

Separable Neuronal Circuitries for Manipulable and Non-manipulable Objects in Working Memory

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Previous work using single-cell recordings in monkeys and neuro-imaging studies in humans has shown that perceiving an object or imaging the action associated with the object recruits the same brain regions in the ventral premotor cortex as performing an action with the object. We used functional magnetic resonance imaging (fMRI) for examining whether similar brain regions are also activated while maintaining information about manipulable objects in working memory. Holding information about manipulable objects in working memory activated the left ventral premotor cortex and the left inferior frontal gyrus (Broca's area). Conversely, non-manipulable objects to be held in working memory co-activated Broca's area and the left angular gyrus. When contrasted directly, manipulable relative to non-manipulable objects activated the left ventral premotor cortex and the anterior intraparietal sulcus, a circuitry that is assumed to mediate the transformation of movement-relevant object properties into hand actions. These results indicate that visual working memory for manipulable objects is based on motor programmes associated with their use. Similar to speech motor programmes in verbal memory tasks, hand motor programmes may allow the maintenance of objects in working memory over short intervals.

Introduction

Everyday life requires maintaining information in mind for short periods of time. Examples include the rehearsal of a person's name, a telephone number or memorizing parts of a street map while driving in an unknown city. One of the striking differences between maintaining verbal and non-verbal information in the mind is that verbal materials can be encoded phonologically, thereby allowing a direct mapping between hearing and articulation. These phonological codes can be accessed by an articulatory rehearsal mechanism that repeatedly refreshes phonological codes and through this enables the maintenance of verbal information in working memory (Baddeley, 1986; Wilson and Emmorey, 1998).

In support of this two-component view of verbal working memory, recent brain imaging studies have suggested that posterior parietal brain areas represent more sensory-related aspects of verbal working memory and prefrontal/premotor areas more action-oriented aspects of verbal working memory (Paulesu *et al.*, 1993; Smith and Jonides, 1998; Mecklinger *et al.*, 2000). Left posterior parietal areas have been shown as being activated in verbal working memory tasks (Cohen *et al.*, 1997; Jonides *et al.*, 1998) and they remain activated after subtracting task components not involved in storage processes (Awh *et al.*, 1996). Broca's area in the posterior inferior frontal gyrus shows activation in verbal working memory tasks (D'Esposito *et al.*, 1998) and in tasks with phonological processing requirements (Fiez, 1997) and through this is assumed to be concerned with the phonological rehearsal component of working memory.

While phonological codes can be used for maintaining verbal materials in working memory, it is still an issue how this is done

for materials for which verbal codes cannot easily be generated. It was suggested that the rehearsal of spatial information relies on implicit eye movement programmes in the same way that subvocal articulation mediates verbal rehearsal (Baddeley, 1986). Others argue that a more general mechanism is recruited for maintaining spatial information in working memory. For example, in an earlier study it was assumed that the mechanisms of spatial selective attention are recruited to serve as a rehearsal-like function for spatial materials (Awh and Jonides, 2001). Alternatively, other models have stressed the role of spatial motor programmes as a potential mechanism for spatial rehearsal (Schneider, 1999). Even though these views put different emphasis on sensory-related and motor-related processes, they share a common assumption, namely that visual working memory, similar to verbal working memory, makes use of systems that are specialized for other processing domains.

While spatial selective attention may act as a rehearsal mechanism for location-specific information of working memory, it is still unclear by which mechanisms more complex visual information, such as line drawings of objects or pictures of natural scenes, is maintained in working memory. In contrast to spatial locations, objects entail large amounts of visual and functional properties, have lexical entries and, through this, can be verbally recoded. Neuropsychological studies showing a selective loss of knowledge about specific object categories (Forde and Humphreys, 1999) have suggested that objects are represented according to their features and attributes in the human brain. We were interested in particular kinds of objects, namely manipulable objects. These objects are unique in that they are strongly associated with a specific hand movement. The relevance of motor properties for the representation of objects has not only been highlighted by visual processing models that assume a common representational basis for sensory-related and action-related aspect of a perceived event (Prinz, 1997), but has also been supported by neuroimaging studies showing that the observation of tools or the silent naming of tools is associated with activity in the hand area of the ventral premotor cortex, i.e. those brain areas that are activated when an action with this object is actually being performed (Decety *et al.*, 1997; Grafton *et al.*, 1997; Decety and Grèzes, 1999). Here we examined whether motor programmes for object use are recruited when information about manipulable objects has to be maintained in working memory. In order to examine this issue we used fMRI in a modified delayed matching to sample task. The participants were required to maintain manipulable objects in working memory for a period of 10 s. Thereafter a test stimulus was presented and they had to decide whether it was identical or a mirror image of the objects held in their memory. Brain activation was examined in the delay interval. An equal number of non-manipulable objects that were equated for familiarity, complexity and name agreement were used as control stimuli. If

the premotor cortex is activated in the retention interval for manipulable but not for non-manipulable objects these results will favour the view that motor programmes for object use play a role in the rehearsal of manipulable objects in working memory.

Methods

Subjects

Sixteen subjects (six males and 10 females) of mean age 23 years and range 21–33 years participated in the study. All subjects were right handed and gave informed consent prior to participation.

Stimuli

The stimuli were 96 line drawings from stimulus materials used in an earlier study (Snodgrass and Vanderwart, 1980). They were selected from a total of 240 objects that were tested for manipulability in a pilot study (with $n = 40$) (Magnié *et al.*, 2002). In the manipulability rating the subjects indicated whether they could easily pantomime the action associated with an object on a five-point rating scale ranging from 'no action can be associated with the object' (rating of 1) to 'only one action can be associated with the object' (rating of 5). All line drawings were also evaluated for symmetry along the vertical axis (i.e. similarity with their mirror image) in a second pilot study. In this test 30 subjects indicated whether the line drawing and its mirror image along the vertical axis were similar or not on a five-point rating scale from very dissimilar (rating of 1) to very similar (rating of 5).

