Visual Exploration of Form and Position with Identical Stimuli: Functional Anatomy with PET

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Abstract: Visual form and position perception in primates is thought to engage two different sets of cortical visual areas. However, the original concept of two functionally different and anatomically segregated pathways has been challenged by recent investigations. Using identical stimuli in the centre of the visual field with no external cues, we examined whether discrimination of form aspects and position aspects would indeed activate occipito-temporal and occipito-parietal areas, respectively. We measured and localised regional cerebral blood flow (rCBF) changes in the brain with positron emission tomography (PET) and ¹⁵O-butanol while the subjects performed four visual tasks: position discrimination (PD), form discrimination (FD), joint form and position discrimination (FPD), and a control task. Discrimination of form contrasted with discrimination of position resulted in rCBF increases in the lateral occipital and fusiform gyri. Discrimination of position contrasted with discrimination of form yielded rCBF increases in the left frontal eye field and middle frontal gyrus. No extra activations were seen when the joint form and position discrimination task was contrasted with either the individual form and position discrimination tasks. When the individual form and position discrimination tasks were contrasted with the control task, form discrimination resulted in activations in both occipito-temporal and occipito-parietal visual cortical regions, as well as in the right middle-frontal gyrus. Position discrimination resulted in activation in occipito-parietal visual cortical regions, the left frontal eye field and the left middle frontal gyrus. These findings are consistent with the view that the processing of visual position information activates occipito-parietal visual regions. On the other hand, the processing of 2D visual form information, in addition to the activation of occipito-temporal neuronal populations, also involves the parietal cortex. Form and position discrimination activated different nonsymmetrical prefrontal fields. Although the visual stimuli were identical, the network of activated cortical fields depended on whether the task was a form discrimination task or a position discrimination task, indicating a strong task dependence of cortical networks underlying form and position discrimination in the human brain. In contrast to former studies, however, these task-dependent macronetworks are overlapping in the posterior parietal cortex, but differentially engage the occipito-temporal and the prefrontal cortex. *Hum. Brain Mapping* 11:104–116, 2000. © 2000 Wiley-Liss, Inc.

INTRODUCTION

One of the most widely accepted hypotheses in recent vision research, originally formulated on the basis of lesion and single-cell recording studies in the primate visual system, claims that the analysis of the identity of an object and that of its spatial relationship to the environment are dissociated into a ventral occipito-temporal 'what' pathway and a dorsal occipito-parietal 'where' pathway [Ungerleider and Mishkin, 1982; Desimone and Ungerleider, 1989; Ungerleider and Haxby, 1994]. Previous functional imaging stud-

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ies on visual cortical processing in human visual system have provided ample supporting evidence for the selective activation of the ventral regions during the analysis of object features, such as colour and shape [Corbetta et al., 1991] as well as faces and of the dorsal occipito-parietal regions during position discrimination tasks [Haxby et al., 1994].

Studies in the past years have questioned the simplicity of the 'two-visual-processing-streams-hypothesis' by further revealing the operational complexity of the primate visual system. Emphasis has been put on the participation of parietal visual regions in, among others, visual-spatial functions, vision-based prehension, action planning, performance, and control [Goodale and Milner, 1992; Goodale et al., 1991, 1994; Rizzolatti et al., 1997; Sakata 1997, 1998; Snyder et al., 1998], visual attention [Wojciulik and Kanwisher, 1999; for review, see Mesulam, 1999; Colby and Goldberg, 1999], visual working memory [Ungerleider et al., 1998], and multimodal integration of spatial information [Andersen, 1997; Qian and Andersen, 1997]. On the other hand, the more subtle role of the occipito-temporal regions in visual form analysis has also been revealed (see, e.g., Kanwisher et al., 1998, 1999). It has also been suggested that a heavy "cross-talk" between the two processing streams exist [Gulyás and Roland, 1994; Gulyás, 1997]. In the monkey there are robust anatomical connections between the two visual subsystems [Morel and Bullier, 1990; Bous-saoud et al., 1990; Andersen, 1997; Felleman and Van Essen, 1991]. It has been hypothesised that by way of such cross-talk, parietal regions can contribute to form-related visual tasks, including feature binding [Friedman-Hill et al., 1995; Treisman, 1998; Ashbridge et al., 1999] and the processing and analysis of visual form [Gulyás et al., 1998; Sereno and Maunsell, 1998; Shen et al., 1999].

Regarding the subtle "division of labour" between the two visual processing streams, recently Köhler et al. [1995] have shown the stimulus- and task-related activations in either the ventral (occipito-temporal) or dorsal (occipito-parietal) set of visual areas in humans, albeit by using different visual stimuli. Identical stimuli with no working memory components were used by Haxby et al. [1991, 1994] to demonstrate activations of occipito-parietal areas in position judgements and occipito-temporal areas in face (i.e., object) judgements. Fink et al. [1997a] also used identical stimuli, but in contrast to previous studies and the prevailing hypothesis, they found the inferior temporal cortex more activated when spatial attributes were judged. However, both these groups used stimuli containing rather strong spatial (position) components in all con-

ditions, such as shift of visual focus between targets [Haxby et al., 1991, 1994] and right-left orientation of markers [Fink et al., 1997a].

In the light of these observations, in the present study we reexamined the hypothesis of separate sets of cortical fields associated with form judgements and spatial judgements, respectively, by using *identical visual stimuli* presented to the center of field of vision and with *no working memory components*. We also reexamined whether form discrimination and position discrimination may activate occipito-parietal and occipito-temporal areas in both cases.

To test whether the cortical neuronal populations participating in visual form information processing versus positional information processing constitute (i) entirely disparate, (ii) overlapping, or (iii) identical cortical patchworks, we designed visual paradigms using (i) identical visual stimuli with (ii) internal ("inherent") instructions cues. The analysis of the different object features (let them be either form related or position related) depended on an inherent feature—the luminance—of the stimulus. Thus, no visual memory component burdened the paradigm. Consequently, the activated cortical regions should display only those neuronal populations participating in the processing of actual visual information. The two visual features, namely *position* and *form*, were used in a most elementary way, in line with the basic meaning of the terms [Oxford English Dictionary, 1971]: *position* indicating "the place occupied by a thing or in which it is put," a "purely space relation," whereas *form* indicating "shape, arrangement of parts, the visual aspect of a thing."

