

Cortical areas with enhanced activation during object-centred spatial information processing

A PET study

Manabu Honda,¹ Steven P. Wise,² Robert A. Weeks,¹ Marie-Pierre Deiber¹ and Mark Hallett¹

¹Human Motor Control Section, Medical Neurology Branch, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda and
²Laboratory of Systems Neuroscience, National Institute of Mental Health, National Institutes of Health, Poolesville, USA

Correspondence to: Mark Hallett, NINDS, NIH, Building 10, Room 5N226, 10 Center Drive, MSC-1428, Bethesda, MD 20892-1428, USA. E-mail: hallett@codon.nih.gov

Summary

The phenomenon of object-centred unilateral neglect suggests that some neural networks process spatial information relative to reference objects. To examine object-centred information processing, we measured regional cerebral blood flow in 11 normal subjects with PET. During each PET scan, a subject viewed a sample stimulus followed by a cue on a video screen. The sample consisted of two polygons, termed 'objects', each located in a corner of the screen. A small target spot appeared in a corner of each polygon. There were two tasks: the visuomotor task and the matching-to-sample task. In the visuomotor task, the subject moved a joystick in a direction indicated by either the location of the target spot inside the object (if object-centred coordinates were operative) or the location of the object relative to the video screen (if screen-centred coordinates were operative). In the matching-to-sample task, the subject moved the

joystick to report whether the relevant spatial information (object- or screen-centred) in the cue matched the sample. In both the visuomotor and the matching-to-sample task, use of object-centred (versus screen- or viewer-centred) information caused augmented activation in the inferior occipitotemporal cortex, bilaterally, in the left superior occipital gyrus, and in both the thalamus and the brainstem. In addition, in the visuomotor task such activation occurred in the right posterior parietal cortex and in the left ventral premotor, dorsolateral prefrontal and anterior supplementary motor areas. These findings suggest the involvement of the occipitotemporal cortex and a broad frontoparietal network when, as in the visuomotor task, object-centred information guides movement. When the same data underlie declarative reports, as in the matching-to-sample task, the occipitotemporal cortex remains engaged but the frontoparietal network diminishes in importance.

Keywords: cerebral blood flow; object-centred coordinate; screen-centred coordinate; occipitotemporal cortex; frontoparietal network

Abbreviations: rCBF = regional cerebral blood flow; SMA = supplementary motor area

Introduction

Patients with unilateral neglect sometimes overlook features on the contralesional side of an object regardless of the object's location within the visual field. This phenomenon, termed object-centred unilateral neglect (see e.g. Marshall and Halligan, 1994; for review see Walker, 1995), suggests the existence of neurons and/or brain regions that bind visual spatial information to objects. This issue can be approached in the context of the view that the primate visual cortex can be functionally segregated into two major pathways in monkeys (Ungerleider and Mishkin, 1982; Desimone and Ungerleider, 1989) and humans (Ratcliff and Newcombe,

1973; Damasio *et al.*, 1982; Haxby *et al.*, 1991, 1994; Courtney *et al.*, 1996). A dorsal pathway is thought to be crucial for spatial vision and a ventral pathway for object vision. However, many behaviours require integration of spatial with non-spatial visual information (Zeki, 1993). For example, in reaching for the handle of a cup, one has to localize a part of an object (the handle) with respect to the reference object (a cup). Spatial location defined relative to a reference object can be referred to as an object-centred coordinate frame. This coordinate system contrasts with a viewer-centred coordinate frame, which specifies location

relative to a viewer, and with other coordinate frames not explicitly referenced to objects. There is evidence for object-centred information processing in the supplementary eye field, part of the frontal oculomotor cortex (Olson and Gettner, 1995).

Although both object-centred coordinate frames (Haxby *et al.*, 1991, 1994) and alternatives (Corbetta *et al.*, 1993, 1995; Jonides *et al.*, 1993; Courtney *et al.*, 1996) have been used in other brain imaging studies, few attempts have been made to examine activation differences due to object-centred coordinate frames explicitly (Fink *et al.*, 1997a). In this report, we examine the effect of object-centred information processing on regional cerebral blood flow (rCBF). Further, by employing two tasks that require a different type of behavioural response, we will distinguish between distributed neural networks used for the sensory/perceptual aspects of information processing and those used for visuomotor control (Sirigu *et al.*, 1991; Goodale and Milner, 1992; Goodale, 1993; Milner and Goodale, 1993).

Method

Subjects

We studied 11 healthy volunteers (eight men, three women) aged 18–34 years (mean, 22.3 years). The subjects were all 100% right-handed according to the Edinburgh Inventory (Oldfield, 1971). The protocol was approved by the Institutional Review Board of the National Institute of Neurological Disorders and Stroke, and the National Institute of Mental Health, National Institutes of Health, USA, and the subjects gave their written informed consent.

Experimental design

During the experiment, the subjects moved a joystick with their right hand in response to visually presented stimuli. The correct joystick movement direction was determined differently according to five conditions, described below. For each condition, visual stimuli were presented on a video computer screen 60 cm from the subject. The display subtended a visual angle of $\sim 35 \times 30^\circ$. The base of the joystick had four orthogonal slots (one each oriented to the upper right, lower right, upper left and lower left relative to the central joystick position). Each slot extended 6.5 cm from the centre to its end point. Joystick position was sampled at 200 Hz. Movement was recorded as completed at the midpoint of its trajectory. A Macintosh IIfx computer (Apple, Cupertino, Calif., USA) and SuperLab (Cedrus, Wheaton, Md, USA) were used to present stimuli and monitor the behavioural data.

The behavioural paradigm was composed of five conditions, including four principal task conditions plus one behavioural control. The two tasks were termed the ‘visuomotor’ and ‘matching-to-sample’ tasks. Both tasks had two versions, which required either the use of ‘object-centred’

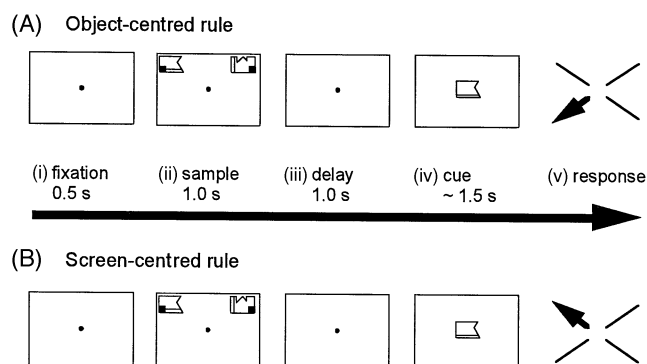


Fig. 1 Visual stimuli used in the visuomotor task. Regardless of the rule, each trial consisted of sequential presentation of (i) an initial blank screen with a fixation spot, (ii) a sample stimulus, (iii) a blank screen for a delayed period and (iv) a cue stimulus. In the sample stimulus, two objects were simultaneously presented in two of the four corners of the screen. Each object had a small target spot within it. In the example illustrated, the target spot was in the lower left part of the object in the upper left corner of the screen, and in the lower right part of the object in the upper right corner. The location of the objects on the screen and relative location of the target spot within each object were varied in random order among trials. In the cue stimulus, one of the two objects without a target spot reappeared at the centre of the screen. The subject was instructed to move the joystick in a direction determined by two different rules. For the object-centred rule (A), the relative location of the target spot within the object on its original presentation determined the correct direction of movement of the joystick. In this example, it is to the lower left (A, v). For the screen-centred rule (B), the corner of the screen in which the object had appeared in the sample stimulus determined the correct direction. In the example illustrated it is to the upper left (B, v). When the correct direction was chosen within 1.5 s, the cue stimulus disappeared immediately. If the direction was incorrect or no movement was performed, the cue stimulus remained visible for a total duration of 1.5 s on the screen and then disappeared. Subsequently, another fixation point was presented, an event that marked the beginning of the next trial.

spatial information or the use of ‘screen-centred’ information to perform the task correctly. Thus, the four principal task conditions consisted of each combination of the two tasks in two parallel versions. In addition, a ‘fixed-response condition’ was used as a behavioural control. In the present task, an ‘object’ is defined as a relatively small polygon on a video display.

