral simultaneous stimulation with almost identical stimuli may impose a substantial requirement for endogenous suppression of signals from the ignored hemifield. Attentional deficits after right frontal lesions point towards a possible role in suppression of signal processing. Habituation to peripheral stimuli in the left visual field, as measured by use of the Troxler fading paradigm, is diminished (Mennemeier *et al.*, 1994) after right frontal lesions. It is not known whether this contralateral over-orienting also occurs after left frontal lesions and why other

functional imaging studies of unilateral attention using bilateral stimuli (Mangun *et al.*, 1997) did not reveal frontal blood flow differences. Possibly, the effect depends upon the degree of similarity between attended and ignored stimuli. To our knowledge, no brain-mapping studies have directly compared conditions with and without bilateral competitors to test this hypothesis. Furthermore, while we contrasted left and right hemifield conditions it is currently not known whether similar effects can be obtained when the distractor is to the left or the right of the target within the same hemifield. Finally, the right prefrontal involvement in all our discrimination tasks might also possibly be related to suppression of distractors regardless of their location, while the hypothetical left prefrontal role in suppression of distractors might be restricted to the contralateral field only.

The absence of any significant effect of shifting in the current study contrasts with neuropsychological evidence that parietal cortex is involved in disengagement of attention (Posner *et al.*, 1987), which constitutes a critical component of shifting operations (Posner *et al.*, 1987). A functional imaging study in normals (Le *et al.*, 1998) has also provided evidence for a role of parietal cortex in non-spatial shifting. In that study subjects had to shift attention back and forth from color to shape each time a target occurred. This was compared to conditions where attention was sustained on a single stimulus feature. Intraparietal sulcus was activated bilaterally during the shifting condition. Other functional imaging studies of visuospatial shifting (Corbetta *et al.*, 1993; Nobre *et al.*, 1997; Gitelman *et al.*, 1999; Kim *et al.*, 1999) have reported parietal activation during spatial shifting of attention in comparison to baseline. However, in the absence of a condition requiring maintained attention within the same experiment these parietal activations cannot be specifically attributed to the shifting component.

Theoretically, subjects might have been dividing attention between the two gratings present in the attended hemifield rather than shifting and focusing depending on which grating was cued. Such a strategy would, however, lack efficiency: indeed, psychophysical experiments have demonstrated a behavioral cost during orientation-discrimination tasks when attention is divided between objects rather than focused on a single object (Duncan, 1993; Vandenberghe *et al.*, 1997; Morgan *et al.*, 1998). Most importantly, in the current experiment shifting trials were associated with slower responses and lower accuracies than maintaining trials (Table 1). This provides strong behavioral evidence that subjects shifted attention during shifting trials relatively more so than during maintaining trials. Although the behavioral data indicate a distinction between shifting and maintaining trials, the absence of any parietal blood flow response to shifting in the current experiment must be interpreted with caution. First of all, the distinction between blocks of shifting trials and blocks of maintaining trials was only relative. We intentionally included 20% of shifting trials in the maintaining conditions and an equal proportion of maintaining trials in the shifting conditions so that predictability and working memory were entirely controlled for between the shifting and maintaining conditions. This may, however, have been at the expense of sensitivity. As a second experimental caveat, shifts between a peripheral location and the centre of the screen may have occurred between trials both during maintaining and shifting conditions. Such shifts may have gone undetected and have saturated any signal changes elicited by the difference between shifting and maintaining trials. To specifically discourage this possibility, cues appeared immediately after the offset of the previous grating display and remained on the screen until the onset of the next display, rendering shifts between periphery and centre less likely. As a final consideration, in the current, blocked-mode experiment, activity is integrated over a relatively long period of time. Even during shifting trials, subjects may spend a substantial amount of time maintaining their attention subsequent to the shifting operation. Event-related functional magnetic resonance imaging potentially provides us with a promising tool to investigate this possibility.

