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THE ROYAL SOCIETY

The role of prefrontal cortex in working memory: examining the contents of consciousness

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Working memory enables us to hold in our 'mind's eye' the contents of our conscious awareness, even in the absence of sensory input, by maintaining an active representation of information for a brief period of time. In this review we consider the functional organization of the prefrontal cortex and its role in this cognitive process. First, we present evidence from brain-imaging studies that prefrontal cortex shows sustained activity during the delay period of visual working memory tasks, indicating that this cortex maintains on-line representations of stimuli after they are removed from view. We then present evidence for domain specificity within frontal cortex based on the type of information, with object working memory mediated by more ventral frontal regions and spatial working memory mediated by more dorsal frontal regions. We also propose that a second dimension for domain specificity within prefrontal cortex might exist for object working memory on the basis of the type of representation, with analytic representations maintained preferentially in the left hemisphere and image-based representations maintained preferentially in the right hemisphere. Furthermore, we discuss the possibility that there are prefrontal areas brought into play during the monitoring and manipulation of information in working memory in addition to those engaged during the maintenance of this information. Finally, we consider the relationship of prefrontal areas important for working memory, both to posterior visual processing areas and to prefrontal areas associated with long-term memory.

Keywords: functional brain imaging; human cognition; functional magnetic resonance imaging; positron emission tomography; visual processing

1. INTRODUCTION

Consciousness: the state of being 'aware of one's own existence, sensations, and thoughts and of one's environment' or of being 'capable of thought, will, or perception'. 'The component of waking awareness perceptible by an individual at a given instant'.

(*Webster's Dictionary*)

Working memory is the process of maintaining a limited amount of information in an active representation for a brief period of time so that it is available for use. There-fore, by definition, working memory includes those processes that enable us to hold in our 'mind's eye' the contents of our conscious awareness, even in the absence of sensory input. Thus, the study of working memory provides a framework for investigating the neural system underlying our awareness of stimuli, memories and knowledge that are no longer tied to perceptual events.

Although the neural system responsible for working memory is known to include a large number of brain regions, there is abundant evidence from neurophysiological and lesion studies in monkeys that prefrontal cortex is a critical component (Fuster 1990; Goldman-Rakic 1990). Recent brain-imaging studies, using positron emission tomography (PET) and functional magnetic resonance imaging (fMRI), have also implicated the human prefrontal cortex in working memory (see, for example, Jonides *et al.* 1993; Petrides *et al.* 1993*b*; McCarthy *et al.* 1994; D'Esposito *et al.* 1995; Fiez *et al.* 1996; Owen *et al.* 1996; Cohen *et al.* 1997; Courtney *et al.* 1997*a*, 1998). However, there remain questions and some dispute about the functional organization of the human prefrontal cortex and its exact role in working memory.

Here we summarize the evidence for working memory-related activity within human prefrontal cortex. We then present evidence for domain specificity within frontal cortex for object working memory as opposed to spatial visual working memory. We also review evidence suggesting an additional dimension of domain specificity for object working memory based on whether the type of representation is analytic or image-like. In addition, we discuss evidence suggesting a third dimension for the specialization of working memory function in prefrontal cortex that distinguishes regions important for the maintenance of the contents held in working memory from regions important for the manipulation of those contents. Finally, we consider the relationship of prefrontal areas important for working memory, both to posterior visual processing areas and to prefrontal areas associated with long-term memory.

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2. TRANSIENT VERSUS SUSTAINED ACTIVITY: IMPLICATIONS FOR PREFRONTAL ORGANIZATION

In monkeys, working memory has typically been studied in either delayed response or delayed match-to-sample tasks. In both types of task, the monkey is given a brief cue at the start of the trial, which it must maintain in memory during a delay of several seconds. At the end of the delay, the monkey is required to make a choice or differential response based on the previous cue. Many studies have found cells in prefrontal cortex whose response to the initial cue is sustained at some level during the delay period (for reviews, see Goldman-Rakic (1990) and Fuster (1995)). Thus, the memory of the cue seems to endure by maintaining the activity of the cells that represent the cue. Depending on the type of cue, cells with this delay activity have also been found in areas outside the prefrontal cortex, such as the inferior temporal cortex for visual pattern or colour cues, and the posterior parietal cortex for spatial cues. However, the sustained activity in these posterior visual processing areas is greatly diminished and made less stimulus-specific by cooling the prefrontal cortex, indicating that sustained activity in these posterior areas might be due to feedback projections from prefrontal cortex (Fuster *et al.* 1985; Goldman-Rakic & Chafee 1994).

To determine whether human prefrontal cortex has a role in working memory similar to that demonstrated in the monkey, it is necessary in brain-imaging studies to distinguish transient, perception-related activity from sustained, memory-related activity. However, it is difficult to make this distinction with PET because the technique integrates activity over 20–60 s, whereas the time-scale of events in a working-memory task is typically only a few seconds. Our first approach to this problem was to design a task in which the delay between the presentation of a stimulus to be held in working memory and the test stimulus was varied parametrically (Haxby *et al.* 1995). The stimuli were pictures of faces. We predicted that different delay intervals would have differential effects on areas principally involved in the perceptual aspects of the task compared with areas principally involved in the mnemonic aspects. This was because, with shorter delay intervals, a greater proportion of time would be spent viewing pictures of faces, whereas with longer delay intervals, a smaller proportion of time would be spent viewing faces but a greater proportion of time would be spent holding a face in memory. We therefore predicted that areas principally involved in perceptual analysis would show increased activity relative to a sensorimotor control task, but that the size of the increase would diminish with increasing delays. In contrast, areas principally involved in working memory would show relatively constant levels of increased activity as a function of the delay interval. The latter prediction was based on the fact that, in the monkey, areas that participate in working memory contain neurons that respond both to stimulus presentation and during memory delays and therefore should be active throughout the face-memory task, regardless of the delay length.