In the visuomotor task (Fig. 1), each trial started when a 0.5° fixation point was presented at the centre of the screen, and remained visible until a cue stimulus appeared, much later in the trial (Fig. 1, i). In the meantime, 0.5 s after the fixation point appeared, two objects, each of which subtended a visual angle of $8 \times 6^\circ$, were simultaneously presented in two of the four corners of the screen as a sample stimulus (Fig. 1, ii). The objects remained visible for 1 s. For example, one object might appear near the upper-left corner, another near the upper-right, as illustrated in Fig. 1. Together, these two stimuli constituted the sample. The same two polygonal objects were used for all trials. Each object had a 0.5° target

spot within it. The relative location of the target spot within one object always differed from that in the other object, and the two objects were always near different corners of the screen. Within these constraints, the locations of the objects on the screen and the relative location of the target spot within each object were varied in random order, trial by trial. In the example shown in Fig. 1, one target spot was in the lower-left part of the object located in the upper-left corner of the screen, and the other target spot was in the lower-right part of the object in the upper-right corner. After the sample stimulus had been presented for 1 s, it disappeared for a 'memory delay period' of 1 s (Fig. 1, iii). At that point in each trial the cue stimulus was presented (Fig. 1, iv); the fixation spot disappeared and, simultaneously, one of the two objects reappeared at the centre of the screen. At the time of the cue stimulus, the polygonal object lacked any target spot.

The subjects had been instructed to move the joystick as quickly and correctly as possible, within 1.5 s of the appearance of the cue stimulus, in a direction determined by one of two different rules (Fig. 1, v). For the object-centred rule (Fig. 1A), the relative location of the target spot within that object, on its original presentation as part of the sample stimulus, determined the correct joystick movement direction. For the screen-centred rule (Fig. 1B), the corner of the screen in which that object had appeared in the sample stimulus guided the direction of movement. For this rule, the relative location of the target spot on its original presentation was irrelevant, although the target spot was nevertheless presented within the object during the sample stimulus. Feedback was given concerning the correctness of the response in the following manner. When the correct direction was chosen within 1.5 s, the cue stimulus disappeared immediately. If the direction was incorrect or no movement was performed, the cue remained visible on the screen for a total duration of 1.5 s and then disappeared. The subjects were limited to one movement of the joystick for each sample-cue presentation (i.e. one behavioural trial). Subsequently, another fixation point was presented, an event that marked the beginning of the next trial. As a result, the intertrial interval varied according to the reaction time in each trial.

In the matching-to-sample task (Fig. 2), the sequence of events was the same as in the visuomotor task until the time of cue stimulus presentation (Fig. 2, i–iii). The same two objects as in the visuomotor task were used. For the object-centred rule (Fig. 2A), one of the two objects reappeared as the cue stimulus at the centre of the screen, and had a target spot inside. The relative location of the spot within the object matched or did not match that on its original presentation (Fig. 2A, iv, upper part for a match, lower part for a non-match). The subjects had to report whether the within-object target spot's location matched the sample. They did so by moving the joystick in one of two predetermined directions: to the upper right to report a match, and to the lower left for a non-match. For the screen-centred rule (Fig. 2B), one of the objects, also with a target spot, reappeared in one of the corners of the screen as the cue stimulus, although never in

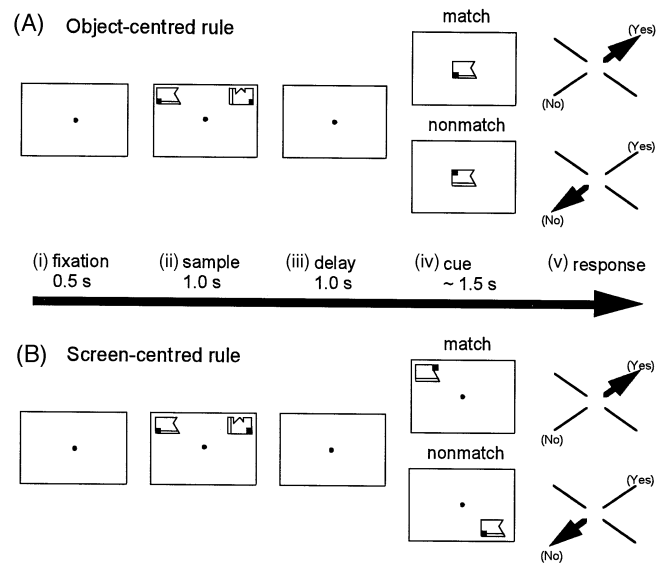


Fig. 2 Visual stimuli used in the matching-to-sample task. Visual stimuli were the same as those in the visuomotor task until the time of cue stimulus presentation (i–iii). For the object-centred rule (A), one of the two objects with a target spot within it reappeared at the centre of the screen as the cue stimulus (A, iv). The relative location of the spot within the object matched or did not match that on its original presentation. The subject moved the joystick in one of two predetermined directions: to the upper right to report a match (A, v, *upper*) and to the lower-left to report a non-match (A, v, *lower*). For the screen-centred rule (B), one of the objects with a target spot reappeared in one of the corners of the screen as the cue stimulus (B, iv). The corner of the screen where the cue stimulus was presented was or was not the same as that of its original presentation. In this condition only, the fixation spot remained until the end of the trial. The subject moved the joystick to the upper right to report a match (B, v, *upper*) and to the lower left to report a non-match (B, v, *lower*). The order of matches and non-matches was controlled in pseudorandom order so that the probability of each was 0.5. The same feedback as that in the visuomotor task was given.

the same corner as the other object that was included in the sample stimulus on that trial. The corner of the screen where the cue stimulus was presented was or was not the same as for that object on its original presentation (Fig. 2B, iv, upper part for a match, lower part for a non-match). In this condition only, the fixation spot remained on until the end of the trial. The subject moved the joystick to the upper right to report that the current location matched the sample location and to the lower left if it did not. Note that a target spot was presented but was not relevant for determining the report at this time. The order of matches and non-matches was controlled in a pseudorandom order so that the probability of each was 0.5. As in the visuomotor task, the subjects were requested to move the joystick within a time limit of 1.5 s, and the same feedback was given.

In the control (fixed-response) condition, the stimuli were the same as those used in the visuomotor tasks (Fig. 1) but were irrelevant, since movement direction was constant, i.e. always to the upper right. The time limit for movement and feedback were the same as those in the other conditions.

