

The neural correlates of human working memory for haptically explored object orientations.

Citation for published version (APA):

Kaas, A. L., van Mier, H., & Goebel, R. W. (2007). The neural correlates of human working memory for haptically explored object orientations. *Cerebral Cortex*, 17(7), 1637-1649. <https://doi.org/10.1093/cercor/bhl074>

Document status and date:

Published: 01/01/2007

DOI:

[10.1093/cercor/bhl074](https://doi.org/10.1093/cercor/bhl074)

Document Version:

Publisher's PDF, also known as Version of record

Document license:

Taverne

Please check the document version of this publication:

- A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
- The final author version and the galley proof are versions of the publication after peer review.
- The final published version features the final layout of the paper including the volume, issue and page numbers.

[Link to publication](#)

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal.

If the publication is distributed under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license above, please follow below link for the End User Agreement:

www.umlib.nl/taverne-license

Take down policy

If you believe that this document breaches copyright please contact us at:

repository@maastrichtuniversity.nl

providing details and we will investigate your claim.

The Neural Correlates of Human Working Memory for Haptically Explored Object Orientations

Amanda L. Kaas^{1,2}, Hanneke van Mier¹ and Rainer Goebel^{1,3}

¹Department of Cognitive Neuroscience, University of Maastricht, Maastricht, The Netherlands, ²Department of Neurophysiology, Max Planck Institute for Brain Research, Frankfurt am Main, Germany and ³F.C. Donders Centre for Cognitive Neuroimaging, Radboud University Nijmegen, Nijmegen, The Netherlands

Skillful object manipulation requires that haptically explored spatial object characteristics like orientation be adequately represented in working memory. In the current functional magnetic resonance imaging study, healthy right-handed participants explored a bar-shaped reference object with the left hand, memorizing its orientation. After a variable delay (0.5, 5, or 10 s), participants used their right hand to match the orientation by rotating a second, identical object. In the first seconds of the delay, right sensorimotor cortex was active, whereas clusters in left anterior prefrontal cortex (aPFC) (Brodmann area 10) became dominant 2 s after the end of exploration, showing sustained activity for several seconds. In contrast, left parieto-occipital cortex was involved toward the end of the delay interval. Our results indicate that a dynamic network of brain areas subserves hapticospatial information processing in the delay between haptic stimulus exploration and orientation matching. We propose that haptic sensory traces, maintained in contralateral sensorimotor cortex, are transformed into more abstract hapticospatial representations in the early delay stages. Maintenance of these representations engages aPFC and parieto-occipital cortex. Whereas aPFC possibly integrates spatial and motor components of hapticospatial working memory, parieto-occipital cortex might be involved in orientation imagery, supporting working memory, and the preparation of haptic matching.

Keywords: fMRI, parieto-occipital cortex, prefrontal cortex, sensorimotor cortex, spatial

Introduction

Working memory, a concept introduced in the 1970s (Baddeley 1998), refers to the short-term maintenance and manipulation of information necessary for upcoming tasks. To date, most research on the neural substrate of (spatial) working memory has employed stimulation in the visual or auditory modality (e.g., Owen 1997; Haxby and others 2000; Wager and Smith 2003). The haptic modality—or active tactile perception—has remained largely untouched. The lack of scientific attention for haptic perception might be due in part to practical problems related to stimulus presentation and response recording in the context of functional neuroimaging, as well as to the dominance of the visual modality in humans. However, haptic stimulus processing plays a key role in the skillful and sensitive interaction with our surroundings, potentially drawing upon a modality specific type of short-term memory system to keep extracted stimulus features online in the course of our daily activities.

There is some evidence that haptic working memory is characterized by 3 different processing stages, similar to other modalities. Most sensory details of a tactile stimulus are retained

up to 500 ms after stimulus offset. During this stage, perceptual masking can occur, raising the intensity required for detection of a subsequent stimulus (Loomis 1981; Craig and Rollman 1999). The second stage is characterized by vivid recollections of uncategorized stimulus information. Although some information is lost, retention is not affected by interfering tasks until approximately 5 s after stimulus offset. The third stage lasts up to 30 s after stimulus offset and requires rehearsal mechanisms to preserve only a limited set of feature values (Burton and Sinclair 2000). Anatomic studies in monkeys support the idea that tactile information from the somatosensory cortex is directed ventrally through the insula to the frontal cortex for short-term storage (Burton and Sinclair 2000; Constantinidis and Procyk 2004). Some nonhuman primate studies of working memory in the somatosensory domain have shown sustained responses in primary somatosensory regions (Zhou and Fuster 1996), parietal area 5 (Koch and Fuster 1989), and prefrontal cortical areas (Romo and others 1999). Recent human functional magnetic resonance imaging (fMRI) studies found activation in ventral prefrontal cortex (PFC) for maintenance of the oblongness of a manually explored object (Stoerckel and others 2003) and left anterior intraparietal sulcus for maintenance of kinesthetic information for subsequent haptic shape discrimination (Stoerckel and others 2004). Dorsal prefrontal activation was observed when a spatiotemporal pattern of pressure pulses had to be maintained online (Numminen and others 2004).

The present study investigated working memory maintenance of spatial representations obtained by haptic (i.e., active tactile) exploration. Haptic perception involves the integration of tactile and proprioceptive information. The existence of distinct exploration strategies to extract different types of information, like object shape and roughness, shows that it is a domain where perception and action are preeminently intertwined (Soechting and others 1996). In addition, haptic spatial perception is intrinsically linked to peripersonal space, the space within a hand's reach. Psychophysical studies have shown that haptic peripersonal space is probably represented in an egocentric reference frame (centered on the body). This is indicated by systematic error patterns on tasks that appeal to allocentric reference frames (centered in the external world), like haptic parallel setting. In such a task, blindfolded participants are asked to match the orientation of a reference bar by turning a test bar to a parallel orientation. Veridical performance requires the hands to assume different postures for each bar. To achieve this, participants would need to be guided by a representation that factors out the orientation of their own body parts. However, the direction of the errors was found to be highly correlated to the natural orientation of the hand in workspace (Kappers 1999, 2004; Kappers and Koenderink

1999; Zuidhoek and others 2003; Kaas and Van Mier 2006). In contrast, a task involving haptic orientation mirroring in the midsagittal plane induced smaller errors. This task can be accurately performed by using a representation of the bar orientation with respect to the hands (Newport and others 2002; Kappers 2004; Kaas and Van Mier 2006). There is modest empirical evidence that such egocentric representations, that is, representations linked to the body, are associated with a different pattern of brain activity than allocentric representations, that is, of objects with respect to other objects. When compared with allocentric judgments, egocentric judgments involving the computation of the midsagittal plane evoked higher bilateral parietofrontal activation with a right-hemisphere emphasis, in fMRI studies using visual tasks (Vallar and others 1999; Galati and others 2000).

The current fMRI study used an allocentric and an egocentric haptic delayed match-to-sample task to investigate the neural correlates of hapticospatial working memory. In a delayed match-to-sample task, participants have to match a test stimulus to a reference stimulus that has been maintained in working memory during a delay interval. The use of delayed match-to-sample tasks in the context of event-related fMRI designs permits the segregation of neural processes related to temporally separable task components (Zarahn 2000; Linden and others 2003; Manoach and others 2003). In the present study, the event-related design allowed the separation of processes related to hapticospatial working memory from processes related to manual exploration and active manual orientation matching. Activation related to stimulus encoding (exploration), maintenance in working memory (delay), and response (haptic matching) was isolated by introducing a variable delay between the haptic exploration and matching response, with the assumption that areas which respond to the parametric increase of the memory delay are likely to represent the neuronal substrate for hapticospatial working memory. The delay lengths were chosen to correspond to the hypothesized first (0.5 s), second (5 s), and third (10 s) haptic working memory stages (Burton and Sinclair 2000). In addition, we explored the possibility that the distribution of activation in the cortical network supporting hapticospatial working memory would be sensitive to task rules favoring either an allocentric or an egocentric representation (Vallar and others 1999; Galati and others 2000).

Materials and Methods

Participants

Seven healthy participants (3 males, average age 23.7 and standard deviation 5.3 years) were paid to participate in the present study. All participants were right handed as assessed by a Dutch translation of the Edinburgh Handedness Inventory (Oldfield 1971). Informed consent was obtained prior to the experiment. Participants were unfamiliar with the setup, the stimulus orientations, and the purpose of the study. Six participants took part in a separate behavioral training session in the week prior to scanning, consisting of at least 2 runs of each task. The seventh participant practiced 1 run of each task on the day of the experiment. The study was approved by the local ethics committee.

Experimental Procedure

Participants were blindfolded and lay supine in the scanner. Their head and arms were stabilized using foam padding. A small table was placed over the scanner bed, below the waistline, close to the bore entrance. The position of the table and the angle of the tabletop were adjusted to a comfortable position. Participants kept both hands on foam padding, just in front of the table. Attached to the tabletop were 2 turn bars (10 ×

1 cm), with a plastic needle at each end. The lateral motion of the arms was limited by the space within the magnet bore; therefore, the bars were separated by the furthest distance that still allowed them to be comfortably reached (35 cm center-center distance).

Each trial was composed of an exploration phase (duration 1.5 s), a delay phase, and a matching phase (duration 2 s). The delay phase could be short (0.5 s), intermediate (5 s), or long (10 s). The onset of each trial was synchronized with the start of the acquisition of a new volume. The intertrial interval (ITI) was 8.33 s. Start and end of the exploration and matching phases were indicated by 4 auditory signals presented through headphones (pure tones, 1000 Hz for the exploration phase and 2000 Hz for the matching phase).