We found that areas showing a significant negative correlation between activity increases and delay were restricted to the ventral occipitotemporal cortex, in areas essentially identical to those identified in studies of face perception (see, for example, Haxby *et al.* 1991, 1994; Puce *et al.* 1995; Clark *et al.* 1996; Kanwisher *et al.* 1997). Thus, these areas are mainly active during the presentation of stimuli, not during memory delays. They are therefore likely to be involved more in the perceptual analysis of faces during the task than in the working-memory component *per se*. In contrast, areas showing a more constant activity increase across all delays were in the prefrontal cortex, indicating that they are active during memory delays as well as during stimulus presentation. Thus, prefrontal regions probably have a more important role in the maintenance of a representation during working memory. Interestingly, hemispheric differences were also observed, with the right prefrontal cortex being more active during short memory delays and the left prefrontal cortex most active during longer delays (see § 3b).

More recently, we have taken advantage of the temporal resolution afforded by fMRI to reinvestigate the functional roles of posterior processing and prefrontal areas in face working memory (Courtney *et al.* 1997a). Multiple regression analysis enabled us to decompose activation in a face working-memory task into three components: (i) a transient, non-selective response to visual stimuli; (ii) a transient, selective response to faces; and (iii) sustained activity over memory delays. Posteriorly, in ventral occipital areas, we found mostly a transient, non-selective response to visual stimuli, which did not differ between faces and non-face control stimuli. More anteriorly, in ventral temporal regions, we found a more selective response to faces than to non-faces, and also a small but significant sustained response over memory delay intervals. Finally, three distinct prefrontal regions were identified, all of which showed greater levels of sustained activity over memory delays, including one in posterior mid-frontal cortex (Brodmann area (BA) 9/44), another in anterior mid-frontal cortex (BA 46), and a third in inferior frontal cortex and the anterior portion of the insula (BA 45/47). These results therefore provide a direct demonstration of memory-related sustained activity in human prefrontal cortex (see also Cohen *et al.* 1997). On the basis of work in the monkey, we had expected sustained activity in the more ventral portion of prefrontal cortex, but had not expected three anatomically distinct regions.

The results also showed that there was a systematic progression in the relative strengths of perception- and memory-related activity from occipital to temporal and through multiple prefrontal areas, indicating that this distributed neural system for object working memory is organized hierarchically (figure 1). In occipitotemporal areas, there was a progression from a mainly non-selective perceptual response in posterior occipital cortex to face-selective perceptual activity in lateral inferior occipital and middle fusiform regions. This progression is consistent with the well-established hierarchical organization of visual cortex in monkeys (Felleman & Van Essen 1991). Although the three prefrontal areas all responded to the presentation of faces, these areas demonstrated different relative amounts of activity related to the presentation of visual stimuli compared with the activity related to the memory delay period. The posterior mid-frontal
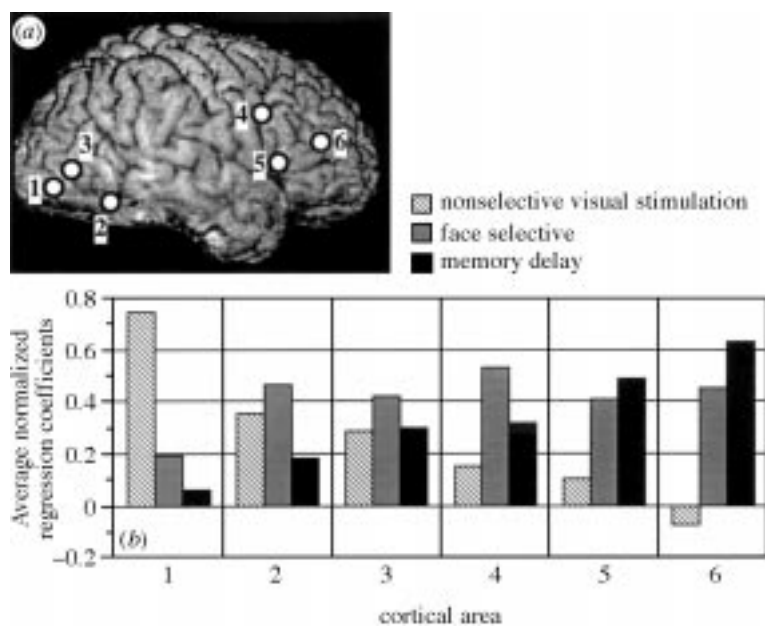
Figure 1. Varying degrees of transient and sustained activity in regions comprising a distributed neural system for face working memory. Averaged locations across subjects of the regions of activation are shown in lateral projection on a human brain (white circles). The regions, numbered in order of decreasing relative amounts of transient activity related to non-selective visual stimulation and increasing relative amounts of sustained activity related to the memory delay, are: (1) posterior lingual and fusiform cortex (BA 18); (2) mid-to-anterior fusiform cortex (BA 37); (3) inferior occipital sulcus (BA 18/19); (4) posterior mid-frontal cortex (BA 9/44); (5) inferior frontal cortex and anterior insula (BA 45/47); and (6) anterior mid-frontal cortex (BA 46). The graph shows the three normalized regression coefficients for each region, averaged across subjects and hemispheres, demonstrating the gradual shift in the relative contributions of each task component to the activity within this distributed neural system. (Adapted from Courtney *et al*. (1997*a*).)