One block for each condition consisted of 32 trials. The location of presentation of objects and target spots was balanced in terms of both the screen-centred and object-centred coordinate frames. Reaction time from the onset of each cue stimulus was calculated on-line. The number and type of errors were also recorded. When an incorrect response was generated within a period of 1.5 s, it was considered a directional error. When no response was generated within the period, it was considered a timing error. Prior to PET scans, the subjects were trained using each task until they had completed one block of trials in every condition in which they attained 70% correct responses. No measurement of eye position was attempted. The mean reaction time and error rate (as a percentage) in each condition were subjected to separate RM-ANOVA (repeated measures analysis of variance) with two within-subject factors—condition (five levels) and repetition (two levels: first and second scans). Greenhouse–Geisser correction for degrees of freedom was employed. The effect of repetition and interaction of condition with repetition reflected an overall effect of potential learning and the difference in a learning effect among conditions, respectively. Predetermined linear contrasts were used to test differences between specific pairs of conditions. For this purpose, the data from the first and second sessions were averaged.

PET procedure

The subjects underwent 10 consecutive rCBF PET scans, two for each condition, using the tracer $H_2^{15}O$ as a marker of neuronal activity. The order of conditions was counterbalanced across subjects. The subject lay supine on a scanner bed in a dimly lit, sound-attenuated room. The joystick was positioned so that the subject could hold it in a natural position and easily move to any of four directions to the end-point. The head was immobilized with an individually fitted thermoplastic face mask. PET was performed with a PC 2048–15B (Scanditronix, Uppsala, Sweden) scanner, which collected 15 contiguous planes with an in-plane resolution of 6.5 mm full-width half-maximum after reconstruction, and with a centre-to-centre distance of 6.5 mm, covering 97.5 mm in the axial direction. Field of view and pixel size of the reconstructed images were 256 and 2 mm, respectively. A transmission scan was obtained with a rotating $^{68}Ge/^{68}Ga$ source. Based on the reconstructed transmission image, the subject's head was positioned so that the scan covered the entire frontal lobe, necessarily sacrificing the anterior portion of the inferior temporal lobe and inferior cerebellum in some subjects. Ten consecutive scans were performed with a 10-min interscan interval. A bolus of 30 mCi of ^{15}O -labelled water was injected into the subject's left cubital vein 10 s after the task began. Reconstructed images were obtained by summing the activity during the 60-s period following the increase in cerebral radioactivity after the injection. No arterial blood sampling was performed, and thus the images collected were those of tissue activity.

Tissue activity recorded by this method is linearly related to rCBF (Fox *et al.*, 1985).

Image processing

rCBF data were analysed by statistical parametric mapping (SPM96 software; Wellcome Department of Cognitive Neurology, London, UK) implemented in MATLAB (Mathworks, Sherborn, Mass., USA). Statistical parametric maps are spatially extended statistical processes used to characterize regionally specific effects in imaging data (Friston *et al.*, 1991, 1994; Worsley *et al.*, 1992). The scans from each subject were realigned using the first image as a reference (Friston *et al.*, 1995a). After realignment, the images were transformed into a standard anatomical space (Talairach and Tournoux, 1988; Friston *et al.*, 1995a). SPM95 was used for this purpose to keep coordinates comparable with previous literature. As a result, each scan was resampled into voxels that were $2 \times 2 \times 4$ mm in the x (right–left), y (anterior–posterior) and z (superior–inferior) directions, respectively. Each image was smoothed with an isotropic Gaussian kernel (full-width half-maximum = 15 mm) to account for the variation in normal gyral anatomy.

To test hypotheses about regionally specific effects of condition, the general linear model was employed at each voxel (Friston *et al.*, 1995b). In total 110 scans (11 subjects \times 10 scans) were subjected to this analysis. In the general linear model, the replication of the same tasks was collapsed as a single condition (i.e. five factors of interest). A systematic difference among subjects and the effect of global differences in rCBF between scans were removed as a confounding effect (i.e. 12 factors of no interest). Consequently, the number of degrees of freedom for the residual errors was 94. The estimates were compared using linear contrasts as described below.

First, each of four conditions requiring the variable responses was separately contrasted with the fixed-response condition, which served as a low-level baseline. These comparisons were useful to observe a basic pattern of increased or decreased brain activity by each task–rule combination relative to the baseline and to avoid confusion in interpreting the later analyses which might have resulted from deactivations relative to the baseline.

The differential effects of the spatial coordinate frame (i.e. the object-centred versus screen-centred rules) and the task (i.e. visuomotor versus matching-to-sample) were then explicitly tested as follows. Ignoring the fixed-response condition, the present paradigm design had a 2×2 factorial nature with two factors (rule and task), each consisting of two levels. Thus, the main effects of rule and task and the rule \times task interaction were estimated employing linear contrasts. For example, [(object- versus screen-centred rule in visuomotor task) versus (object- versus screen-centred rule in matching-to-sample task)] was used to study the interaction effect. Based on the observation that rule \times task interactions essentially reflected differences in rule effects between the

two tasks, we characterized the areas according to whether the rule effect was common to the two tasks or was specific to either task. For this purpose, all the voxels were divided according to task \times rule interaction (cut-off level of $P = 0.05$ for each voxel). Voxels that showed a significant main rule effect but did not show a significant interactive term were considered common to the two tasks. Voxels showing a positive interactive term were subjected to *post hoc* contrasts to further explore the nature of the rule effect. In these *post hoc* tests we contrasted object- versus screen-centred rules for the visuomotor task and examined the same contrast separately for the matching-to-sample task. Thus, for the rule effect we report those effects common to the two rules and those specific to either rule. For task effects, only the main effects are reported.

The resulting set of voxel values for each contrast constituted a statistical parametric map of the t statistic. The t values were transformed to the unit normal distribution (Z scores), which was independent of the degree of freedom of the error, and thresholded at 2.33. To account for multiple non-independent comparisons, the significance of the activation in each brain region detected was estimated by the use of distributional approximations from the theory of Gaussian fields in terms of spatial extent and/or peak height (Friston *et al.*, 1994). An estimated P value of 0.05 was used as a final threshold for significance. The resulting set of Z scores for the significant brain regions was mapped on a standard spatial grid (Talairach and Tournoux, 1988).

Results

Behavioural data

Although the intertrial interval depended on the reaction time, the number of movements performed during different conditions was within a reasonable range. The number of movements during the 1-min PET scan was maximal in the fixed-response condition (21.2 ± 0.8 movements, mean \pm SD, corresponding to 0.35 Hz) and minimal for the object-centred rule in the matching-to-sample task (17.4 ± 0.3 movements, corresponding to 0.29 Hz). As for mean reaction time, RM-ANOVA revealed significant main effects of condition [$F(4,40) = 163.15$, $\epsilon = 0.46$, $P < 0.0001$] and repetition [$F(1,10) = 10.33$, $\epsilon = 1.0$, $P < 0.01$], but no interaction of condition with repetition [$F(4,40) = 1.11$, $\epsilon = 0.53$, $P = 0.35$]. For error rate, there was a significant main effect of condition for total, directional and timing error [total, $F(4,40) = 27.65$, $\epsilon = 0.54$, $P < 0.0001$; directional, $F(4,40) = 15.01$, $\epsilon = 0.47$, $P < 0.001$; timing, $F(4,40) = 6.33$, $\epsilon = 0.68$, $P < 0.01$]. In contrast, no significant effect was observed in terms of repetition (total, $P = 0.41$; directional, $P = 0.31$; timing, $P = 0.75$) and condition \times repetition interaction (total, $P = 0.91$; directional, $P = 0.61$; timing, $P = 0.51$). These findings indicate that there was systematic improvement in mean reaction time between the first (overall mean, 677 ms) and second (655 ms) scans, but shortening of reaction time was not

significantly different among the conditions. Improvement of error rate was not statistically significant between the first (overall mean of total error, 8.0 %) and second (6.8 %) scans.