During each trial, the first auditory signal indicated that the participant had to feel the orientation of the left reference bar with the left hand. The second auditory cue signaled the end of the exploration phase and the beginning of the variable delay. Upon this cue, the participant stopped the exploration of the reference bar and positioned the left hand in the resting position on the foam padding, next to the right hand. The third auditory cue signaled the end of the delay and the beginning of the matching phase, during which the participant used the right hand to turn the test bar to an orientation matching the orientation of the reference bar (see Fig. 1). At the last auditory cue, indicating the end of the matching phase, the participant positioned the right hand next to the left hand in the resting position, until the start of the next trial, at which time the procedure described above was repeated (see Fig. 1a).

A different matching criterion was used in each of the 2 experimental conditions. In the mirror task, the test bar had to be turned in such a way that its orientation matched the mirror image of the left bar with respect to the midsagittal plane of the body (see Fig. 1b). In the parallel task, the orientation of the test bar had to be turned parallel to the reference bar (see Fig. 1c).

During all experimental runs, 2 assistants were present in the scanner room. For each trial, the first assistant set the reference orientations. The second assistant noted the orientation of the test bar and returned it to a default position (either 55° or 125°, depending on the run). Accuracy for setting and recording of the orientations by the assistants was tested in advance and was found to be within 0.5°. Six different orientations were used for the reference bar (0°, 30°, 60°, 90°, 120° and 150°, see Fig. 3). Participants performed two 12-min runs for each task. Each run was made up of a pseudorandom series of 36 trials (3 delays × 6 orientations × 2 repetitions) of either the parallel or the mirror task. Parallel and mirror runs were alternated, and the order was counterbalanced over participants. At the end of the experiment, participants were asked to elaborate on the strategy they had used to perform the tasks.

Behavioral Data Analysis

Signed errors were calculated for every trial by subtracting the orientation of the (left) reference bar from the orientation of the (right) response bar. In the mirror task, matching errors were expressed as deviations from the inverse reference orientation (i.e., 60° → -60°). Errors were subsequently normalized to lie in the range -89° < 0 < 90° and were analyzed using a 3 (delay) × 2 (task) within-subjects analysis of variance (ANOVA).

Image Acquisition

A high-resolution anatomical image was obtained from each participant in a 1.5-T magnetic resonance scanner using a T_1 -weighted magnetization-prepared rapid gradient-echo sequence (Magnetom Sonata, Siemens Medical Systems, Erlangen, Germany; matrix 256 × 256 × 176, voxel size 1 × 1 × 1 mm³). fMRI data were subsequently acquired in the same session using a T_2^* -weighted echo-planar sequence (matrix 64 × 64 × 25, voxel size 4 × 4 × 4.5 mm³, echo time/time repetition (TR) = 40/1970 ms, flip angle = 90°) covering the whole brain with the exception of the lower cerebellum. All images were obtained in one scanning session, which comprised 4 functional runs of on average 338 volumes. Presentation of the first auditory cue was synchronized with the fMRI sequence at the beginning of each trial.

The fMRI Data Analysis

The first 2 volumes of each run were discarded to remove T_1 saturation effects. Standard preprocessing was performed, including motion

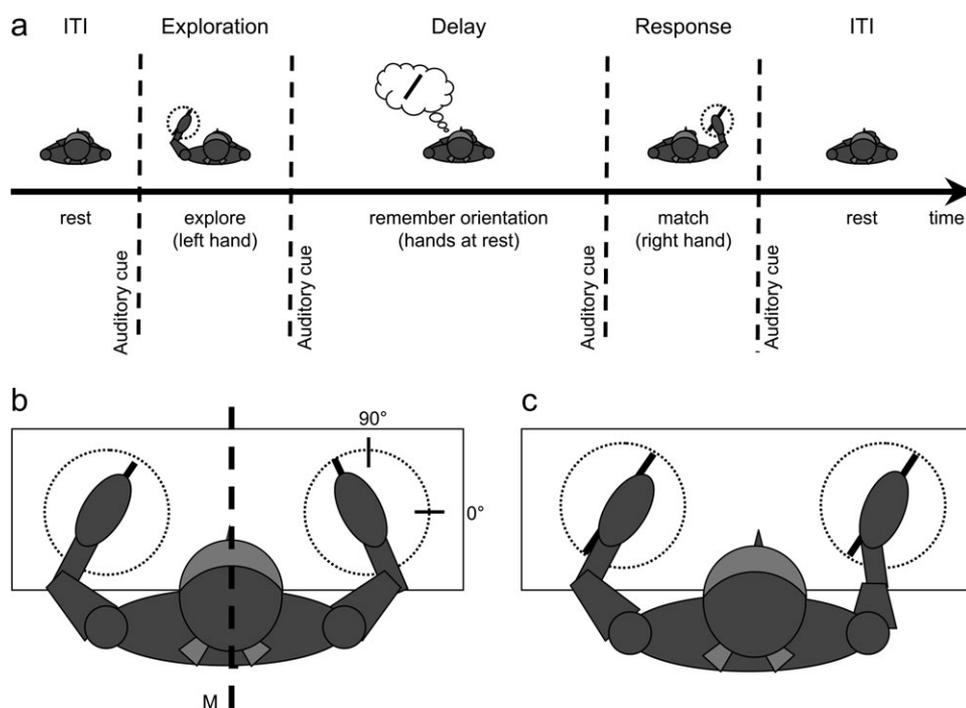


Figure 1. (a) Diagram illustrating the temporal succession of task events. Panels (b) and (c): schematic illustration of the mirror (b) and parallel (c) matching tasks, viewed from behind the head for a participant lying in the scanner. The Kaasplank tabletop was not orthogonal with respect to the scanner bed, but slightly tilted to obtain a comfortable orientation. In the mirror task, the orientation of test bar and right hand had to be the mirror image of the orientation and hand posture on the left with respect to the midsagittal plane, which is indicated by the dashed line “M” in part (b).

correction, temporal smoothing (high-pass filter, 5 cycles per run), slice scan time correction, and linear trend removal, as implemented in the BrainVoyager software package 4.9/QX1.1 (Brain Innovation B.V., Maastricht, the Netherlands; Goebel and others 2006). Functional images from different runs were aligned to the first run and coregistered with the Talairach-transformed anatomical images, interpolating the functional images to obtain a volume time course with a resolution of $3 \times 3 \times 3 \text{ mm}^3$. The resulting fMRI time series were analyzed with a general linear model. We used a design that aimed to separate different trial phases (exploration, delay, and matching) and trial lengths (short, intermediate, and long), using stick predictors with a width of 1 TR. This resulted in 2 predictors for the short-delay trial (1 exploration, 0 delay, and 1 matching predictor), 4 predictors for the intermediate-delay trial (1 exploration, 2 delay, and 1 matching predictor), and 7 for the long-delay trial (1 exploration, 5 delay, and 1 matching predictor), adding up to a total of 13 predictors for each run. The predictors were shifted forward in time by 2 volumes (3.94 s) to account for hemodynamic sluggishness (see Fig. 2).

We chose stick predictors because we did not want to make assumptions about the specific shape of the hemodynamic response, which is unlikely to be the same for all brain areas involved in the task. In addition, stick predictors allow visualization of the foci of mass activation within each TR of the delay. Previously, stick predictors were successfully applied for the detection of temporally restricted activation in the delay of a visual working memory task (Linden and others 2003). To identify those predictors mainly reflecting the delay-related activity, we used the standard assumption that the hemodynamic response peaks approximately 4 s after the stimulus or neural event.

A fixed effects group analysis was performed on 26 runs, 14 for the parallel task and 12 for the mirror task, correcting for serial correlations (one of the mirror task runs was missing in 2 participants, due to technical problems). In addition, single-subject analyses were performed to rule out dominance of the results by a small number of participants. Statistical maps were interpolated to a resolution of $1 \times 1 \times 1 \text{ mm}^3$ and projected on the average of the Talairach brains of all participants. For the contrast analyses described below, only those

clusters are reported that fell within gray matter and that were over 50 mm^3 in size.

The fMRI Contrast Analyses

Haptic Exploration and Matching Response

A conjunction of the exploration and matching predictors from the short- and long-delay trials was used to visualize the activation in the exploration and response phases. The predictors from the short- and long-delay trials were used because they were most similar (see Fig. 2). The matching predictor of the intermediate-delay trial also included a small portion of the end of the delay, due to the uneven delay length of 5 s. The same conjunction of long and short trials was then also used for the exploration phase, to be able to maintain the same threshold for these very similar trial phases. In addition, the contrasts between parallel and mirror task were computed separately for exploration and matching to check for areas related to the performance of these different tasks.

Delay-Related Activity

To disclose areas showing potential task differences, the parallel versus mirror contrast was computed for the delay phase. Subsequently, 2 different contrast analyses were used to evaluate delay-related activation. The first analysis was performed to identify brain areas showing a greater or longer response with increasing delay length, by computing the unbalanced contrast maps of all 4 intermediate-delay trial predictors minus the 2 short-delay trial predictors and all 7 long-delay trial predictors minus all 4 intermediate-delay trial predictors. Exploration- and matching-related differences will cancel out in this analysis because all trials were identical except for the length of the delay. In this way, regions were revealed showing a greater or longer response for increasing delay lengths. In the short-delay trial, potential nonlinearities in the summation of the blood oxygen level-dependent (BOLD) response related to exploration and matching were assumed to be reduced or precluded by the fact that exploration and matching are carried out by different hands, with the restriction that this holds true for lateralized areas, but not for areas responding more or less independent of hand use.

