

Functional localization of the system for visuospatial attention using positron emission tomography

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Summary

PET was used to image the neural system underlying visuospatial attention. Analysis of data at both the group and individual-subject level provided anatomical resolution superior to that described to date. Six right-handed male subjects were selected from a pilot behavioural study in which behavioural responses and eye movements were recorded. The attention tasks involved covert shifts of attention, where peripheral cues indicated the location of subsequent target stimuli to be discriminated. One attention condition emphasized reflexive aspects of spatial orientation, while the other required controlled shifts of attention. PET activations

agreed closely with the cortical regions recently proposed to form the core of a neural network for spatial attention. The two attention tasks evoked largely overlapping patterns of neural activation, supporting the existence of a general neural system for visuospatial attention with regional functional specialization. Specifically, neocortical activations were observed in the right anterior cingulate gyrus (Brodmann area 24), in the intraparietal sulcus of right posterior parietal cortex, and in the mesial and lateral premotor cortices (Brodmann area 6).

Keywords: PET; covert visuospatial attention; anterior cingulate; frontal eye fields; posterior parietal cortex

Abbreviations: BA = Brodmann area; ERP = event-related potential; fMRI = functional MRI; FWHM = full-width half-maximum; LIP = lateral bank of the intraparietal sulcus; LVF = left visual field; MANCOVA = multivariate analyses of covariance; MANOVA = multivariate analyses of variance; rCBF = regional cerebral blood flow; RVF = right visual field; SMA = supplementary motor area; SOAs = stimulus-onset asynchronies; SPM = statistical parametric mapping; STS = superior temporal sulcus

Introduction

The ability to direct attention to a location in extrapersonal space is a requisite step toward conscious perception (James, 1890). Knowledge about the system of brain regions involved in spatial attention has come primarily from the study of patients with brain lesions. Deficits in spatial attention can result from lesions to different cortical and subcortical regions. Visuospatial deficits occur most frequently and are more enduring following lesions to the right cerebral hemisphere, suggesting dominance of the right hemisphere (Heilman and Van Abell, 1980; Mesulam, 1981; Weintraub and Mesulam, 1987). Visuospatial neglect can be dissociated

from perceptual or motor problems, and specific behavioural characteristics depend on the brain regions affected (Mesulam, 1990).

The precise anatomical regions important to spatial attention in the human brain remain unresolved. In monkeys, the localization of relevant brain regions has been possible through neuroanatomical, neurophysiological and lesion research. Critical areas are located in the inferior parietal lobule of the posterior parietal cortex (Heilman *et al.*, 1970; Lynch and McLaren, 1989) and in the general area of the frontal eye fields (Kennard, 1939; Welsh and Stuttenville, 1958;

Latto and Cowey, 1971; Schiller *et al.*, 1980). Neurons in the posterior parietal cortex and in the frontal eye fields are sensitive to attentional demands in tasks and show functional specialization for spatial orientation and exploratory eye movements, respectively (Bushnell *et al.*, 1981; Andersen *et al.*, 1985a; Bruce and Goldberg, 1985; Goldberg and Segraves, 1987; Andersen, 1989). These two brain regions are directly interconnected and have convergent patterns of efference to the cingulate gyrus and subcortical sites in the thalamus and striatum (Mesulam *et al.*, 1977; Seltzer and Pandya, 1980; Barbas and Mesulam, 1981; Petrides and Pandya, 1984; Selemon and Goldman-Rakic, 1988).

Mesulam (1990) has proposed a neural model for spatial attention which integrates data across methodologies in monkey and man. The right hemispheric dominance for spatial attention was hypothesized to result from the ability of the right hemisphere to direct attention to both sides of extrapersonal space and the ability of the left hemisphere to direct attention only contralaterally (Mesulam, 1981). Three cortical regions with distinct functional properties form the core of the network: a dorsolateral posterior parietal region, the frontal eye fields and the cingulate cortex. The parietal region builds a sensory representation of extrapersonal space. The frontal regions map orienting and exploratory movements in space. The cingulate area apportions motivational potential. Subcortical regions also participate. The pulvinar nucleus of the thalamus and the striatum are interconnected with all three cortical regions (Yeterian and VanHoesen, 1978). The reticular activating system, which has a well-established role in arousal (Goodman, 1968; Plum and Posner, 1972; Ray *et al.*, 1982), has a distributed but specific pattern of innervation which includes regions of the proposed attentional network (Scheibel and Scheibel, 1967).

Neuroimaging studies have begun to unveil the architecture and functional properties of the attentional system in the human brain. Most of the studies have been performed using PET and have relied on data averaged across subjects. The resulting spatial resolution has been insufficient to resolve the anatomical regions involved. Nevertheless, the overall pattern of results has been consistent with evidence from cognitive neurology. Two PET studies have investigated the brain regions comprising the system of spatial attention directly. Corbetta *et al.* (1993) used tasks of visuospatial attention and observed activation of superior parietal cortex, superior frontal cortex in the premotor region and midline areas which may have included the anterior cingulate gyrus. The tasks involved many parameters thought to contribute to attention, such as spatial priming, expectancy, visual field location, direction of shifts and differential response requirements. Parietal and frontal regions displayed different sensitivities. The superior parietal cortex was sensitive to stimulus location, whereas the frontal activation was more bound to overt motor responses. Furthermore, the parietal activation showed hemispheric asymmetry. Two foci were present in the right hemisphere, linked to shifts toward each visual field. Only one focus appeared in the left hemisphere,

present when attention was directed to the contralateral visual field. Gitelman *et al.* (1996a) extended the study of spatial attention to examine the regions involved in non-visual exploratory-motor aspects of attention. Subjects explored a surface with the right hand to identify targets or performed a repetitive circular motion. The cortical regions of activation during exploration were similar to those obtained for visuospatial attention: posterior parietal, premotor and anterior cingulate cortex. The activations were strongly lateralized to the right hemisphere, despite the usage of the right hand.

Posterior parietal activation has also been reported during tasks involving attention to feature conjunctions (Corbetta *et al.*, 1995), vigilance (Pardo *et al.*, 1991) and cued arm movements (Deiber *et al.*, 1991). Activation of anterior cingulate has been reliable in a variety of tasks that engage cognitive effort and decisions, such as Stroop interference (Pardo *et al.*, 1990), willed action (Frith *et al.*, 1991) and semantic categorization (Petersen *et al.*, 1988). Activation of premotor cortex has been reported consistently in neuroimaging studies of spatial working memory (*see* McCarthy, 1995) and in tasks requiring attention to or decisions about movements (Deiber *et al.*, 1991; Mitz *et al.*, 1993).

In monkeys, the frontal eye fields are located in the posterior part of area 8 (Schiller, 1980). The location of the frontal eye fields in humans has been investigated directly by neuroimaging studies of eye movements. PET studies using grouped data have suggested that eye movements engage brain regions in motor and premotor regions, including Brodmann areas (BA) 4 and 6 (Melamed and Larsen, 1979; Fox *et al.*, 1985; Petit *et al.*, 1993; Anderson *et al.*, 1994). The location of the human frontal eye fields was also recently investigated in individual subjects by Darby *et al.* (1996) using a novel functional magnetic resonance method linked to blood perfusion (Edelman *et al.*, 1994). Lateral brain areas engaged by voluntary saccades included precentral area 4 and premotor area 6 in most subjects. Combined, these studies support a relatively more posterior location for the frontal eye fields in man than would have been expected on the basis of cytoarchitectonic homologies to BA 8 in monkey (Brodmann, 1909).

The main goal of the present paper was to improve the resolution of the anatomical localization of regions of the visuospatial attention network using PET. To this end, the experiment was adapted for single-subject analysis. Hemispheric lateralization of the brain regions and variability of activation patterns across subjects were analysed. The second objective was to establish a simple behavioural protocol for systematic study of the functional specialization of brain regions involved in attention. The attention tasks involved covert peripheral shifts of attention directed by peripheral cues. The proportion of shifts to either visual field and the requirement for non-reflexive spatial shifts were manipulated across conditions.

Methods

Subjects

Six subjects participated in the PET experiment. These subjects were selected on the basis of performance in a pilot behavioural experiment. All subjects showed significant effects of attentional cueing and were able to maintain central eye fixation during the pilot tasks. Eye movements were monitored using a head-mounted infra-red eye tracker as well as with horizontal and vertical electrooculogram. The eye tracker had a resolution superior to 1° of visual angle and was calibrated before each experimental block. Detectable eye movements occurred in 11% of the trials (range across subjects, 5–28%) and did not differ across experimental conditions.

Handedness was assessed by the modified Edinburgh Inventory (Oldfield, 1971). All subjects were right-handed, with an average handedness score of 93% (range 73–100%). Subjects were briefed on the procedures and risks of PET, and participated voluntarily after signing informed-consent forms. The study protocols were approved by the local hospital ethics committee and the Administration of Radioactive Substances Advisory Committee (UK).

Behavioural tasks

There were two attention tasks. The tasks were identical except for the spatial contingency between the cue and target stimuli. In both cases, the background display consisted of a small central diamond (0.5° wide) and two peripheral squares (1° wide), centred at 7° eccentricity in each visual field. In the same-side condition, a brief brightening of one peripheral square (100 ms duration) indicated the ensuing appearance of a target within that box 80% of the time. In this task condition, the location of the target was spatially primed by the cue on valid trials. This condition emphasized reflexive aspects of spatial orientation, since the attentional shifts could be carried out reflexively. However, contribution from controlled attentional processes such as spatial expectancy could not be ruled out. In the opposite-side condition, the brief brightening of one of the peripheral boxes (100 ms duration) indicated the ensuing appearance of a target within the box in the opposite visual field 80% of the time. This condition emphasized controlled aspects of attention, since it required a non-reflexive shift from the brightened box toward the contralateral location.

In both conditions, targets followed cues at stimulus-onset asynchronies (SOAs) of 200, 400 or 800 ms in pseudo-randomized and balanced order. Inter-trial intervals were co-varied with the SOAs so that each trial lasted 2 s. Target stimuli were either a diagonal cross (×) or an upright cross (+) which appeared briefly (50 ms duration). Subjects were required to discriminate between these stimuli covertly, using only peripheral vision, and to respond as quickly and as accurately as possible every time they detected the '×' target. Subjects were informed about the contingencies between the

cues and targets, and were encouraged to use the cues to improve performance.