region had the greatest transient response to visual stimuli and the smallest amount of sustained activity during the memory delay; the inferior frontal region had intermediate amounts of perception- and memory-related activity; and the anterior mid-frontal region had the smallest perception-related response and the greatest amount of sustained delay activity. This progression suggests that these prefrontal regions, like those in occipitotemporal cortex, might also be organized hierarchically.

What roles might these prefrontal regions have in working memory? Although we do not yet have the answer to this question, results from other imaging studies might provide some clues. The posterior mid-frontal region, which had the greatest non-selective response to visual stimuli, has been activated during a wide range of working-memory tasks, including verbal, spatial and object (see, for example, Haxby *et al*. 1995; Courtney *et al*. 1996*b*, 1997*a*; Fiez *et al*. 1996; McCarthy *et al*. 1996; Smith *et al*. 1996; Cohen *et al*. 1997). This region therefore seems to contribute to working-memory processes independent of the type of information. The inferior prefrontal region is close to a ventrolateral prefrontal area identified by Petrides and colleagues (Petrides *et al*. 1993*b*; Owen *et al*. 1996) which, they propose, is involved in the encoding and retrieval of information held in posterior cortical areas. Verbal semantic functions have also been associated with this inferior frontal area (McCarthy *et al*. 1993; Demb *et al*. 1995), suggesting that its activation in the present study might also reflect verbal processing of the face stimuli; however, it is unlikely that this could account for our findings because we often observe that the activation in this region is bilateral or even lateralized to the right hemisphere (Haxby *et al*. 1995; Courtney *et al*. 1996*b*, 1997*a*). The anterior mid-frontal region, which showed the greatest activation during working-memory delays, is similar to an area activated in a recent study by Schacter *et al*. (1997). In their study, this anterior prefrontal area had a longer response latency than other prefrontal areas during performance of an episodic long-term memory

task. A similar anterior prefrontal area was activated in a dual-task paradigm by D'Esposito *et al*. (1995). Taken together, these results suggest that this anterior mid-frontal area might be responsible for 'executive' functions, such as rehearsal and monitoring, that occur after the disappearance of the stimulus (see § 3*c*).

3. DOMAIN SPECIFICITY IN HUMAN FRONTAL CORTEX

(a) *Segregation for object versus spatial processing*

Goldman-Rakic and colleagues (Wilson *et al*. 1993; O'Scalaidhe *et al*. 1997) have shown that, in monkeys, the dorsal prefrontal areas that are reciprocally connected with parietal visual areas exhibit sustained delay activity that is primarily related to spatial information. In contrast, they found that the ventral prefrontal areas that are reciprocally connected with temporal visual areas exhibit sustained delay activity that is primarily related to information about pattern, colour, object and face. On the basis of these results, Goldman-Rakic (1995) proposed that the segregation of spatial and object information processing between parietal and temporal cortices, respectively, is maintained within the prefrontal cortex for working memory. Thus, dorsal prefrontal cortex, specifically cortex within the principal sulcus (BA 46), is proposed to be specialized for spatial working memory, whereas ventral prefrontal cortex, specifically the inferior convexity (BA 12), is proposed to be specialized for object working memory.

Does this dorsal versus ventral model of domain specificity for object versus spatial working memory apply to the human prefrontal cortex as well? Much of the human imaging data so far has been inconclusive, leading to a controversy in the literature. Owen (1997) and D'Esposito *et al*. (1988) have argued that human prefrontal areas are not segregated according to the type of information held in working memory. Instead, they propose that prefrontal areas are functionally organized according to the level of processing. We shall address this possibility below. Their main argument against domain specificity based on the

type of information comes from meta-analyses that show that spatial, object, and verbal working-memory tasks all seem to activate BA 9/46 in the mid-dorsolateral prefrontal cortex as well as BA 45/47 in inferior (ventrolateral) prefrontal cortex, the same general regions associated with, respectively, spatial and object working memory in monkeys.

Meta-analyses of the existing literature, however, might fail to distinguish between activation of different strengths in prefrontal regions because they lump together studies in which the comparison task varies widely. This is an important consideration because a recent physiological study by Rao *et al.* (1997) has provided evidence in monkeys that, whereas different parts of lateral prefrontal cortex might emphasize processing of different kinds of information, the segregation of processing between information types might not be absolute. Rao *et al.* demonstrated that during a task that required the maintenance of both object and spatial information, more than half of the prefrontal neurons with delay activity showed both object and spatial tuning. If there is, indeed, a great deal of integration of spatial and object information within prefrontal cortex, as Rao *et al.* suggest, one would expect both dorsal and ventral prefrontal regions to be 'activated' when compared with a low-level control task. A dissociation based on the relative strengths of activation during working memory for different information types might then be demonstrated only by contrasting, in a single study, activation during carefully matched working-memory tasks. Comparison of tasks that are not matched for difficulty and memory load can give misleading results because these factors influence both the amplitude and spatial extent of prefrontal activation during working-memory tasks (Cohen *et al.* 1997).