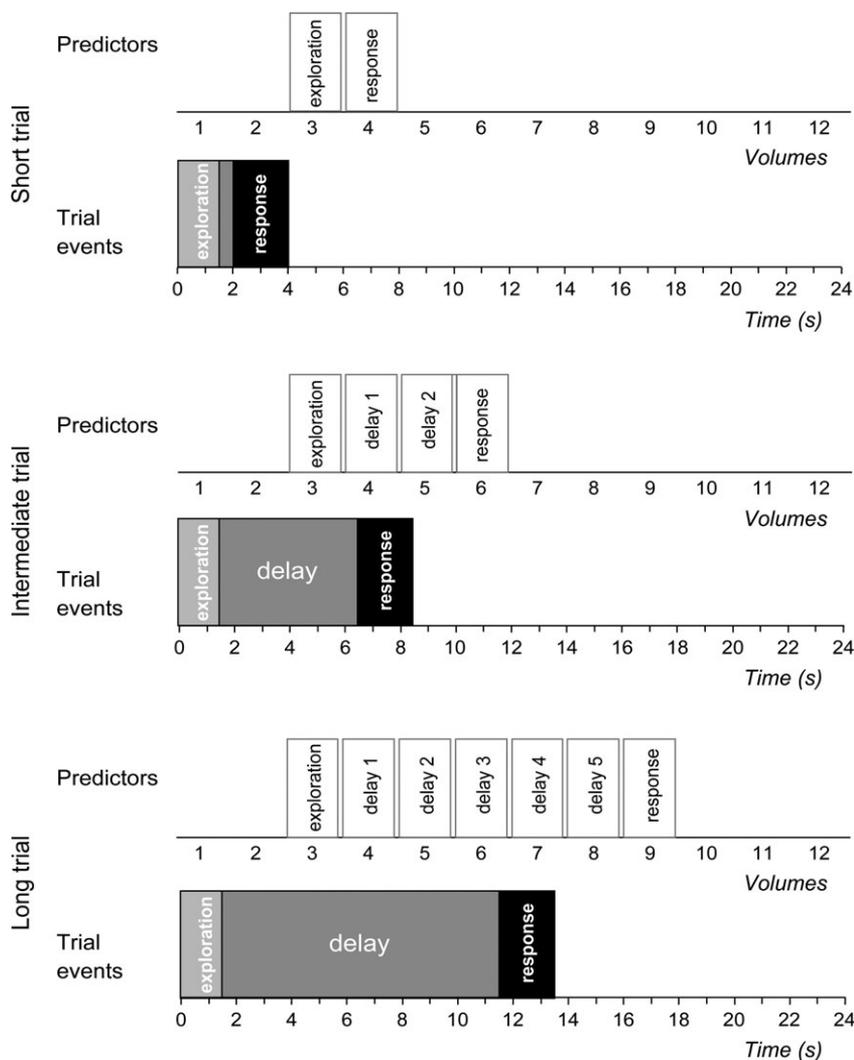


Figure 2. Trial events for each trial type (short, intermediate, and long delay) and corresponding stick predictors shifted forward in time by 2 volumes to account for the hemodynamic delay. Separate stick predictors model the exploration and response phases. The intermediate and long delays are modeled by 2 and 5 separate stick predictors, respectively.

The second analysis aimed to illustrate the temporal evolution of activation across the (longest) delay phase. For this purpose, a contrast map was computed for separate 2-s epochs of the delay phase against ITI. Only delay epoch 2, 3, and 4 were considered, from 2 s after exploration offset to 2 s before matching onset, to reduce overlap with the descending tail of the exploration BOLD response as well as the ascending slope of the matching response. The predictor for delay epoch 2 was available from both the intermediate- and long-delay trials (see Fig. 2); for that reason, a conjunction of the contrasts of this predictor against ITI from the intermediate- and long-delay trials was used to visualize the activation corresponding to delay epoch 2. The predictors for delay epoch 3 and 4 were only available from the long-delay trial. Areas that were stimulus related but had a longer or shorter hemodynamic delay (time to peak) were potentially included in the delay-epoch analysis. Therefore, this analysis was used complementary to the first, and only areas that were also found in the first delay analysis, comparing trials of different delay lengths, were interpreted.

A statistical threshold of q (FDR) < 0.05 (false discovery rate; Genovese and others 2002) was used for all group analyses. However, the exploration and matching phases, which entailed perceptual and motor activity, were associated with higher BOLD responses than the delay phase, which involved only cognitive processes. Therefore, the significance thresholds for Figure 4 and Tables 1 and 2 were set to

$t_{8695} > 3.75$, $q(\text{FDR}) < 0.001$. Single-subject analyses were thresholded at $P < 0.05$ (uncorrected) for all participants. In some cases (20%), the threshold was raised to prevent clusters spreading to clearly unrelated anatomical regions.

Results

Behavioral Performance

The 3 (delay) \times 2 (task) within-subject ANOVA on the signed matching errors did not reveal significant effects for delay lengths ($F_{2,14} = 0.90$, $P = 0.91$) or between mirror and parallel task ($F_{1,7} = 1.21$, $P = 0.31$). The mean signed matching error was -2.5° (standard error [SE] = 4.0) for the parallel task, displaying a clockwise deviation, and 1.4° (SE = 2.5) for the mirror task, showing a counter clockwise deviation (see Fig. 3).

Six out of 7 participants reported having used a strategy involving some form of visualization for the parallel task. Five participants used a similar visualization strategy for the mirror task, 4 of whom explicitly stated that they directly recoded the reference orientations by mirroring in the 90° axis of the left

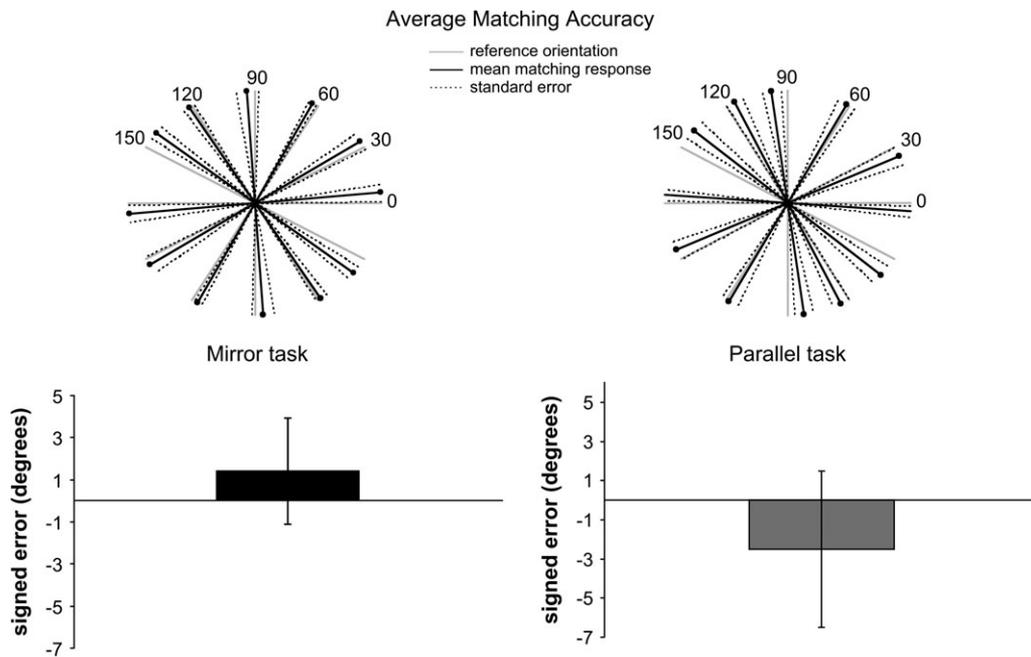


Figure 3. Average matching accuracy for mirror and parallel haptic matching. The top panel is a graphical display of the reference orientations (gray lines) and the corresponding average matching response (black lines). Dotted lines indicate the average matching response plus/minus 1 SE. The panel below shows the average matching response and SE across reference orientations.

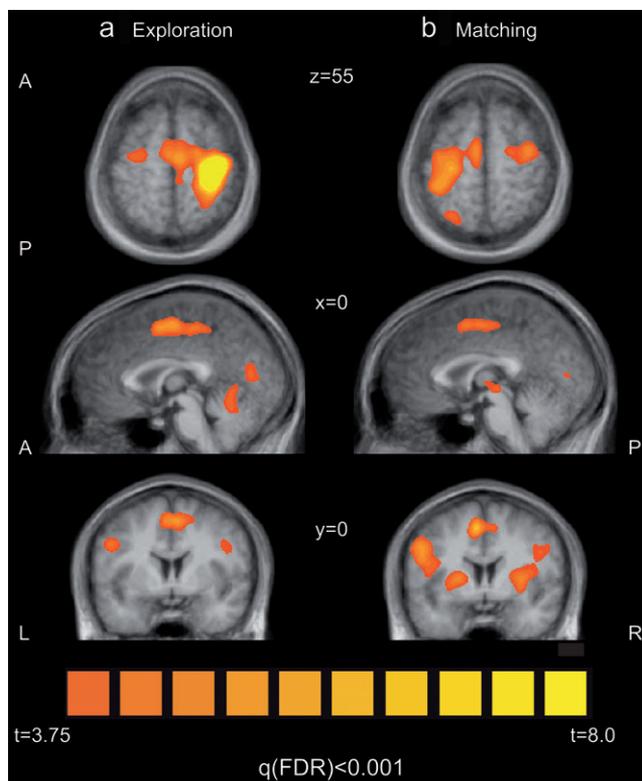


Figure 4. Statistical maps for the contrast against ITI of (a) the exploration phase and (b) the matching phase. Maps were obtained from the fixed effects group ($N = 7$) general linear model analysis and are projected on the average of the Talairach normalized brains of all participants. The statistical threshold was set to $t > 3.75$, $q(\text{FDR}) < 0.001$. Only clusters over 50 voxels are shown, which t -values exceeded the threshold in both short- and long-delay trials.

turntable, therefore in effect performing a parallel matching with respect to this recorded reference. Two participants mentioned having used a more somatosensory strategy on the mirror task.