Sixty trials comprised one experimental block, in which all task contingencies were satisfied (48 valid trials, 12 invalid trials; 30 left targets, 30 right targets; 30 '×' targets; 30 '+' targets; 20 short SOAs, 20 medium SOAs; 20 long SOAs). Each experimental block lasted 2 min.

The tasks were designed specifically to study covert peripheral cueing of attention with neurophysiological procedures. In addition to the present PET experiment, the tasks were also used in combination with functional MRI (fMRI) (Nobre *et al.*, 1996a, b) and electrophysiological event-related potentials (ERPs) (Sebestyen and Nobre, 1996). The advantage of this task design is that it enabled the investigation of different directions and types of attentional shifts following the identical physical stimulus. Depending on instruction and stimulus contingencies, a given peripheral cue could signal a shift to either hemisphere and with different contributions from reflexive and controlled processes. A discrimination response was chosen instead of simple detection in order to fractionate processes linked to response execution using ERPs. The presence of validly and invalidly cued targets enabled the confirmation of the ability of these particular tasks to direct visuospatial attention. The three SOAs permitted some analysis of the time-course of the underlying cognitive processes.

Behavioural procedures

Twelve PET scans were performed. In total there were four replications of each attention task condition (same-side and opposite-side) and four replications of a rest condition, in which the subject was asked to relax and look toward a static display, which contained only the background display.

In all cases, subjects were engaged in the task for 1 min prior to the onset of signal measurement from the brain. During the first 30 s of PET scanning, the most sensitive period, the shifts of attention were biased to either the left visual field (LVF) or the right visual field (RVF) in the attention conditions. This was achieved by controlling the trial order so that only valid trials involving shifts to one visual field were presented during this interval. All other task parameters remained intermixed throughout the scanning time. The resulting protocol followed a factorial design which manipulated type of shift (same-side and opposite-side) and side of shift (LVF and RVF). There were two replications of each experimental cell: same-side LVF, same-side RVF, opposite-side LVF, opposite-side RVF. Rest conditions were always performed as the first, sixth, seventh and twelfth scans. The four conditions of each attention task were imaged in a blocked fashion (scans 2–5 or scans 7–11) that was counterbalanced across subjects. The order of the scans emphasizing RVF and LVF shifts within each task was also counterbalanced.

A repeated-measures multivariate analysis of variance (MANOVA) assessed differences in reaction time across task

condition (same-side, opposite-side), cue validity (valid trials, invalid trials), target side (LVF, RVF) and SOA (short, medium, long).

Imaging procedures

Subjects were positioned in the PET scanner to sample the superior part of the brain. A venous line was placed in their left arm. A computer monitor was positioned perpendicular to the subject's natural forward gaze at the distance required to maintain the correct visual angles. The display was controlled by a Macintosh Powerbook. Subjects responded with their right hand on the space-bar of the Powerbook keyboard, which was placed at their side at a comfortable position.

Images of brain regional cerebral blood flow (rCBF) were obtained using a CTI Model 953B PET scanner (CTI, Knoxville, Tenn., USA) with the collimating septa retracted. Twelve scans were obtained at 10-min intervals by measuring the distribution of radioactivity following a 20-s intravenous bolus of $H_2^{15}O$ at a concentration of 55 Mbq/ml and a flow rate of 10 ml/min. Structural images of the subjects' brains were obtained with T_1 -weighted MRI on a separate day.

Image analysis

Images were reconstructed with a Hanning filter (cut-off frequency 0.5 cycles per pixel) into 31 transaxial planes with $8.5 \times 8.5 \times 4.3 \text{ mm}^3$ resolution at full-width half-maximum (FWHM). A transmission scan was used to correct for the attenuating effects of the tissues of the head.

PET images were analysed using statistical parametric mapping (SPM), which combines the approaches of general linear model and the theory of Gaussian fields to make statistical inferences about regional changes in signal (Friston *et al.*, 1991, 1994). PET scans from each subject were realigned to the structural MRI using a least squares approach (Friston *et al.*, 1995). The structural MRI and the realigned PET images were spatially normalized into a standardized neuroanatomical space (Talairach and Tournoux, 1988) using a reference template image (Friston *et al.*, 1995). PET images were smoothed using an isotropic Gaussian kernel in order to conform the data to a Gaussian-fields model. Two values of smoothing were used. A 16-mm kernel was chosen as the suggested practical value of smoothing to twice the original FWHM of the data (J.-P. Poline, personal communication). The image matrix was interpolated into $65 \times 87 \times 26$ voxels with $2 \times 2 \times 4 \text{ mm}^3$ dimension and $16.6 \times 18.6 \times 17.5 \text{ mm}^3$ FWHM resolution. An 8-mm smoothing kernel was also used in order to evaluate the effects of spatial filtering on the patterns of activation. The resulting resolution at FWHM was $9.9 \times 11.5 \times 11.6 \text{ mm}^3$.

The PET data from the group of subjects were analysed with multivariate analyses of covariance (MANCOVA), in which global flow was treated as a covariate of no interest and the twelve scans were treated as factors. Linear contrasts

tested the effects of task conditions and side of visual shifts. SPMs were obtained, in which the value of each voxel was a t statistic (SPM $\{t\}$) or a Z score (SPM $\{z\}$). Voxels were considered significant if their Z scores were significant at $P < 0.01$ after correction for multiple comparisons. In addition, voxels within the brain regions hypothesized to be involved in spatial attention were considered significant at $P < 0.001$ uncorrected. Cortical areas hypothesized to be engaged during the attention tasks were the anterior cingulate gyrus, the posterior parietal cortex and frontal cortex in the premotor and prefrontal areas. Subcortical areas hypothesized to be involved included the pulvinar nucleus of the thalamus and the striatum. The superior colliculi were not imaged consistently across subjects.

PET data from each individual subject were also analysed separately with MANCOVAs using the task replications as factors. The hypotheses for these analyses were guided by the results from the group analysis. Single-subject analysis added precision to the anatomical localization of brain activations and assessed individual variability. A threshold of $P < 0.01$ was set for brain regions activated in the group analyses.

Results

Behavioural results

Behavioural performance during the PET experiment yielded main effects of task condition [$F(1,5) = 8.04$, $P < 0.05$], cue validity [$F(1,5) = 18.01$, $P < 0.01$] and SOA [$F(2,10) = 5.49$, $P < 0.05$]. On average subjects responded faster in the same-side task (398 ms) than in the opposite-side task (415 ms), and they responded much faster to validly cued targets (375 ms) than to invalidly cued targets (439 ms). Subjects responded more slowly to the trials with short SOAs (415 ms) and about the same to trials with medium and long SOAs (403 and 402 ms, respectively). Subjects responded more quickly to targets on the RVF (401 ms) than the LVF (412 ms), but this was not statistically significant. A significant interaction between task condition and cue validity [$F(1,5) = 32.81$, $P < 0.01$] indicated that subjects differed more on invalid trials than on valid trials across the task conditions. In the opposite-side condition subjects were more slowed to respond to invalidly cued targets (373 ms valid, 458 ms invalid) than in the same-side task (377 ms valid, 420 ms invalid). They performed more similarly to the valid trials in each task condition.

Reaction times were also analysed for the individual subjects in the PET experiment using t tests adjusted for multiple comparisons. Five of the six subjects had significantly faster reaction times to valid trials relative to invalid trials in the same-side task. All six showed validity effects in the opposite-side task. In the same-side task, three of the six subjects showed significant speeding of the reaction times to targets presented in the RVF, while one subject showed the opposite effect. Two subjects showed no

Table 1 All regions of significant activation in the same-side task, relative to baseline

Region	Coordinates	Structure (BA)	Z	P	$P(Z_{\max} > u)$
1	0, 4, 52	Medial SMA (6)	5.71	0.000	0.000
	10, 8, 56	Medial SMA (6)	5.03	0.000	0.002
	8, 16, 44	Anterior cingulate (24)	4.35	0.000	0.033
2	42, -2, 44	Right lateral premotor (6)	5.24	0.000	0.001
	44, -12, 44	Right lateral premotor (6)	4.36	0.000	0.033
3	-40, 0, 40	Left lateral premotor (6)	4.41	0.000	0.027
4	-22, -28, 4	Left thalamus (pulvinar)	4.15	0.000	0.071
5	34, -68, 36	Right posterior parietal	4.01	0.000	0.112
6	58, -50, 16	Right superior temporal sulcus	3.97	0.000	0.128
7	12, -76, -28	Right cerebellum	3.63	0.000	0.345

significant differences. In the opposite-side task, five of the six subjects responded more rapidly to right visual-field targets, but only two of the effects were statistically significant. The sixth subject had the identical average reaction time across visual fields.

PET activations during same-side task

Four main cortical areas were significantly activated by the same-side task relative to the control condition. These areas were located in the right anterior cingulate gyrus, right posterior parietal cortex, bilateral premotor frontal cortex and medial frontal cortex. In addition, a focus in the (right) superior temporal sulcus (STS) was observed, which had not been hypothesized, but which tended toward significance after correction for multiple comparisons. Subcortical activation was observed in the thalamus. Activation in the right cerebellum did not reach the imposed threshold of significance. No other brain areas were activated at $P \leq 0.001$. Table 1 summarizes all the significant activations obtained. Table 2 shows the sites of activation for each significant lateral cortical region when the shifts of attention were biased to either the LVF or RVF.