These meta-analyses have also assumed that any segregation between spatial and object working memory would be between BA 9/46 and BA 45/47, respectively, on the basis of areas that have been described in the monkey. (Human BA 47 is assumed to be the homologue of monkey BA 12; see Petrides & Pandya 1994.) Our results and those of others, however, indicate that the performance of spatial working-memory tasks activates frontal areas in addition to those in BA 9/46. In particular, our studies indicate that the region specialized for spatial working memory in humans is in the superior frontal sulcus rather than in BA 9/46, as is commonly assumed.

Activation in the superior frontal sulcus has been observed consistently in many studies of spatial working memory (Jonides *et al.* 1993; Baker *et al.* 1996; Courtney *et al.* 1996b, 1998; Mellet *et al.* 1996; Owen *et al.* 1996; Petit *et al.* 1996; Smith *et al.* 1996), but has generally been dismissed because the activated region was assumed to be located within premotor cortex or the frontal eye field (FEF), and thus related to either hand or eye movements (but see Courtney *et al.* 1996b, 1998; Mellet *et al.* 1996; Petit *et al.* 1996). Indeed, the spatial resolution of PET makes it difficult to determine whether spatial working-memory activation occurs within regions outside those related to movement. However, even without the explicit dissociation of activation related to hand movement, eye movement and working memory, there was still a suggestion from several PET studies that the superior frontal

sulcus activation could not be solely attributable to motor control. For example, spatial working-memory studies conducted by Jonides *et al.* (1993) and Smith *et al.* (1995) required fixation and the same motor response for both the memory and control tasks, yet memory-related activation was still observed near the superior frontal sulcus. A spatial imagery task by Mellet *et al.* (1996) also activated this region in the complete absence of eye and hand movements. Finally, we found the superior frontal sulcus to be preferentially activated during a spatial as opposed to a face working-memory task, even though the tasks used identical stimuli and were designed to have identical hand and eye movements.

In our PET study, subjects had to retain either the identity or the location of three faces presented sequentially in three different locations on the screen (Courtney *et al.* 1996b). Both the spatial location and face identity tasks used the same stimuli. At 500 ms after the presentation of the third face, a test stimulus was shown. The test stimulus was a face in a variable location. For the face working-memory task, the subject indicated whether that face was in the memory set, regardless of the location in which it was initially presented. For the spatial working-memory task, the subject indicated whether the location of the test stimulus was one of the locations in the memory set, regardless of the identities of the faces used to mark those locations.

Direct comparison of activity during performance of the two tasks revealed differences between ventral and dorsal frontal cortices. The face working-memory task showed greater activation in the right inferior and mid-prefrontal cortex (BA 45/47 and 9/44/46). The spatial working-memory task differentially activated an area located in the superior frontal sulcus. The results therefore demonstrated that working memory for different types of information preferentially activate separate frontal regions. Working memory for objects (for example, for faces) activates predominantly ventral frontal cortex, whereas working memory for spatial locations (for example, the spatial locations of faces) activates predominantly dorsal frontal cortex.

Despite this convergence of evidence, however, an explicit demonstration of the role of the superior frontal sulcus in spatial working memory was needed. Two questions remained. First, was the activity in the superior frontal sulcus related to spatial perception rather than working memory? The PET studies mentioned above could not distinguish between transient, perception-related activity and sustained, memory-related activity (Jonides *et al.* 1993; Smith *et al.* 1995; Courtney *et al.* 1996b). Second, was the activity related to oculomotor control, i.e. was the activity in the FEF or in an area distinct from it? In the monkey, the area specialized for spatial working memory is located just anterior to the FEF. We therefore predicted that in humans, if a spatial working-memory area did exist, it would also lie just anterior to the FEF.