Mean reaction time and error rate averaged across all subjects are listed with their standard deviations in Table 1, in which the data of the first and second scans are averaged. Note that the values presented for reaction times are systematically overestimated because the movement was recorded at the midway point of the joystick trajectory. In all conditions requiring variable responses (i.e. the four principal conditions in the visuomotor and matching-to-sample task), mean reaction times were significantly longer than in the fixed-response condition. When rules were contrasted, mean reaction times were always longer for the object-centred rule than for the screen-centred rule. When tasks were contrasted, mean reaction times were always longer in the matching-to-sample task than in the visuomotor task.

The total error rate was higher with the object-centred rule than with the screen-centred rule or the fixed-response condition. There was no significant difference between the screen-centred rule and the fixed-response condition. Error rate was higher in the matching-to-sample task than in the visuomotor task, but only within the object-centred rule, not within the screen-centred rule. Directional and timing errors generally corresponded to the total error rate, although the timing errors were less variable by rule and task.

Contrasts with the fixed-response condition

Figure 3 shows brain regions with significant increases of activity during the four conditions that required variable responses compared with the fixed-response condition (corrected $P < 0.05$). All experimental conditions yielded robust activation in the bilateral parieto-occipital cortex. Additional activated regions, common to all conditions, were the left anterior supplementary motor area (pre-SMA) and the cerebellar vermis, bilaterally. The dorsal premotor cortex was bilaterally activated in all tasks and rules except for the right dorsal premotor cortex during the object-centred rule of the matching-to-sample task. The bilateral fusiform gyri, inferior temporal gyri, the ventral aspect of the left premotor cortex, brainstem and thalamus were activated only when object-centred rules were contrasted with the fixed-response condition (Fig. 3A and C). The anterior part of the right insula was activated (Fig. 3C) only during the screen-centred rule of the matching-to-sample task.

Analysis using 2×2 factorial design

Rule effects

Common effects. In both tasks, the bilateral inferior occipitotemporal cortex, including the fusiform gyrus, left superior occipital gyrus, brainstem and thalamus showed significantly increased activity for the object-centred rule

Table 1 Grand average of mean reaction time and accuracy during PET scan

Condition	Reaction time (ms)	Error rate (%)		
		Total	Directional	Timing
Fixed-response condition	336 ± 100	1.8 ± 2.1	0	1.8 ± 2.1
Visuomotor task				
Object-centred rule	708 ± 91 ^{*†}	10.1 ± 6.6 ^{*†}	7.7 ± 6.6 ^{*†}	2.4 ± 1.5
Screen-centred rule	610 ± 65 [*]	3.0 ± 2.3	1.1 ± 1.4	1.8 ± 1.8
Matching-to-sample task				
Object-centred rule	951 ± 67 ^{*†‡}	18.6 ± 6.2 ^{*†‡}	13.4 ± 8.3 ^{*†‡}	5.3 ± 3.1 ^{*†‡}
Screen-centred rule	725 ± 85 ^{*†}	3.4 ± 2.3	2.0 ± 1.9	1.4 ± 1.3

Data are means ± SD. *Significantly different from the fixed-response task; †significantly different from the screen-centred rule within the same task; ‡significantly different from the visuomotor task within the same rule. $P < 0.05$.

when contrasted with the screen-centred rule (Fig. 4 and Table 2).

Conversely, the screen-centred rule showed greater activity than the object-centred rule in the bilateral superior and middle temporal gyrus [maximum Z score = 5.47 at the coordinate of $(x, y, z) = (52, -40, 16)$ for the right, and maximum Z score = 3.70 at $(54, -32, 8)$ for the left, not illustrated] and a medial prefrontal region [maximum Z score = 3.70 at $(x, y, z) = (4, 52, 36)$]. However, when each condition was separately contrasted with the fixed-response condition, these areas always showed decreased activity (i.e. Z scores were always negative). Thus, the observed changes in this comparison reflect significant differences in decreased rather than increased activity. As a result, no region was more 'activated' during the screen-centred rule than during the object-centred rule.

Task-specific effects. Only the voxels with positive interaction terms were subjected to these analyses. Our examination of interactive effects involved testing for four differential rule effects: object-centred > screen-centred in the visuomotor task, object-centred > screen-centred in the matching-to-sample task, screen-centred > object-centred in the visuomotor task and screen-centred > object-centred in the matching-to-sample task. Only contrasts of the first type were significant. Figure 5 shows brain regions with significantly greater activity for the object-centred rule specifically in the visuomotor task. Significant regions of activation are listed in Table 3 with local maxima of significance. These areas include the dorsolateral prefrontal cortex, left ventral premotor cortex, right posterior parietal cortex and left pre-SMA. Figure 6 shows the mean and standard deviation of the adjusted rCBF across subjects at each local maximal point for the four areas. In all the illustrated areas, the object-centred rule in the visuomotor task showed the greatest activity. We note that the left posterior parietal cortex was just below the predetermined threshold of significance [maximal $Z = 4.12$ at $(x, y, z) = (26, -74, 36)$].

Response task effects

Brain regions showing significantly different activity during the visuomotor task relative to the matching-to-sample task are illustrated in Fig. 7. Identified regions are listed in Table 4 with local maxima of significance. The two rules were analysed together in this analysis. The left anterior parietal cortex and left dorsal premotor cortex had significantly greater activity during the visuomotor task compared with the matching-to-sample task. The left primary sensorimotor cortex was included in the cluster, although the local maximum of the significance was not situated in the primary sensorimotor cortex. There was a significant increase of activity in the right dorsolateral prefrontal cortex during the matching-to-sample task versus the visuomotor task.

Discussion

Object-centred versus screen-centred information processing

We examined two hypotheses by comparing rCBF during object-centred versus screen-centred information processing: (i) that there are brain areas with greater activation during the processing of object-centred spatial information than during the processing of other kinds of spatial information, as suggested by the phenomenon of object-centred neglect; and (ii) that visuomotor information processing dominates the blood flow signal in a network that differs from and is more dorsally situated than the areas that are most important for the processing of the same information for perception and declarative reports, based on the ideas of Milner and Goodale and their colleagues (Goodale and Milner, 1992; Goodale, 1993; Milner and Goodale, 1993). Our data support both hypotheses and point to a broad frontoparietal network that is more activated when object-centred information is used to guide a spatially directed hand movement than when the same information is used for declarative reports.