The mean manipulability scores were 3.95 ± 0.46 (mean \pm SD; range = 3.2–4.8) for the 48 manipulable objects selected for the present study and 1.99 ± 0.39 (range = 1.05–2.51) for the 48 non-manipulable objects. Stimuli were assigned to the two groups of manipulable and non-manipulable objects with the constraint that in both groups the objects' symmetry index was comparable. The mean symmetry scores were 2.60 for the manipulable objects (range = 1.64–4.23) and 2.61 for the non-manipulable objects (range = 1.33–4.46). The line drawings in both groups were also equated for name agreement (82% versus 84% for manipulable and non-manipulable objects respectively), familiarity (3.5 versus 3.5 for the manipulable and non-manipulable objects respectively) and complexity (2.6 versus 2.8 for the manipulable and non-manipulable objects respectively) (Snodgrass and Vanderwart, 1980). All line drawings were restricted to categories of inanimate objects. There were no significant differences between the manipulable and non-manipulable objects for all the above-mentioned control variables ($P > 0.20$).

Procedure

In each trial an object was presented for 100 ms and 4 s later the task cue was shown indicating that, upon presentation of S2 (6 s after the task cue), the memory task or the control task had to be performed. In the memory task, the participants indicated whether the object presented at S2 was identical or the mirrored version of the object presented at S1. In the control task, the participants indicated whether the two digits presented to the left and right of the object were identical or not (see Fig. 1). In both tasks the subjects responded by pressing one of two response buttons with the index and middle finger of their right hand. The next trial started 6000 ms after S2 onset.

A total of 192 trials were presented, half in the memory task (96) and half in the control task (96). In both tasks, half the trials contained manipulable (48) and the other half non-manipulable (48) objects. Each object was presented once in the memory task and once in the control task, with the order of presentation (presented in the memory or in the control task first) balanced across subjects. The order of the memory and control tasks was randomized. The participants were not informed about the manipulability or similarity rating performed before the fMRI experiment.

fMRI Procedures

Imaging was performed with a 3 T MR scanner and a T_2^* -sensitive echo planar sequence was used for functional imaging ($T_R = 1000$ ms and $T_E = 30$ ms). Structural whole brain images were acquired using a T_1 -weighted three-dimensional segmented MDEFT in a separate session. In order to

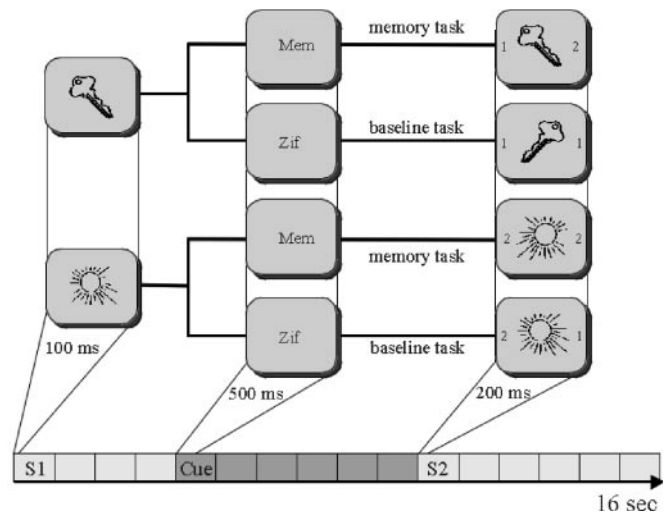


Figure 1. The working memory and control tasks. In the memory tasks the subjects had to indicate whether the same object or its mirror image was presented at S2. In the control tasks they had to indicate whether or not two digits presented at S2 (together with the object) were identical or not. Two objects with low (keys) and high (sun) symmetry ratings are presented as examples.

align the functional and the three-dimensional images conventional T_1 -weighted anatomical images in plane with the echo-planar images were acquired in the same session in which the functional images were recorded. A standard birdcage head coil was used and the participants were supine on the scanner bed, with a stereotactic fixation system used for reducing head motion. Sixteen functional volumes were taken for each trial. An acquisition volume consisted of eight axial slices [parallel to the plane intersecting the anterior and posterior commissures (the AC-PC plane)] of 5 mm thickness and 1 mm inter-slice distance, resulting in a voxel size of 3 mm \times 3 mm \times 5 mm. The lower edge of the most inferior slice was identical with the AC-PC plane.

The fMRI data were processed using the software package LIPSIA (Lohmann *et al.*, 2001). During pre-processing low-frequency artefacts were removed by applying a 1/55 s high-pass filter. A Gaussian filter was applied (FWHM = 5.28 mm) for spatial smoothing. The fMRI signals evoked by the task cues for each subject were correlated with a reference function, i.e. a boxcar function convolved with a Gaussian kernel that followed the time course of the cue-S2 interval (i.e. 6 s). In order to account for the physiological delay of the haemodynamic response, the reference function was shifted by 4 s (Buckner *et al.*, 1998). Orthogonal contrasts were calculated between the memory tasks and the control tasks for the manipulable and non-manipulable objects respectively using this reference function. Only trials with a correct performance were entered into this analysis. The resulting individual z-maps were transformed into stereotactic Talairach space. Group analyses were performed with a random effect model by applying a one-sample *t*-test.