Recently, we have taken advantage of the temporal and spatial resolution of fMRI to test this prediction and, further, to distinguish between transient, perception-related and sustained, memory-related activity. By comparing activation evoked during tasks involving spatial working memory, face working memory and eye
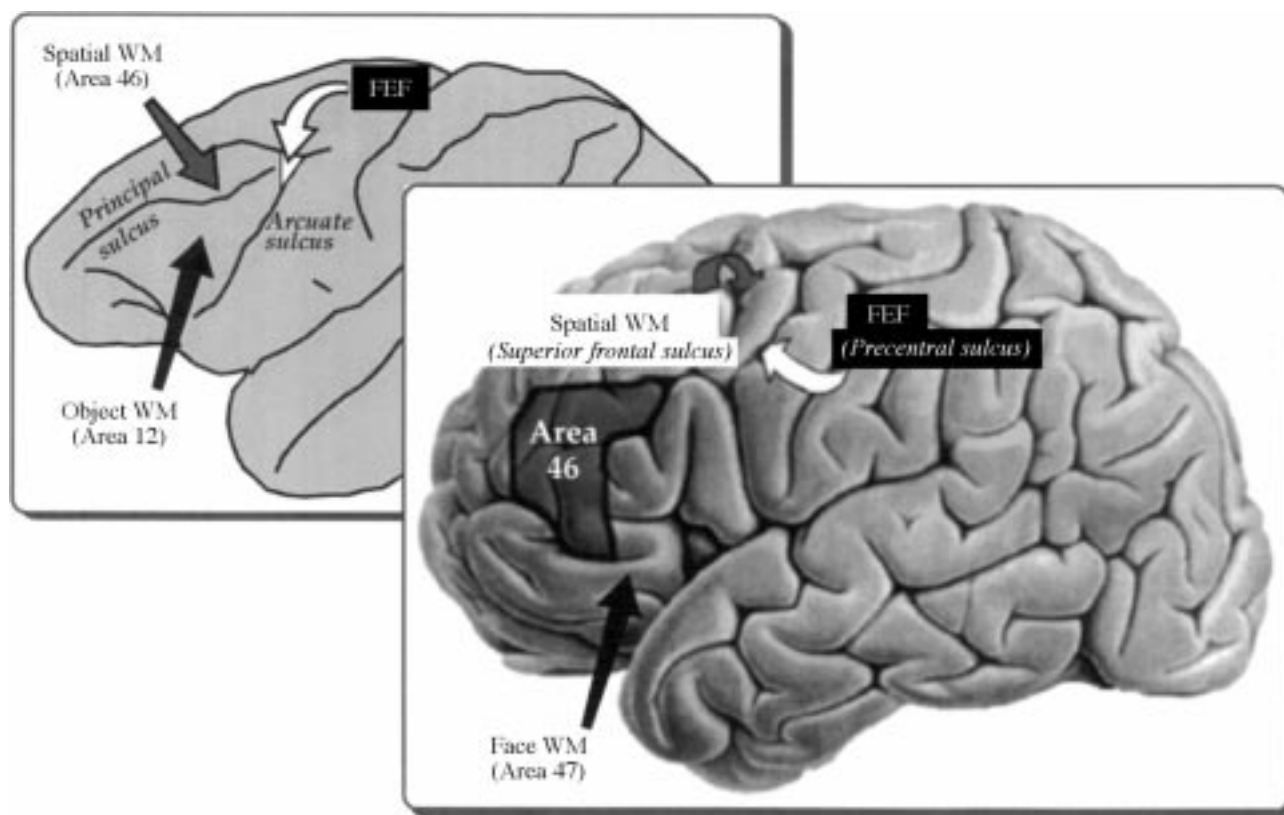
Figure 2. Locations of areas specialized for spatial working memory in monkeys and humans relative both to the frontal eye field (FEF) and to areas specialized for object working memory. In monkeys, the area specialized for spatial working memory is located in the principal sulcus (BA 46) and the FEF is located just posterior to it in the arcuate sulcus. In humans, the area specialized for spatial working memory is located within the superior frontal sulcus, and the FEF is located just posterior to it in the precentral sulcus. Thus, although the two areas occupy a more posterior and dorsal location in humans compared with monkeys, the topological relationship between them is the same. In both monkeys and humans, the area specialized for object (or face) working memory is located in a more ventral portion of prefrontal cortex.

movements, we found that the activity in the superior frontal sulcus was (i) sustained over spatial working-memory delays; (ii) selective for spatial relative to face working memory; and (iii) distinct from activity in the FEF related to oculomotor control (Courtney *et al.* 1998). The activation was also not related to the hand movements during the task, as this component was identical in the spatial and face working-memory tasks. These results therefore provide evidence that areas in human frontal cortex, like posterior visual perceptual areas, are functionally organized according to the type of information being processed. As predicted, in humans, as in monkeys, the area specialized for spatial working memory lies just anterior to the FEF. In monkeys, the spatial working-memory area is within the principal sulcus and the FEF is just posterior to it within the arcuate sulcus. In humans, the spatial working-memory area is within the superior frontal sulcus and the FEF is just posterior to it within the precentral sulcus (see also Paus 1996; Petit *et al.* 1997; Luna *et al.* 1998). Thus, in humans, compared with monkeys, both areas occupy a more dorsal and posterior location, although the topological relationship between them has been conserved (figure 2).

In summary, in humans, as in monkeys, object working memory is mediated by more ventral lateral frontal cortex. Although spatial working memory in both

monkeys and humans is mediated by more dorsal lateral frontal cortex, the region in humans is in the superior frontal sulcus and therefore occupies a more dorsal and posterior location. The functional segregation of these dorsal and ventral frontal areas might not be absolute, however. The evidence for segregation came from a comparison of the relative amounts of sustained activity during spatial and face working-memory tasks rather than from a demonstration of the presence or absence of activity. Had we simply compared activity during each working-memory task with activity during a low-level control task, we would not have found evidence for segregation. This partly explains the lack of evidence for dorsal–ventral segregation for object and spatial working memory in meta-analyses reported so far. In addition, the meta-analyses focused on a comparison between area 9/46 dorsally and area 45/47 ventrally. In fact, the dorsal area in the superior frontal sulcus was not considered. Had the meta-analyses included this area, some segregation might have been apparent.