Anterior cingulate and medial premotor cortex

Group analysis. A large focus of activation was obtained with its primary peak in the medial supplementary motor area (SMA) in premotor cortex [Talairach and Tournoux coordinates: 0, 4, 52; $Z(54) = 5.71$, $P < 0.001$, $P(Z_{\max} > u) = 0.000$]. According to the Talairach and Tournoux (1988) atlas, the activation was located in BA 6. The activated region had two additional sub-peaks, whose magnitudes were also statistically significant after multiple comparisons. One of the subpeaks also fell in the medial premotor area [coordinates: 10, 8, 56; $Z(54) = 5.03$, $P < 0.001$, $P(Z_{\max} > u) = 0.002$]. The other was located in the anterior portion of the right cingulate gyrus [BA 24, coordinates: 8, 16, 44; $Z(54) = 4.35$, $P < 0.05$, $P(Z_{\max} > u) = 0.03$]. Figures 1A and 2A show the activations in SMA and anterior-cingulate,

Table 2 Locations of sub-peaks of activation in the right and left cortex when shifts of attention were biased toward one visual field

	Right hemisphere				Left hemisphere			
	x,	y,	z	Z	x,	y,	z	Z
Premotor cortex								
Right-rest	38,	-4,	44	4.27	-44,	-2,	40	4.37
	42,	2,	40	4.20	-38,	-10,	40	3.86
	46,	10,	36	3.73				
Left-rest	42,	-2,	44	4.63	-40,	0,	0	3.01
	42,	14,	40	3.01				
Parietal cortex								
Right-rest	36,	-70,	32	3.84	-26,	-62,	6	2.81
	34,	-60,	36	3.54				
Left-rest	34,	-68,	36	2.86				
Superior temporal sulcus								
Right-rest	58,	-50,	16	3.74	-40,	-56,	4	3.82
	54,	-60,	12	3.38	-40,	46,	16	2.84
Left-rest	54,	-54,	16	3.12				
	58,	-48,	4	2.56				

respectively, superimposed upon the average of the subjects' structural MRIs. Analysis using the narrow spatial filter did not alter the pattern of activation. Again, three foci were observed: two in the medial premotor area and one in the right anterior cingulate area. When the narrow filter was used, the medial prefrontal activation appeared more bilateral. Two foci were identified in the region, one in each hemisphere [right hemisphere coordinates: 4, 14, 44; $Z(54) = 4.82$, $P < 0.001$, $P(Z_{\max} > u) = 0.02$; left hemisphere coordinates: -4, 4, 52; $Z(54) = 5.87$, $P < 0.001$, $P(Z_{\max} > u) = 0.000$].

Individual analysis. Five of the six subjects had significant foci of activity in the medial premotor cortex and four of the six subjects had significant foci in the anterior cingulate gyrus. In the individual analysis these foci often appeared as separate regions. In four of the five subjects with medial frontal activation, the focus fell in BA 6. In one case the focus was more anterior, and might have been located in medial area 8. The activations were on the midline. There

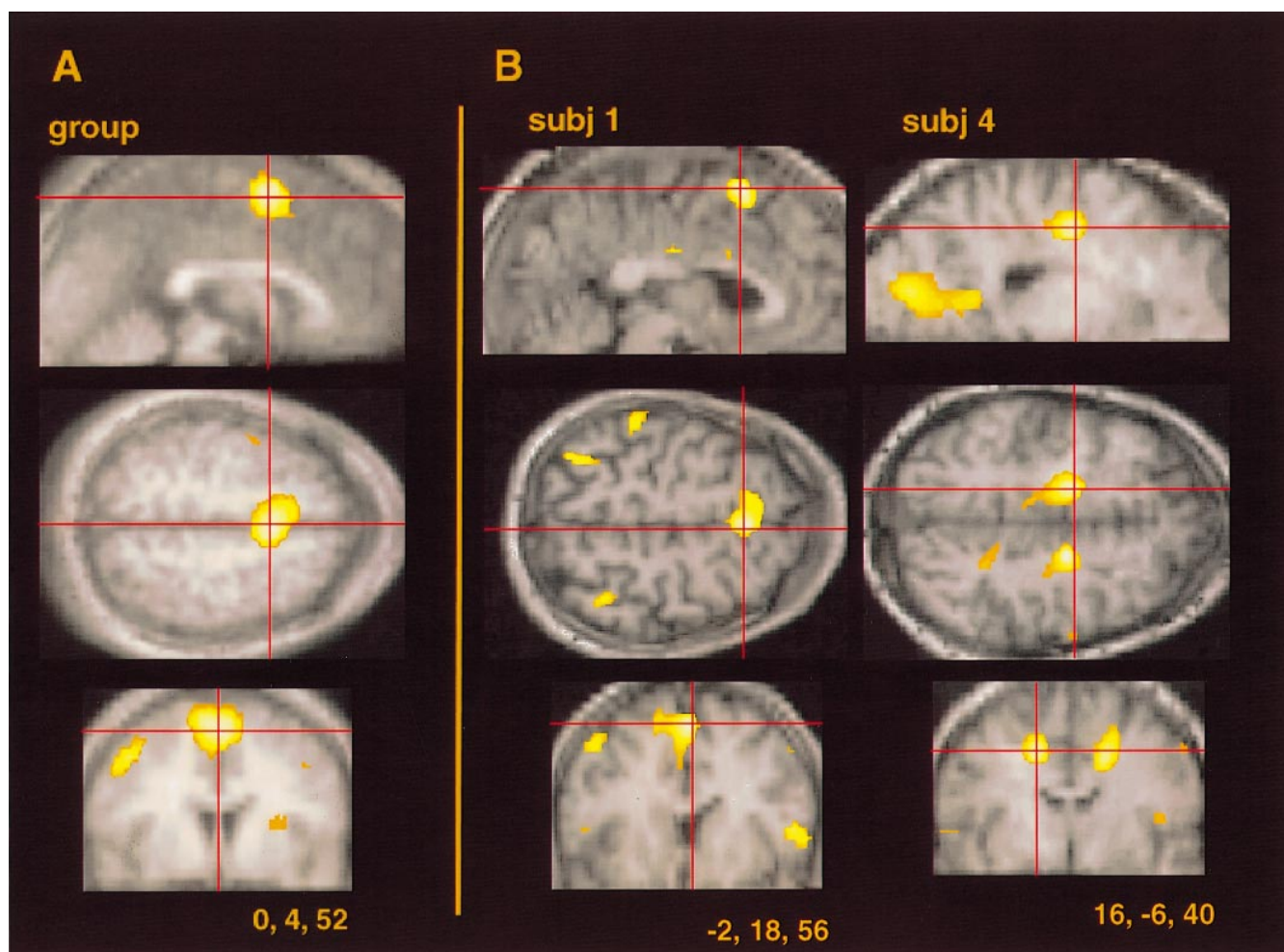


Fig. 1 Significant PET activations in the medial premotor cortex during the same-side task relative to baseline. The format for presentation of PET activations is the same across figures. The orientation of the brain follows radiological convention. The right side of the brain is shown on the left side of the brain image. In sagittal and axial sections, the anterior part of the brain is on the right of the image. Part **A** shows the location of the group activation superimposed upon the average MRI from the six subjects. The threshold for group-activation maps is $P < 0.001$. Part **B** shows the locations of the activations in two individual subjects. The threshold for individual-activation maps is $P < 0.01$. The red lines bisect the peak of the activations, and the numbers on the bottom right of each column are the corresponding standardized normalized coordinates (Talairach and Tournoux, 1988). Individual data are presented from one subject (Subject 1) in common across figures and from one additional different subject each time.

was no systematic bias toward either cerebral hemisphere. Figure 1B shows the location of the medial frontal activation in two representative subjects. The first individual-subject activation shown comes from the same subject (Subject 1) in all figures. The second case always comes from a different subject.

Activation in the anterior cingulate occurred in the right hemisphere and in BA 24 in all cases. Examples from two subjects are shown in Fig. 2B. Two subjects had two foci in the cingulate gyrus. In one case the additional focus was more posterior, towards area 23. In the other case the additional focus was more anterior, near the head of the corpus callosum.

Laterality. The visual field, toward which peripheral shifts were made did not alter the location of the peak activations in the medial premotor cortex or anterior cingulate gyrus. In

both cases the activation of the medial premotor cortex occurred along the midline and the activation of the anterior cingulate was right-sided.

Lateral premotor and prefrontal cortex

Group analysis. The lateral frontal cortex was activated bilaterally during peripheral shifts of attention. The magnitudes of the activations in both hemispheres were significant at the thresholds for multiple comparisons. The peak foci of the activations were located in BA 6 in the anterior precentral or premotor gyri. Two significant foci were observed in the right hemisphere [one with coordinates 42, -2, 44; $Z(54) = 5.24$, $P < 0.001$, $P(Z_{\max} > u) = 0.001$, the other with coordinates 44, -12, 44; $Z(54) = 4.36$, $P < 0.001$, $P(Z_{\max} > u) = 0.03$]. One peak was obtained in

