

Content-specific activation during associative long-term memory retrieval

Patrick Khader,^{a,*} Michael Burke,^a Siegfried Bien,^b Charan Ranganath,^c and Frank Rösler^a

^aExperimental and Biological Psychology, Philipps-University, 35032 Marburg, Germany

^bNeuroradiology, Department of Medicine, Philipps-University Marburg, Germany

^cCenter for Neuroscience and Department of Psychology, University of California at Davis, CA 95616, USA

Received 7 October 2004; revised 21 April 2005; accepted 5 May 2005

Available online 16 June 2005

We tested whether visual stimulus material that is assumed to be processed in different cortical networks during perception (i.e., faces and spatial positions) is also topographically dissociable during long-term memory recall. With an extensive overlearning procedure, 12 participants learned paired associates of words and faces and words and spatial positions. Each word was combined with either one or two positions or one or two faces. fMRI was recorded several days later during a cued recall test, in which two words were presented and the participants had to decide whether these were linked to each other via a common mediator, i.e., a face or a position. This paradigm enforces retrieval from long-term memory without confounding recall with perceptual processes. A network of cortical areas was found to be differently activated during recall of positions and faces, including regions along the dorsal and ventral visual pathways, such as the parietal and precentral cortex for positions and the left prefrontal, temporal (including fusiform gyrus) and posterior cingulate cortex for faces. In a subset of these areas, the BOLD response was found to increase monotonically with the number of the to-be-re-activated associations. These results show that material-specific cortical networks are systematically activated during long-term memory retrieval that overlap with areas also activated by positions and faces during perceptual and working memory tasks.

© 2005 Elsevier Inc. All rights reserved.

Keywords: Functional magnetic resonance imaging; Long-term memory; Face memory; Spatial memory

Introduction

Theories about the role of the neocortex in storing the long-term memory representations postulate that permanent information storage is mediated by modified synaptic connectivities in

neocortical cell assemblies (McClelland et al., 1995; O'Reilly and Rudy, 2001; Squire, 1992; Squire and Alvarez, 1995). Moreover, it is assumed that the engrams are located in those cortical areas that are also involved in the initial perceptual processing of the later stored information (Damasio, 1989; McClelland et al., 1995). Therefore, long-term memory representations should be re-activated in topographically distinct cortical cell assemblies with the localization depending on the kind of material.

One fundamental topographical dissociation found relevant for visual perception is the distinction between the dorsal and ventral visual processing pathway. Based on findings that monkeys with lesions of the superior parietal cortex had deficits in spatial discrimination, whereas monkeys with lesions of the inferior temporal cortex were impaired in discriminating visual features (Pohl, 1973; Ungerleider and Mishkin, 1982), two different routes of higher visual processing were proposed for spatial and object information, i.e., the dorsal processing stream from primary visual areas up to the superior parietal cortex and the ventral stream from primary visual cortex into the inferior temporal cortex (Mishkin et al., 1983). Adhering to the distributed model of memory representations described above, recalling visual objects from long-term memory should re-activate the primary and secondary visual areas of the occipital and temporal cortex (Felleman and Van Essen, 1991; Livingstone and Hubel, 1988; Mishkin et al., 1983), whereas recalling spatial information should re-activate regions of the parietal cortex in which information about spatial positions and coordinates is processed (Mishkin et al., 1983; Ungerleider and Mishkin, 1982).

The available evidence from neuroimaging and neurophysiological studies seems to support this proposal. The role of the parietal cortex in spatial memory was investigated, for example, in a PET study by Smith et al. (1996, Exp. 2), who found bilateral activation of the posterior parietal and premotor cortex in a spatial 3-back working memory task, in which the positions of letters had to be compared that appeared successively at random locations. Accordingly, single-cell recordings of the posterior parietal cortex showed sustained neural activity during the retention interval of spatial

* Corresponding author. Fax: +49(0)6421 2828948.