(b) *Segregation for analytic versus image-based processing*

To our knowledge, there are only three other studies (Smith *et al.* 1995; Baker *et al.* 1996; McCarthy *et al.* 1996) that have directly contrasted activation during object and

spatial working-memory tasks. In all three, the objects were non-meaningful shapes. Two used match-to-sample tasks for spatial location (Smith *et al.* 1995; McCarthy *et al.* 1996), whereas the third used delayed response (Baker *et al.* 1996). All three studies reported greater activation in the right prefrontal cortex during the spatial task, and two out of the three (Smith *et al.* 1995; Baker *et al.* 1996) reported greater activation in the left prefrontal cortex during the object task. Thus, these studies suggested that domain specificity for spatial and object working memory is primarily a hemispheric laterality effect, rather than a dorsal–ventral distinction. We shall first consider the evidence supporting right hemispheric dominance for spatial working memory, and then we shall discuss the evidence supporting left hemispheric dominance for object working memory.

The evidence supporting right hemispheric dominance for spatial working memory is based, in all three studies, on activation largely in mid- and inferior prefrontal cortex (BA 46, 44, 47). These results contrast with our own, in which there was no evidence for laterality effects in these prefrontal regions during spatial working memory. In addition, as we have already discussed, these areas in humans are not specialized for spatial working memory. Activation in the area that is specialized for spatial working memory, the superior frontal sulcus, was directly compared during spatial and object working memory in only one other study besides our own, and that study found bilateral activity for spatial working memory (Baker *et al.* 1996), just as we did. Therefore, spatial working memory does not seem to be lateralized to the right frontal cortex.

The evidence supporting left hemispheric dominance for object working memory is based on activation in inferior prefrontal cortex (BA 44) in one study (Smith *et al.* 1995) and dorsolateral prefrontal cortex (presumably BA 46) in another (Baker *et al.* 1996). We believe that the left hemispheric dominance observed in these studies does not reflect a left hemispheric dominance for objects *per se*, but instead might reflect the type of working-memory strategy used. Indeed, we propose that when analytic-based representations of objects are held in working memory, left hemisphere activation will dominate, whereas when image-based representations of objects are held in working memory, right hemisphere activation will dominate.

In our previously described PET study of face working memory (Haxby *et al.* 1995), in which we parametrically varied the length of the delay between sample and test stimuli, right prefrontal activity tended to diminish at the longer delays, whereas left prefrontal activity showed the largest activity increases (figure 3). In other imaging studies of face working memory, we observed (i) right lateralized activity in a task with short delay intervals (4.5 s) and a memory set size of three faces (Courtney *et al.* 1996*b*); (ii) bilateral activations in a task with intermediate delay intervals (8 s) and a memory set size of one face (Courtney *et al.* 1997*a*); and (iii) left lateralized activity in a task with longer delay intervals (13 s) and a memory set size of three faces (Courtney *et al.* 1998). Thus, longer delay intervals and a larger memory set size seem to shift face working memory-related activity from the right to the left hemisphere. One possible explanation
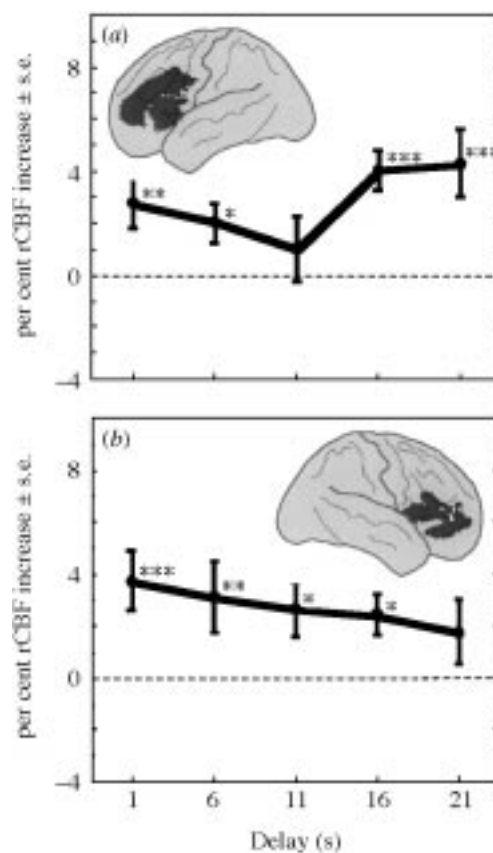

Figure 3. Areas in left (*a*) and right (*b*) prefrontal cortex that were activated during performance of a face working-memory task. Activity in these regions, as measured by regional cerebral blood flow (rCBF), was significantly more sustained across memory delay lengths than was activity in ventral temporal cortex, indicating that these regions are more active during the memory delays after the stimuli are removed from view. Note that whereas the right prefrontal region showed a tendency to have a diminished increase in activity at longer delays, the left prefrontal region showed the greatest activity increase at longer delays. Single, double, and triple asterisks indicate significant difference from control rCBF at the $p = 0.05$, 0.01 and 0.001 levels, respectively. (Adapted from Haxby *et al.* (1995).)

for these hemispheric differences is that right hemisphere activity is associated with an icon-like image of a face that is difficult to maintain in working memory for a long period of time, whereas left hemisphere activity is associated with a face representation that is more durable, based perhaps on an analysis, which might be partly verbal, of distinctive features and attributes.