A two-step procedure was used for all statistical analyses. First, the main effects of memory task versus control task across both object types was calculated at a threshold of $P < 0.001$. Only voxels that showed this overall experimental effect were considered for further analyses (Chao and Martin, 2000). The results of this overall contrast were used for restricting the search space for the specific contrasts, in which both object classes (manipulable and non-manipulable) were either examined separately or directly contrasted with each other. Because the main interest of the present study was in the maintenance of relevant information in working memory, the voxels were selected based on their overall response in the memory task. Thus, by selecting voxels based on their memory-related response rather than on their differential response to manipulable objects, the statistical analysis was not biased for a particular object class.

A threshold of $P < 0.01$ was applied (uncorrected for multiple comparisons) for the specific contrasts between the memory and control trials. Only regions with contiguous clusters of more than five voxels with

$Z > 2.33$ ($P < 0.01$), corresponding to an activated volume of 225 mm^3 , were interpreted. In order to protect against false-positive activations, a region was only considered significant if it passed the statistical criteria and the spatial extent criterion described above. A region of interest analysis was employed for specific analyses. Spherical regions with 3 mm radius were defined around peak activations revealed in the initial analyses and mean Z -scores were computed for each region of interest (Bosch, 2000). The mean Z -scores were then subjected to repeated-measure ANOVAs.

Results

Performance Results

The reaction times in the memory trials were not significantly different for the manipulable ($913 \pm 42 \text{ ms}$, mean \pm SE) and non-manipulable objects ($924 \pm 43 \text{ ms}$). In the control trials the mean reaction times were 878 ± 41 and $882 \pm 38 \text{ ms}$ for the manipulable and non-manipulable trials, respectively. A two-way repeated-measure ANOVA with the factors task and manipulability revealed neither significant main effects nor an interaction ($P < 0.15$). The error rates were slightly lower for manipulable ($9.4 \pm 1.6\%$) than for non-manipulable memory trials ($12.3 \pm 1.9\%$), whereas no such differences were obtained for the control trials ($8.0 \pm 1.5\%$) and ($7.9 \pm 1.2\%$). The ANOVA revealed a main effect of task [$F(1,15) = 7.95$ and $P < 0.05$], but not of manipulability [$F(1,15) = 3.9$ and $P < 0.07$].

fMRI Results

In this section we first report the results of the overall comparison between the memory and control trials. In a second step the specific comparisons for both object classes will be reported. Figure 2 shows the across-subject activation pattern for all memory trials relative to the control trials. The memory trials activated the left ventral premotor cortex [Brodmann's area (BA) 6], the right middle frontal gyrus (BA 9), the left superior frontal gyrus (BA 10), the inferior frontal gyrus (BA 44), the left anterior intraparietal sulcus (BA 40) and the left angular gyrus (BA 39).

The mean activation pattern evoked by the task cue for the manipulable and non-manipulable objects relative to the control tasks are illustrated in Figure 3A,B respectively. Maintaining manipulable objects in memory resulted in prominent activations in the left ventral premotor cortex, the inferior portion of Broca's area and in the right middle frontal gyrus. In contrast, maintaining non-manipulable objects in working memory resulted in prominent activation patterns in Broca's area and in the left angular gyrus. Notably, no reliable activity was found for non-manipulable objects in the left ventral premotor cortex, even with a lowered statistical threshold of $P < 0.05$. The significant areas are summarized in Table 1.

The time courses of the blood oxygen level-dependent (BOLD) response for manipulable objects in the memory and control trials for the relevant areas are illustrated in Figure 4. There are two peaks, i.e. 4–6 s after S1 and S2 respectively, reflecting enhanced haemodynamic responses to both stimuli. Taking into account a temporal delay of the BOLD response of ~4 s (Buckner *et al.*, 1998), the figure suggests that activation differences

between the memory and control trials start to emerge in the pre-cue period, reach their maximum in the cue–S2 interval and approximately decline with the onset of S2.

These findings show that the ventral premotor cortex is activated when manipulable objects have to be maintained in working memory and that these memory-related differences were most pronounced in the post-cue period of the retention interval. This may suggest that motor schemata for object use mediated by the ventral premotor cortex play a role when information about manipulable objects is held in working memory. In order to examine this pattern of results further we directly contrasted the brain activity evoked by memory trials with the manipulable and non-manipulable objects (see Fig. 5). This comparison revealed significantly larger left ventral premotor cortex activation for the manipulable than non-manipulable objects. It was accentuated ~1 cm inferior to the premotor cortex activation obtained in the memory versus control task comparison. A second activation difference between the manipulable and non-manipulable objects was found in the anterior (ascending) branch of the left intraparietal sulcus (BA 40). The time course of these activation patterns in the retention interval is illustrated in the upper part of Figure 5. The haemodynamic response for manipulable objects in the ventral premotor cortex remained elevated in the post-cue interval and was attenuated for non-manipulable objects. This difference due to manipulability started ~3–4 s after the task cue and had an extension of ~6–7 s, i.e. approximately the length of the cue–S2 interval. Visual inspection indicated that this effect started ~3 s earlier in the left intraparietal sulcus, suggesting that this brain region was already affected by object manipulability in the pre-cue period.