In considering these two hypotheses, four general issues concerning the present experimental design need to be

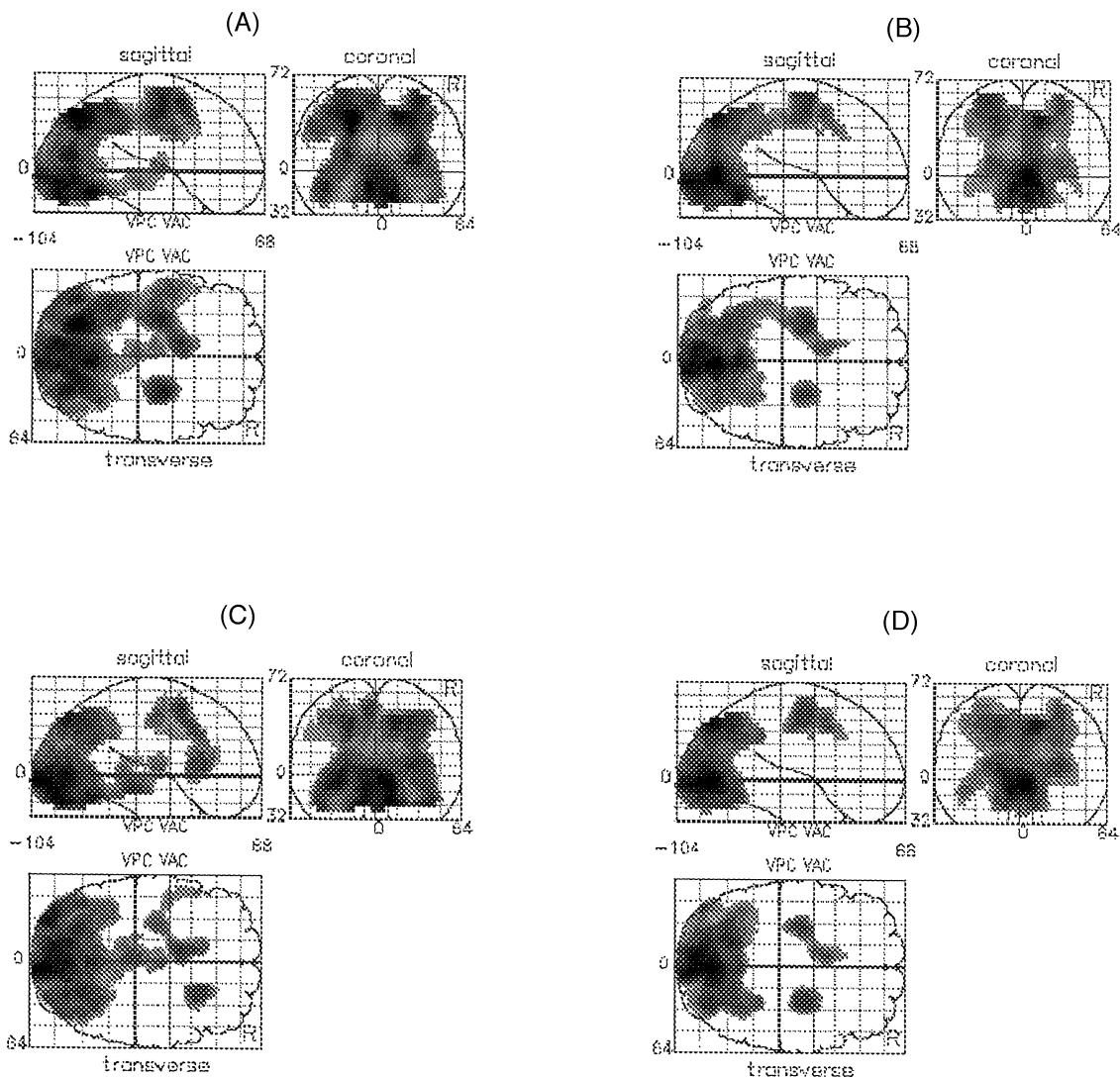


Fig. 3 Statistical parametric maps contrasting the control with each condition with either the object-centred rule or the screen-centred rule. Maps of Z scores for the regions where activity was significantly increased compared with the control ($P < 0.05$ with correction for multiple comparisons) are shown in a standard anatomical space (Talairach and Tournoux, 1988) viewed from the back (coronal view), the right side (sagittal view) and the top (transverse view) of the brain. Maps are illustrated using a grey scale, with the lower Z scores represented in light grey and the higher ones in dark grey. (A) Visuomotor task, object-centred rule. (B) Visuomotor task, screen-centred rule. (C) Matching-to-sample task, object-centred rule. (D) Matching-to-sample task, screen-centred rule. All are contrasted with the fixed-response condition.

discussed: (i) the relationship of the tasks to the concepts of declarative versus visuomotor function; (ii) the validity of the spatial coordinate frames used; (iii) the contrasting difficulty of the object-centred versus the screen-centred rules; and (iv) eye movement confounds.

(i) We considered the matching-to-sample task as an example of a perceptual, declarative report task. Once the subjects had judged whether the sample and cue stimuli matched, the joystick movement was performed in one of the arbitrary, predetermined directions. In other words, regardless of the rule, the movement direction was determined by the explicit, binary intention to report 'yes' or 'no', i.e. match or non-match. This approach allowed us to control for the execution of a joystick movement *per se* (i.e. by contrast

with the fixed-response condition). During the visuomotor task, however, the joystick movement direction was analogically instructed by the spatial information contained in the visual stimuli. Therefore, the visuomotor task should reflect spatial information processing that is similar to many forms of visually guided reaching. Note, however, that the task differed from the kind of veridical visually guided movement that typically occurs in reaching. The subjects did not reach directly for a spatial target, but rather mapped spatial targets as viewed on the video screen on to a joystick movement.

(ii) A screen-centred coordinate system may include several different frames of reference, including among others retinocentric, craniocentric and hand- or shoulder-centred

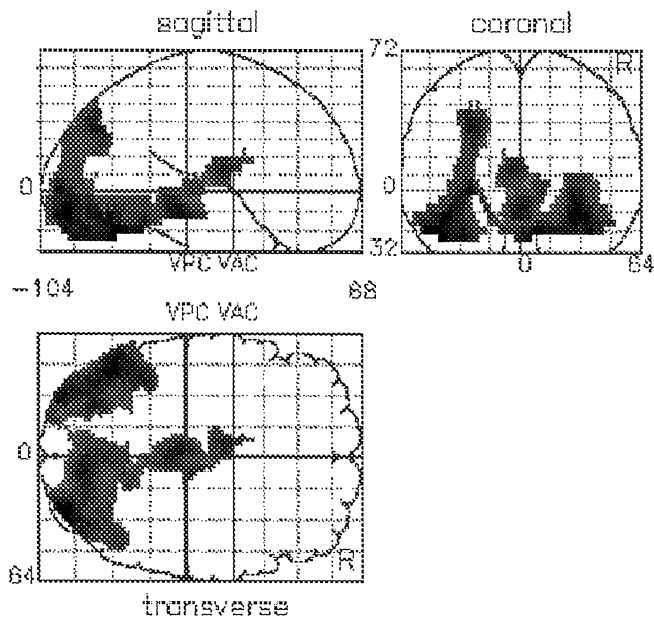


Fig. 4 Statistical parametric maps directly contrasting the object-centred rule with the screen-centred rule. For this analysis, data from both the visuomotor and the matching-to-sample task were included; voxels with a positive rule \times task interaction were excluded. Maps show the regions where activity was significantly greater during the object-centred rule than during the screen-centred rule without a positive rule \times task interaction.