The fact that delay did not result in a significant deterioration of performance shows that memory traces and maintenance strategies for haptic stimuli were still effective at 10 s retention intervals, comparable with psychophysical tactile studies showing retention up to at least 15 s (Bowers and others 1990; Kiphart and others 1992; Burton and Sinclair 2000; Woods and others 2004). Other studies reported significantly higher accuracy for mirror matching compared with parallel matching (Newport and others 2002; Kappers 2004; Kaas and Van Mier 2006). However, these studies used larger distances between the turn bars in the frontoparallel plane. Decreasing the distance between the turn bars decreased the error size in haptic parallel matching (Kappers 1999), whereas mirror matching remained unaffected (Kaas and Van Mier 2006).

Imaging Data

Haptic Exploration and Matching Response

The statistical contrast between the parallel and mirror task did not yield significant results for exploration or matching. The contrast of exploration predictors against ITI revealed that haptic exploration with the left hand was associated with a large activated region in the right hemisphere with its center of gravity in the central sulcus (primary motor cortex, M1). In addition, there was a large patch of activation in right lateral sulcus, including secondary somatosensory cortex and primary auditory cortex, and a smaller focus was found in right putamen. In the left hemisphere, activation was found in the cerebellar vermis, superior temporal cortex, left precentral sulcus, pre-cuneus, frontal eye fields (FEFs), medial occipital cortex, and

Table 1
Haptic exploration network

Brain region (COG)	BA	x	y	z	Number of voxels	In number of subjects
L anterior cerebellum (vermis)		-5	-59	1	13 394	7
L superior temporal cortex	22/42	-48	-33	12	9317	7
L inferior frontal sulcus (vPMA)	44	-44	3	29	1390	6
L precentral sulcus	6	-27	-10	53	1295	7
L precuneus	7	-16	-73	44	330	6
L middle frontal gyrus (FEF)	8	-31	25	37	325	6
L medial occipital cortex	19	-39	-71	13	247	7
L thalamus		-7	-20	1	64	4
R central sulcus (M1)	4	22	-20	53	35 251	7
R superior temporal cortex	42	39	-24	15	17 090	7
R inferior frontal sulcus (vPMA)	44	43	6	29	1966	7
R putamen		28	-6	-1	78	6

Note: Areas activated for the exploration versus the ITI contrast, conjoined for short and long trials. Voxel size is 1 mm³. Talairach coordinates of the centers of gravity (COG) of significantly activated clusters, over 50 voxels in size, at $q(\text{FDR}) < 0.001$, $t_{6695} > 3.75$. The group map was spatially smoothed with a Gaussian kernel of 8 mm full width at half maximum (FWHM). L = left, R = right, M1 = primary motor cortex, vPMA = ventral premotor cortex.

Table 2
Haptic response network

Brain region (COG)	BA	x	y	z	Number of voxels	In number of subjects
L central sulcus (M1)	4	-12	-16	52	26 949	7
L putamen		-27	-3	13	15 293	7
L superior temporal cortex	22/42	-51	-35	12	6379	7
L middle frontal gyrus (FEF)	8	-34	28	37	1733	6
L superior occipital cortex	19	-19	-73	41	1288	6
L superior parietal lobule	7	-23	-59	57	806	6
L inferior temporal cortex	37	-41	-62	2	224	5
L parieto-occipital sulcus	31	-15	-69	19	148	6
L precuneus	7	-10	-49	49	77	5
Cuneus		0	-76	9	87	6
R insula		36	5	16	9118	7
R superior temporal cortex	41	46	-27	13	2655	7
R parieto-occipital sulcus	31	14	-64	14	1952	6
R postcentral gyrus (S1)	2	33	-32	48	963	7
R inferior parietal lobule	40	47	-39	28	57	5

Note: Areas activated for the response versus ITI contrast, conjoined for short and long trials. Voxel size is 1 mm³. Talairach coordinates of the centers of gravity (COG) of significantly activated clusters, over 50 voxels in size, at $q(\text{FDR}) < 0.001$, $t_{6695} > 3.75$. The group map was spatially smoothed with a Gaussian kernel of 8 mm full width at half maximum (FWHM). L = left, R = right, M1 = primary motor cortex.

thalamus. Bilateral activation was observed in the ventral premotor area (vPMA) (see Fig. 4a and Table 1).

The contrast of matching predictors against the ITI revealed the highest levels of activation in the left hemisphere. The center of gravity of the largest cluster was localized in the left primary motor cortex, consistent with use of the right hand during matching. Additional left hemispheric clusters were found in the putamen, superior temporal cortex, FEFs, superior occipital cortex, superior parietal lobule, inferior temporal cortex, and left precuneus. In the right hemisphere, activation clusters were centered in the insula, superior temporal gyrus, postcentral gyrus (S1), and right inferior parietal lobule. Bilateral activity was observed in cuneus and parieto-occipital sulcus (see Fig. 4b and Table 2).

Delay-Related Activity

The contrast of intermediate- versus short-delay trials revealed areas in the left parieto-occipital cortex (Brodmann area [BA] 19) and the ventral premotor cortex (BA 44). In the right

Table 3
Contrast intermediate minus short trial

Region	BA	x	y	z	Number of voxels
Subject					
L mIFG (vPMA)	44	-38	21	32	187
Mean (N = 5)		-39	20	30	953
2		-41	22	28	45
3		-36	24	34	21
5		-46	15	24	3008
6		-38	18	28	1681
7		-32	20	34	12
L SOG (POC)	19	-22	-72	16	93
Mean (N = 4)		-25	-74	15	678
1		-29	-74	14	188
4		-21	-71	16	48
5		-27	-73	17	506
7		-21	-79	13	1970
R CS (M1)	4	32	-26	58	3611
Mean (N = 7)		31	-29	60	4319
1		31	-19	62	391
2		35	-36	56	1166
3		38	-33	60	4776
4		28	-28	62	12 371
5		27	-33	63	3619
6		31	-25	55	7750
7		29	-27	60	158
R lingual gyrus	18	12	-86	-9	156
Mean (N = 6)		10	-86	-7	1313
1		28	-90	-4	900
2		14	-85	-6	268
3		15	-87	-9	102
4		0	-82	-14	1824
5		6	-83	-6	1507
7		-2	-90	-5	3275

Note: Center of gravity Talairach coordinates from group analysis clusters significant at $q(\text{FDR}) < 0.05$ and corresponding clusters from individual analyses significant at (uncorrected) $P < 0.05$, $t > 2.0$. The group map was spatially smoothed with a Gaussian kernel of 4 mm full width at half maximum (FWHM). Voxel size is 1 mm³. L = left, R = right. Group analysis $t_{6695} > 2.9$. mIFG = middle inferior frontal gyrus, SOG = superior occipital gyrus, POC = parieto-occipital cortex, CS = central sulcus, M1 = primary motor cortex.

hemisphere, primary motor cortex (M1) and occipital cortex (BA 18) were activated (see Table 3). By contrasting the long-minus intermediate-delay trials, significant t -values were found for voxel clusters in left calcarine sulcus (BA 17), left parieto-occipital cortex (BA 19), left anterior prefrontal cortex (aPFC) (BA 10), left putamen, bilateral middle occipital gyrus (BA 18), and right anterior cingulate gyrus (see Table 4). For the majority of the participants, these areas were also found to be active in single-subject analyses (see Tables 3 and 4). Figure 5 displays selected activated regions and corresponding event-related time courses for both contrasts overlaid onto anatomical images, as well as the equivalent regions from the single-subject analyses. The averaged event-related time course from the primary sensorimotor cluster shows a reactivation of this area in the matching phase. By contrast, left parieto-occipital cluster (POC) becomes reactivated near the end of the delay, well before the start of the matching phase, whereas left aPFC shows a sustained response during the first half of the long delay. The matching cue for the intermediate-delay trials occurred 6500 ms after trial onset, that is, just after volume 3 (5910 ms). The curves for left aPFC start to diverge at the next time point, at volume 4 (7880 ms), and the long-delay trial remains high until volume 5.

The results from the epoch analysis illustrating the spatio-temporal dynamics in the delay interval are presented in Figure 6 and Table 5. The conjunction of the contrasts against ITI of the second delay predictor showed left-hemisphere activation in

Table 4

Contrast long minus intermediate trial

Region	BA	x	y	z	Number of voxels
Subject					
L SOG (POC)	19	-26	-82	32	313
Mean (N = 6)		-30	-79	33	1194
2		-46	-62	37	2089
3		-19	-79	26	33
4		-29	-75	36	4296
5		-25	-84	39	284
6		-24	-88	29	232
7		-35	-84	29	229
L putamen		-26	10	-9	142
Mean (N = 7)		-22	8	-10	517
1		-24	20	-7	1431
2		-27	7	-15	379
3		-19	6	-11	173
4		-28	4	-11	288
5		-11	7	-10	997
6		-23	9	-7	38
7		-19	6	-11	313
L MOG	18	-11	-95	7	104
Mean (N = 6)		-17	-93	9	816
2		-22	-96	18	295
3		-9	-93	-1	184
4		-6	-97	2	574
5		-17	-96	11	1615
6		-35	-80	10	1637
7		-15	-96	13	593
L CaS (V1)	17	-5	-78	7	93
Mean (N = 5)		-7	-58	5	293
3		-5	-84	0	849
4		-6	-76	6	351
5		-5	-76	8	195
6		-1	-82	0	180
7		-3	-76	8	22
L middle frontal gyrus (aPFC)	10	-21	49	10	57
Mean (N = 6)		-23	47	9	158
2		-34	46	15	115
3		-20	50	4	21
4		-16	52	9	77
5		-21	39	11	603
6		-22	49	3	25
7		-23	45	11	107
R ACG	24	2	32	25	53
Mean (N = 7)		5	16	18	518
1		-3	39	14	2760
2		1	35	26	56
3		0	23	25	9
4		29	-85	10	147
5		1	34	16	505
6		0	34	21	54
7		4	33	16	95
R MOG	18	26	-91	9	51
Mean (N = 6)		26	-89	13	1305
2		37	-87	16	133
3		28	-82	11	278
4		27	-93	6	167
5		23	-88	24	5530
6		25	-86	11	676
7		16	-98	9	1044

Note: See Table 3. Group analysis: $t_{6995} > 3.3$. SOG = superior occipital gyrus, ACG = anterior cingulate gyrus, MOG = medial occipital gyrus, CaS = calcarine sulcus, V1 = primary visual area.

the vermis of the cerebellum, aPFC (BA 10), and inferior parietal lobule (BA 40) and right-hemisphere activation in the lingual and fusiform gyrus (BA 18 and 19) and the pericentral cortex (M1/S1). The contrast against ITI of the third delay predictor, available for the long-delay trial only, corresponded to activation in left aPFC (BA 9, 10) and left inferior frontal gyrus (BA 47). The contrast of the fourth delay predictor against ITI revealed significant left-hemisphere clusters in the aPFC (BA 10), presupplementary motor area, and the parieto-occipital cortex (BA 19).