We further examined the neuronal networks sensitive to object manipulability by analysing the effects of task demands. As the task used here required a decision about whether or not the object maintained in memory was identical or the mirror image of the object presented at S1, the task may have been more demanding for high symmetry objects (that are similar to their mirror image) than for low symmetry objects (that are dissimilar to their mirror image). A median split of the manipulable and non-manipulable objects was performed according to their symmetry score, yielding 24 high symmetry and 24 low symmetry objects for both object classes. The performance data are presented in Table 2. Analyses of the reaction times and error rates in the memory trials revealed main effects of symmetry [reaction times, $F(1,15) = 65.12$ and $P < 0.001$ and error rates, $F(1,15) = 44.91$ and $P < 0.001$], indicating that it took more time and it was more difficult to judge similar than dissimilar objects. Moreover, the two-way interactions between symmetry and manipulability were significant [reaction times, $F(1,15) = 5.63$ and $P < 0.03$ and error rates, $F(1,15) = 5.30$ and $P < 0.03$], indicating that the reaction times and error rates were higher for high symmetry non-manipulable objects than for the other object types ($P < 0.02$).

The brain activation patterns for low symmetry and high symmetry objects are summarized in Table 3. Low symmetry

Figure 2. Activation patterns averaged across all subjects showing enhanced BOLD responses for the memory trials relative to the control trials. Axial, coronar and lateral views of a normalized T_1 structural image of one subject are shown. Activations exceeding a threshold of $Z = 2.6$ are shown in this and in the following figures. Memory trials were associated with increased activation in the left ventral premotor cortex, the right middle frontal gyrus, the left inferior frontal gyrus (Broca's area) and the left angular gyrus. Not visible but also activated in this contrast were the left superior frontal gyrus and the left anterior intraparietal sulcus (for further details see the Methods and Results sections).

Figure 3. Activation patterns averaged across all subjects showing enhanced BOLD responses to (A) manipulable objects and (B) non-manipulable objects relative to the control task. Axial, coronar and lateral views of a normalized T_1 structural image of one subject are shown.

Figure 2:

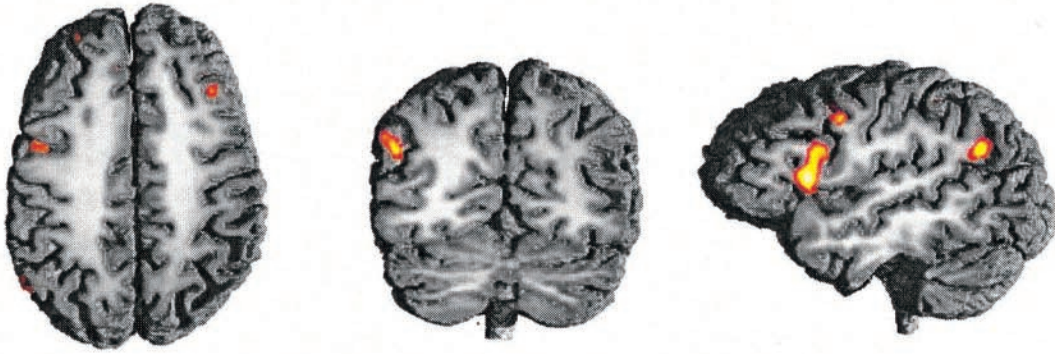


Figure 3a:

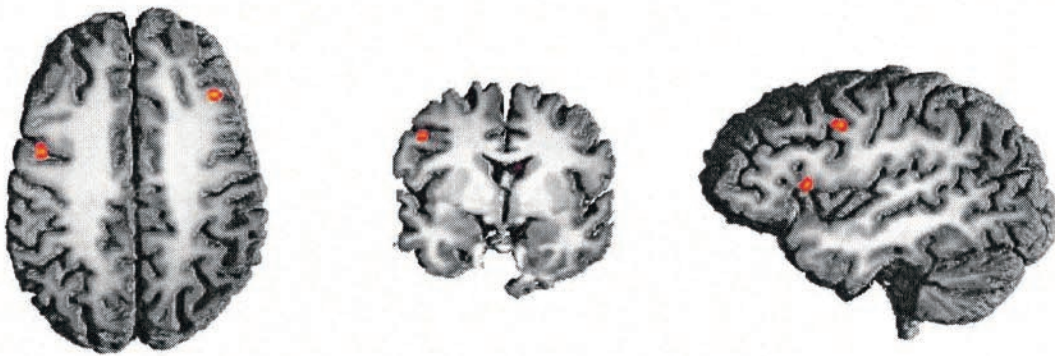


Figure 3b:

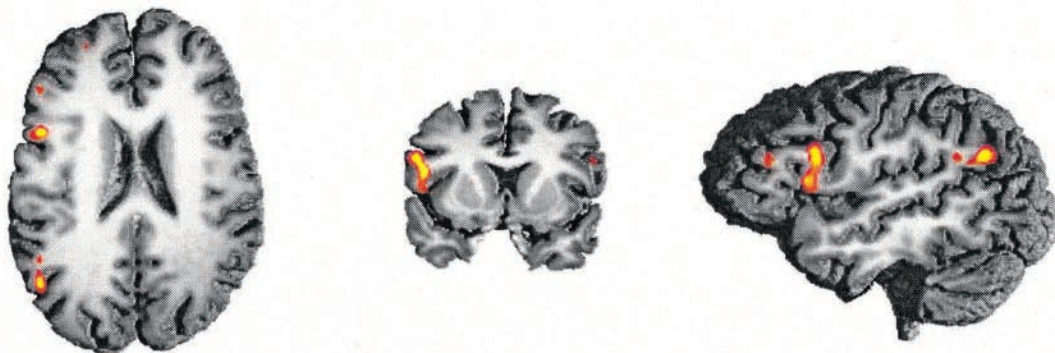


Table 1

Anatomical location (in Talairach coordinates) of the regions activated by the manipulable and non-manipulable objects ($P < 0.01$ and size larger than five voxels)