Table 2 Regions of the brain with a significant increase in rCBF during object-centred rule relative to screen-centred rule commonly observed in both the visuomotor and the matching-to-sample task

Brain region	Coordinates			Z score
	x	y	z	
Left GF and GOi (19, 37) (OTi)	-44	-64	-24	4.76
Right GF and GOi (18, 19) (OTi)	28	-88	-12	4.70
Brainstem	0	-32	-8	4.32
Left GOs (19)	-26	-74	32	4.20
Thalamus	-6	-8	12	3.90

Each coordinate indicates the location of maximal significance in each brain region. GF = fusiform gyrus; GOi = inferior occipital gyrus; GOs = superior occipital gyrus; OTi = inferior occipitotemporal region. Numbers in parentheses are Brodmann areas, according to the atlas of Talairach and Tournoux (1988).

frames; most of these can be considered ‘viewer-centred’. Previous studies suggested that the differential effect of these distinct coordinates could be evident in some patients with spatial neglect (e.g. Karnath *et al.*, 1996; Ladavas *et al.*, 1997). In this experiment, however, we did not differentiate among these possibilities. Because the subject’s head and body, as well as the video screen, were all in a fixed position and the subjects were instructed to fixate the centre of the screen during all of the experimental conditions, these coordinate systems were essentially equivalent in the present experiment. We presumed that human subjects, familiar with

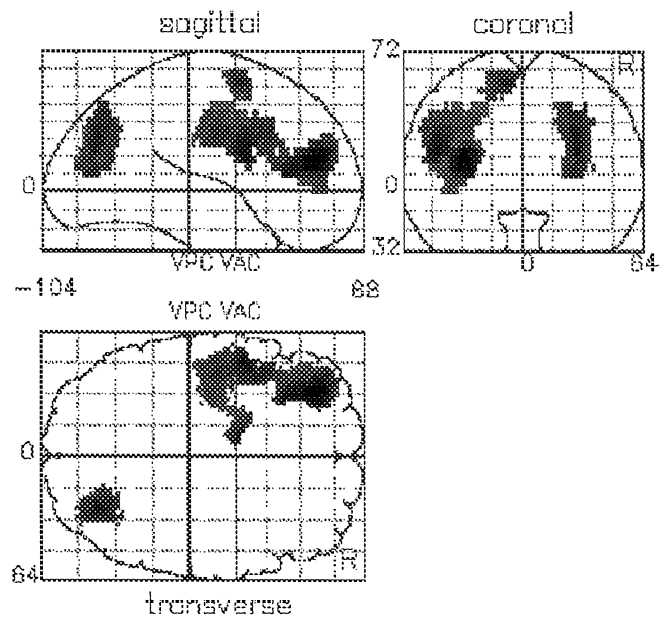


Fig. 5 Statistical parametric maps directly contrasting the object-centred rule with the screen-centred rule within the visuomotor task. For this analysis voxels without a positive rule \times task interaction were excluded. Therefore, maps consist of the voxels with the increased activity for the object-centred rule observed in the visuomotor task but not in the matching-to-sample task.

Table 3 Regions of the brain with a significant increase in rCBF during object-centred rule relative to screen-centred rule selectively observed in the visuomotor task

Brain region	Coordinates			Z score
	x	y	z	
Left dorsolateral prefrontal cortex (46)	-32	40	16	4.72
Left ventral premotor cortex (6, 44)	-46	2	20	4.26
Right posterior parietal cortex (7, 19)	28	-76	20	4.16
Left presupplementary motor area (6)	-12	2	56	3.72

Each coordinate indicates the location of maximal significance in each brain region. Numbers in parentheses are Brodmann areas, according to the atlas of Talairach and Tournoux (1988).

viewing video or cinematic scenes in which the content of a screen represents visual space, would interpret that information in terms of visual space rather than as part of a larger object. This would create a viewer-centred coordinate frame. Furthermore, the spatial relationship between the reference (i.e. the video screen) and the viewer (i.e. subject) was never changed in this experiment, and the video screen subtended $>30^\circ$ of visual angle, occupying most of the subject’s visual field. Although we assume it to be unlikely, we cannot rule out the possibility that subjects construed the video monitor as an object and processed the location of the polygons in object-centred coordinates relative to the screen. Accordingly, we use the term ‘screen-centred’ rather than ‘viewer-centred’ in this report.

(iii) Systematic differences in the mean reaction time and

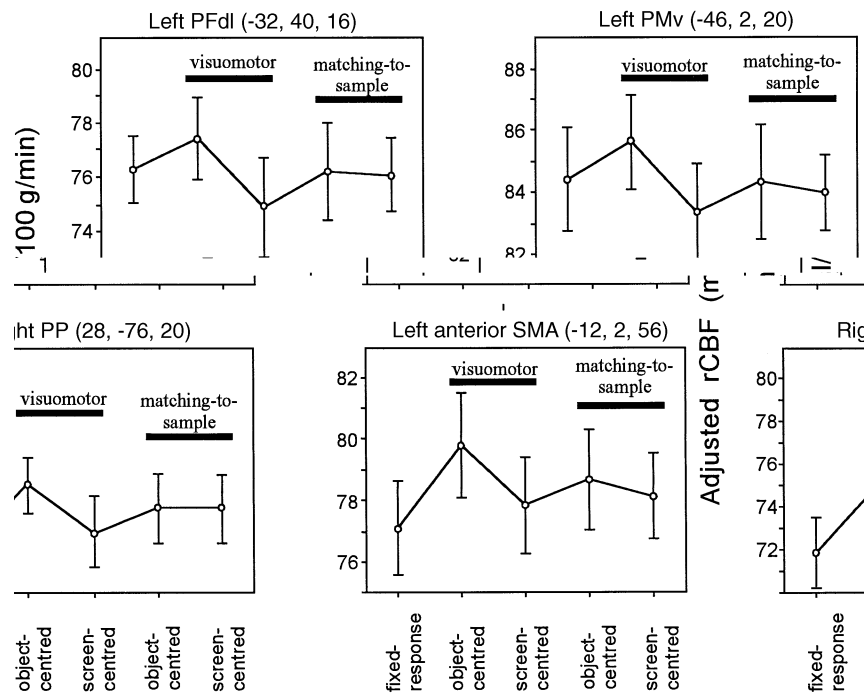


Fig. 6 The mean adjusted rCBF and standard deviations in the regions activated during the object-centred rule compared with the screen-centred rule, exclusively under the visuomotor task. Values are plotted at the voxel of maximum Z score in each region. Pfdl = dorsolateral prefrontal region; PMv = ventral premotor region; PP = posterior parietal cortex.

error rate were observed from rule to rule and task to task. These data indicate that the object-centred rule was more difficult. We elected not to balance task difficulty because we postulated that it may reflect an essential distinction between the object-centred and screen-centred coordinate frames. The screen-centred coordinate frame might be implicitly used even when only the object-centred coordinate was relevant for the task. This could happen because the subjects were likely to shift their attention using screen-based spatial information (e.g. relative to the fixation point). Therefore, object-centred information processing, as highlighted in the present study, might involve additional integration of screen-based with object-based information. This interpretation is compatible with the observation that the screen-centred information processing did not induce more activation than the object-centred rule. However, we recognize that the object-centred rule required greater attentional and mnemonic resources, as well as more intensive integration of viewer-based with object-based information. A further difference in difficulty might have been caused by the difference in size between the smaller target spot, relevant only for the object-centred rule, and the larger object. In addition, the higher error rate (in the object-centred rule) caused the subjects to receive more variable feedback about their performance, which, as discussed for the dorsolateral prefrontal cortex below, may have prompted a learning component that was negligible in the screen-centred rule. All these consequences of increased task difficulty for the object-

centred rule might have contributed to the observed contrasts in rCBF. However, we think that this account is unlikely for most cortical areas because, as shown in Fig. 6, the object-centred rule showed the highest activity in the visuomotor task when the extra difficulty engendered by the object-centred rule was less pronounced than in the matching-to-sample task. In addition, by our performance measure, the error rate did not show significant improvement between the two repeated sessions. Although only the reaction time showed significant improvement between two scans, the degree of improvement was not different across the conditions, as demonstrated by a negative interaction effect of condition \times repetition. Nevertheless, the difference in task difficulty and its many consequences need to be considered when interpreting the results.