Likewise, the absence of an interaction between shifting and direction of attention must be interpreted with caution. We compared shifting within left or right hemifield but did not tease out the effects related to the direction of shifts, leftward or rightward. Parietal direction-sensitivity may be related to the direction of shifting and not only to the hemifield in which shifts occur (Mesulam, 1999).

To conclude, the current study provides further evidence that left frontal convexity is sensitive to the direction of spatial attention to the left or the right. Higher left frontal blood flow levels during leftward in comparison to rightward attention are a robust finding obtained across a variety of experimental conditions. The study also partially confirms previous findings of parietal direction-sensitivity (Corbetta *et al.*, 1993; Nobre *et al.*, 1997). This parietal effect, however, is weaker than would be expected on the basis of neuropsychological data (Weintraub and Mesulam, 1987). Also in contrast with predictions on the basis of neuropsychological evidence (Baynes *et al.*, 1986; Posner *et al.*, 1987; Posner and Petersen, 1990), parietal responses were not significantly altered by the frequency of spatial-attentional shifts. The predicted responses may have gone undetected for experimental or methodological reasons. This said, strong parietal recruitment by attentional shifting is certainly questioned by these data.

Notes

Address correspondence to Rik Vandenberghe, M.D., Ph.D., Cognitive Neurology and Alzheimer's Disease Center, Northwestern University Medical School, 320 East Superior Street Suite 11–461, Chicago, IL 60611, USA. Email: r-vandenberghe@nwu.edu.

References

Baynes K, Holtzman J, Volpe B (1986) Components of visual attention: alterations in response pattern to visual stimuli following parietal lobe infarction. Brain 109:99–114.

Brefczynski J, DeYoe E (1999) A physiological correlate of the 'spotlight' of visual attention. Nature Neurosci 2:370–374.

Butter C, Rapcsak S, Watson R, Heilman K (1988) Changes in sensory inattention, directional akinesia and release of the fixation reflex following a unilateral frontal lesion: a case report. Neuropsychologia 26:533–545.

Corbetta M, Miezin F, Shulman G, Petersen S (1993) A PET study of visuospatial attention. J Neurosci 13:1202–1226.

Coull J, Frith C, Frackowiak R, Grasby P (1996) A fronto-parietal network for rapid visual information processing: a PET study of sustained attention and working memory. Neuropsychologia 34:1085–1095.

Duncan J (1993) Similarity between concurrent visual discriminations: dimensions and objects. Percept Psychophys 54:425–430.

Friston K, Ashburner J, Poline J, Frith C, Heather J, Frackowiak RSJ (1995a) Spatial realignment and normalization of images. Hum Brain Map 2:165–189.

Friston K, Holmes A, Worsley K, Poline J, Frith C, Heather J, Frackowiak RSJ (1995b) Statistical parametric maps in functional imaging: a general approach. Hum Brain Map 2:189–210.

Gitelman D, Nobre A, Parrish T, LaBar K, Kim Y, Meyer J, Mesulam M (1999) A large-scale distributed network for covert spatial attention. Brain 122:1093–1106.

Heinze H, Mangun G, Burchert W, Hinrichs H, Scholz M, Munte TF, Gos A, Scherg M, Johannes S, Hundeshagen H, Gazzaniga MS, Hillyard SA (1994) Combined spatial and temporal imaging of brain activity during visual selective attention in humans. Nature 372:543–546.

Kim Y, Gitelman D, Nobre A, Parrish T, LaBar K, Mesulam M (1999) The large-scale neural network for spatial attention displays multifunctional overlap but different asymmetry. NeuroImage 9:269–277.

Kinahan P, Rogers J (1989) Analytic 3D image reconstruction using all detected events. IEEE Trans Nucl Sci 36:964–968.

Le T, Pardo J, Hu X (1998) 4 T-fMRI study of nonspatial shifting of selective attention: cerebellar and parietal contributions. J Neurophysiol 79:1535–1548.