| | X | Y | Z | Z-score | mm ³ |
|---|-----|-----|----|---------|-----------------|
| Manipulable objects: memory versus control trials | | | | | |
| Right middle frontal gyrus | 35 | 31 | 25 | 3.19 | 281 |
| Left ventral premotor cortex | -46 | 5 | 31 | 3.02 | 253 |
| Left inferior frontal gyrus (Broca's area) | -46 | 14 | 4 | 3.04 | 218 |
| Non-manipulable objects: memory versus control trials | | | | | |
| Left inferior frontal gyrus (Broca's area) | -46 | 12 | 13 | 3.71 | 1200 |
| Left angular gyrus | -48 | -60 | 32 | 3.55 | 576 |
| Manipulable versus non-manipulable memory trials | | | | | |
| Left anterior intraparietal sulcus | -44 | -46 | 42 | 2.95 | 241 |
| Left ventral premotor cortex | -47 | 4 | 22 | 3.91 | 436 |

objects, when non-manipulable, activated the left angular gyrus and the anterior portion of the left intermediate frontal sulcus (BA 10), whereas no reliable activation pattern was obtained for low symmetry manipulable objects. Conversely, high symmetry objects, when manipulable, activated the left ventral premotor cortex and, when non-manipulable, resulted in pronounced activation in Broca's area.

This pattern of results suggested that the differential brain activation pattern for manipulable and non-manipulable objects was most pronounced for visually similar high symmetry objects, that is when the line drawing and its mirror image were not easily discernible by the orientation of the object's main axis and, therefore, the participants had to encode and memorize the figurative details of the line drawings. The differential activation for those manipulable and non-manipulable line drawings that presented high symmetry was further examined by means of a region of interest analysis. The mean activation pattern of spherical regions, which were centred around the peak activations in the lateral premotor cortex and Broca's area, were entered in a two-way ANOVA with the factors manipulability and region of interest. This analysis revealed a significant interaction [$F(1,15) = 11.50$ and $P < 0.004$]. Broca's area was more activated by non-manipulable objects whereas the ventral premotor cortex activation was more pronounced for manipulable objects under increased task demands, i.e. for high symmetry visually similar objects.

Discussion

In this study we examined the effects of an objects's manipulability on brain activation patterns in a working memory task. The participants performed a modified delayed matching to sample task in which they memorized line drawings of objects for 10 s and subsequently judged whether an object was identical or a mirror image of the object held in memory. The objects differed in their manipulability (the ease with which the action associated with the object can be pantomimed) and were equated for characteristics that are known to influence object processing, i.e. name agreement, complexity, familiarity and category membership (Martin *et al.*, 1996). fMRI activation was measured time locked to the task cue in a retention interval of 6 s.

The direct contrast of the memory and control trials revealed activation in a neuronal network including lateral and ventral prefrontal, premotor and posterior parietal areas. These areas have repeatedly been found in a variety of working memory studies and have been taken to reflect the multiple subprocesses that underlie working memory for non-verbal materials (Smith

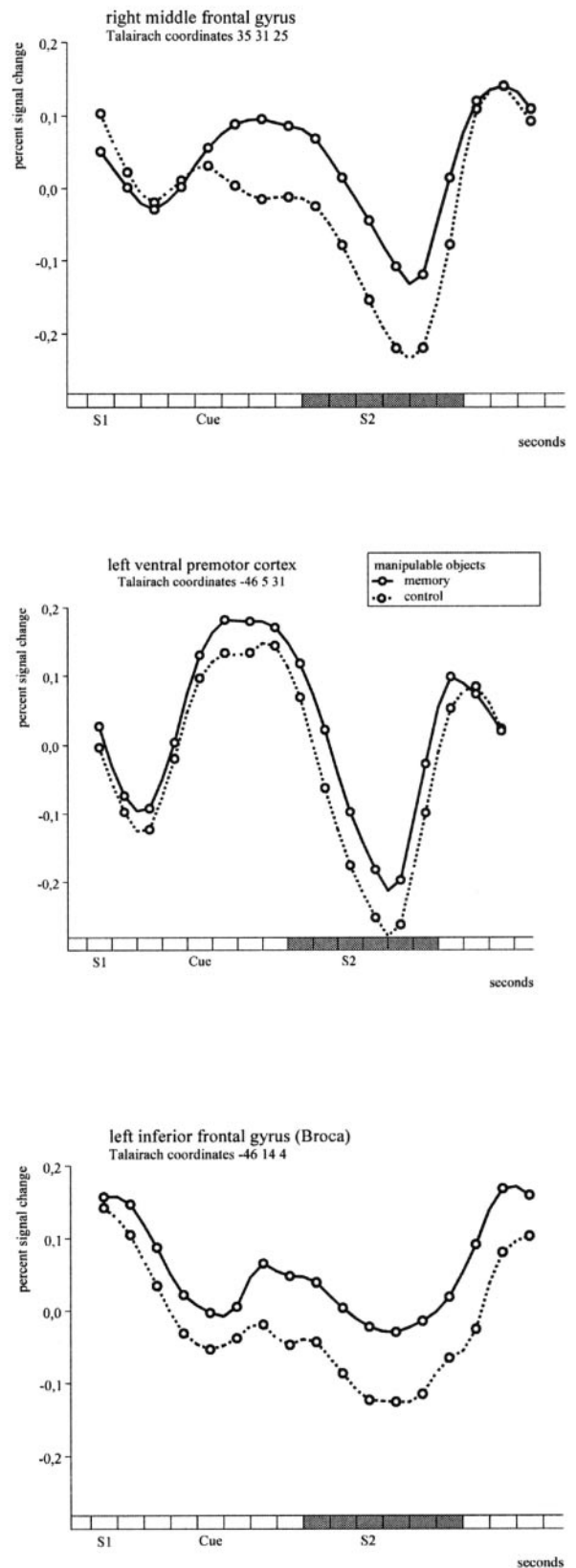


Figure 4. Percent signal change (relative to the mean value across all scans) for single voxels in the regions showing significantly enhanced responses to manipulable objects in the memory trials relative to the control trials. The shaded area indicates the location and duration of the reference function used for modelling the haemodynamic response.