In the light of the above stimulus requirements and constraints, four different tasks (whereof one was the control) were used. The stimulus display and response conditions were identical during the tasks. Based on the luminance of the stimulus (i.e., darker-lighter), in the form task the subjects had to scrutinise one of two form-features of the stimulus and make discrimination strategies. In the position discrimination task they had to scrutinise one of two possible dislocations of the stimulus and make a discrimination. In the joint form and position discrimination task they discriminated either form or position. Thus, during this latter task the subjects could not apply a sustained selective attention throughout the whole scanning period toward spatial or form aspects of the stimuli. Therefore, a comparison of the joint form and position discrimination task to the form and position discrimination tasks allows us to investigate whether there are any additional activations due to the alternation between position and form processing during the joint form

and position discrimination task as compared to selective form or position processing.

METHODS

Subjects

Seven right-handed, healthy male volunteers (age 21–36) participated in the experiment. Informed consent was obtained from all subjects, in line with the Helsinki Declaration, and the study was approved by the Ethics Committee and the Radiation Safety Committee of the Karolinska Hospital.

Scanning procedures and image post processing

Each subject wore an individually moulded plastic helmet [Greitz et al., 1980; Bergström et al., 1981] that held the head in identical position during the MR and PET scanning procedures. First, a high resolution nuclear magnetic resonance (NMR) scan (GE Signa scanner, 1.5 Tesla) was acquired for each brain. The MR images were used to guide the head positioning in the PET scanner. The MR and PET images were placed in register and the MR images were used to standardise individual brains, as well as to localise anatomical structures underlying functional changes in the individual brains. The PET measurements were made in ECAT EXACT HR PET scanner in 3D mode. During the PET experiment each subject received 12 bolus injections of 14 mCi ^{15}O -butanol. Data were acquired during the first 60 sec. Images were reconstructed with a ramp filter to a resolution of 5 mm in the plane. Subsequently, the last 11 images for each subject were realigned to one another with AIR software [Woods et al., 1992]. All images were filtered with a Gaussian filter of 8 mm FWHM. Regional cerebral blood flow (rCBF) images were calculated with an autoradiographic method [Meyer, 1989]. The MR images were transformed to a standard anatomical space [Roland et al., 1994], and the information obtained in this transformation was subsequently used to transform the rCBF images into the same space.

Statistical evaluation

The data were modeled using a general linear model [Ledberg et al., 1998]. The factors included were task, subject, and repetition, giving 72 degrees of freedom. The design matrix of the study is shown in Figure 1. The t -images for the investigated contrasts were searched for the largest clusters above a threshold of $t > 3.43$. The significance of these clusters was

Figure 1.

The design matrix of the experiment. The first four vertical columns indicate the tasks (control, FD, PD, FPD), the mid seven columns indicate the subjects, and the last four columns indicate the repetitions. In fact, in each subject, the tasks were randomly interleaved and repeated three times.

determined by a permutation analysis [Holmes et al., 1996]. A cluster was classified as significant if it had an omnibus probability of $P < 0.05$ [Ledberg et al., 1998].

In addition to the above model, we also used a VOI-based statistical analysis. The seven VOIs were identical with the seven significant activation clusters found in the comparison between the FPD task and the control condition.

Stimulus characteristics

Stimuli were displayed on a colour monitor at a viewing distance of 110 cm. On each trial a circular stimulus containing horizontal and vertical gratings (diameter 3.1 deg) was presented randomly in one of the four different positions (up-right, up-left, down-right, and down-left) displaced between 0.5 to 1.0 deg from the centre of the screen. Four different grating configurations varied randomly in the circle during the stimulus display: (i) The six strips of both the vertical and horizontal gratings were of the same width, forming symmetrical grating patterns with a spatial frequency of about two cycles/degree; (ii) three out of the six vertical strips were 1.5 times thicker than the other three, while horizontal strips

Figure 2.

A. Examples of the stimulus. **B.** The flowchart of paradigm-related executive functions during task performance.

remained identical; (iii) three horizontal strips were 1.5 times thicker and the vertical identical; (iv) both the vertical and horizontal grating contained three thicker strips. The phase of the gratings and the relative location of the thick and normal strips varied randomly during stimulus display (Fig. 2A).

This target was always displayed inside a square frame (6.2 deg in size), which had a constant central position, for a duration of 500 msec. The interstimulus interval (ISI) was 1,500 msec. The luminance of the displayed stimulus together with the frame varied randomly between 4.51 and 8.42 cd/m² (whereas the background monitor luminance remained 6.34 cd/m²). During ISI a central fixation square was displayed (0.2 deg in size), which is composed of four small squares. To avoid any cueing effect from the fixation point, the luminance of the two small squares laying along one of the diagonals was 4.51 cd/m² whereas the luminance of the other two squares was 8.42 cd/

m². The subjects were instructed to maintain fixation on the fixation point or during stimulus presentation in the centre of the display.

Tasks

Four different tasks were designed during which the stimulus presentation and the motor component of the responses were identical. In the control task the subjects were simply discriminating between the two luminance values of the target stimulus. If the displayed circle stimulus had the higher luminance value (i.e., it was lighter than the display background), the subjects were instructed to press the left button of the mouse, while if it had the lower value (i.e., darker than the background), they had to press the right button (Fig. 2B).

In the other three tasks, luminance was used as the cue and different discrimination strategies were conditioned to them. In the form discrimination task (FD), on the basis of the luminance of the target stimulus, the subjects had to make the discrimination along a form-feature of the stimulus ("regularity of pattern"), by choosing between two FD instructions. If the displayed target had higher luminance than the background, the subjects had to determine whether the strips in the vertical grating were of the same width or were different and press the right or the left response button, respectively. On the other hand, if the displayed stimulus had lower luminance than the background, the subjects discriminated whether the width of the horizontal strips were the same or different and had to press the right or the left mouse button, respectively. The position discrimination task (PD) was very similar to FD, but instead of FD, the subjects were required to execute one of the previously conditioned PD tasks based on the same luminance cues. If the displayed stimulus had the higher luminance value, subjects had to decide whether the circle was presented above or below the centre of the screen using the centrally positioned rectangular frame as a reference. When the stimulus luminance was lower than that of the background, the subjects had to indicate, by pressing the appropriate mouse button, whether the circle had been presented left or right of the centre. The joint form and position discrimination task (FPD) was a combination of the form and position discrimination tasks. When in this task the stimulus had the higher luminance value, just as in FD, the subjects had to discriminate whether the width of the vertical lines were identical or different; whereas in the case when the stimulus had the lower luminance value, the subjects had to indicate (as in PD) whether the circle was located on the left or on the right side of the centre (Fig. 2B).