Discussion

A dynamical cortical network of brain areas was revealed, using a haptic orientation matching task with a variable delay between stimulus exploration and active matching response, showing higher or sustained activation for trials of increasing delay length. Right primary sensorimotor cortex, left vPMA, right lingual gyrus (BA 18), and left parieto-occipital cortex were the main foci of activation when contrasting intermediate versus short trials, whereas left aPFC (BA 10), left parieto-occipital and bilateral medial occipital gyrus were the most important areas activated in the contrast between long- and intermediate-delay trials. Analysis of separate 2-s delay epochs uncovered the temporal flow of mass activation in the middle of the longest delay interval, with right primary somatosensory, aPFC, and parieto-occipital cortex appearing in subsequent time intervals.

Activation in Exploration and Matching Phases

The areas revealed in the exploration and matching phases correspond to areas commonly reported to be involved in haptic sensorimotor processes (Van Mier and others 1998, 2004; Stoeckel and others 2003; Numminen and others 2004; Lehericy and others 2006). The pattern of lateralization can be explained by the fact that the left hand was used for exploration and the right hand for matching of the stimulus bars. The activation in bilateral superior temporal regions is most likely related to the processing of the auditory stimuli, whereas the activations in left inferior temporal cortex in the matching phase are in-line with previous reports of activation in this area during exploration of tactile objects (Pietrini and others 2004). The involvement of occipital and parieto-occipital regions (POCs) in exploration and matching is consistent with subjective reports of visual imagery from the majority of our participants and the important role of (higher order) visual areas for spatial processing (e.g., Zangaladze and others 1999; Sathian and Zangaladze 2002; Merabet and others 2004; Zhang and others 2004, 2005).

Effect of Task

The contrast of parallel versus mirror task, separately performed for the exploration, delay, and matching predictors, did not reveal any areas that responded differently during parallel or mirror task. This might indicate that the tasks are subserved by overlapping neuronal networks, which cannot be disentangled with the current spatiotemporal resolution and experimental design. The absence of a significant difference in both the behavioral measure and the imaging data might also be the result of a ceiling effect in haptic matching performance: former studies have shown that the error size for parallel matching decreases with smaller distances between the bars (Kappers 1999; Kaas and Van Mier 2006). However, the results could also indicate that both tasks were solved in the same, visuospatial reference frame. This interpretation would be in accordance with the reports of 5 out of 7 participants stating that they had used the same strategy for both tasks.

First 4 s of the Delay: from Sensory Trace to Hapticospatial Imagery

The activity in right primary somatosensory cortex found in the contrast of intermediate and short trials and in the second (2–4 s) epoch of the delay is in-line with previous findings of involvement of areas belonging to the somatosensory pathway

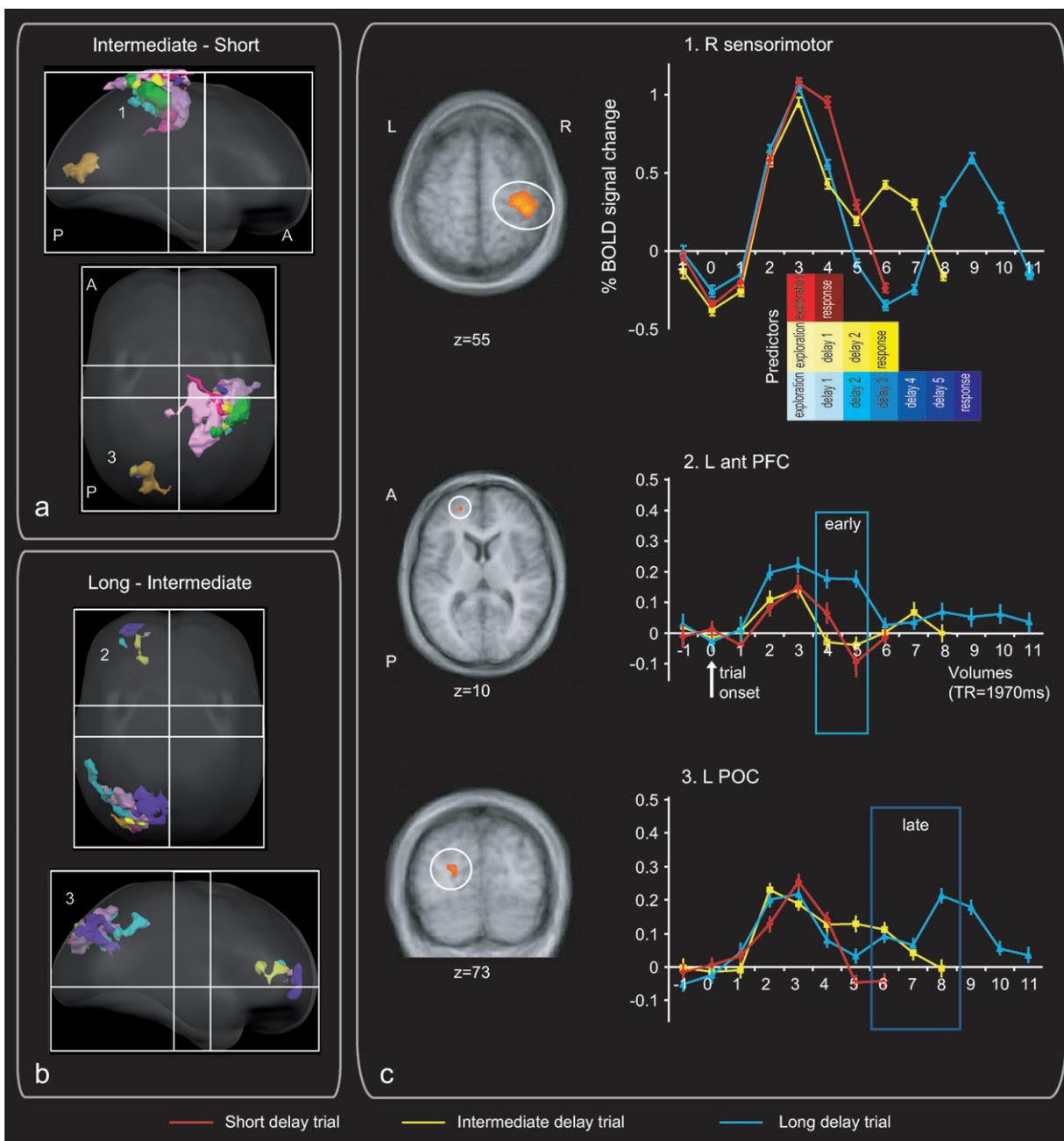


Figure 5. Selected delay-length dependent areas from single-subject (*a* and *b*) and group analyses (*c*). Individual regions of interest for the contrast of intermediate minus short trials (*a*) and long minus intermediate trials (*b*) are projected in a glass brain (right and top views). 1 = right sensorimotor cortex, 2 = left aPFC, 3 = left parieto-occipital cortex (POC). Clusters (*c*): the right sensorimotor cluster was obtained from the contrast of intermediate- minus short-delay trials (group: $t > 2.9$, $q(\text{FDR}) < 0.05$; single subject: $t > 2$, $P < 0.05$) and the left aPFC cluster from the contrast of long minus intermediate trials (group: $t > 3.3$, $q(\text{FDR}) < 0.05$; single subject: $t > 2$, $P < 0.05$). A similar left POC was found in both contrast analyses; displayed is the time course from the cluster found by subtracting short from intermediate trials. A square window indicates the time points of interest for the left aPFC and left POC. The group clusters were projected on the group average of the Talairach normalized brains. Note that the slight spilling of the clusters from the glass brain surface is due to the fact that the surface does not reach until the superior end of Talairach space.

in tactile memory (Koch and Fuster 1989; Zhou and Fuster 1996; Romo and others 1999; Burton and Sinclair 2000; Stoeckel and others 2003; Constantinidis and Procyk 2004; Numminen and others 2004). The corresponding event-related time course showed substantial coactivation of the ipsilateral hemisphere in the matching phase (see Fig. 5). The activation of left cerebellar vermis, showing up in the second delay epoch, did not appear in the contrast of intermediate- versus short-delay trials. Still, the role of the right primary somatosensory area in the delay is

difficult to establish based on the current fMRI study. Our interpretation would be that primary somatosensory cortex is involved in the early sensory stage of haptic working memory. This is in-line with the model by Burton and Sinclair (2000) and with previous studies reporting involvement of primary somatosensory cortex in short-term maintenance of vibrotactile stimuli (Harris and others 2002) and tactile texture stimuli (Zhou and Fuster 1996). These studies circumvented the problem of the hemodynamic confound in fMRI by using