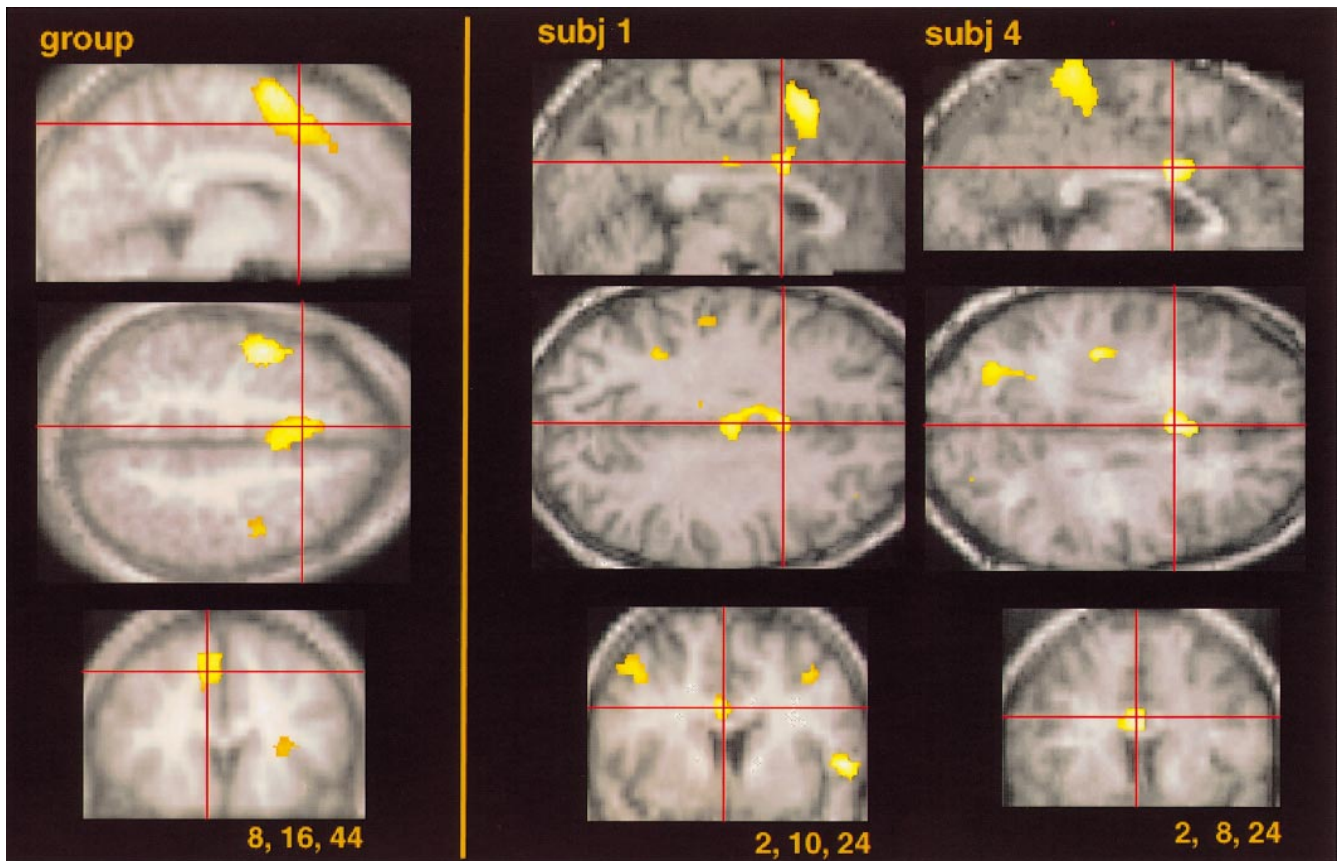


Fig. 2 Significant PET activations in the anterior cingulate cortex during the same-side task relative to baseline. *See* legend to Fig. 1 for details.

the left hemisphere [coordinates: $-40, 0, 40$; $Z(54) = 4.41$, $P < 0.001$, $P(Z_{\max} > u) = 0.03$]. The strength and reliability of the premotor effects were augmented by the wider spatial filter, but the location of the peak activations were unchanged. Figure 3A shows the premotor activation superimposed upon the average structural MRI. No separate foci of activation were observed in primary motor cortex in either hemisphere. Individual analysis. Five of the six subjects had significant activations in premotor cortex. The majority of these subjects had more prominent activations in the right hemisphere. In one case, however, the activation was restricted to the left hemisphere. In all cases the activations were centred over BA 6. In two cases, subjects had another focus of activation more anteriorly in the right prefrontal cortex, in BA 8. Figure 3B shows the location of premotor activations in two subjects. In Subject 6, an activation in the right prefrontal cortex can be observed.

Laterality. Differences in sites of activation across right and left peripheral shifts fell within the limits of the FWHM resolution. In both cases, however, there were more sub-peaks located in the right hemisphere than in the left hemisphere (*see* Table 2). The right premotor cortex had three sub-peaks associated with right shifts of attention and two associated with left shifts. The left premotor cortex had

two sub-peaks associated with right shifts and only one associated with left shifts. The activations in the right hemisphere also reached more anterior locations, which might have been situated in prefrontal rather than premotor sites. Figure 4 shows the locations of the activations for shifts directed to each visual field.

Right posterior parietal cortex

Group analysis. The right posterior parietal cortex was engaged in peripheral shifts of attention [coordinates: $34, -68, 36$; $Z(54) = 4.01$, $P = 0.000$, $P(Z_{\max} > u) = 0.11$]. Using the standardized Talairach and Tournoux atlas, we found that the activation was located in the general area of the intraparietal sulcus, which is straddled by the superior parietal lobule and the supramarginal and angular gyri. The anatomical features in this region were not well defined in the average structural MRI because of the high variability in sulcal and gyral anatomy in this part of the human brain. The posterior parietal activation for the group of subjects is shown in Fig. 5A.

Individual analysis. The sulcal and gyral anatomy was much clearer in the individual MRI scans, enabling

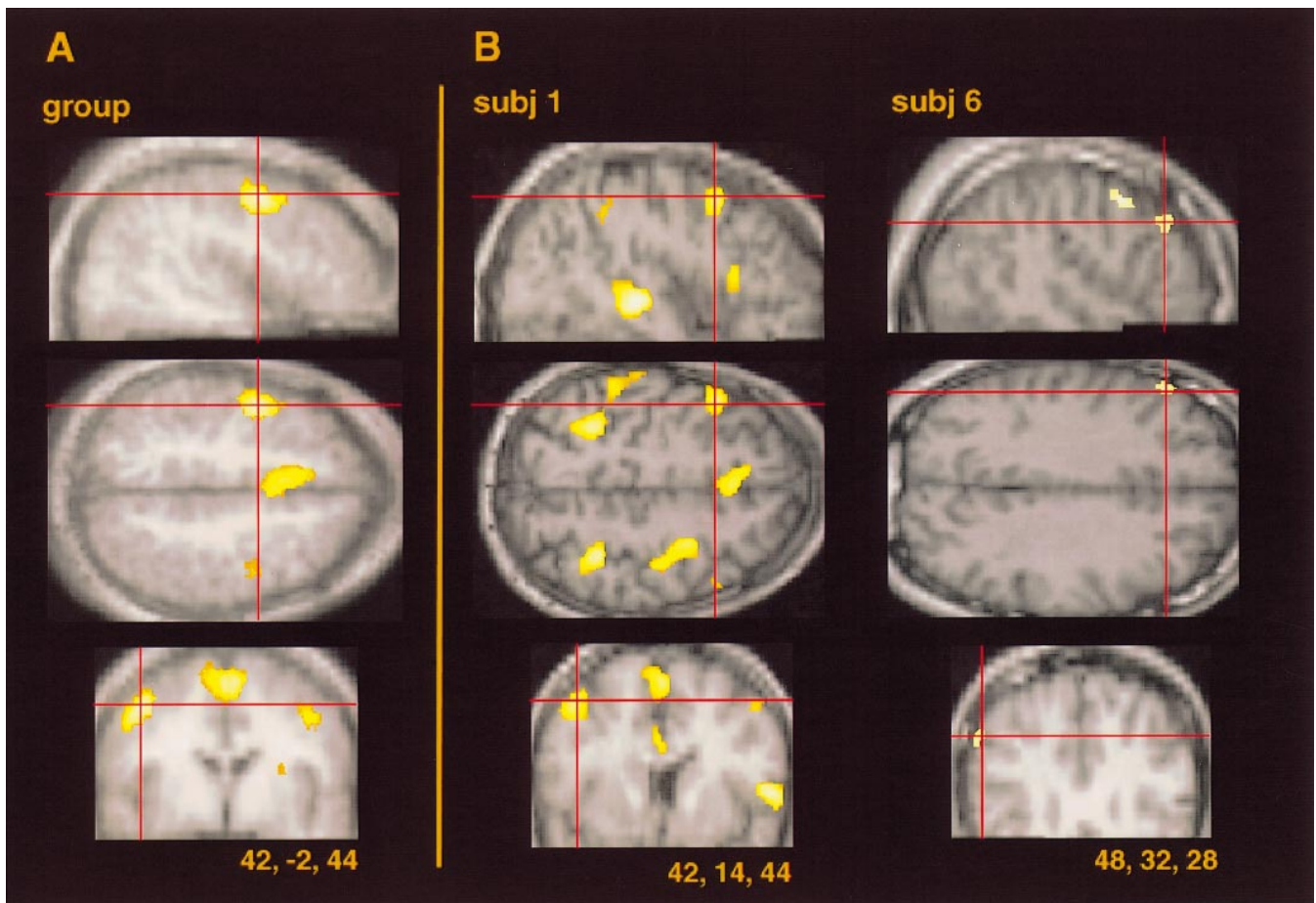


Fig. 3 Significant PET activations in the lateral premotor cortex during the same-side task relative to baseline. See legend to Fig. 1 for details.

localization of the right posterior parietal activations to the banks of the intraparietal sulcus. Five of the six subjects showed significant activations in the posterior parietal cortex, with three predominantly in the right hemisphere. Two representative cases are shown in Fig. 5B. Subject 1 showed bilateral activation, though more extensive on the right side. Subject 4 had exclusively right-sided activation. In all cases the activation followed the intraparietal sulcus.

Laterality. Posterior parietal cortex was only activated in the right hemisphere in the group analysis of the same-side task. In individual subjects, left parietal activation occurred in four of the six cases. When the activations were analysed by visual field in the group of subjects, more foci were obtained in the right hemisphere than in the left (see Table 2). When attention was drawn to the LVF, only one focus was obtained, located in the right hemisphere. When attention was drawn to the RVF, a similar region was activated in the right hemisphere, but included two sub-peaks and extended more anteriorly. A focus in the left hemisphere was also present. These results are displayed graphically in Fig. 6.

Right superior temporal sulcus

Group analysis. A small focus of activation in the right STS approached significance at the threshold for multiple comparisons [coordinates: 58, -50, 16; $Z(54) = 3.97$, $P = 0.000$, $P(Z_{\max} > u) = 0.13$]. Figure 7A shows the location of the activation.

Individual analysis. Individual-subject analysis supported the validity of this result. Five of the subjects showed activations in the STS. Two representative results are shown in Fig. 7B. Three subjects showed activation bilaterally, while the two additional subjects each showed foci in the opposite hemispheres.