In their studies, Smith *et al.* (1995) attributed the left lateralization of object working memory to rehearsal of a symbolically or linguistically encoded representation of the object. We suggest that this argument can be extended: laterality effects in visual working memory might be influenced by a variety of factors, such as length of the memory retention interval, memory set size and even item familiarity, all of which might affect the extent to which subjects engage in analytical or verbal, as opposed to image-based, encoding and rehearsal of information about objects. Therefore, we propose that, in humans, a division might exist between processing in the left and right hemispheres, but that this division reflects

analytical-based versus image-based processes rather than object versus spatial ones.

(c) *Segregation for maintenance, or manipulation of representations?*

According to the original model proposed by Baddeley & Hitch (1974, 1994), working memory can be divided into at least three components: (1) a 'phonological loop' for maintaining auditory–verbal information; (2) a 'visuospatial sketch pad' for maintaining information about the visual properties of objects and about spatial locations; and (3) a 'central executive' for attentional control and for coordinating the manipulation and use of information held in both the phonological loop and the sketch pad. Thus, the concept of working memory encompasses both the informational content of our consciousness and the wilful use and manipulation of that information.

In working-memory tasks, such as ours, using delayed match-to-sample or delayed response, information is held 'on-line' for a brief period of time, but manipulation of that information is not required. These working-memory tasks contrast with others in which monitoring or manipulation of the information held in working memory is required. One example of such a task is the '*n*-back' task (Cohen *et al.* 1994; Smith *et al.* 1996). In this task, subjects are required to respond if the current item being shown is the same as that shown one, two, or three items earlier in a constant stream of stimuli. This requires maintaining a list of items in working memory that must be constantly updated by discarding the oldest items while maintaining and adding more recent ones. Another example of a task that requires monitoring of the contents of working memory is the 'self-ordered' task developed by Petrides for use in patients with frontal lobe lesions (Petrides & Milner 1982). In this task, subjects are presented with a set of stimuli that vary in their relative positions from trial to trial. The subjects are required to point to a different stimulus on each trial until all have been selected. Thus, the subjects have to monitor their responses and update, during each trial, the remembered set of previously selected items, to avoid pointing to the same stimulus twice. Therefore, *n*-back and self-ordered tasks require, in addition to simple maintenance of information, cognitive processes related to the central executive component of working memory that are not required by delayed match-to-sample and delayed-response tasks.

Are there prefrontal areas that are brought into play during the monitoring and manipulation of information in working memory in addition to those engaged during the maintenance of this information? In monkeys, lesions restricted to cortex within the principal sulcus impair spatial delayed-response tasks (Mishkin & Manning 1978). However, lesions that are slightly more dorsal, which spare the principal sulcus but involve dorsal BA 9, do not affect performance on spatial delayed-response tasks, but do impair performance on both spatial and non-spatial self-ordered tasks that require, in addition to maintenance, monitoring and manipulation of information in working memory (Petrides 1994). It therefore seems that, at least in monkeys, there might be an area that is required for the executive processes involved in the self-ordered tasks, that is adjacent to but distinct from the area involved in maintaining spatial information in working memory.

Is there evidence from brain-imaging studies for a similar distinction in the human frontal cortex? There have been four studies that have compared frontal activation during working-memory tasks requiring monitoring and manipulation to activation during versions of the task that only required maintenance (Petrides *et al.* 1993*a*; Awh *et al.* 1996; Owen *et al.* 1996; Cohen *et al.* 1997). Three regions have been identified in these studies as being associated with monitoring and/or manipulation. BA 6/8 was identified in all four studies, anterior cingulate in three of the four (Petrides *et al.* 1993*a*; Owen *et al.* 1996; Cohen *et al.* 1997), and BA 9/46 in two of the four (Petrides *et al.* 1993*a*; Owen *et al.* 1996). There is therefore some indication that there are frontal areas brought into play during the monitoring and manipulation of information in working memory in addition to those engaged during the maintenance of this information, but the evidence is currently insufficient to answer the question with confidence.

4. DISTRIBUTED NEURAL SYSTEMS

(a) *Relationship of frontal working-memory areas to posterior visual processing areas*

One advantage of functional brain imaging, compared with physiological recording, is the ability to obtain simultaneously measures of activity in the entire brain, thereby allowing observations across entire neural systems. The individual regions in these systems might make different functional contributions to a given cognitive task, and each contribution might or might not be critical for successful performance. For example, in monkeys performing object working-memory tasks, the presentation of distracting items during the memory delay interval completely eliminates sustained activity of inferior temporal neurons that is normally seen during the delay, despite the fact that the monkeys continue to perform the task successfully. In contrast, the sustained activity of prefrontal neurons is not interrupted by the presentation of distracting items during the memory delay interval (Miller *et al.* 1996). This finding indicates that sustained activity within the inferior temporal cortex of monkeys is not critical for their performance of the working-memory task. By implication, the small amount of sustained activity that we observed in the ventral temporal cortex during face working memory might reflect interactions with, and feedback from, prefrontal regions.