Figure 5:

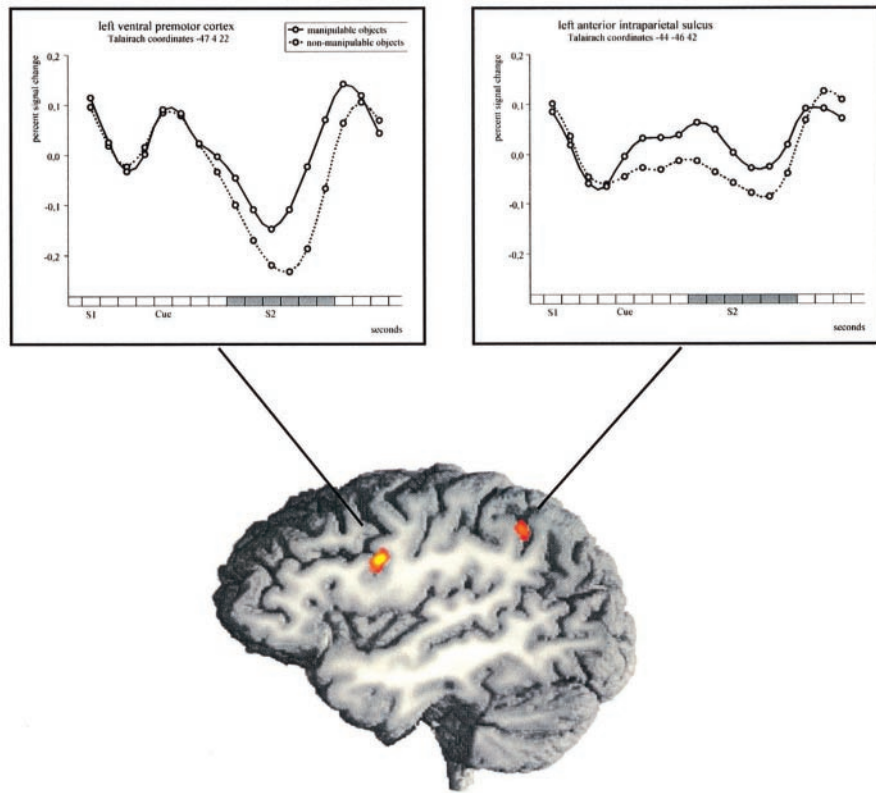


Figure 5. Brain regions showing enhanced BOLD responses for manipulable relative to non-manipulable objects in the memory task. The time course of the BOLD response (percent signal change relative to the mean value across all scans) in the left ventral premotor cortex and in the left anterior intraparietal sulcus for both object types is shown in the upper part of the figure. The spacing of the x-axis is 1 s and the shaded area indicates the location and duration of the reference function used for modelling the haemodynamic response.

Table 2

Performance results (reaction times and percentage of errors) for the manipulable and non-manipulable memory trials separately for objects being similar (high symmetry) or dissimilar (low symmetry) with their mirror image

| | Reaction times | % errors |
|-------------------------|----------------|------------|
| Manipulable objects | | |
| High symmetry | 931 ± 40 | 12.5 ± 1.8 |
| Low symmetry | 896 ± 45 | 6.7 ± 1.7 |
| Non-manipulable objects | | |
| High symmetry | 985 ± 44 | 17.9 ± 2.5 |
| Low symmetry | 873 ± 44 | 6.1 ± 1.8 |

Values are mean ± SEM.

and Jonides, 1998; Postle and D'Esposito, 1999; Mecklinger *et al.*, 2000).

Interestingly, while the reaction times and error rates were not affected by the manipulability of the objects, a clear dissociation in the haemodynamic response to both object classes in the retention interval was found. Relative to a memory-free control task equated for sensory and motor processing demands, manipulable objects activated the ventral part of the premotor cortex, the inferior part of Broca's area and the right middle frontal gyrus. Non-manipulable objects activated the inferior and superior portion of Broca's area and the left angular gyrus adjacent to the posterior part of the intraparietal sulcus. Consistent with the cueing procedure employed in the present

Table 3

Anatomical location (in Talairach coordinates) of the regions activated by low symmetry and high symmetry objects ($P < 0.01$ and size larger than five voxels)

| | X | Y | Z | Z-score | mm ³ |
|---|-----|-----|----|---------|-----------------|
| Low symmetry | | | | | |
| Non-manipulable objects: memory versus control trials | | | | | |
| Left angular gyrus | -53 | -56 | 37 | 3.59 | 853 |
| Left intermediate frontal sulcus (anterior portion) | -25 | 53 | 8 | 3.02 | 381 |
| Manipulable objects: memory versus control trials | - | - | - | | |
| High symmetry | | | | | |
| Non-manipulable objects: memory versus control trials | | | | | |
| Left inferior frontal gyrus (Broca's area) | -45 | 12 | 9 | 3.75 | 705 |
| Manipulable objects: memory versus control trials | | | | | |
| Left ventral premotor cortex | -44 | 3 | 31 | 3.13 | 337 |

study, these manipulability effects were most pronounced in the post-cue interval, when the participants either continued (memory trials) or stopped remembering the object (control trials).