Laterality. In the overall group analysis, the superior temporal sulcus was only activated in the right hemisphere. Analysis by VF of visuospatial shifts showed that right STS activation occurred when shifts of visuospatial attention were directed to either hemisphere. The locations of the activations for RVF and LVF shifts did not differ beyond the image

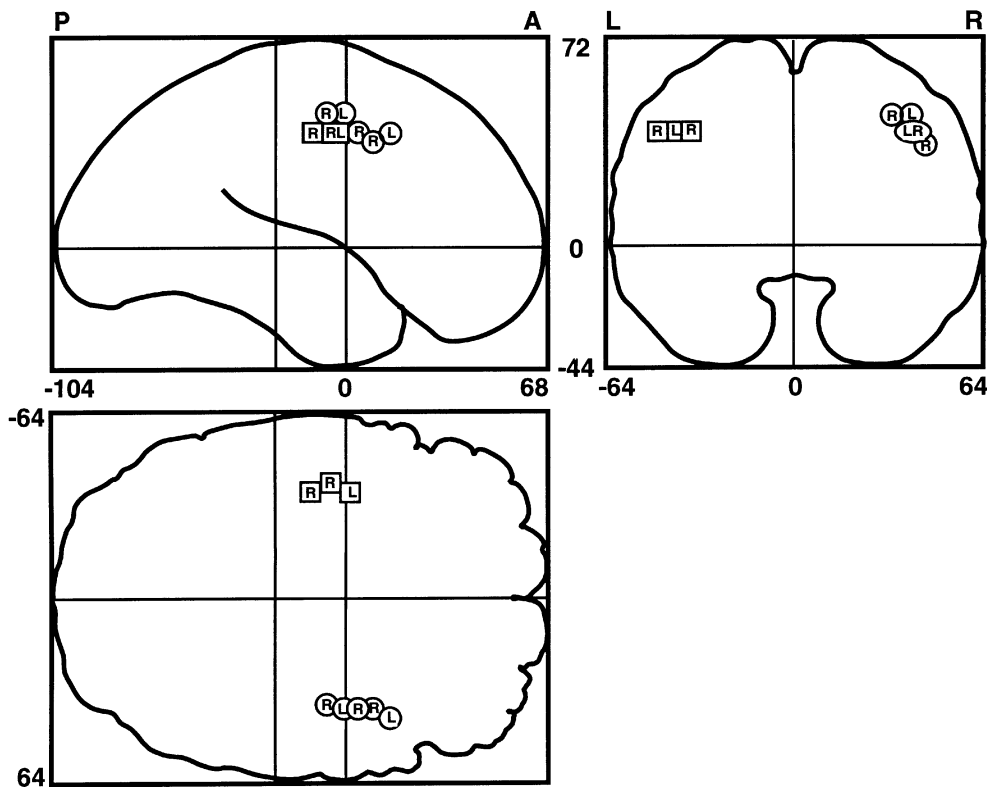


Fig. 4 Laterality of premotor activations when shifts of visuospatial attention were biased toward the left (L) and right (R) visual fields during the same-side task relative to baseline. The locations of peak activation were plotted onto glass-brain projections of the brain in standardized normalized space (Talairach and Tournoux, 1988). Left hemisphere activations are shown in squares and right-hemisphere activations in circles.

resolution. Left STS activation occurred only after shifts directed toward the RVF (see Table 2).

Subcortical regions

The only subcortical activation which tended to be significant occurred in the left thalamus [coordinates: $-22, -28, 4$; $Z(54) = 4.15$, $P < 0.001$, $P(Z_{\max} > u) = 0.07$]. According to the Talairach and Tournoux atlas (1988) this activation was located in the pulvinar nucleus. This activation was also observed when only shifts to the RVF were analysed [coordinates: $-22, -28, 4$; $Z(54) = 4.40$, $P < 0.001$, $P(Z_{\max} > u) = 0.03$]. No significant activation of the pulvinar was obtained during shifts to the LVF. Foci in the striatum and cerebellum were less significant, and did not survive the statistical thresholds.

Activations during opposite-side task

Cortical structures

The cortical pattern of activation obtained during opposite-side task was very similar to that obtained during same-side task. Significant cortical activations were obtained in medial frontal cortex, premotor cortex and posterior parietal cortex. A direct contrast between the two active conditions revealed

no areas of significantly different activation after correction for multiple comparisons. The left parietal cortex was relatively more active during the opposite-side task [coordinates: $-34, -76, 40$; $Z(54) = 3.32$, $P < 0.001$, $P(Z_{\max} > u) = 0.64$; and coordinates: $-26, -76, 44$; $Z(54) = 3.26$, $P = 0.001$, $P(Z_{\max} > u) = 0.70$]. Since the posterior parietal cortex was hypothesized *a priori* to participate in visuospatial shifts, its differential activation was considered significant.

Discussion

Behavioural consequences of visuospatial shifts

A network of brain regions was engaged by tasks involving shifts of visuospatial attention. The tasks differed mainly in their spatial cueing properties. In one case, an attention-grabbing stimulus predicted the subsequent appearance of a target stimulus to be discriminated at that same location (i.e. same-side task) with 80% probability. This type of task has been used widely to probe reflexive shifts of attention, since the cueing stimulus primes its location in space. However, nothing prevents subjects from developing controlled strategies or expectancies based upon the predictive information carried in the cue stimulus. The second task required non-reflexive attentional processes. In the opposite-side task, the appearance of a peripheral cue predicted the

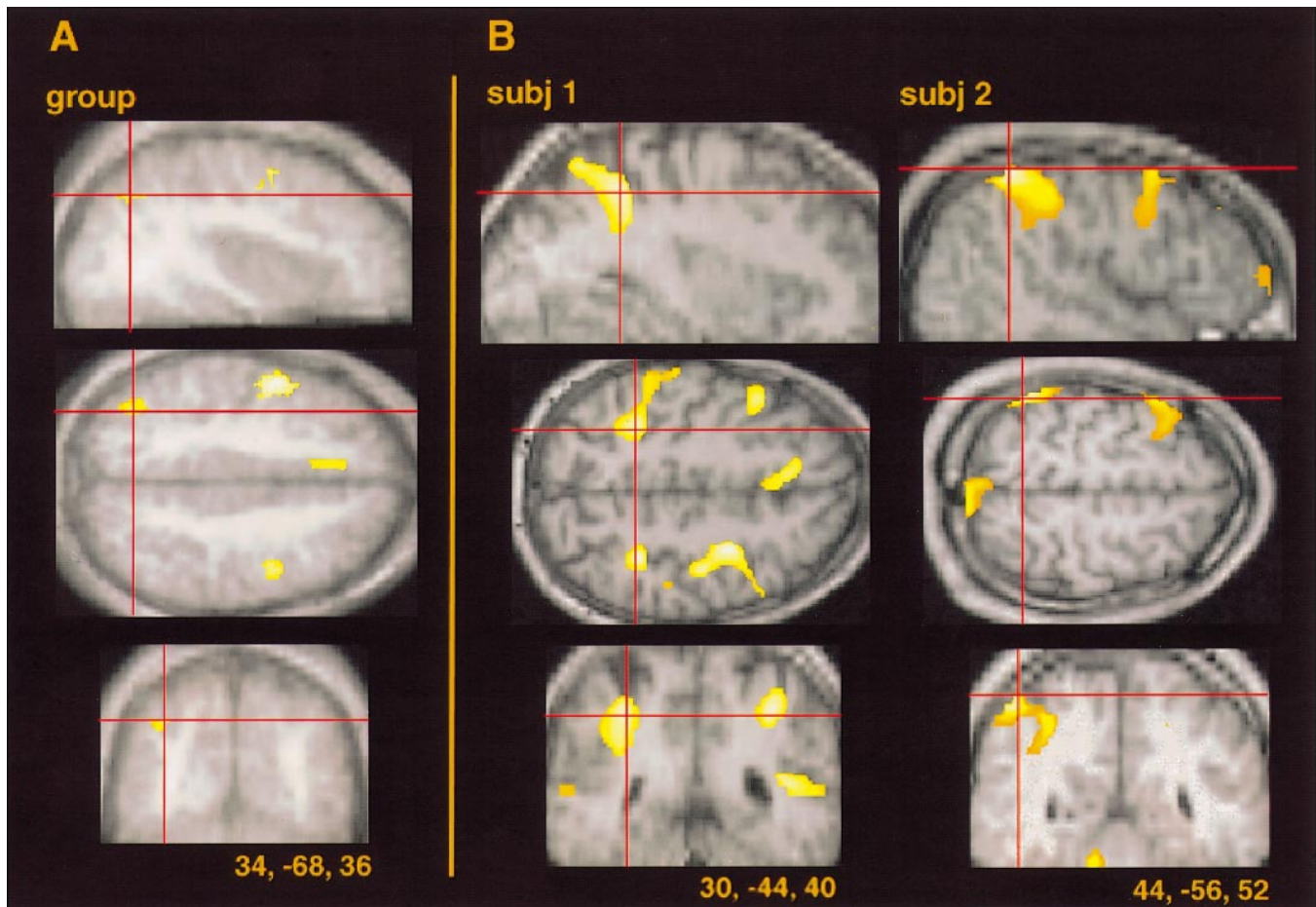


Fig. 5 Significant PET activations in the posterior parietal cortex during the same-side task relative to baseline. See legend to Fig. 1 for details.

subsequent appearance of the target in the symmetrical location in the opposite visual field. Controlled shifts were required and reflexive shifts might have needed to be inhibited or overridden.

The ability of the tasks to drive covert shifts of visuospatial attention was demonstrated by the significant behavioural benefits of valid cues in both tasks. Subjects were significantly faster in response to targets that occurred in the predicted location in space. The highly statistically significant validity effects replicated the well-established advantage that spatial cueing confers to behaviour. In both tasks, subjects were additionally speeded following inter-stimulus intervals >150 ms. The added advantage conferred by longer-latency intervals has been interpreted as evidence for the contribution of a controlled, non-reflexive process to attentional systems (Posner and Snyder, 1975; Neely, 1977). In this light, both tasks can be interpreted to have combined reflexive and non-reflexive processes. Overall, reaction times were faster for targets in the same-side task during the PET experiment, suggesting that additional controlled aspects of attention may have operated in the opposite-side task. Perhaps the requirement to inhibit or override reflexive aspects during visuospatial shifts contralateral to an attention-grabbing stimulus delayed cognitive processing. This possibility was

supported by the significant interaction obtained between task condition and cue validity. Subjects were relatively slower on invalid trials in the opposite-side task, suggesting an additional cost of remaining at, or returning to, the invalid location.

PET activations during peripheral shifts of visuospatial attention

The network of regions imaged by PET in the main same-side task relative to the rest control included all the cortical regions hypothesized to form the core of the network for visuospatial attention proposed by Mesulam (1990). Analysis of the group results included foci of activation in the right posterior parietal cortex, the right anterior cingulate, and in the lateral and medial premotor cortex bilaterally. In addition to the cortical areas that were predicted *a priori*, a small focus of activation tended toward significance in the right superior temporal sulcus.