TABLE I. Performance and response parameters during the tasks

	Reaction time	Performance
Task	(Mean reaction time)	(percent correct)
Control	397 ± 94	97 ± 3
FD	834 ± 212	81 ± 8
PD	792 ± 185	86 ± 6
FD (during FPD)	825 ± 178	83 ± 9
PD (during FPD)	787 ± 194	85 ± 11

All subjects went through a 2 h training session a day before the PET scanning. After having been instructed about the different task conditions, they learned the task-specific discrimination instructions in association with the luminance cue. When the subjects were able to recall the different conditioned discrimination strategies for all three tasks, they went through a training session consisting of repetitions of each of the task blocks (80 trials in each blocks) until they performed all three discrimination tasks at a performance level of around 75%. During the training of the PD task the dislocation of the displayed circle in the rectangular frame was set to obtain a performance level similar to that in the FD (ranging between 0.5 and 1 deg in both axes).

Eye movement monitoring

Due to the fact that the PET scanner gantry's high voltage electronic components interfere with eye movement measurements, the on-line monitoring of eye movements was not possible during the PET measurements. For this reason we monitored eye movements in a pilot "sham" experiment with electro-oculogram (EOG) in three subjects (Siemens Mingograph, 100× amplification) [Gulyás and Roland, 1994]. Two skin electrodes were located above the lateral and inferior edges of the orbit on both sides. As measured in preliminary tests, the recording gave information about the frequency, amplitude and movement trajectory of eye movements > 1 deg in amplitude. Fine eye movements < 1 deg in amplitude could not be monitored with precision with this method. There was no significant difference between the tasks with regard to the frequencies and amplitudes of eye movements.

RESULTS

Performance

The reaction times and performance levels are shown in Table I. To provide a better comparison with

other tasks and to reveal possible task effects on either type of discrimination, during FPD both reaction time and performance for PD and FD were registered and analysed separately. The performance levels between the PD and FD tasks, the PD component of the FDL task and the FD component of the FPD task, and the PD and FD tasks and the FD and PD components of the FPD task did not differ significantly (one-way ANOVA, $P > 0.6$). Similarly, there was no significant task effect on the reaction times (one-way ANOVA, $P > 0.05$). There were no significant differences between the task conditions with regard to the frequencies and amplitudes of eye movements.

Cortical activations during the FPD task as compared to control

There were seven brain regions exhibiting significantly higher rCBF during FPD task compared to the control task. Bilateral activations were found in the posterior part of the middle-frontal gyrus (pmFG), in the parietal cortex and in the posterior part of the lateral occipital gyrus. The seventh activation was found in the right fusiform gyrus. The significant rCBF increase in the left hemisphere in the posterior part of the middle-frontal gyrus was 10 mm anterior and lateral compared to the right-sided activation. The activations in the parietal and occipital cortices were asymmetrical the ones in the right hemisphere being larger. We found a large cluster of activation in the right parietal cortex extending from the junction between the occipital and parietal cortex through the superior parietal cortex into the intraparietal sulcus. The center of gravity of the activated cluster in the left parietal cortex was in the intraparietal sulcus. In the occipital cortex significant rCBF increases extended from the lateral posterior occipital regions to the fusiform/lateral occipital gyrus.

These seven clusters, found in the 'FPD-control' contrast, were used as volumes of interest (VOI) and applied to the rCBF images of the FD and PD tasks.

Comparison of the three discrimination tasks

There were no significant rCBF differences when the FPD task was contrasted to either the FD or PD tasks within the general linear model. The comparison of the FD and PD tasks yielded a significant bilateral activation in the lateral posterior occipital cortex extending into the fusiform gyri (Table II; Fig. 3G). When PD was contrasted to FD, the left frontal eye field region was the only region significantly more activated during PD (Fig. 3H).

TABLE II. Regions of significant rCBF increases during task conditions

Comparison and anatomical location		Talairach coordinates			Size mm ³	Seen Fig. 3
		x	y	z		
FD-PD						
Lateral occipital gyrus	R	32	−84	−5	1,350	G
Lateral occipital gyrus	L	−34	−83	−8	580	G
PD-FD						
Frontal eye field	L	−30	−5	45	520	H
FPD-control						
Posterior middle-frontal gyrus	R	39	11	31	990	
Posterior middle-frontal gyrus	L	−46	18	33	930	F
Lateral occipital gyrus	R	30	−84	3	2,310	
Fusiform gyrus	R	40	−53	−10	830	E, F
Lateral occipital gyrus	L	−30	−81	−9	530	F
Posterior superior parietal cortex	R	22	−68	42	3,700	
Intraparietal cortex	L	−31	−54	34	940	E, F
FD-control						
Posterior middle-frontal gyrus	R	40	11	32	1,170	
Lateral occipital gyrus	R	34	−75	−3	7,470	A, B
Lateral occipital gyrus	L	−34	−81	−9	2,300	A, B
Posterior superior parietal cortex	R	25	−68	37	5,590	A
Posterior superior parietal cortex	L	−12	−75	39	730	A, B
Intraparietal sulcus	L	−26	−63	31	890	B
PD-control						
Posterior middle frontal gyrus	L	−44	20	30	1,800	
Frontal eye field	L	−30	−2	50	870	
Posterior superior parietal cortex	R	23	−68	39	7,440	C, D
Posterior superior parietal cortex	L	−14	−74	39	1,870	
Inferior parietal cortex	L	−40	−53	47	760	
Intraparietal sulcus	L	−29	−55	32	3,070	C

Analysis with the VOIs representing the significant clusters of the FPD-control contrast revealed that the rCBF was significantly higher ($P < 0.01$) in the left posterior part of the middle frontal gyrus-VOI, when the PD task was compared to the FD task. It was also found that during the FD task the rCBF was significantly higher both in the left and the right posterior lateral occipital VOIs and also in the right fusiform VOI as compared to the PD task (for all the three VOIs, $P < 0.001$). There were no significant rCBF differences in the parietal VOIs between the FD and PD tasks ($P > 0.5$).