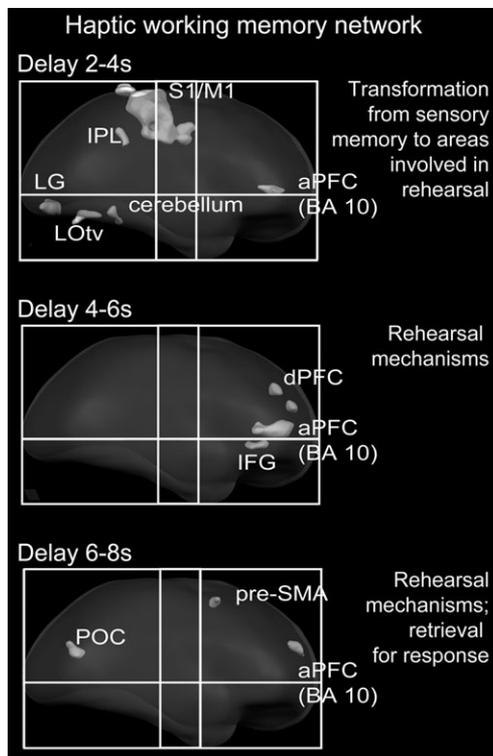


Figure 6. Surface projection of volumes of interest in a glass brain (right view), representing the dynamical neural network activated in the middle of the working memory delay. Volumes of interest for the 3 middle delay epochs (2–8 s) were obtained from the contrasts of separate delay predictors against baseline (Table 5).

temporally resolved transcranial stimulation (TMS) and single-cell recordings, respectively.

The contrast of intermediate- versus short-delay trials also revealed activity in left ventral premotor cortex (BA 44), which might correspond to a region involved in visuomotor transformations for grasping and manipulating objects in macaques (Rizzolatti and others 2002) and humans (Binkofski and others 1999; Johnson-Frey and others 2005). Lesions of left ventral premotor cortex are observed in patients suffering from ideomotor apraxia (Haaland and others 2000), a pathological condition characterized by the performance of spatiotemporal

errors when pantomiming transitive tool-use gestures, as well as intransitive gestures, for example, waving goodbye (Choi and others 2001). The fact that this region remained when subtracting short from intermediate trials, but not when calculating long minus intermediate trials, suggests that the long- and intermediate-delay trials involve equal activation levels in vPMA, whereas different pathways are used for the sensorimotor transformations in the short trials.

The left POC revealed in the contrast between intermediate and short trials is similar to clusters found in the delay epoch 6–8 s after exploration offset and in the contrast between long and intermediate trials. These POCs might be involved in directing hapticospatial attention (Simon and others 2002). An area posteromedial from POC has been interpreted as the neural substrate of tactile position recognition because of its role in integrating proprioceptive posture information on visuotactile matching trials performed with crossed hands (Misaki and others 2002). Alternatively, the POC region might support specific hapticospatial orientation imagery, supporting haptic working memory. Visual imagery has been shown to activate primary and secondary (parieto-occipital) visual areas (Amedi and others 2005). The area found in the current study might be the human homologue of the macaque V6 complex, which contains a large representation of the periphery of the contralateral visual hemifield (Pitzalis and others 2006). Alternatively, it might be functionally homologous to the region known as caudal intraparietal sulcus in the macaque, which responded selectively to the longitudinal axis of elongated objects that were presented visually (Sakata and others 2005). Left-hemisphere areas with more dorsal coordinates than POC were reported to show preferential activation for tools as compared with other classes of objects (Johnson-Frey 2004). In addition, parietooccipital areas have been found to be of vital importance for tactile discrimination of macrostructural object attributes such as orientation in normally sighted humans (Sathian and others 1997; Zangaladze and others 1999; Sathian and Zangaladze 2002; Zhang and others 2005). Orientation-selective adaptation effects related to visual higher order shape processing were found in a right POC area (Talairach coordinates: 22, –81, 19; Valyear and others 2006).

In-line with the lingual gyrus activation in the present study, Stoeckel and others (2003) found left lingual gyrus activity when a manipulandum was explored with the right hand,

Table 5

Delay-related network

Delay	Brain region (COG)	BA	x	y	z	Number of voxels	In number of subjects
2–4 s	L middle frontal gyrus (aPFC)	10a	–25	44	3	542	3
	L cerebellum		–10	–47	–13	317	4
	L inferior parietal lobule		–28	–43	38	316	4
	R central sulcus (M1)	4	31	–25	53	10 761	7
	R lingual gyrus	18	6	–84	–8	1251	4
4–6 s	R fusiform gyrus (LOtv)	19	48	–64	–14	408	6
	L middle frontal gyrus (aPFC)	10a	–20	44	7	2198	7
	L inferior frontal gyrus	47	–41	33	–3	437	7
	L superior frontal gyrus (aPFC)	10b	–13	54	21	371	6
	L superior frontal gyrus	9	–12	44	32	350	6
6–8 s	L superior occipital gyrus (POC)	19	–27	–71	20	464	6
	L superior frontal gyrus (aPFC)	10b	–13	56	23	334	6
	L medial superior frontal gyrus (preSMA)	6	–15	9	53	320	7

Note: Areas activated for the contrast of each of the 3 predictors for the middle of the delay interval against ITI. Center of gravity (COG) Talairach coordinates for significantly activated clusters over 300 voxels in size at $q(\text{FDR}) < 0.05$ (corresponding to $t_{6895} > 2.5$). Group maps were spatially smoothed with a Gaussian kernel of 8 mm full width at half maximum (FWHM). Voxel size is 1 mm³. L = left, R = right, M1 = primary motor cortex, LOtv = lateral occipital tactile-visual area, POC = parieto-occipital cortex, SMA = supplementary motor area.

interpreting the activation as the neural correlate for a visual imagery strategy for the encoding of geometric properties. Primary and secondary visual areas were also reported in a study involving mental rotation of tools (Vingerhoets and others 2002). In our study, right medial lingual gyrus (BA 18) activity was accompanied by right lateral occipital tactile-visual area (BA 19; Amedi and others 2001) and left inferior parietal activity in the 2-s epoch approximately 2 to 4 s after exploration offset. This constellation of areas might support a hapticospatial imagery strategy that aids working memory maintenance of haptic macrospatial features.

In general, the recruitment of visual areas at various stages in the current haptic orientation matching task is consistent with the dominance of vision over haptics in macrospatial tasks (Lederman and Klatzky 2004). The functional relevance of visual areas for haptic tasks has been demonstrated by impaired haptic performance after disruption of occipital cortex by TMS (Zangaladze and others 1999; Merabet and others 2004). Recruitment of visual areas can be accompanied by subjective experiences of visual imagery (Kosslyn and others 2001; Ganis and others 2004; Zhang and others 2004). In the present study, 6 out of 7 participants reported having used a visual imagery strategy.

Four to Ten Seconds into the Delay: the Neural Correlate of Hapticospatial Maintenance

In the delay epoch from approximately 4–6 s after exploration, activation moved entirely to the prefrontal areas, with 4 activated clusters: 1 in dorsal (BA 9), 1 in ventral PFC (BA 47), and 2 in aPFC (BA 10). The last cluster was also found in the contrast of long- versus intermediate-delay trials, possibly representing abstract working memory maintenance of information relevant to the upcoming task (e.g., Courtney and others 1996, 1998; D'Esposito and others 1998; Linden and others 2003).

Working memory theorists have long attempted to unravel the organizational principles governing the functional topography of working memory in the PFC. One view, supported by differential anatomical connectivity and functional data, is that there is a segregation based on content domain, with working memory for objects, faces, and the color or pattern of a stimulus engaging ventral portions of PFC and spatial working memory engaging more dorsal prefrontal areas (Courtney and others 1996, 1998; D'Esposito and others 1998; Linden and others 2003; Romanski 2004; Mohr and others 2006). On the other hand, evidence has been found that working memory in PFC is organized based on the kind of cognitive processing required (Owen 1997; Nyberg and others 2003), with maintenance processes activating ventral areas and manipulation processes activating dorsal areas. The exact nature of the processes reflected is subject of debate. For instance, it has been argued that dorsolateral PFC supports response selection processes rather than working memory per se (Rowe and others 2000). In a number of studies in the visual modality, activity in PFC has been suggested to be instrumental in biasing sensory processing and response selection to ultimately achieve a desired behavioral outcome (Wallis and Miller 2003; Reynolds and Chelazzi 2004).

Christoff and Gabrieli (2000) proposed a rostrocaudal hierarchical organization in PFC. In their account, ventrolateral regions (BA 45/47/12) are at the bottom of the hierarchy,

being involved in the maintenance of one or only a few items. Dorsolateral regions (BA 9/46) have a role in the evaluation of externally generated information, and finally, frontopolar prefrontal regions (BA 10) are at the top of the hierarchy, involved in the evaluation of internally generated information. In a review integrating anatomical and functional knowledge on the aPFC (frontopolar) (BA 10), Ramnani and Owen (2004) conclude that this region has a specific role in the integration of the outcomes of 2 or more separate cognitive operations in the pursuit of a higher behavioral goal. The aPFC has been labeled as the neural substrate for prospective memory, allowing the execution of an intended act after a delay, keeping a mental agenda of what to do when (Burgess and others 2001). In-line with these interpretations, we suggest that in the present study, aPFC might integrate the different sources of information necessary for the subsequent reproduction of the haptically explored spatial orientation, whereas at the same time anticipating the cue for the matching response. The aPFC might bring into register the information of areas involved in hapticospatial imagery, for example, (parieto-)occipital cortex (BA 17/18) and the information from ventral premotor cortex (BA 44) on visuomotor transformations required for object manipulation, unleashing motor preparatory processes in areas such as supplementary motor cortex, cingulate motor cortex, and premotor cortex (Van Mier and others 1998, 2004; Toni and others 2001, 2002; Cunnington and others 2003) some time before the anticipated cue for the start of the matching.