E-mail address: Khader@staff.uni-marburg.de (P. Khader).

URL: <http://staff-www.uni-marburg.de/~cablab> (P. Khader).

Available online on ScienceDirect (www.sciencedirect.com).

delayed-matching-to-sample tasks (Funahashi et al., 1989; Pesaran et al., 2002). In comparable object memory tasks, sustained neural activity was found in the inferior temporal cortex with single-cell recordings (Desimone et al., 1984; Miller et al., 1993; Miyashita and Chang, 1998), as well as with functional MRI (Ranganath et al., 2004). Activation of the inferior temporal lobe (i.e., the fusiform gyrus) was also found in face recognition tasks (Henson et al., 2003; Vaidya et al., 2002). In the study of Vaidya et al. (2002), recognition memory judgments about words encoded as pictures compared to words encoded as words activated the fusiform and inferior temporal gyrus, primarily in the left hemisphere.

Other studies directly compared memory retrieval for spatial and object information. In a delayed recognition task, in which participants had to store either the location or the shape of visual objects, Postle and D'Esposito (1999) found fMRI activations in the superior parietal cortex for the spatial and in the ventral posterior temporal cortex for the object task (see also Belger et al., 1998; D'Esposito et al., 2000; Postle et al., 2000 for related results). However, a study by Banich et al. (2000) was not able to substantiate comparable posterior differences in activation between spatial and object memory using a shape and a location version of the Stroop task. Instead, material-specific dissociations were found within the prefrontal cortex with positions showing more dorsal and colors showing more ventral activations (see also Levy and Goldman-Rakic, 2000 for a review of related results obtained from lesions and electrophysiological recordings, suggesting a specialization of the dorsolateral prefrontal cortex for spatial and of the ventrolateral prefrontal cortex for object information).

The present study further investigates whether the dissociation between the dorsal and ventral visual processing pathways also implies a topographical dissociation if spatial positions and faces have to be recalled after full consolidation from long-term memory. To test the theory of material-specific long-term storage systems in the neocortex, we employed a task that explicitly triggered access to permanently stored representations by separating the encoding phase from the probing of the acquired memory structure by at least 1 day. Furthermore, we wanted to avoid the neural *activation* elicited by the perception of a specific type of stimulus to get confounded with the activity that is directly associated with *re-activation* from long-term memory. Therefore, the design of the present study separates the processing of external stimuli from recalling them by probing the retrieval of both faces and spatial positions by means of the same type of cue, i.e., visually presented nouns. Thus, the to-be-retrieved information varied, while the retrieval cues remained constant.

In an acquisition phase, either one or two pictures of faces or spatial positions had to be associated with a noun. During retrieval, probe stimuli comprising pairs of nouns were presented, and participants had to recall the respective associations, activate the respective stimulus representations of faces and positions and then had to decide whether the nouns are linked to each other via a commonly associated spatial position or face. If the two words were associated with one position/face each, participants had to make only one comparison to give the correct answer. If one word was associated with one and the other word with two positions/faces, one or two comparisons were required, and if both words were associated with two stimuli, participants had to make up to four comparisons. Thus, each correct response to a word pair requires activation of a varying number of associations in long-term memory, depending on the word pair's level of associative fan

(Anderson, 1974). Therefore, both the quality (face vs. position) and the quantity (associative fan) of the activated representations were varied systematically while holding constant the stimuli and response requirements.

Considering the work on the dorsal and ventral visual pathway, we predicted that the recall of faces and spatial positions should be accompanied by topographically distinct activation patterns, with an involvement of parietal areas during the recall of positions and of occipital and temporal areas during face recall. Furthermore, we predicted that the amplitude of the BOLD signal should increase systematically with the level of associative fan during retrieval, indicating increased activity in the material-specific neural networks as the number of stimulus representations that have to be activated in long-term memory gets larger.