When contrasted directly, the memory trials with manipulable objects led to stronger activations in the ventral premotor cortex and in the anterior part of the intraparietal sulcus. The differential processing of both object types was even more pronounced when the analysis was restricted to trials with high task demands, i.e. trials with high symmetry objects that were

not easily discernible from their mirror images. In this condition, Broca's area was more strongly activated for non-manipulable objects and activation in the ventral premotor cortex was larger for manipulable objects.

The Neuronal Circuitry for Maintaining Manipulable Objects

The direct contrast between the memory trials with manipulable and non-manipulable objects revealed a left hemisphere co-activation of the anterior intraparietal sulcus and the ventral premotor cortex. The anterior intraparietal sulcus receives input from somatosensory areas and projects to the ventral premotor cortex (Luppino *et al.*, 1999). The anterior intraparietal sulcus region is clearly separable from the posterior parietal area, which is centred along the posterior (descending) branch of the intraparietal sulcus and is critical for the allocation of spatial attention (Gitelman *et al.*, 1999). It has been found that the anterior intraparietal sulcus is activated during motor preparation (Deiber *et al.*, 1996) or when subjects attend to movements (Deiber *et al.*, 1998). It is assumed to be important for attention in relation to limb movements (Rushworth *et al.*, 2001). In the animal brain, neurons in the anterior intraparietal sulcus area (AIP) are highly responsive to movement-relevant object properties, such as the handle of a cup or the upper border of a cup (Rizzolatti *et al.*, 1995). In humans, lesions centred around the intraparietal sulcus lead to stronger impairments in grasping than in reaching (Binkofski *et al.*, 1998), thereby suggesting a similar functional organization of the intraparietal sulcus in the monkey and human brain. The anterior intraparietal sulcus is reciprocally connected with the ventral premotor cortex and supplies premotor areas with sensory information that is relevant for movements in relation to objects (Schubotz and Von Cramon, 2001). Within the lateral premotor cortex the ventral part can be separated on cytoarchitectonic (He *et al.*, 1993) and functional grounds from the dorsal part, which is strongly connected with the dorsal prefrontal cortex (Rushworth *et al.*, 2001). This suggests that the anterior intraparietal sulcus and the rostral part of the inferior premotor cortex form neuronal circuitries that transform intrinsic object properties into hand actions (Rizzolatti *et al.*, 1998).

In support of this view, co-activation of anterior intraparietal sulcus and ventral premotor cortex neurons has been reported in several recent neuroimaging studies with humans. Interestingly, the tasks employed in these studies required the processing of object features in the absence of any overt movements. A recent study (Schubotz and Von Cramon, 2001) examined brain activation while stimulus sequences had to be monitored for deviant stimuli, as defined by either object-based, spatial-based or temporal characteristics. Co-activation of the left ventral premotor cortex and the anterior intraparietal sulcus was obtained mainly in the object task and less so in the other two monitoring tasks. An earlier study (Chao and Martin, 2000) reported highly similar co-activation when subjects viewed man-made manipulable objects (i.e. tools) and another study (Grèzes and Decety, 2002) found combined left anterior parietal and premotor activation when the participants were presented with graspable objects across a variety of tasks. A common feature of these studies may have been that viewing of or attending to visual object features triggered the retrieval of information about hand movements associated with the objects, even in the absence of any motor requirements with these objects. The present findings confirm and extend these observations. They indicate that information about manipulable objects is maintained in working memory by object-specific motor programmes.

Notably, as suggested by Figure 5, the manipulability effects in the ventral premotor cortex and in the anterior intraparietal sulcus differed in their temporal characteristics. In the ventral premotor cortex it was present in the post-cue period only, whereas in the anterior intraparietal sulcus manipulability effects emerged ~3 s earlier. This may suggest that the anterior intraparietal sulcus is more sensitive to sensory features of manipulable objects (presented at S1) than the ventral premotor cortex.

The late onset of manipulability effects in the pre-cue period seems to be surprising in the light of studies that have shown ventral premotor cortex activation during the perceptual encoding of man-made manipulable objects (Chao and Martin, 2000; Grèzes and Decety, 2002). One explanation for this apparent discrepancy could be that our task may have lacked the statistical power for finding encoding-related differences in the ventral premotor cortex. As the main focus of our study was on delay-related activation, the present analyses focused on the memory versus control trial contrast, which could not be applied in the pre-cue interval. Alternatively, the brief object presentation time (100 ms) at S1 in combination with the retention demands of the working memory task may have delayed ventral premotor cortex activation until the participants were fully engaged in mnemonic processing of the stimuli. Further studies will be required in order to examine the issue of differential sensitivity of the ventral premotor cortex and the anterior intraparietal sulcus to perceptual and mnemonic processing of manipulable objects.

When manipulable objects were contrasted with control trials the ventral premotor cortex activation was accentuated more superiorly. However, the substantial overlap of both ventral premotor cortex activations and the fact that both activations are located in the hand region of the premotor cortex (Deiber *et al.*, 1991) suggest that they are functionally similar. This latter analysis revealed two differences to the aforementioned direct comparison of manipulable and non-manipulable objects: relative to control trials, manipulable objects activated the right middle frontal gyrus and no anterior intraparietal sulcus activation was found. Dorsolateral prefrontal cortex activation along the banks of the inferior frontal sulcus and in the adjacent middle frontal gyrus has been shown in a large variety of working memory studies (Smith and Jonides, 1998; Rypma and D'Esposito, 2000) and has been associated with the selection and organization of motor responses (Owen *et al.*, 1996; Mecklinger *et al.*, 2000; Rushworth *et al.*, 2001). In the present study this activation may be related to differential response selection or preparation requirements between the memory and control trials.