Cortical activations during the FD and PD compared to control

In both FD and PD there were significant activations in the pMFG and in the parietal cortex compared to control. In the FD, task the rCBF was significantly higher in the right pMFG; while in the PD, task acti-

vation was observed in the left pMFG. However, these regions were not symmetrically located (Fig. 4). This indicates that the left pMFG region is different from the right pMFG region. The right pMFG then being associated with from discrimination and the left pMFG with position discrimination.

Activations in the parietal cortex during both FD and PD were present in both hemispheres, they were asymmetrically located in the right and left hemispheres, and activations in the right hemisphere exceeded in size those in the left hemisphere. In the right posterior parietal cortex we have found a large cluster of activation in both tasks with almost identical centers-of-gravity (x, y, z coordinates: 25, -68, 37, and 23, -68, 39, FD and PD tasks, respectively). In the left parietal cortex two separate clusters were found. One was located in the posterior superior parietal cortex and the other in the intraparietal sulcus. In the PD task in addition we found a third cluster located in the left anterior inferior parietal cortex.

Figure 3.

Significant activations in the brain during various task comparisons. The activations (each cortical field in different colour) are projected onto the standard MR brain of the HBA [Roland et al., 1994]. Radiological convention: left hemisphere is in the right side and vice versa. For the identification of the regions, see Table II. **A–B.** FD-Control comparison. **A.** Coronal slice, $y = -74$ mm. **B.**

Sagittal slice, $x = -33$ mm. **C–D.** LD-Control comparison. **C.** Coronal slice, $y = -54$ mm. **D.** Sagittal slice, $x = -33$ mm. **E–F.** FLD-Control comparison. **E.** Coronal slice, $y = -52$ mm. **F.** Sagittal slice, $x = -33$ mm. **G.** FD-LD comparison. Coronal slice, $y = -86$ mm. **H.** LD-FD comparison. Sagittal slice, $x = 29$ mm.

In the occipital cortex, significant rCBF increases were found in FD. The activation extended from the lateral posterior occipital regions to the fusiform/lateral occipital gyrus. There was one large cluster in both left and right hemispheres, but the activation on the right side was substantially larger and extended more anterior in the inferior temporal cortex than the cluster on the left side. In the PD task no activation was observed inferior to the junction between the occipital and parietal cortex.

DISCUSSION

Main effects

The form and position discrimination tasks used in the present study were matched for both input and output components. The stimulus display and response conditions during all three tasks and during the luminance discrimination control condition were identical. This indicated that the differences observed were unlikely due to stimulus differences or motor components (response differences and eye movements). Psychophysical measurements of the response parameters revealed that there were no significant differences in response times and performance levels

during selective form and position discrimination tasks. These observations indicate that general attention and differences in difficulty of the tasks could not account for the observed rCBF differences.

Comparison of the PD task with the control task revealed significant activations in the parietal lobes (bilaterally in the posterior superior parietal cortices and in the left intraparietal sulcus and inferior parietal cortex), as well as in the left frontal eye field and middle frontal gyrus. These observations are in line with widely held expectations, namely that the discrimination of relative positions results in activation in the dorsal (occipito-parietal) visual pathway.

Comparison of the FD task with the control task revealed significant activations bilaterally in the inferior part of the lateral occipital gyri, the fusiform gyrus, as well as in the posterior superior parietal cortices, in the left intraparietal gyrus, and in the right middle frontal gyrus. The activations in the parietal cortex challenge the view that the processing and analysis of visual form information takes place only in these ventral areas, and indicate the involvement of parietal neuronal populations in the discrimination of visual form.

Figure 4.

The prefrontal fields in the posterior part of the middle frontal gyri, activated by FD (in yellow; x, y, z coordinates of its center of gravity: 40, 11, 32) and PD (in red; x, y, z coordinates of its center of gravity: -44, 20, 30). In fact, the field activated by PD was in the left prefrontal cortex, whereas the field activated in FD was in the right prefrontal cortex. In order to demonstrate the nonoverlapping locations of the two prefrontal fields, the PD field was mirrored across the midsagittal line onto the right hemisphere (left side in the figure).

Cortical fields activated in the selective form and position discrimination tasks

We found that rCBF was significantly higher bilaterally in the lateral occipital gyrus and in the right fusiform gyrus during FD compared to PD. The activations in the lateral occipital gyrus, according to fMRI retinotopic mapping studies in humans [Sereni et al., 1995; DeYoe et al., 1996], may correspond to the ventral V3/VP, to the ventral V4 and/or a region termed the lateral occipital complex (LO) [Malach et al., 1995]. The lateral parts of the activations were overlapping with the LO region [Grill-Spector et al., 1998]. The fusiform gyrus, close to the regions found in the present study, was also found activated in previous studies during face [Haxby et al., 1994; Courtney et al., 1996, 1997] and shape [Corbetta et al., 1991; Kanwisher et al., 1997] processing. The discrimination between different gratings during the form task has activated also a field in the right fusiform gyrus com-

pared to the PD task, in similar location to the region found during face and/or object processing [Haxby et al., 1994; Courtney et al., 1996, 1997]. This region of the fusiform gyrus was found to be activated also during recognition of large-field visual patterns [Roland and Gulyás, 1994]. The consistent activations of the lateral occipital and the fusiform gyri in FD and FPD versus control and FD versus PD were thus in accordance with the view that these regions contribute to the processing and analysis of visual forms and patterns.

Comparison of the PD task to the FD task revealed that there were no significant differences in occipital and parietal cortices between the two tasks. The fact that there was no significant rCBF increase in the dorsal occipitoparietal region during PD compared to FD implies that FD also led to the activation of this region. This is supported by the comparison of the FD task to control, which revealed significant activations, in addition to activated regions in the dorsal occipital cortex, the superior parietal, and the intraparietal cortical regions.