Mangun G, Hopfinger J, Kussmaul C, Fletcher E, Heinze H (1997)

Covariations in ERP and PET measures of spatial selective attention in human extrastriate visual cortex. Hum Brain Map 5:273–279.

Martinez A, Anllo-Vento L, Sereno M, Frank L, Buxton R, Dubowitz D, Wong E, Hinrichs H, Heinze H, Heinze S (1999) Involvement of striate and extrastriate visual cortical areas in spatial attention. Nature Neurosci 2:364–369.

Mennemeier M, Chatterjee A, Watson R, Wertman E, Carter L, Heilman K. (1994) Contributions of the parietal and frontal lobes to sustained attention and habituation. Neuropsychologia 32:703–716.

Mesulam M (1999) Spatial attention and neglect: parietal, frontal and cingulate contributions to the mental representation and attentional targeting of salient extrapersonal events. Phil Trans R Soc Lond B 354:1325–1346.

Morgan M, Ward R, Castet E (1998) Visual search for a tilted target: tests of spatial uncertainty models. Q J Exp Psychol A Hum Exp Psychol 51:347–370.

Nobre A, Sebestyen G, Gitelman D, Mesulam M, Frackowiak RSJ, Frith C (1997) Functional localization of the system for visuospatial attention using positron emission tomography. Brain 120:515–533.

Paus T, Kalina M, Patockova L, Angerova Y, Cerny R, Mecir P, Bauer J, Krabec P (1991) Medial vs lateral frontal lobe lesions and differential impairment of central-gaze fixation maintenance in man. Brain 1991:2051–2067.

Posner M, Petersen S (1990) The attention system of the human brain. Annu Rev Neurosci 13:25–42.

Posner M, Walker J, Friedrich F, Rafal R (1987) How do the parietal lobes direct covert attention? Neuropsychologia 25:135–145.

Schiltz C, Bodart J, Dubois S, Dejardin S, Michel C, Roucoux A, Crommelinck M, Orban GA (1999) Neuronal mechanisms of perceptual learning: changes in human brain activity with training in orientation discrimination. NeuroImage 9:46–62.

Snodgrass J, Corwin J (1988) Pragmatics of measuring recognition memory: applications to dementia and amnesia. J Exp Psychol Gen 117:34–50.

Talairach J, Tournoux P (1988) Co-planar stereotaxic atlas of the human brain. New York: Thieme.

Tootell R, Hadjikhani N, Hall E, Marrett S, Vanduffel W, Vaughan J, Dale A (1998) The retinotopy of visual spatial attention. Neuron 21: 1409–1422.

Vandenberghe R, Dupont P, De Bruyn B, Bormans G, Michiels J, Mortelmans L, Orban GA (1996) The influence of stimulus location on the brain activation pattern in detection and orientation discrimination. Brain 119:1263–1276.

Vandenberghe R, Duncan J, Dupont P, Ward R, Poline J, Bormans G, Michiels J, Mortelmans L, Orban GA (1997) Attention to one or two features in left or right visual field: a positron emission tomography study. J Neurosci 17:3739–3750.

Weintraub S, Mesulam MM (1987) Right cerebral dominance in spatial attention. Arch Neurol 44:621–624.

Woldorff M, Fox P, Matzke M, Lancaster J, Veeraswamy S, Zamarripa, F, Seabolt M, Glass T, Gao J, Maftin C, Jerabek P (1997) Retinotopic organization of early visual spatial attention effects as revealed by PET and ERPs. Hum Brain Map 5:280–286.

Woldorff M, Fox P, Matzke M, Veeraswamy S, Jerabek P, Martin C. (1995) Combined PET and ERP study of sustained visual spatial attention and visual target detection. Hum Brain Map 2:49.

Worsley K, Marrett S, Neelin P, Vandal A, Friston K, Evans A (1996) A unified statistical approach for determining significant signals in images of cerebral activation. Hum Brain Map 4:58–73.