The absence of anterior intraparietal sulcus activation in the memory versus control task comparison may reflect the fact that the anterior intraparietal sulcus was also activated in the retention interval of the control trials with manipulable objects. This interpretation was at least tentatively confirmed by a *post hoc* analysis that directly contrasted control trials with manipulable and non-manipulable objects. In this analysis, anterior intraparietal sulcus activation was stronger for manipulable than for non-manipulable objects (maximum *Z*-value = 2.67). However, this result was restricted to two measured voxels, only.

Non-manipulable Objects and the Potential Role of Verbal Rehearsal

Non-manipulable objects relative to control trials led to stronger activations in Broca's area and in the left angular gyrus. Broca's area has most often been related to speech motor processes,

particularly phonological processing (Poldrack *et al.*, 1999). In verbal working memory tasks, Broca's area has been associated with subvocal rehearsal processes (Paulesu *et al.*, 1993; Cohen *et al.*, 1997). It has been suggested that Broca's area, which is located anterior to the inferior precentral sulcus, similar to the ventral premotor cortex, is concerned with movement representations, namely articulatory movements (Grafton *et al.*, 1997; Binkofski *et al.*, 1999; Schubotz and Von Cramon, 2001). In support of this view, activation in Broca's area has been reported during tool naming (Chao and Martin, 2000) and tool use naming (Grafton *et al.*, 1996). Broca's area activation has also been found during language comprehension, in particular when syntactic aspects are in focus (Dapretto and Bookheimer, 1999; Caplan *et al.*, 2000; Friederici *et al.*, 2000). Moreover, besides language-related tasks, Broca's area has also been activated by a variety of non-linguistic tasks, such as tasks that require the timing of movements, e.g. the synchronization of movements with sensory events (Rao *et al.*, 1997), the perceptual analysis of temporal patterns (Schubotz and Von Cramon, 2001) or the cognitive analysis of musical structures (Maess *et al.*, 2001). This suggests a functional overlap between language and non-linguistic processes and a more general functional role of Broca's area in the coordination and regulation of sequential activities in different effector domains (Schubotz *et al.*, 2000).

Insofar as Broca's area activation was found for both the non-manipulable and manipulable objects, our findings may indicate that both types of objects were, to some extent, phonologically recoded and subvocally rehearsed during the retention interval. However, the reasons as to why Broca's area activation was stronger for the non-manipulable than manipulable objects in a memory task that stressed spatial rather than linguistic features remain open. Since both object classes were equated along a number of dimensions, including name agreement and led to similar performance measures, both in reaction times and error rates, it is unlikely that the differential activation of Broca's area results from uncontrolled factors.

It is still possible that subvocal rehearsal played a more important role for the non-manipulable objects than for the manipulable ones because it would be the most readily usable strategy. In contrast, other strategies, such as imaging the mirror transformation with the object as required in the present memory task, would probably be more efficient for manipulable objects. However, it may also be that the differential activation of Broca's area for manipulable and non-manipulable objects reflects the general coordination requirements for sequential activities evoked by the task cues, such as the initiation of a mirror transformation or the activation of an appropriate stimulus-response mapping for the upcoming S2 comparison. As the anticipation of the mirror transformation for manipulable objects may have been supported by the activation of motor programmes for object use, these coordination requirements may have been lower for this object class. This latter interpretation is supported by reports of co-activation of Broca's area and the ventral premotor cortex in a motor attention task, i.e. in an interval in which the participants prepared for a finger movement (Rushworth *et al.*, 2001).

Beside Broca's area, non-manipulable objects activated the left angular gyrus, which has been reported as being activated in a variety of verbal (Paulesu *et al.*, 1993; Jonides *et al.*, 1998) and non-verbal working memory tasks (Mecklinger *et al.*, 2000). Angular gyrus activation was most pronounced for low symmetry, non-manipulable objects, for which the response times were faster and error rates lower, than for high symmetry objects. As the task required a mirror image comparison

subsequent to the retention interval, the subjects may have encoded and mentally rotated those object features that were most beneficial for the upcoming mirror comparison, e.g. the orientation of the object's main axis. In support of this view, inferior parietal activation centred around the angular gyrus, as in the present study, has been found in tasks that involve spatial transformations of objects, such as mirror image discrimination (Alivisatos and Petrides, 1996), size or principle axis discrimination (Faillenot *et al.*, 1999) or mental rotation (Cohen *et al.*, 1996; Kosslyn *et al.*, 1998). Given this, it is reasonable to assume that the angular gyrus activation for non-manipulable objects, in particular when highly dissimilar with their mirror image, reflects spatial transformations of objects' features performed in the retention interval in anticipation of the upcoming mirror comparison.

In conclusion, the present results provide evidence for different neuronal circuitries that allow the retention of manipulable and non-manipulable objects in visual working memory. In showing different haemodynamic responses to both object classes while object class did not affect performance, the results also indicate that haemodynamic measures can provide important complementary information about the architecture of working memory processes. Manipulable objects to be held in working memory co-activate ventral premotor cortex and anterior intraparietal sulcus areas, a neuronal circuitry that transforms movement-relevant object properties into hand actions. No ventral premotor cortex and anterior intraparietal sulcus activation was found for non-manipulable objects to be held in working memory. This opens the intriguing possibility that visual working memory for manipulable objects is based on object-specific motor programmes, i.e. information about actions associated with their use. Similar to speech motor actions in verbal working memory tasks, hand motor actions may allow the maintenance of objects in working memory over short intervals.

Notes

This research was supported by the German Research Society (DFG) (grant ME 1588/3-1). We wish to thank Angela Friederici and Bertram Opitz for helpful comments on earlier versions of the manuscript.

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