Although the design of the present study did not aim at drawing specific conclusions with respect to the various models of prefrontal involvement in working memory, our results do indicate that many pivotal areas in the above-mentioned models are also engaged in haptic working memory. A dynamical pattern of activation was revealed in prefrontal regions across the haptic working memory delay, involving aPFC (BA 10) as well as additional foci of activation were observed in dorsal and ventral prefrontal areas (BA 9, 47). This suggests that various prefrontal regions might be involved in the haptic working memory delay, reflecting the hierarchical organization proposed by Christoff and Gabrieli (2000). In our view, future attempts to formulate a comprehensive theoretical perspective on human working memory should no longer be based on a subset of the human sensory modalities, but should (among others) incorporate the tactile sense, which despite its pre-eminent importance for goal-directed behavior, has until recently been largely ignored.

Specific Implications for Theories of Haptic Working Memory

Our study provides important insights into the neural bases of hapticospatial working memory, identifying a network of areas supporting this crucial human function. Integrating the results obtained from the different delay analyses and comparing them with results reported in the literature, few areas emerge that are likely to represent the neuronal correlate of haptic memory (see Fig. 7). The first region is located around the right central sulcus, the second in the left parieto-occipital cortex, and the third in left aPFC. The 3 processing stages in tactile memory proposed by Burton and Sinclair (2000) might be reflected by subsequent dominance of each of these regions in the working memory delay. Consequently, the first stage of haptic sensory memory might be subserved by the right primary sensorimotor

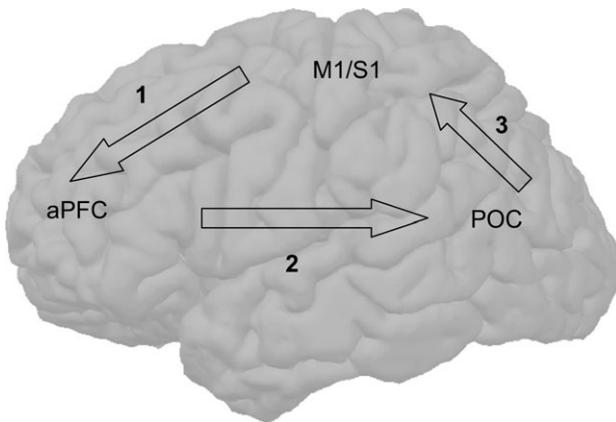


Figure 7. Schematic illustration of selected brain areas involved in haptic working memory and potential temporal order of activation. (1.) The sensory trace first stored in sensorimotor cortex (S1/M1) (2.) is transformed to a more abstract hapticospatial representation, maintained in aPFC. This representation is converted to hapticospatial imagery by parieto-occipital cortex (POC) in the latest stages of the delay (3.) preparing the haptic matching response.

cortex for stimuli explored with the left hand, whereas prefrontal areas might be the most important neuronal correlate for the third stage. The second stage, characterized by vivid recollections of uncategorized stimulus information and immunity to interfering tasks, might be brought about by the temporal overlap of the descending activation in the primary somatosensory cortex and increasing dominance of occipital-parietal areas as well as prefrontal regions.

The pattern of lateralization observed in the sensorimotor and occipital areas might be largely attributable to the use of the left hand for haptic exploration and the right hand for matching. We consider it less likely that the left lateralization observed in the anterior frontal areas be influenced by a change in hand use. The involvement of right dorsolateral PFC has been found to be independent of the hand used for tactile shape discrimination (Harada and others 2004). Although the effect of hand use on the lateralization of haptic working memory remains to be tested, left lateralized brain activity was also revealed in the delay of the only other haptic working memory study known to us (Stoessel and others 2003). The participants in this study used their right hand for both exploration and discrimination.

Each component of the proposed memory network might provide an interesting focus for future investigation, eventually aiming to disentangle the precise contribution and functional relevance of the subprocesses involved in hapticospatial working memory.

Conclusion

This study represents a first attempt to unravel the dynamical cortical network involved in hapticospatial working memory. By parametrically varying the delay length in a hapticospatial delayed match-to-sample task, we were able to spatially map the cortical areas that showed increased activation during longer working memory delays.

Our results indicate that a dynamical network of brain areas underlies working memory maintenance of hapticospatial information in the delay between haptic stimulus exploration and orientation matching. We propose that the haptic sensory trace, maintained in contralateral sensorimotor cortex, is transformed into a more abstract hapticospatial image in the early stages of

the delay. The maintenance of this hapticospatial representation engages aPFC and parieto-occipital cortex. Whereas the aPFC possibly integrates the spatial and motor components of hapticospatial working memory, the parieto-occipital cortex might be involved in hapticospatial orientation imagery, supporting working memory and the preparation of haptic orientation matching.

The results of this study constitute a first step to spatiotemporally disentangle and label the subcomponents of the neural network involved in hapticospatial working memory. Haptic working memory intricately links somatosensory, motor, and cognitive processes, forming a crucial relay station between cognition and action, enabling us to shape the world around us.

Notes

This study was supported by a grant from the Netherlands Organization for Scientific Research (NWO # 410-20-205). We thank Paul Gaalman and the technical personnel of the Donders Center for Cognitive Neuroscience for their kind assistance and A. Sack, J. Reithler, and the reviewers for helpful comments. *Conflict of Interest:* None declared.

Address correspondence to Amanda L. Kaas, Department of Neurophysiology, Max Planck Institute for Brain Research, Deutschordenstrasse 46, 60528 Frankfurt am Main, Germany. Email: kaas@mpih-frankfurt.mpg.de.

References

- Amedi A, Malach R, Hendler T, Peled S, Zohary E. 2001. Visuo-haptic object-related activation in the ventral visual pathway. *Nat Neurosci* 4:324–330.
- Amedi A, Malach R, Pascual-Leone A. 2005. Negative BOLD differentiates visual imagery and perception. *Neuron* 48:859–872.
- Baddeley AD. 1998. Recent developments in working memory. *Curr Opin Neurobiol* 8:234–238.
- Binkofski F, Buccino G, Posse S, Seitz RJ, Rizzolatti G, Freund H-J. 1999. A fronto-parietal circuit for object manipulation in man: evidence from an fMRI-study. *Eur J Neurosci* 11:3276–3286.
- Bowers RL, Mollenhauer MS, Luxford J. 1990. Short-term memory for tactile and temporal stimuli in a shared-attention recall task. *Percept Mot Skills* 70:903–913.
- Burgess PW, Quayle A, Frith CD. 2001. Brain regions involved in prospective memory as determined by positron emission tomography. *Neuropsychologia* 39:545–555.
- Burton H, Sinclair RJ. 2000. Attending to and remembering tactile stimuli: a review of brain imaging data and single-neuron responses. *J Clin Neurophysiol* 17:575–591.
- Choi SH, Na DL, Kang E. 2001. Functional magnetic resonance imaging during pantomiming tool-use gestures. *Exp Brain Res* 139:311–317.
- Christoff K, Gabrieli JDE. 2000. The frontopolar cortex and human cognition: evidence for a rostrocaudal hierarchical organization within the human prefrontal cortex. *Psychobiology* 28:168–186.
- Constantinidis C, Procyk E. 2004. The primate working memory networks. *Cogn Affect Behav Neurosci* 4:444–465.
- Courtney SM, Petit L, Maisog JM, Ungerleider LG, Haxby JV. 1998. An area specialized for spatial working memory in human frontal cortex. *Science* 279:1347–1351.
- 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.
- Craig JC, Rollman GB. 1999. Somesthesia. *Annu Rev Psychol* 50:305–331.
- Cunnington R, Windischberger C, Deecke L, Moser E. 2003. The preparation and readiness for voluntary movement: a high-field event-related fMRI study of the Bereitschafts-bold response. *Neuroimage* 20:404–412.
- D'Esposito M, Aguirre GK, Zarahn E, Ballard D, Shin RK, Lease J. 1998. Functional MRI studies of spatial and nonspatial working memory. *Brain Res Cogn Brain Res* 7:1–13.