According to the hypothesis of independent and parallel dissociated visual processing channels, spatial vision would activate primarily the dorsal pathway and not the ventral one, while object vision would preferentially activate neuronal populations in the ventral pathway. Previous imaging studies have shown that selective attention to locations [Haxby et al., 1994] and spatial working memory tasks [Courtney et al., 1996] were associated with selective rCBF increases in dorsal occipital and superior parietal regions bilaterally. In line with these findings, in the present study activation during PD was also restricted to the dorsal pathway and no activation was observed in the ventral occipital and inferotemporal cortices.

As for the activations during object vision, the results of previous reports are equivocal. Some of the previous studies have found selective activation of the ventral pathway during face and shape matching to sample and WM tasks and no rCBF increase in the dorsal regions [Haxby et al., 1994; Courtney et al., 1996, 1997]. However, in a recent PET study, Faillenot et al. [1997] found that during nonspatial delayed matching to sample task, in addition to the activation of the ventral regions, there was also activation in the superior parietal and intraparietal cortex. Bilateral medial superior parietal activation was also reported when subjects judged whether a square was on the right or left of a line [Fink et al., 1997b].

(i) The simplest possible explanation of the activation of the parietal cortex in FD contrasted to control is that the subjects moved their eyes. Although EOG measurements have demonstrated infrequent and

small eye movement during FD, there were no significant eye movement differences between this task and the control task or the other tasks. (ii) Another possible hypothesis in this regard may be related to activations in different cortical regions in global versus local processing of visual information. Fink et al. [1996] showed that processing the global aspects of a figure activated the lingual gyrus, whereas processing the local aspects activated the inferior occipital gyrus. A shift of attention between the local and global aspects was correlated with temporal and parietal activation. In our case, global processing would correspond to PD, whereas local processing may correspond to FD. Since the contrast PD-FD did not show anything, the global-local aspect may, in our experiments, be of less importance. Neither did we find the activations reported in the Fink et al. [1997b] study in the FD-PD contrast. In the FPD, subjects may have switched from processing the global (position) to the local (gratings) within the central field of view, but this was not associated with any parietal or other rCBF differences in the FPD-PD and FPD-FD contrasts. This makes it unlikely that the parietal activation in the FD-control contrast and the lack of parietal differences in the PD-FD contrast were related to specific global or spatial processing in the FD. (iii) A further possibility, suggested by Kosslyn et al. [1995] and Faillenot et al. [1997], that local processing of an object, including shifts of attention to its different parts, requires spatial information and therefore would lead to activation in the occipito-parietal areas. We cannot exclude that a possible shift in processing of the different stimulus parts may have contributed to the parietal activation seen consistently when all tasks were contrasted to control. The same parietal regions were activated in FD, PD, and FPD when contrasted to control. This might indicate that a task-related common denominator would have caused this activation. One can also reason that all tasks in the present study consist of both local processing and binding of different object features. Simultaneous processing and binding of different object features is impaired after lesion in the parietal cortex [Friedman-Hill et al., 1995; Treisman, 1996].

The region, showing significantly higher rCBF during PD compared to FD, was found in the left frontal cortex, located on the rostral lip of the precentral sulcus. This region may correspond to the human frontal eye field. However, earlier PET and fMRI studies have suggested two different regions of the posterior part of the middle frontal gyrus as related to fixation and eye movements. The caudal part of the frontal convexity, identified as human FEF, has been

found activated during different types of eye movements, including saccadic (for review, see Paus, 1996) and pursuit eye movement [Petit et al., 1997]. However the exact position of the FEF in humans is still controversial. Two regions of the posterior part of the middle frontal gyrus seem related to fixation and eye movements and, possibly, visuo-spatial attention [Paus, 1996]. The present activation we discovered, corresponds to the medial and superior locations of FEF, as described by Paus [1996].

Since there was no difference in eye movement frequencies and amplitudes during the form and position discrimination tasks, as revealed by our post hoc investigation of these parameters, the reason for FEF activation during PD compared to FD may be related primarily to the increased demand in visuospatial attention in this task. Several previous imaging studies have shown bilateral activation of the presumed premotor cortex (FEF?) during both reflexive and controlled covert shifts of visual attention (for review, see Nobre et al., 1997). These studies revealed a right hemisphere dominance for spatial attention. The reason for left FEF and left pMFG activation during the PD compared to FD in the present study is not known. The comparison of the FD and PD tasks to control and the VOI analysis revealed that both FD and PD bilaterally activated similar regions of the posterior middle frontal gyrus and that the activation of the left pMFG during PD is significantly higher than in the FD task.

According to the model of compartmentalised working memory (WM) [Goldman-Rakic, 1995], different subregions of the dorsal prefrontal cortex (PFC) maintain on-line representation of different informational domains such as position and features of objects. This view is supported by single-cell electrophysiological studies on monkeys [Funahashi et al., 1990; Wilson, 1993], showing that neurons responsive during the performance of object working memory tasks are located more ventrally than those responsive during the performance of spatial working memory tasks. Since the two processing pathways of the monkey visual system have separate anatomical projections to prefrontal cortex [Jones and Powell, 1970; Barbas, 1988; Ungerleider et al., 1989; Petrides and Pandya, 1994; Schwartz and Goldman-Rakic, 1984; Cavada and Goldman-Rakic, 1989], there is also an anatomical basis for the dissociation of spatial and non-spatial WM functions in the PFC. The results of brain imaging studies aiming to test this hypothesis in human prefrontal cortex led to the conclusion that this type of functional specialization in the prefrontal cortex of humans does not correspond strictly to the monkey data and it depends on the processing re-

quirements of the tasks (for review, see McCarthy et al., 1996; Owen, 1997; Belger et al., 1998). Because in our case there was no visual working memory component in the tasks, the activations of different parts of the posterior part of the middle frontal gyri should be related to the differences in activations between FD and PD. We showed that PD was associated with a specific activation of the left middle frontal gyrus at a more lateral and inferior position than the right-sided activation in the FD. Thus form discrimination and position discrimination is associated with a differential activation of the lateral prefrontal cortex, which cannot be attributed to visual working memory.

Limited shift in activation between the FPD task and the selective form and position discrimination tasks

Comparison of the FPD task to the FD and PD tasks revealed no significant rCBF changes between the tasks. Concerning the prefrontal activations during the FPD task compared to control, it was found that mPFG was bilaterally active during this task. The prefrontal activations were in similar positions as in the FD and PD tasks, and they were similarly strong in both hemispheres. These results are consistent with the psychophysical data, showing no significant difference in the performance levels during FPD and the selective tasks and implicating that no additional cognitive component was elicited by this task.