During the most sensitive portion of the PET scans, the tasks were biased to contain only valid trials. Cognitive processes linked to invalid trials, such as the breaching or updating of expectations probably did not contribute substantially to the pattern of brain activation observed.

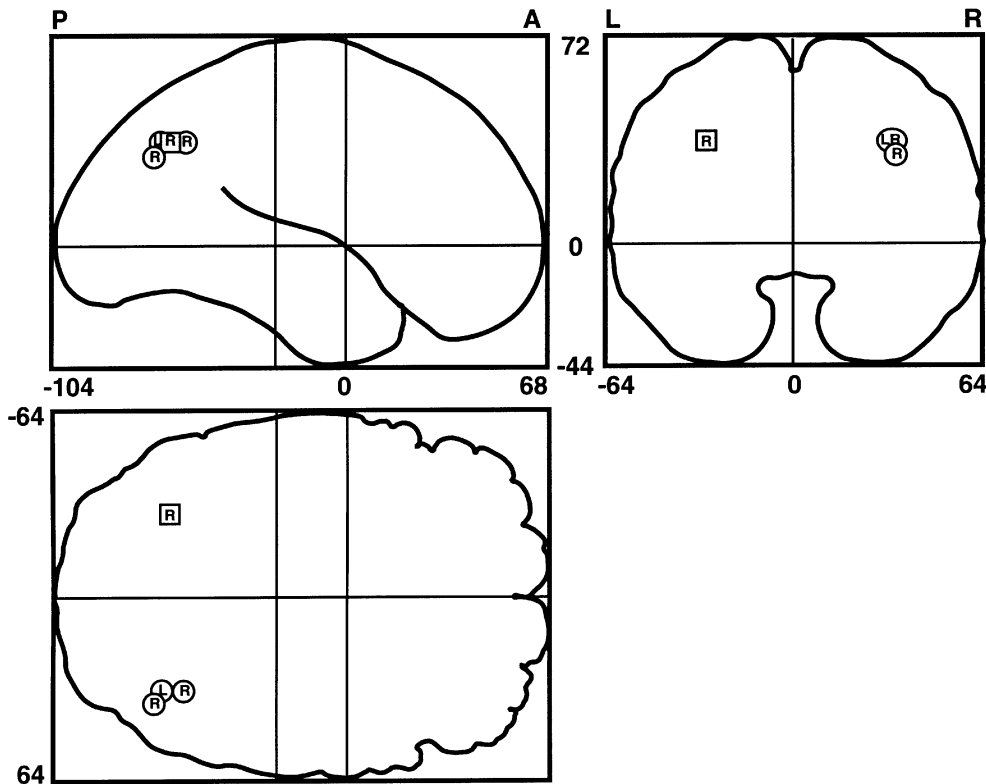


Fig. 6 Laterality of posterior parietal activations when shifts of visuospatial attention were biased toward the left (L) and right (R) visual fields during the same-side task relative to baseline. The locations of peak activation were plotted onto glass-brain projections of the brain in standardized normalized space (Talairach and Tournoux, 1988). Left hemisphere activations are shown in squares and right-hemisphere activations in circles.

Effects of non-reflexive components to visuospatial shifts

Behavioural dissociations suggest that reflexive and non-reflexive shifts of visuospatial attention may rely upon distinct systems (Posner and Raichle, 1994). To test this notion, the patterns of activation obtained with same-side and the opposite-side tasks were compared. These tasks engaged non-reflexive components to different extents, but both employed exactly the same physical stimuli and required the same motor decisions and responses. In general, the data did not support the existence of separate systems for reflexive and non-reflexive shifts of visuospatial attention. Nearly equivalent patterns of brain activation were observed across tasks that engaged reflexive and non-reflexive processes to different extents. The results were more consistent with the existence of a large-scale neural system for spatial orientation, composed of specialized brain regions.

The only difference across tasks of possible significance was the symmetry of the involvement of the posterior parietal cortex. When the two attention tasks were compared directly, the left posterior parietal region was relatively more active during the task which emphasized non-reflexive shifts. When each task was compared with the rest condition, activation in the posterior parietal cortex during the opposite-side task

was more symmetrical and included significant peaks in the left hemisphere.

Differences in parietal activation were deemed worthy of further consideration and investigation since the posterior parietal cortex has been associated with a special role in covert shifts of visuospatial attention (Corbetta *et al.*, 1993). Additional parietal involvement could have occurred in the opposite-side task for different reasons. The opposite-side task may have engaged more covert shifts than the other condition. Parietal activation has been correlated with the number of covert visuospatial shifts in previous studies (Corbetta *et al.*, 1993). Another, related, possibility is that additional parietal involvement resulted from the requirement to disengage attention in the opposite-side task. The posterior parietal cortex has been proposed to disengage attention from its present focus (Posner *et al.*, 1984). Another possibility is that the opposite-side task involved not only shifts across space, but also between objects. Subjects had to shift their focus from the peripheral square containing the cue to the other square, where target appearance was predicted. Inter-object shifts of attention have been associated with left posterior parietal cortex (Egley *et al.*, 1994). Finally, involvement of the left posterior parietal cortex may have been linked to additional requirements of distinct cognitive functions that show left hemisphere specialization. For

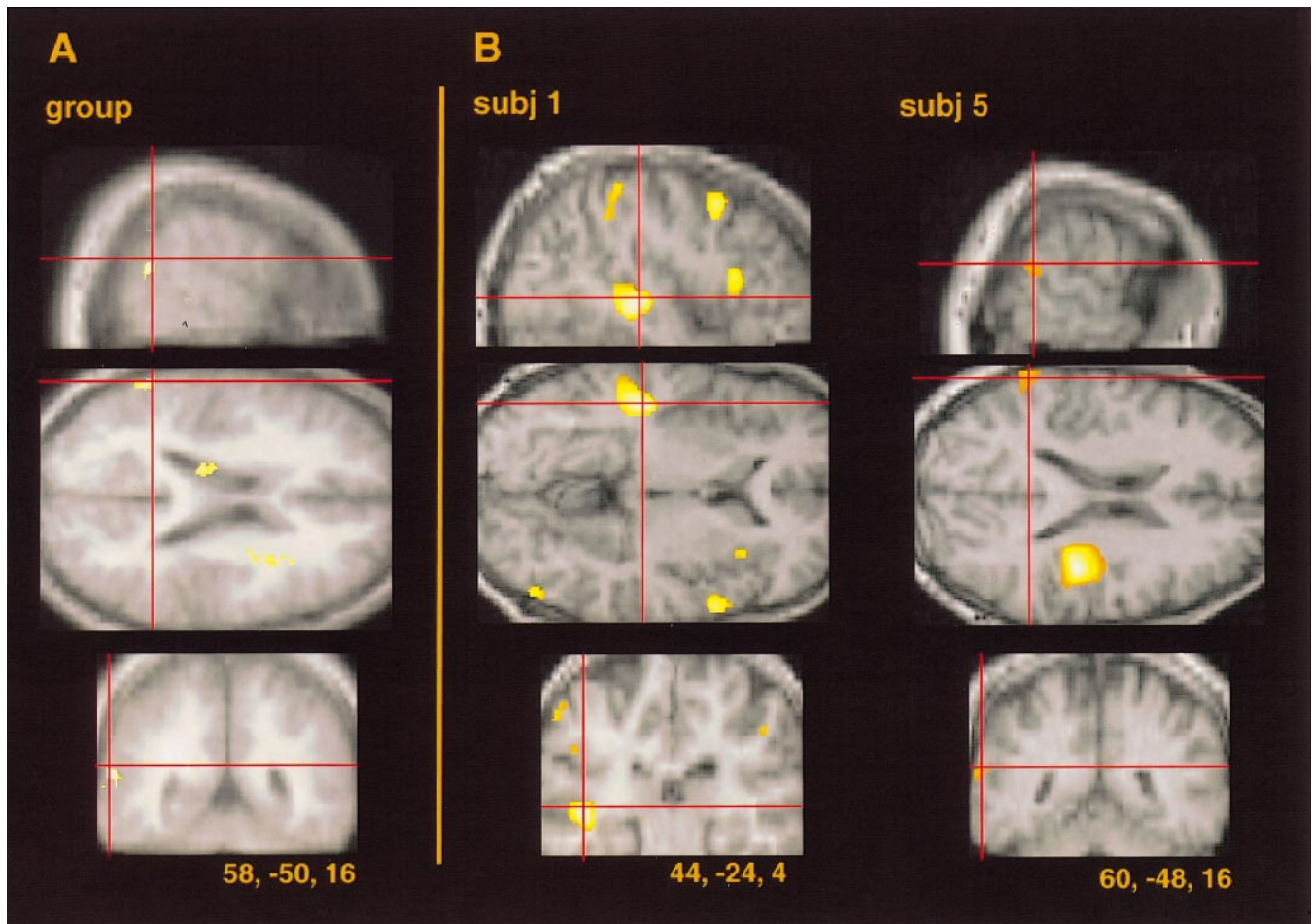


Fig. 7 Significant PET activations in the superior temporal sulcus during the same-side task relative to baseline. See legend to Fig. 1 for details.

instance, the left posterior parietal cortex may have integrated or used verbal or other top-down cues to form spatial expectations or to initiate covert shifts of visuospatial attention.

Lateralization of brain areas

Lateralization and localization of the cortical areas involved in visuospatial attention were main objectives of the experiment. The pattern of lateralization obtained was consistent with a right-hemisphere dominance for visuospatial attention. Three of the cortical regions were activated primarily in the right hemisphere in the group analysis when shifts to both visual fields were considered together: the anterior cingulate gyrus, posterior parietal cortex and superior temporal sulcus. In addition, the lateral cortical areas showed differential activation when shifts to the two visual fields were considered separately. Overall, there were more foci of activation in the posterior parietal cortex in the right hemisphere than in the left. During shifts to the LVF, only the right posterior parietal cortex was activated. However, bilateral activations were obtained during shifts toward the RVF. The right hemisphere also contained more activations

in the region of the lateral premotor cortex. During shifts to the LVF, two peaks of activation occurred in the right hemisphere, and only one in the left hemisphere. One of the right-hemisphere peaks was located more anteriorly, in the prefrontal cortex. When RVF shifts were made, three peaks occurred in the right hemisphere, while two occurred in the left. Again the peaks in the right hemisphere extended more anteriorly into prefrontal areas. Activation of the superior temporal sulcus was also asymmetrical. Shifts to the RVF engaged STS bilaterally, whereas LVF shifts engaged the right hemisphere only.