- Galati G, Lobel E, Vallar G, Berthoz A, Pizzamiglio L, Le Bihan D. 2000. The neural basis of egocentric and allocentric coding of space in humans: a functional magnetic resonance study. *Exp Brain Res* 133:156-164.
- Ganis G, Thompson WL, Kosslyn SM. 2004. Brain areas underlying visual mental imagery and visual perception: an fMRI study. *Brain Res Cogn Brain Res* 20:226-241.
- Genovese CR, Lazar NA, Nichols T. 2002. Thresholding of statistical maps in functional neuroimaging using the false discovery rate. *Neuroimage* 15:870-878.
- Goebel R, Esposito F, Formisano E. 2006. Analysis of FIAC data with BrainVoyager QX: from single-subject to cortically aligned group GLM analysis and self-organizing group ICA. *Hum Brain Mapp* 27:392-401.
- Haaland KY, Harrington DL, Knight RT. 2000. Neural representations of skilled movement. *Brain* 123:2306-2313.
- Harada T, Saito DN, Kashikura K, Sato T, Yonekura Y, Honda M, Sadato N. 2004. Asymmetrical neural substrates of tactile discrimination in humans: a functional magnetic resonance imaging study. *J Neurosci* 24:7524-7530.
- Harris JA, Miniussi C, Harris IM, Diamond ME. 2002. Transient storage of a tactile memory trace in primary somatosensory cortex. *J Neurosci* 22:8720-8725.
- Haxby JV, Petit L, Ungerleider LG, Courtney SM. 2000. Distinguishing the functional roles of multiple regions in distributed neural systems for visual working memory. *Neuroimage* 11:380-391.
- Johnson-Frey SH. 2004. The neural bases of complex tool use in humans. *Trends Cogn Sci* 8:71-78.
- Johnson-Frey SH, Newman-Norlund R, Grafton ST. 2005. A distributed left hemisphere network active during planning of everyday tool use skills. *Cereb Cortex* 15:681-695.
- Kaas AL, Van Mier H. 2006. Haptic spatial matching in near peripersonal space. *Exp Brain Res* 170:403-413.
- Kappers AM. 1999. Large systematic deviations in the haptic perception of parallelity. *Perception* 28:1001-1012.
- Kappers AM, Koenderink JJ. 1999. Haptic perception of spatial relations. *Perception* 28:781-795.
- Kappers AML. 2004. The contributions of egocentric and allocentric reference frames in haptic spatial tasks. *Acta Psychol* 117:333-340.
- Kiphart MJ, Hughes JL, Simmons JP, Cross HA. 1992. Short-term haptic memory for complex objects. *Bull Psychon Soc* 30:212-214.
- Koch C, Fuster JM. 1989. Unit activity in monkey parietal cortex related to haptic perception and temporary memory. *Exp Brain Res* 76:292-306.
- Kosslyn SM, Ganis G, Thompson WL. 2001. Neural foundations of imagery. *Nat Rev Neurosci* 2:635-642.
- Lederman SJ, Klatzky RL. 2004. Multisensory texture perception. In: Calvert G, Spence C, Stein BE, editors. *The handbook of multisensory processes*. Cambridge, MA: The MIT Press. p 107-122.
- Lehéricy S, Bardinet E, Tremblay L, Van de Moortele PF, Pochon JB, Dormont D, Kim DS, Yelnik J, Ugurbil K. 2006. Motor control in basal ganglia circuits using fMRI and brain atlas approaches. *Cereb Cortex* 16:149-161.
- Linden DE, Bittner RA, Muckli L, Waltz JA, Kriegeskorte N, Goebel R, Singer W, Munk MH. 2003. Cortical capacity constraints for visual working memory: dissociation of fMRI load effects in a fronto-parietal network. *Neuroimage* 20:1518-1530.
- Loomis JM. 1981. Tactile pattern perception. *Perception* 10:5-27.
- Manoach DS, Greve DN, Lindgren KA, Dale AM. 2003. Identifying regional activity associated with temporally separated components of working memory using event-related functional MRI. *Neuroimage* 20:1670-1684.
- Merabet L, Thut G, Murray B, Andrews J, Hsiao S, Pascual-Leone A. 2004. Feeling by sight or seeing by touch? *Neuron* 42:173-179.
- Misaki M, Matsumoto E, Miyauchi S. 2002. Dorsal visual cortex activity elicited by posture change in a visuo-tactile matching task. *Neuroreport* 13:1797-1800.
- Mohr HM, Goebel R, Linden DEJ. 2006. Content- and task-specific dissociations of frontal activity during maintenance and manipulation in visual working memory. *J Neurosci* 26:4465-4471.
- Newport R, Rabb B, Jackson SR. 2002. Noninformative vision improves haptic spatial perception. *Curr Biol* 12:1661-1664.
- Numminen J, Schurmann M, Hiltunen J, Joensuu R, Jousmaki V, Koskinen SK, Salmelin R, Hari R. 2004. Cortical activation during a spatiotemporal tactile comparison task. *Neuroimage* 22:815-821.
- Nyberg L, Marklund P, Persson J, Cabeza R, Forkstam C, Petersson KM, Ingvar M. 2003. Common prefrontal activations during working memory, episodic memory, and semantic memory. *Neuropsychologia* 41:371-377.
- Oldfield RC. 1971. The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* 9:97-113.
- Owen AM. 1997. The functional organization of working memory processes within human lateral frontal cortex: the contribution of functional neuroimaging. *Eur J Neurosci* 9:1329-1339.
- Pietrini P, Furey ML, Ricciardi E, Gobbi MI, Wu WH, Cohen L, Guazzelli M, Haxby JV. 2004. Beyond sensory images: object-based representation in the human ventral pathway. *Proc Natl Acad Sci USA* 101:5658-5663.
- Pitzalis S, Galetti C, Huang R-S, Patria F, Comitteri G, Galati G, Fattori P, Sereno MI. 2006. Wide-field retinotopy defines human cortical visual area V6. *J Neurosci* 26:7962-7973.
- Ramnani N, Owen M. 2004. Anterior prefrontal cortex: insights into function from anatomy and neuroimaging. *Nat Rev Neurosci* 5:184-194.
- Reynolds JH, Chelazzi L. 2004. Attentional modulation of visual processing. *Annu Rev Neurosci* 27:611-647.
- Rizzolatti G, Fogassi L, Gallese V. 2002. Motor and cognitive functions of the ventral premotor cortex. *Curr Opin Neurobiol* 12:149-154.
- Romanski LM. 2004. Domain specificity in the primate prefrontal cortex. *Cogn Affect Behav Neurosci* 4:421-429.
- Romo R, Brody CD, Hernandez A, Lemus L. 1999. Neuronal correlates of parametric working memory in the prefrontal cortex. *Nature* 399:470-473.
- Rowe JB, Toni I, Josephs O, Frackowiak RS, Passingham RE. 2000. The prefrontal cortex: response selection or maintenance within working memory? *Science* 288:1656-1660.
- Sakata H, Tsutsui K-I, Taira M. 2005. Toward an understanding of the neural processing for 3D shape perception. *Neuropsychologia* 43:151-161.
- Sathian K, Zangaladze A. 2002. Feeling with the mind's eye: contribution of visual cortex to tactile perception. *Behav Brain Res* 135:127-132.
- Sathian K, Zangaladze A, Hoffman JM, Grafton ST. 1997. Feeling with the mind's eye. *Neuroreport* 8:3877-3881.
- Simon SR, Meunier M, Piettre L, Berardi AM, Segebarth CM, Boussaoud D. 2002. Spatial attention and memory versus motor preparation: premotor cortex involvement as revealed by fMRI. *J Neurophysiol* 88:2047-2057.
- Soechting JF, Tong DC, Flanders M. 1996. Frames of reference in sensorimotor integration: position sense of the arm and hand. In: Haggard P, Wing AM, Flanagan RJ, editors. *Hand and brain: the neurophysiology and psychology of hand movements*. San Diego, CA: Academic Press. p 151-168.
- Stoeckel MC, Weder B, Binkofski F, Buccino G, Shah NJ, Seitz RJ. 2003. A fronto-parietal circuit for tactile object discrimination: an event-related fMRI study. *Neuroimage* 19:1103-1114.
- Stoeckel MC, Weder B, Binkofski F, Choi H-J, Amunts K, Pierperhoff P, Shah NJ, Seitz RJ. 2004. Left and right superior parietal lobule in tactile object discrimination. *Eur J Neurosci* 19:1067-1072.
- Toni I, Thoenissen D, Zilles K. 2001. Movement preparation and motor intention. *Neuroimage* 14:S110-S117.
- Toni I, Thoenissen D, Zilles K, Niedeggen M. 2002. Movement preparation and working memory: a behavioural dissociation. *Exp Brain Res* 142:158-162.
- Vallar G, Lobel E, Galati G, Berthoz A, Pizzamiglio L, Le Bihan D. 1999. A fronto-parietal system for computing the egocentric spatial frame of reference in humans. *Exp Brain Res* 124:281-286.
- Valyear KF, Culham JC, Sharif N, Westwood D, Goodale MA. 2006. A double dissociation between sensitivity to changes in object identity and object orientation in the ventral and dorsal visual streams: a human fMRI study. *Neuropsychologia* 44:218-228.
- Van Mier H, Tempel LW, Perlmutter JS, Raichle ME, Petersen SE. 1998. Changes in brain activity during motor learning measured with

- PET: effects of hand of performance and practice. *J Neurophysiol* 80:2177-2199.
- Van Mier HI, Perlmutter JS, Petersen SE. 2004. Functional changes in brain activity during acquisition and practice of movement sequences. *Motor Control* 8:500-520.
- Vingerhoets G, de Lange FP, Vandemaele P, Deblaere K, Achten E. 2002. Motor imagery in mental rotation: an fMRI study. *Neuroimage* 17:1623-1633.
- Wager TD, Smith EE. 2003. Neuroimaging studies of working memory: a meta-analysis. *Cogn Affect Behav Neurosci* 3:255-274.
- Wallis JD, Miller EK. 2003. From rule to response: neuronal processes in the premotor and prefrontal cortex. *J Neurophysiol* 90:1790-1806.
- Woods AT, O'Modhrain S, Newell FN. 2004. The effect of temporal delay and spatial differences on cross-modal object recognition. *Cogn Affect Behav Neurosci* 4:260-269.
- Zangaladze A, Epstein CM, Grafton ST, Sathian K. 1999. Involvement of visual cortex in tactile discrimination of orientation. *Nature* 401:587-590.
- Zarahn E. 2000. Testing for neural responses during temporal components of trials with bold fMRI. *Neuroimage* 11:783-796.
- Zhang M, Mariola E, Stilla R, Stoesz M, Mao H, Hu X, Sathian K. 2005. Tactile discrimination of grating orientation: fMRI activation patterns. *Hum Brain Mapp* 25:370-377.
- Zhang M, Weisser VD, Stilla R, Prather SC, Sathian K. 2004. Multisensory cortical processing of object shape and its relation to mental imagery. *Cogn Affect Behav Neurosci* 4:251-259.
- Zhou YD, Fuster JM. 1996. Mnemonic neuronal activity in somatosensory cortex. *Proc Natl Acad Sci USA* 93:10533-10537.
- Zuidhoek S, Kappers AM, van der Lubbe RH, Postma A. 2003. Delay improves performance on a haptic spatial matching task. *Exp Brain Res* 149:320-330.