Though no significant changes were revealed between the FPD task and the FD and PD tasks, during the FPD task the activity in the visual cortex was weaker when compared to the FD and PD tasks. Since the sensory processing during the FPD form and position discrimination trials is equal to the sensory processing during the FD and PD trials, respectively, the FPD task might be considered from this point of view as a task consisting of 50% FD and 50% PD trials. Thus the observed weaker activation in the extrastriate cortex in the FPD task compared to the corresponding visual cortical regions in the FD and PD tasks are in line with the recent imaging findings, demonstrating a correlation between the number of trials or presentation rate and rCBF increase in the sensory cortical areas [Price et al., 1996; Rees et al., 1997]. The fact that the FEF activation in FPD did not reach the significance level indicates a similar relationship between this region and the number of executed trials.

On the other hand, the fact that the individual contrasts between the FPD task and the FD and PD tasks did not display any significant difference is somewhat surprising on the basis of earlier observations regard-

ing the role of the superior parietal cortex in conjunction tasks—a typical example of which was our FPD task [Corbetta et al., 1995]. A possible interpretation of the absence of extra activation in the parietal cortex may be related to the fact that a shift between form processing and position processing took place within the central field of view.

Comparison of the present findings with those obtained in similar investigations

In contrast to our paradigm, earlier imaging studies aiming at the exploration of form and position processing pathways in the human brain used rather complex visual stimuli, often with strong positional markers. In their pioneering PET studies, Haxby et al. [1991, 1994] used a matching-to-sample task with identical visual stimuli and no working memory components to explore cortical regions. The stimuli were composite as they contained three images during one stimulus presentation and the subjects had to investigate three panels in order to solve the task. In the face-matching task the authors have found selective activations tasks in the fusiform gyri and in the prefrontal cortex, whereas the spatial vision tasks generated activations in the occipito-parietal cortex [Haxby et al., 1994; Tables II, III, V, VI]. Köhler et al. [1995] also used complex visual displays with three different objects on them and the subjects had to investigate either the display arrangement (object location task) or the individual constituents of the display (object identification task). By contrasting the task with each other (a similar operation to our FD-PD and PD-FD contrasts), they have shown positive contrast differences in the occipito-parietal cortex (right inferior parietal lobule) in the object location task and a set of occipito-temporal areas in the object identification task. Fink et al. [1997a] used a controlled noncueing nonblocked paradigm using the simplest possible geometrical figures (a line with a square at one end) in a restricted number of spatial arrangements (left or right of a fixation dot). In contrast to the aforementioned studies by Haxby et al. [1991, 1994] and Köhler et al. [1995], Fink et al. [1997a] have found strong activations in the parietal cortex during both object-based and space-based processes, and the inferior temporal cortex was more activated during space-based processes, as well.

In contrast to Haxby et al. [1991, 1994] and Köhler et al. [1995], our stimuli were simpler and contained only geometrical figures. In this regard, however, they were more complex than those found in the experiments of Fink et al. [1997b]. Under time-controlled stimulus presentation, one figure per stimulus was

shown at a time. The stimulus feature to be discriminated (the discriminanda: form or position) and the cue were identical—the stimulus itself. In agreement with the main findings of the previous two studies, we have also found activations in occipito-temporal regions during our form task, and occipito-parietal activations in our position task. However, in contrast to these studies, we have found activation in the parietal cortex during the form task, too. And this observation is in line with the findings of Fink et al. [1997] on activations in the parietal cortex during their object-based condition. On the other hand, in contrast to Fink et al. [1997b] regarding activations in the space-based task, we have not found activation in occipito-temporal cortex in our position task.

Another remarkable finding was that whereas contrasting the object task with the spatial task in the study by Köhler et al. [1995] produced activations in the occipito-temporal cortex, similar to the activations found by us in the FD-PD contrast, in our study the contrast between PD and FD does not result in activations in the parietal cortex. It resulted, instead, in activation in the left frontal eye field, indicating its possible role in position discrimination processes.

CONCLUSION

The present experiments aimed at the exploration of cortical regions participating in the processing and analysis of visual information related to form and position discrimination during visual tasks containing no visual memory components. The results clearly indicate the role of the occipito-parietal and an occipito-temporal visual areas in form and position discrimination. Whereas, in line with earlier findings, visual position discrimination activates occipito-parietal visual regions, form discrimination engage both occipito-temporal and occipito-parietal regions. As we can exclude the contribution of *specific attentional tuning*, visual memory components, eye movement changes between the various tasks, the latter finding indicates the possible role of parietal cortical regions in visual form perception. The two discrimination processes activated different regions in the prefrontal cortex, indicating that selective neuronal populations were responsible for form- and position-related visual discrimination processes in the prefrontal cortex.