(iv) The subjects' eye movement could, possibly, also confound the interpretation of the present data. However, the subjects were instructed to fixate the centre of the screen, and they reported that they did so after the experiment. The object-centred rule required more detailed information from the peripheral stimuli, and thus might result in a larger number of unintentional eye movements. Indeed, the region of parietal cortex activated in this study has been shown to be critical for the visuomotor control of eye movement (e.g. Colby *et al.*, 1995). However, it is unlikely that such extra eye movements would be introduced only during the visuomotor task, for which the frontoparietal regions showed object-centred enhancement.

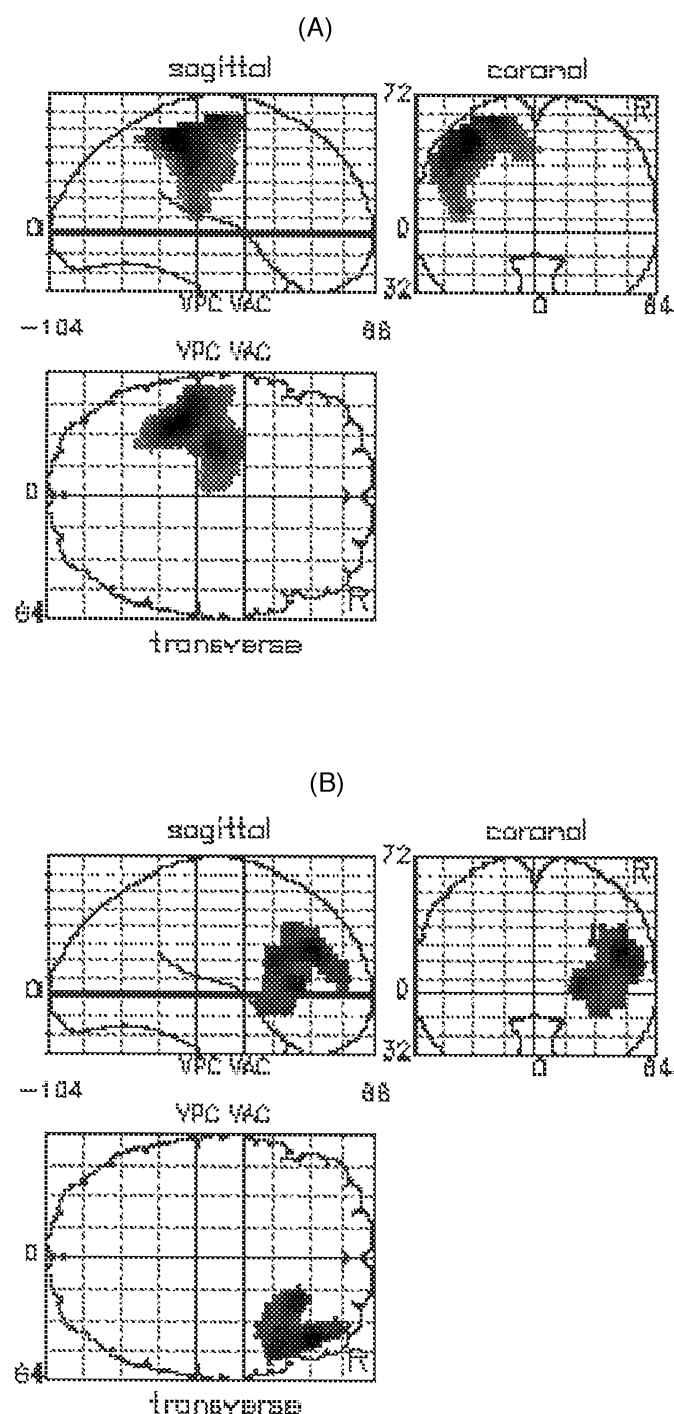


Fig. 7 Statistical parametric maps contrasting the visuomotor task with the matching-to-sample task. For this analysis, data from both the object-centred and the screen-centred rule are included. Maps show regions where the activity was significantly increased (A) and decreased (B) during the visuomotor task relative to the matching-to-sample task.

Enhancement for object-centred information processing in both tasks

We observed one general cortical region in which the use of an object-centred rule induced higher rCBF than the use of a screen-centred rule, and did so for both the visuomotor and

matching-to-sample tasks. This region was located in a broad inferior occipitotemporal region including a part of the superior occipital gyrus. The activation in the inferior occipitotemporal region was primarily bilateral, although the activation of the superior occipital gyrus was more predominant in the left. Since our subjects consisted of eight men and three women, putative sex differences in spatial cognition, thought to be more bilateral in females (e.g. Corsi-Cabrera *et al.*, 1997), might have contributed to the unilateral predominance of the activation that we observed. We interpret the increased activity in the inferior occipitotemporal region as a reflection of enhanced visual information processing when object-centred coordinates must be used. This emphasis on visuospatial information processing in the ventral visual stream might appear to conflict with its well known role in processing non-spatial information about objects. However, recent findings support the view that the ventral stream can process spatial information, and it may preferentially do so when object-centred coordinates are important. For example, electrophysiological studies (Ferrera *et al.*, 1992, 1994) have shown that the magnocellular pathways (M), usually associated with the dorsal stream, and parvocellular pathways (P), more often considered in the context of ventral stream function, make an almost equally significant contribution to the ventral visual processing stream. It seems likely, therefore, that the ventral visual stream receives both spatial and non-spatial visual information (Zeki, 1993). Further, neurons in area V4 of monkeys have increased sensitivity to a visual stimulus situated at a certain location relative to the monkey's current focus of attention (Connor *et al.*, 1996, 1997). A location relative to the current focus of attention, when attention is focused on an object, can be equivalent to coding object-centred coordinates under certain conditions.

Enhancement in the visuomotor task only

In contrast to the inferior occipitotemporal area, which showed object-centred rCBF enhancement in both tasks, a second set of areas, consisting of the pre-SMA, posterior parietal cortex, ventral premotor cortex and dorsolateral prefrontal cortex, showed this effect only in the visuomotor task. This specificity may reflect the use of visual information for spatially guided movement, perhaps specifically for objects on which attention has focused. At the single-neuron level this has been referred to as an object-centred motor field (Olson and Gettner, 1996).