The interactions between frontal cortex and posterior visual processing areas might differ, however, for the dorsal spatial working-memory system and the ventral object working-memory system. Indeed, there is evidence to support this idea. Whereas the ventral temporal cortex shows a small amount of sustained activity during face working-memory delays, the parietal cortex shows approximately the same level of sustained activity as frontal cortex during spatial working-memory delays (Courtney *et al.* 1995, 1996*a*). This finding suggests that the functions of perception and working memory might typically be more tightly coupled for spatial information than for object information. When attempting to maintain an active representation of a spatial location, one can generally attend directly to that location in space, even if the location is no longer marked by a visual stimulus.

When keeping an object in working memory after it is removed from view, however, one must attend to the internal representation of that object.

(b) *Relationship of frontal working-memory areas to frontal areas associated with long-term memory*

The regions activated in our object working-memory tasks seem similar to the regions of prefrontal cortex activated in long-term memory tasks (Buckner 1996; Haxby *et al.* 1996). It has typically been found that encoding of long-term memories preferentially activates the left prefrontal cortex, whereas the retrieval of those memories activates the right prefrontal cortex. These findings have led Tulving *et al.* (1994) to propose a 'hemispheric encoding-retrieval asymmetry' (HERA) model for long-term memory. Does such a hemispheric asymmetry exist for working memory?

We recently examined the difference in activation during encoding and retrieval within the context of working memory for faces; that is, the difference between the transient response to the sample stimuli to be remembered and the transient response to stimuli shown in the test of recognition (Courtney *et al.* 1997*b*). Encoding of the sample faces resulted in a greater activation of bilateral ventral temporal and left prefrontal cortices, whereas recognition of the test faces resulted in a greater activation of right prefrontal cortex. This is exactly the finding reported by Haxby *et al.* (1996) in a long-term memory study of the encoding and recognition of faces.

Interestingly, the transient encoding and recognition responses seen in the face working-memory study tended to be in regions of prefrontal cortex that were adjacent to but distinct from those regions that showed sustained activity during the working-memory delays. Although both sets of regions occupy similar locations to those activated during long-term memory encoding and retrieval, it is not known whether either set of working-memory regions is identical to the regions activated during long-term memory encoding and retrieval. If the same areas are activated during both long-term and working-memory tasks, there are several possible interpretations of this result. Performance of a working-memory task by an individual might involve recruitment of long-term memory processes to provide a more durable representation that could be used if an active representation is disrupted. Additionally, retrieval of long-term memories might typically lead to an active representation of the recalled material, much like the active representation of material held during a working-memory delay. Finally, prefrontal activation associated with long-term memory encoding and retrieval might be due to encoding and retrieving the circumstances of the event during which learning occurred. Encoding and retrieval of the temporal–spatial context of an event is the hallmark of episodic memory, and working memory might maintain active representations of the information that comprises that context.

5. CONCLUSIONS

Many of the brain-imaging studies of working memory in humans have been modelled on those conducted in physiological studies of monkeys. In the monkey, the evidence for prefrontal involvement in working memory has been the presence of sustained neuronal activity during memory delay intervals. Presumably such activity indicates an active on-line representation of the sample stimulus that bridges the memory delay and enables successful performance of the task. We have demonstrated that areas in human frontal cortex also show sustained activity during working-memory delays. As in the monkey, sustained activity in more ventral frontal regions is associated with working memory for objects, and sustained activity in more dorsal frontal regions is associated with working memory for spatial locations. Three major differences emerged between monkey and human, however. First, there are three separate prefrontal regions associated with object working memory in humans, whereas only one has been identified in monkeys. Second, the frontal region associated with spatial working memory in humans occupies a more dorsal and posterior location relative to the homologous area in monkeys. However, as in the monkey, in which the area specialized for spatial working memory is located just anterior to the FEF, the same topological relationship exists in the human. Third, there is no evidence in monkeys for hemispheric lateralization of working-memory processes, whereas in humans the left hemisphere seems to dominate for analytical-based object representations, and the right for image-based object representations.

The difference between monkeys and humans in the exact location of both the FEF and the spatial working-memory area might have implications for human brain evolution. The more dorsal and posterior location of these areas in humans suggests that they were displaced by the expansion of the dorsolateral portion of prefrontal cortex. A comparison of monkey and human functional neuroanatomy indicates that the displacement of regions in the human brain might be due to the emergence of phylogenetically newer regions. For example, posterior areas specialized for spatial vision have a more superior location in parietal cortex in the human than in the monkey, whereas those specialized for object vision have a more inferior location in temporal cortex (for reviews see Ungerleider & Haxby (1994) and Ungerleider (1995)). Displacement of both sets of visual areas away from the posterior perisylvian cortex might be related to the emergence of language mediated by phylogenetically newer cortical areas, such as BA 39 and BA 40. The specific displacement of functional areas in dorsal frontal cortex that we have identified might likewise be related to new functional areas in prefrontal cortex, perhaps created through the duplication and differentiation of older areas. One could speculate that BA 46 in the monkey was duplicated during primate evolution and now comprises at least two areas in the human brain: a spatial working-memory area located in the superior frontal sulcus and one or more areas in what is now known as human BA 46. If so, human BA 46 might have acquired new processing functions mediating cognitive abilities that are either distinctively human or greatly elaborated in humans. Examples of these abilities might include abstract reasoning, complex problem solving, and planning for the future, consistent with behavioural symptoms in patients with frontal lobe damage (Stuss & Benson 1986).

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