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REFERENCES

- Andersen RA (1997): Multimodal integration for the representation of space in the posterior parietal cortex. *Philos Trans R Soc Lond B Biol Sci* 352:1421–1428.
- Ashbridge E, Cowey A, Wade D (1999): Does parietal cortex contribute to feature binding? *Neuropsychologia* 37:999–1004.
- Bergström M, Boethius J, Eriksson J, Greitz T, Ribbe T, Widén L (1981): Head fixation device for reproducible positron alignment in transmission CT and positron emission tomography. *J Comput Assist Tomogr* 5:136–141.
- Barbas H (1988): Anatomic organization of basoventral and mediodorsal visual recipient prefrontal regions in the rhesus monkey. *J Comp Neurol* 276:313–342.
- Belger A, Puce A, Krystal JH, Gore JC, Goldman-Rakic P, McCarthy G (1998): Dissociation of mnemonic and perceptual processes during spatial and nonspatial working memory using fMRI. *Hum Brain Mapp* 8:14–32.
- Boussaoud D, Ungerleider LG, Desimone R (1990): Pathways for motion analysis: cortical connections of the medial superior temporal and fundus of the superior temporal visual areas in the macaque. *J Comp Neurol* 296:462–495.
- Cavada C, Goldman-Rakic PS (1989): Posterior parietal cortex on rhesus monkey: II. Evidence for segregated corticocortical networks linking sensory and limbic areas with the frontal lobe. *J Comp Neurol* 287:422–445.
- Colby CL, Goldberg ME (1999): Space and attention in parietal cortex. *Ann Rev Neurosci* 22:319–349.
- Corbetta M, Miezin FM, Dobmeyer S, Shulman GL, Petersen SE (1991): Selective and divided attention during visual discriminations of shape, color, and speed: functional anatomy by positron emission tomography. *J Neurosci* 11:2383–2402.
- Corbetta M, Shulman GL, Miezin FM, Petersen SE (1995): Superior parietal cortex activation during spatial attention shifts and visual feature conjunction. *Science* 270:802–805.
- Courtney SM, Ungerleider LG, Keil K, Haxby JV (1996): Object and spatial visual working memory activate separate neural systems in human cortex. *Cereb Cortex* 6:39–49.
- Courtney SM, Ungerleider LG, Kell K, Haxby JV (1997): Transient and sustained activity in a distributed neural system for human working memory. *Nature* 386:608–611.
- Desimone R, Ungerleider LG (1989): Neural mechanisms of visual processing in monkeys. In: Goodglass H, Dumasio AR, editors. *Handbook of neuropsychology*. Amsterdam: Elsevier, p 267–300.
- DeYoe EA, Carman GJ, Bandettini P, Glickman S, Wieser J, Cox R, Miller D, Neitz J (1996): Mapping striate and extrastriate visual areas in human cerebral cortex. *Proc Natl Acad Sci USA* 93:2382–2386.
- Faillenot I, Toni I, Decety J, Gregoire MC, Jeannerod M (1997): Visual pathways for object-oriented action and object recognition: functional anatomy with PET. *Cereb Cortex* 7:77–85.
- Felleman DJ, Van Essen DC (1991): Distributed hierarchical processing in the primate cerebral cortex. *Cereb Cortex* 1:1–47.

- Fink GR, Marshall JC, Halligan PW, Frith CD, Frakowiak RSJ, Dolan RJ (1997a): Hemispheric specialization for global and local processing: the effect of stimulus category. *Proc R Soc Lond B* 264:487–494.
- Fink GR, Dolan RJ, Halligan PW, Marshall JC, Frith CD (1997b): Space-based and object-based visual attention: shared and specific neural domains. *Brain* 120:2013–2028.
- Friedman-Hill SR, Robertson LC, Treisman A (1995): Parietal contributions to visual feature binding: evidence from a patient with bilateral lesions. *Science* 269:853–855.
- Funahashi S, Bruce CJ, Goldman-Rakic PS (1990): Visuospatial coding of primate prefrontal neurons revealed by oculomotor paradigms. *J Neurophysiol* 61:1–19.
- Goldman-Rakic PS (1995): Architecture of the prefrontal cortex and the central executive. *Ann NY Acad Sci* 769:71–83.
- Goodale MA, Meenan JP, Bulthoff HH, Nicolle DA, Murphy KJ, Racicot CI (1994): Separate neural pathways for the visual analysis of object shape in perception and prehension. *Curr Biol* 4:604–610.
- Goodale MA, Milner AD, Jakobson LS, Carey DP (1991): A neurological dissociation between perceiving objects and grasping them. *Nature* 349:154–156.
- Goodale MA, Milner AD (1992): Selective visual pathways for perception and action. *Trends Neurosci* 15:20–25.
- Greitz T, Bergström M, Boëthius J, Kingsley D, Ribbet T (1980): Head fixation device for integration of radiodiagnostic and radiotherapeutic procedures. *Neuroradiology* 19:1–6.
- Grill-Spector K, Kushnir T, Hendler T, Edelman S, Itzhak Y, Malach R (1998): A sequence of object-processing stages revealed by fMRI in the human occipital lobe. *Hum Brain Mapp* 6:316–328.
- Gulyás B, Roland PE (1994): Processing and analysis of form, colour and binocular disparity in the human brain: functional anatomy by positron emission tomography. *Eur J Neurosci* 6:1811–1828.
- Gulyás B (1997): Functional organisation of human visual cortical areas. In: Rockland KS, Kaas JH, Peters A, editors. *Cerebral cortex, volume 12: extrastriate cortex in primates*. New York: Plenum Press. p 743–775.
- Gulyás B, Kovács G, Vidnyánszky Z, Cowey A, Heywood CA, Popplewell DA, Roland PE (1998): “What” activation in the “where” pathway. *Neuroimage* 7:S333.
- Haxby JV, Grady CL, Horwitz B, Ungerleider LG, Mishkin M, Carson RE, Herscovitch P, Schapiro MB, Rapoport SI (1991): Dissociation of object and spatial visual processing pathways in human extrastriate cortex. *Proc Natl Acad Sci USA* 88:1621–1625.
- Haxby JV, Horwitz B, Ungerleider LG, Maisog JM, Pietrini P, Grady CL (1994): The functional organization of human extrastriate cortex: a PET-rCBF study of selective attention to faces and locations. *J Neurosci* 14:6336–6353.
- Holmes AP, Blair RC, Watson JDG, Ford I (1996): Nonparametric analysis of statistic images from functional mapping experiments. *J Cereb Blood Flow Metab* 16:7–22.
- Jones EG, Powell TPS (1970): An anatomical study of converging sensory pathways within the cerebral cortex of the monkey. *Brain* 93:793–820.
- Kanwisher N, Woods RP, Iacoboni M, Mazziotta JC (1997): A locus in human extrastriate cortex for visual shape analysis. *J Cogn Neurosci* 9:133–142.
- Kanwisher N, Tong F, Nakayama K (1998): The effect of face inversion on the human fusiform area. *Cognition* 68:B1–B11.
- Kanwisher N, Tanlet D, Harris A (1999): The fusiform face area is selective for faces not animals. *Neuroreport* 18:183–187.
- Kosslyn SM, Alpert NM, Thompson WL (1995): Identifying objects at different levels of hierarchy: a PET study. *Hum Brain Mapp* 3:107–132.
- Kohler S, Kapur S, Moscovitch M, Winocur G, Houle S (1995): Dissociation of pathways for object and spatial vision: a PET study in humans. *Neuroreport* 6:1865–1868.
- Ledberg A, Åkerman S, Roland PE (1998): Estimation of the probability of 3D clusters in functional brain images. *J Neuroimage*, in press.
- Malach R, Reppas JB, Benson RR, Kwong KK, Jiang H, Kennedy WA, Ledden PJ, Brady TJ, Rosen BR, Tootell RB (1995): Object-related activity revealed by functional magnetic resonance imaging in human occipital cortex. *Proc Natl Acad Sci USA* 29: 8135–8139.
- McCarthy G, Puce A, Constable RT, Krystal JH, Gore JC, Goldman-Rakic P (1996): Activation of human prefrontal cortex during spatial and nonspatial working memory tasks measured by functional MRI. *Cereb Cortex* 6:600–611.
- Mesulam MM (1999): Spatial attention and neglect: parietal, frontal and cingulate contributions to the mental representation and attentional targeting of salient extrapersonal events. *Philos Trans R Soc Lond B Biol Sci* 354:1325–1346.
- Meyer E (1989): Simultaneous correction for tracer arrival delay and dispersion in CBF measurements by the H₂¹⁵O autoradiographic method and dynamic PET. *J Nucl Med* 30:1069–1078.
- Morel A, Bullier J (1990): Anatomical segregation of two cortical visual pathways in the macaque monkey. *Vis Neurosci* 4:555–578.
- Nobre AC, Sebestyen GN, Gitelman DR, Mesulam MM, Frackowiak RSJ, Frith CD (1997): Functional localization of the system for visuospatial attention using positron emission tomography. *Brain* 120:515–533.
- Owen AM (1997): The functional organization of working memory processes within human lateral frontal cortex: the contribution of functional neuroimaging. *EJN* 9:1329–1339.
- Oxford English Dictionary. 1971. Oxford: Oxford University Press.
- Paus T (1996): Location and function of the human frontal eye-field: a selective review. *Neuropsychologia* 34:475–483.
- Petit L, Clark VP, Ingeholm J, Haxby JV (1997): Dissociation of saccade-related and pursuit-related activation in human frontal eye fields as revealed by fMRI. *J Neurophysiol* 77:3386–3390.
- Petrides M, Pandya DN (1994): Comparative architectonic analysis of the human and the macaque frontal cortex. In: Boller F, Grafman J, editors. *Handbook of neuropsychology*, Vol. 9. Amsterdam: Elsevier, p 17–58.
- Price CJ, Moore CJ, Frackowiak RSJ (1996): The effect of varying stimulus rate and duration on brain activity during reading. *Neuroimage* 3:40–52.
- Rees G, Frackowiak R, Frith C (1997): Two modulatory effects of attention that mediate object categorization in human cortex. *Science* 275:835–838.
- Rizzolatti G, Fogassi L, Gallese V (1997): Parietal cortex: from sight to action. *Curr Opin Neurobiol* 7:562–567.
- Roland PE, Graufelds CJ, Wählin J, Ingelman L, Anderson M, Ledberg A, Pedersen J, Åkerman S, Dabringhaus A, Zilles K (1994): Human brain atlas: for high-resolution functional and anatomical mapping. *Hum Brain Mapp* 1:173–184.
- Roland PE, Gulyás B (1994): Visual memory, visual imagery, and visual recognition of large field patterns by the human brain: Functional anatomy by positron emission tomography. *Cereb Cortex* 1:79–93.
- Sakata H, Taira M, Kusunoki M, Murata A, Tanaka Y (1997): The TINS lecture: The parietal association cortex in depth perception and visual control of hand action. *Trends Neurosci* 20:350–357.