Regarding the medial premotor areas, Olson and Gettner (1995) showed that the activity of most neurons studied in the supplementary eye field depended on the targeted direction of the impending eye movement with respect to a reference object, regardless of the eye movement direction in craniocentric coordinates. Although our subjects made limb movements instead of eye movements, the observed change in the pre-SMA lends support to the idea that medial premotor areas are somehow involved in object-centred action. The posterior parietal cortex has dense connections with the

Table 4 Regions of the brain with a significant change in rCBF in visuomotor task relative to matching-to-sample task

Brain region	Coordinates			Z score
	x	y	z	
Visuomotor task greater than matching-to-sample task				
Left inferior parietal lobule (40)	-36	-36	48	5.59
Left dorsal premotor cortex (6)	-24	-16	60	5.04
Matching-to-sample task greater than visuomotor task				
Right dorsolateral prefrontal cortex (46)	42	36	24	4.29

Each coordinate indicates the location of maximal significance in each activated brain region. Numbers in parentheses are Brodmann areas, according to the atlas of Talairach and Tournoux (1988).

extrastriate visual cortex (Blatt *et al.*, 1990; Morel and Bullier, 1990; Baizer *et al.*, 1991; Distler *et al.*, 1993) as well as the frontal lobe (Caminiti *et al.*, 1996; Wise *et al.*, 1997), and is considered to be the bridge between perception and action (Milner and Goodale, 1993). The posterior parietal cortex also processes signals according to different spatial coordinates, presumably for sensory-to-motor transformations (Colby *et al.*, 1993; Andersen, 1995; Caminiti *et al.*, 1996). Thus, the greater activity in the posterior parietal cortex during the object-centred visuomotor task may reflect such transformations. Previous neuroimaging studies showed that the posterior parietal cortex was involved in visuomotor tracking (Grafton *et al.*, 1992), grasping and pointing (Grafton *et al.*, 1996b), reaching (Kertzman *et al.*, 1997) and recalibration of visuomotor reaching movement (Clower *et al.*, 1996). The present finding is in good agreement with these data as well as with a recent PET study on object-oriented action. That study revealed greater activity in the posterior parietal cortex when subjects grasped an object than when they pointed towards the object (Faillenot *et al.*, 1997). A role of the inferior parietal lobule in grasping movements has also been proposed in monkeys (for review see Jeannerod *et al.*, 1995). Grasping an object probably requires the use of object-centred coordinates because the subjects have to shape their hand precisely, based on the object's shape. Increased posterior parietal cortex activation in the object-centred rule may also be partly explained by the additional reorientation of spatial attention (Corbetta *et al.*, 1993, 1995) required to evaluate the target spot within the objects, which was required for the object-centred but not for the screen-centred rule.

For the lateral premotor cortex, we distinguished the dorsal premotor cortex and the ventral premotor cortex, based on the transverse level of the frontal eye field, as reported in previous PET studies (Fox *et al.*, 1985; Anderson *et al.*, 1994), although an alternative proposal for the definition of the ventral premotor cortex (Fink *et al.*, 1997b) is also in good agreement with the interpretation of the present findings about the ventral premotor cortex. Neurophysiological evidence (Kurata, 1991; Mushiake *et al.*, 1991; Boussaoud and Wise, 1993; Boussaoud *et al.*, 1993) suggests that the

ventral premotor cortex is involved in the visual guidance of movement, possibly converting visuospatial to body-centred coordinates (Graziano and Gross, 1993, 1998; Graziano *et al.*, 1994; Kurata, 1994). Lesions of the ventral premotor cortex cause apparent neglect of objects (Rizzolatti *et al.*, 1983). In the present study, the posterior parietal cortex was selectively activated when movement was directionally instructed by object-centred visual information. This points to a role for the posterior parietal cortex in object-centred visuomotor control. Recent studies on observation and imagination of grasping objects have shown a role of the inferior frontal region (Brodmann areas 44 and 45) (Grafton *et al.*, 1996a; Rizzolatti *et al.*, 1996), which is included in the areas activated in the present study. Part of the posterior parietal cortex in monkeys (area F5 in the terminology of Rizzolatti *et al.*, 1996) is considered as a part of the circuit for grasping objects (Jeannerod *et al.*, 1995). The present findings, together with the previous work, are consistent with the suggestion that the posterior parietal cortex is specialized for the control of movements relative to parts of an object (Wise *et al.*, 1996). The dorsal premotor cortex, in contrast, was activated during all variable-movement conditions compared with the fixed-response condition, and no differential rule effect was observed.

As for the dorsolateral prefrontal cortex, one possible explanation of its object-centred enhancement might be that the object-centred rule required greater spatial working memory resources. However, the rule effect was prominent only for the visuomotor task and not for the matching-to-sample task (Fig. 6). Because both tasks involved a higher spatial working memory load for the object-centred rule, this factor alone cannot explain the present results. Differences in learning and performance for the two rules should also be considered. As shown in several PET studies (Jenkins *et al.*, 1994; Raichle *et al.*, 1994; Deiber *et al.*, 1997), activity in the prefrontal cortex is higher when tasks are unfamiliar. At the time of the PET scans, the subjects were, by our performance measure, still learning the task reflected as the improvement of reaction time between repetition of the two sessions, although error rate was not different between the two. However, as discussed above, this idea cannot explain

why the object-centred increase in rCBF was not observed for the matching-to-sample task: in this task, performance according to the object-centred rule was associated with even more errors and had a longer reaction time than for the visuomotor task. As an alternative explanation, perhaps the need to reject strictly screen-based stimulus–response mapping for the object-centred rule in the visuomotor task contributed to the increased activity in the left dorsolateral prefrontal cortex. The rejection of that information would not need to occur in the screen-centred rule of the visuomotor task, nor would it be required in either rule of the matching-to-sample task. This explanation may be in accord with recent findings on analogical reasoning in which increased activity was observed in the left dorsolateral prefrontal cortex during an analogical matching task compared with a standard matching task (Wharton *et al.*, 1998). In this context, analogical reasoning may require the subjects to actively reject information that is not relevant for the analogical matching but would be relevant to a standard matching task.

The present results are comparable with the recent report by Fink *et al.* (1997a). These authors used a verbal response, ‘left’ or ‘right’, to report on object-based or space-based information. Thus, their task was similar to our matching-to-sample task in that the responses consisted of a declarative report. During object-based (versus space-based) attention, Fink *et al.* (1997) reported activation in the left prestriate cortex, a region that is part of an area activated by the object-centred rule in both tasks of the present study. The authors also reported increased activity in the dorsolateral prefrontal cortex and in the right inferior temporal cortex during their space-based task. In the present study, these areas or areas in their vicinity showed increased activity for the screen-centred rule when directly compared with the object-centred rule, but also showed decreased activity for both rules when compared with the fixed-response condition. Because Fink *et al.* (1997a) did not report the activity in their ‘space-based’ areas during the control condition, the possibility that the areas they reported might reflect differences in decreased activity cannot be ruled out.

Visuomotor task versus matching-to-sample task

When the visuomotor tasks were contrasted with the matching-to-sample tasks (Fig. 7), the anterior parietal lobe and the dorsal premotor cortex contralateral to the moving hand, both of which were adjacent to the primary sensorimotor cortex, showed greater activity during the visuomotor tasks. By contrast, the right dorsolateral prefrontal cortex was more activated during the matching-to-sample task. The matching-to-sample task required highly explicit, cognitive operations, whereas the visuomotor task did not require declarative reports and could have been performed more implicitly. Since the tasks were not designed with this issue in mind, this interpretation needs considerable caution, and we could not rule out the possibility that subjects performed the visuomotor task explicitly, even without the requirement of doing so.

Notwithstanding these reservations, this finding is compatible with previous observations in sequence-learning tasks (Grafton *et al.*, 1995; Honda *et al.*, 1996): implicit learning tended to involve the motor areas (including the dorsal premotor cortex) whereas explicit learning tended to involve a frontoparietal network (including predominant activation in the right dorsolateral prefrontal cortex).

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