The pattern of laterality obtained in the posterior parietal cortex and in the lateral premotor cortex concurred with the proposal by Mesulam (1981) to explain right-hemisphere dominance for visuospatial attention. Lesions to the right hemisphere result in neglect of the left hemisphere more often and more profoundly because the left hemisphere does not control the allocation of attention to the ipsilateral left hemisphere. The right hemisphere, in contrast, is capable of controlling attention to the entire visual field. It is important to note that the pattern of activations seen in neuroimaging studies and the pattern of deficits that follow neurological lesions need not coincide in this manner to be compatible.

Neuroimaging is inherently a correlational measure, and areas of activation could be observed in brain regions which are not critical for the behaviour under study.

The pattern of right-hemisphere bias in activations in the posterior parietal cortex was also consistent with previous studies. Corbetta *et al.* (1993) found a similar pattern of posterior parietal laterality. Bilateral activations occurred for shifts to the RVF, but only right-hemisphere activations occurred for shifts to the LVF. However, in their study, the frontal activations were not biased to the right hemisphere, but contralateral to the visual field of the stimuli. In the present study, the lateral premotor activation was bilateral, but tended to be more extensive in the right hemisphere, despite the fact that subjects used the right hand to respond. Similar predominant right-hemisphere involvement was observed by Gitelman *et al.* (1996a) in a spatial exploratory motor task, despite the use of the right hand for exploration.

Localization of brain areas

Primary sensory and motor areas. Areas linked to visual processing or to motor output were not conspicuous in the results, despite the passive nature of the rest control condition. Motor responses occurred at an average rate of one every 4 s. This may have been too infrequent to observe the engagement of the primary motor areas (Jenkins *et al.*, 1994). The visual stimuli were presented very briefly as small black line drawings over a bright white background. They may not have been salient enough to activate the visual areas significantly more than during the passive viewing of the background display. This finding is orthogonal to and does not contradict studies which have shown selective modulation of visual areas by visuospatial attention (VanVoorhis and Hillyard, 1977; Mangun, 1987; McCarthy and Nobre, 1993; Heinze *et al.*, 1994).

Premotor and prefrontal areas. Strong activations were observed in lateral premotor cortex bilaterally, as well as in the medial premotor cortex. The major peaks of these activations were located in BA 6. The location of these activations are consistent with the location of the frontal eye fields in the human brain as indicated by previous neuroimaging studies of eye movements (Paus, 1996). Activations during eye-movement studies in humans have consistently been observed in the lateral premotor cortex (BA 6), occasionally extending posteriorly to the anterior portion of the precentrally gyrus (BA 4) (Fox *et al.*, 1985; Petit *et al.*, 1993; Anderson *et al.*, 1994; Darby *et al.*, 1996). Medial premotor activations, consistent with those seen in the present study, have been proposed as the location of the supplementary eye fields in the human brain (Petit *et al.*, 1993; Darby *et al.*, 1996). Figure 8 compares the locations of lateral premotor foci in this and previous oculomotor and visual attention studies.

The variability in the reported loci of premotor activation

in eye-movement and visuospatial-attention studies is not negligible, and remains a point for further discussion and investigation. One possibility is that processes linked to decision or execution of hand movements contributed to the premotor activations, since the control condition did not require motor responses. This possibility seems unlikely given the low frequency of the responses made (Jenkins *et al.*, 1995). Final assessment of the contribution of hand and eye-movement control to the premotor activations must await further investigations in which motor decisions, hand movements and eye movements are manipulated directly in single subjects.

If the activations in premotor areas represent engagement of frontal eye fields, it is worthy of note that the tasks were covert in nature. Eye monitoring during a separate session indicated that only few trials were contaminated by saccades. The involvement of the frontal eye fields in a task of covert attention is not obvious. It is possible that some activity in the frontal eye field is independent of the motor execution of eye movements, but still sensitive to attentional shifts or exploration. Alternatively, the frontal eye field could be engaged automatically by activity in other regions of the attentional network, as if primed to elicit eye movements. The activation could represent such priming, or the active inhibition of activity. Imagery of eye movements could also have contributed.

Frontal eye field activation did not differ across the two active task conditions. To the extent that the opposite-side task engaged additional non-reflexive attentional components, these did not affect activation in the frontal eye field significantly. Null findings do not carry much weight, since the failure to detect change might have resulted from insufficient statistical power or methodological limitations. Nevertheless, the findings appear consistent with the recent proposal by Paus (1996) that the frontal eye field is more sensitive to oculomotor variables than to attentional or other cognitive variables in the tasks employed to date. However, the role of the frontal eye field in the mapping or control of exploratory movements cannot be fully assessed with the data available (Table 3). Most oculomotor or visuospatial attention tasks, including this one, have not manipulated exploratory motor variables. One exception is the study by Gitelman *et al.* (1996a), which did report enhanced premotor activation to exploratory hand movements as compared with non-attentional repetitive movements. The correspondence between premotor regions which control hand and eye movements, however, remains to be drawn.

Anterior cingulate. The region of activation in medial premotor cortex extended into the right anterior cingulate cortex, where a distinct local peak was obtained in BA 24. The focus was located near the level of the anterior commissure along the anterior-posterior dimension. In individual subjects, cingulate activation was observed as separate from premotor activation. Additional foci were occasionally observed more posteriorly and more anteriorly,

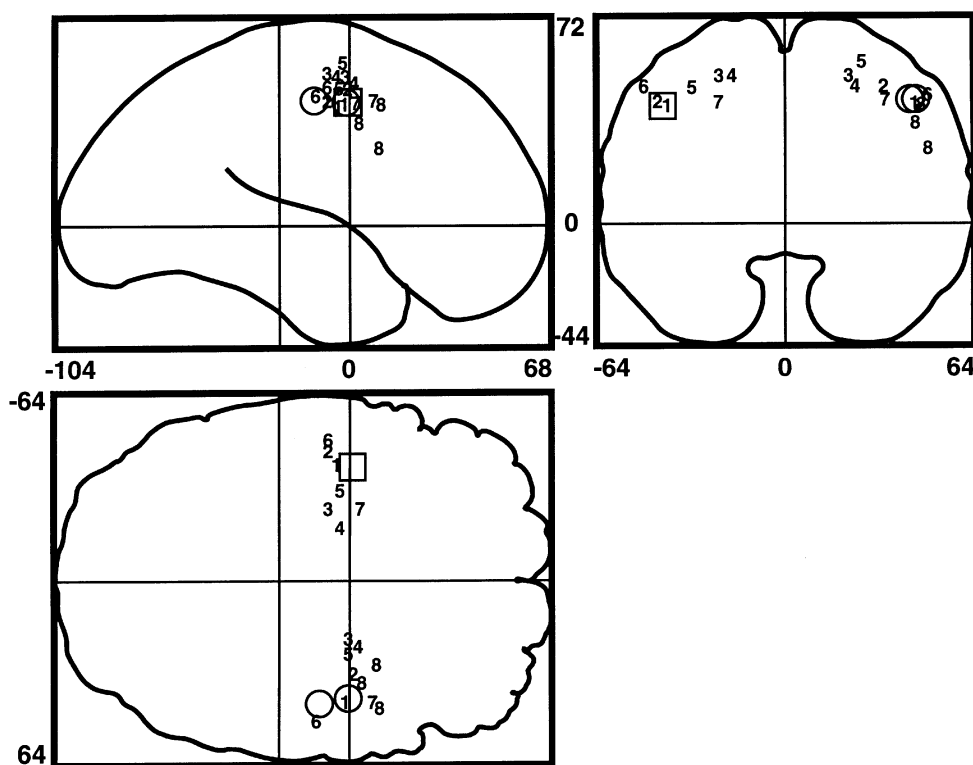


Fig. 8 Comparison of lateral premotor activations obtained in the present experiment relative to previous reports. The peak of activations were plotted onto glass-brain projections of the brain in standardized normalized space (Talairach and Tournoux, 1988). The circles and the square denote activations in the right and left hemispheres, respectively. The numbers plot activations observed in previous studies, and correspond to the references in Table 3.

Table 3 Locations of frontal eye fields reported in this and previous studies

No.	Reference	Task	x, y, z coordinates					
			R hemisphere			L hemisphere		
	Present study	Covert visuospatial attention	42,	-2,	44	-40,	0,	40
1	Fox <i>et al.</i> (1985)	Oculomotor: directed saccades	44,	-12,	44	-39	-5,	41
2	Paus <i>et al.</i> (1993)	Oculomotor: pro-saccades	34,	-2,	48	-44,	-6,	44
3	Anderson <i>et al.</i> (1994)	Oculomotor: pro-saccades	20,	-2,	52	-24,	-6,	52
4	Anderson <i>et al.</i> (1994)	Oculomotor: remembered saccades	22,	2,	48	-18,	-2,	52
5	O'Driscoll <i>et al.</i> (1995)	Oculomotor: anti-saccades	25,	-2,	56	-31,	-3,	48
6	Paus <i>et al.</i> (1995)	Oculomotor: internal saccades	50,	-12,	47	-48,	-6,	50
7	Corbetta <i>et al.</i> (1993)	Visuospatial attention	35,	9,	46	-23,	7,	44
						-25,	5,	42

but the reliability of these observations would require further experimental evidence.

The anterior cingulate, a limbic structure, has been proposed to contribute a mapping of emotive or motivational factors to the system of visual spatial attention (Mesulam 1990). More broadly, the anterior cingulate has been hypothesized to play a key role in an executive attention system, which participates in maintaining events in working memory and selecting actions (Posner and Raichle, 1994). Activation of the anterior cingulate has been observed in a variety of tasks which require different types of attention or cognitive engagement. Examples are studies of willed action

(Frith *et al.*, 1991) and attention tasks using Stroop stimuli (Pardo *et al.*, 1990). Cingulate activation has been shown to shift its focus across verbal, manual and oculomotor tasks; suggesting functional specialization according to the sensorimotor systems (Paus *et al.*, 1993). The specificity of the cingulate focus obtained in this study to visuospatial attention remains to be determined. In a previous study of visuospatial attention, it was not possible to separate cingulate from medial frontal activation (Corbetta *et al.*, 1993).