-
- Sakata H, Taira M, Kusunoki M, Murata A, Tanaka Y, Tsutsui K (1998): Neural coding of 3D features of objects for hand action in the parietal cortex of the monkey. *Philos Trans R Soc Lond B Biol Sci* 353:1363–1373.
- Schwartz ML, Goldman-Rakic PS (1984): Callosal and intrahemispheric connectivity of the prefrontal association cortex in the rhesus monkey: relation between intraparietal and principal sulcal cortex. *J Comp Neurol* 226:403–420.
- Sereno MI, Dale AM, Reppas JB, Kwong KK, Belliveau JW, Brady TJ, Tootell RBH (1995): Borders of multiple visual areas in humans revealed by functional magnetic resonance imaging. *Science* 268:889–893.
- Sereno AB, Maunsell JH (1998): Shape selectivity in primate lateral intraparietal cortex. *Nature* 395:500–503.
- Shen L, Hu X, Yacoub E, Ugurbil K (1999): Neural correlates of visual form and visual spatial processing. *Hum Brain Mapp* 8:60–71.
- Snyder LH, Grieve KL, Brothie P, Andersen RA (1998): Separate body- and world-referenced representations of visual space in parietal cortex. *Nature* 394:887–891.
- Treisman A (1996): The binding problem. *Curr Opin Neurobiol* 6:171–178.
- Treisman A (1998): Feature binding, attention and object perception. *Philos Trans R Soc Lond B Biol Sci* 353:1295–1306.
- Ungerleider LG, Haxby JV (1994): “What” and “where” in the human brain. *Curr Opin Neurobiol* 4:157–165.
- Ungerleider LG, Mishkin M (1982): Two cortical visual systems. In: Ingle DJ, Goodale MA, Mansfield RJW, editors. *Analysis of visual behavior*. Cambridge, MA: MIT Press, p 549–586.
- Ungerleider LG, Gaffan D, Pelak VS (1989): Projections from inferior temporal cortex to prefrontal cortex via the uncinate fascicle in rhesus monkeys. *Exp Brain Res* 76:473–484.
- Ungerleider LG, Courtney SM, Haxby JV (1998): A neural system for human visual working memory. *Proc Natl Acad Sci USA* 95:883–890.
- Wilson FAW, Scalaidhe SPO, Goldman-Rakic PS (1993): Dissociation of object and spatial processing domains in primate prefrontal cortex. *Science* 260:1955–1958.
- Wojciulik E, Kanwisher N (1999): The generality of parietal involvement in visual attention. *Neuron* 23:747–764.
- Woods RP, Cherry SR, Mazziotta JC (1992): Rapid automated algorithm for aligning and reslicing PET images. *J Comput Assist Tomogr* 16:620–633.
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