Posterior parietal cortex. The parietal cortex has been the brain structure most often associated with visuospatial

Table 4 Locations of posterior parietal activations reported in this and previous studies

No.	Reference	Task	x, y, z coordinates					
			R hemisphere			L hemisphere		
1	Present study	Covert visuospatial attention same-side task minus baseline opposite-side minus same-side task	34,	-68,	36			
						-34,	-76,	40
2	Anderson <i>et al.</i> (1994)	Oculomotor: pro-saccades				-26,	-76,	44
4	Anderson <i>et al.</i> (1994)	Oculomotor: remembered saccades				-18,	-68,	36
						-14,	-44,	52
						-18,	-56,	48
						-30,	-34,	40
3	Corbetta <i>et al.</i> (1993)	Visuospatial attention	33,	-45,	46	-29,	-51,	36
						-27,	-43,	46
4	Corbetta <i>et al.</i> (1995)	Visual shifts	21,	-61,	50	-17,	-59,	58
			23,	-47,	52			
5	Corbetta <i>et al.</i> (1995)	Attention to feature conjunctions	23,	-79,	46	-27,	-55,	54
			31,	-47,	54	-31,	-53,	44
			33,	-69,	50			
6	Gitelman <i>et al.</i> (1996a)	Sensorimotor exploration	29,	-44,	52			
			30,	-44,	48			
			45,	-41,	40			

attention and hemispatial neglect (e.g. Mesulam, 1981; Kinsbourne, 1987; Rafal and Robertson, 1994). The precise region critical for visuospatial attention in the human brain, however, had not yet been settled (Table 4). Neuroimaging studies have implicated the superior parietal lobule (Corbetta *et al.*, 1993, 1995; Anderson *et al.*, 1994). However, these studies have relied upon group analysis and have not included structural brain-imaging of the individuals studied. The human posterior parietal cortex is highly variable and asymmetrical in surface anatomy (Witelson and Kigar, 1992). Therefore, analyses relying upon average activations in groups of subjects and standardized anatomical atlases may be misleading. Results from neuropsychological and behavioural neurological studies have implicated the inferior parietal lobule, in the area of the temporal parietal junction (Rafal and Robertson, 1995). Localization based upon lesions in the human brain, however, can also be misleading because of the variable relationship between the lesions and the functional anatomical boundaries, and because lesions can disconnect functional regions instead of damaging the regions *per se*.

The correspondence between the areas in the posterior parietal cortex of monkeys and humans has not been straightforward (*see* Andersen, 1989). Understanding these relationships would greatly help clarify the specializations of the posterior parietal areas in the human brain. Two areas in the posterior parietal lobe of monkeys have been linked to visuospatial attention and oculomotor functions: area 7a and an area in the lateral bank of the intraparietal sulcus (LIP). The homologues of both of these regions are likely to participate in visual attention functions in humans and to cause aspects of neglect when damaged by brain lesions. Area 7a in the inferior parietal lobule in monkeys has been linked to visuospatial attention by lesion and neurophysiological studies. Lesions to area 7a result in hemispatial

neglect and visuospatial deficits in monkeys (Heilman *et al.*, 1970; Petrides and Iversen, 1979; Lynch and McLaren, 1989). Neuronal firing is modulated by stimulus relevance in visuospatial tasks (Bushnell *et al.*, 1981; Goldberg and Segraves, 1987). Area 7a appears capable of integrating eye-position and retinotopic information to form a head-centred spatial map (Zipser and Andersen, 1988; Barash *et al.*, 1991). Area 7a is interconnected with higher-order areas in the cingulate gyrus, superior temporal sulcus and dorsolateral prefrontal cortex (Mesulam *et al.*, 1977; Andersen *et al.*, 1985b; Selemon and Goldman-Rakic, 1988). Area LIP in monkeys also appears to be involved in visuospatial functions, perhaps more closely related to the planning and control of eye movements. Area LIP contains neurons that respond in association with eye movements (Andersen *et al.*, 1985a) and stimulation of the area can generate saccades (Shibutani *et al.*, 1984). LIP also has strong interconnections with the frontal eye fields (Gnadt and Andersen, 1988).

In the present study, the location of the posterior parietal activation across the group of subjects was difficult to interpret relative to Brodmann's areas. Using the Talairach and Tournoux atlas as a guide, the activation appeared to straddle BAs 7, 39 and 40. Figure 9 compares the locations of posterior parietal activations in this and previous oculomotor and visual attention studies.

Given the high degree of variability in the anatomical surface features in this region, localization relied upon analysis of data from single subjects. The most parsimonious description of the site of posterior parietal activation is that it followed the intraparietal sulcus. The inherent resolution of the PET images did not permit a finer grain description, such as resolving which bank of the sulcus was primarily engaged. These activations are likely to have reflected activity in the human homologues of both areas LIP and 7a in the monkey. More precise localization within the intraparietal

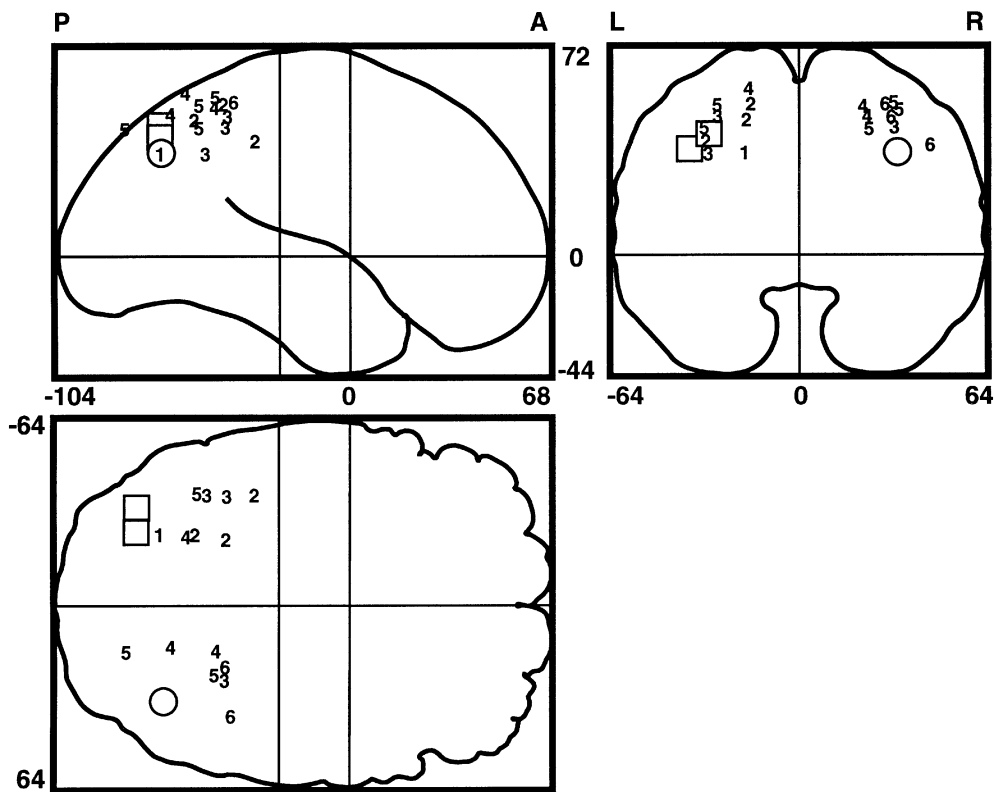


Fig. 9 Comparison of posterior parietal activations obtained in the present experiment relative to previous reports. The peak of activations were plotted onto glass-brain projections of the brain in standardized normalized space (Talairach and Tournoux, 1988). Activation in the same-side task relative to baseline was plotted as a square, and activation in the opposite-side task as squares. The numbers plot the activations observed in previous studies, and correspond to the references in Table 4.

sulcus and further fractionation of the functional properties of this region may have to be evaluated using fMRI, in which repeated studies with higher spatial resolution can be performed in individuals (Gitelman *et al.*, 1996*b, c*; Nobre *et al.*, 1996*a, b*).

Superior temporal sulcus. A region of the right superior temporal sulcus tended to be activated by visuospatial shifts of attention. Technically, this region did not meet the criteria established for significance. However, it was also observed in the majority of the individual analyses. The involvement of the STS in a task of visuospatial shifts of attention was not surprising. The STS in monkeys is polysensory (Bruce *et al.*, 1981; Hikosaka *et al.*, 1988) and some neurons are linked to saccades and smooth pursuit (Dursteler *et al.*, 1987). The STS is strongly interconnected to other regions in the spatial attentional network, such as the posterior parietal cortex, the frontal eye fields and the pulvinar nucleus of the thalamus (Barbas and Mesulam, 1981; Cavada and Golman Rakic, 1989; Stanton *et al.*, 1989; Seltzer and Pandya, 1989, 1994). Lesions to the STS in the monkey have also been reported to result in neglect (Watson *et al.*, 1994). Its involvement in visuospatial attention in humans and its role within the spatial attentional network remains to be validated and investigated further.

Subcortical structures. In general, the subcortical activations were less reliable than cortical activations, and were difficult to pinpoint anatomically. The only subcortical region activated significantly during this experiment was the pulvinar nucleus of the thalamus, suggested to partake in visuospatial attention (Petersen *et al.*, 1985). Some subcortical regions thought to be involved in visuospatial attention were not imaged consistently because of the limited size of the array of PET detectors. This was the case with the superior colliculi and with brainstem structures of the reticular activating system. The involvement of these regions in the present task, therefore, could not be evaluated.

Concluding remarks

The present experiment has helped resolve longstanding questions about the anatomical loci of brain regions involved in visuospatial attention. The results support the existence of a large-scale neural system for visuospatial orientation. The cortical regions involved displayed a right-hemispheric bias in their layout. Future studies that vary systematically the relevant factors for attention should build upon the present findings to provide understanding of the regional functional specializations of the attention system in the human brain.

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