One set of the fMRI data reported here were obtained as part of a more extended EEG/fMRI study, which consisted of an acquisition and two retrieval phases. EEG was recorded during acquisition and the first retrieval phase (see Khader et al., *in press*), while the fMRI was recorded during the second retrieval phase. To control for the possibility that the first retrieval phase (with EEG measurements) could have had an influence on the subsequent fMRI retrieval phase – in the sense of a reconsolidation phase – a second independent sample of participants was tested, who learned the material on day one and performed the fMRI retrieval phase on day two, without an intervening EEG retrieval phase.

Materials and methods

Participants

The first sample consisted of 12 students (8 female) of the University of Marburg (out of the 17 who had participated in an EEG study; see Khader et al., *in press*). Their mean age was 23.4 years with a range of 19–31 years. These participants learned the material, performed the retrieval test once with the EEG recorded and a second time in the scanner. The additional sample consisted of 7 participants (mean age = 20.9 years, range = 20–21, 5 female), who learned the material on day one and performed the fMRI retrieval phase on day two, without an intervening EEG retrieval phase. All participants were right-handed, healthy with corrected or normal vision and native speakers of German. They were naive with respect to the objective of the experiment, gave written consent to participate and received either monetary compensation or course credits.

Material and procedure

During the *acquisition phase*, 54 written nouns were linked to 9 different faces and 9 spatial positions. Only highly abstract words (e.g., “KONZEPT”, engl. concept) were chosen to minimize visual associations that could interfere with the acquisition of new associations. To further prevent any systematic effect of inherent word associations on the experimentally created associative links, all words were randomly assigned to the stimuli for each participant. Half of the words (27) were associated with either one (18) or two (9) of the 9 spatial positions and the other half with either one or two of the 9 faces, respectively. The face stimuli were taken from a standardized picture set (courtesy of S. Sporer, see Sporer, 1999) consisting of grayscale whole-head photographs of male students (cf. Fig. 1). To account for variability in head size,

the distance between the eyes was kept constant. The spatial positions were defined by means of locations in a 5 × 5 grid of dark gray squares (cf. Fig. 1) which changed their luminance to light gray when relevant in a given trial. In order to keep the presentation of the spatial positions as comparable as possible to the presentation of the faces, two separate matrices with one active position in each matrix were presented when two positions had to be associated with one word.

The protocol of the *acquisition phase* was the same in both samples. Each trial started with a centrally presented small white fixation cross followed by a white frame (width = 7.5 cm, height = 6 cm) with an upper and a lower section after 1.5 s (see Fig. 1). Two seconds later, a word appeared in the lower section followed by one or two position(s) or face(s) in the upper section (SOA = 6.5 s). Participants were instructed to carefully inspect the stimuli and to encode the association between the words and the face(s) or position(s) by forming an integrated picture of the display. All stimuli remained on the screen until the participants started the next trial by pressing the space key of a computer keyboard. All 54 trials were presented three times in a randomized order. The resulting 162 trials were presented in 27 blocks of 6 items, separated by an obligatory pause, which the participants could terminate by pressing a button. The acquisition phase was followed by an *overlearning phase*, in which the 5 × 5 matrix of squares or, alternatively, a 3 × 3 grid depicting the 9 faces was presented in each trial, and 1 out of the 54 words appeared below. The associated spatial position(s) or face(s) had to be selected by pressing buttons on a special keyboard consisting of 25 black buttons. In case of an error, the correct position(s) or face(s) subsequently appeared on the screen. On average, participants had to work on 7–8 sets until they made less than three errors in one complete set of 54 trials (93% correct). This took about 1–2 h. To

ensure that the acquired associative memory structure was equally accessible in all participants during the fMRI retrieval phase, participants again had to work through training sets prior to the fMRI scan until they reached the overlearning criterion again, which took about 15–30 min. This refreshing procedure was not applied to the second group of participants who were scanned immediately 1 day after acquisition.

Each retrieval cue in the *retrieval phase* consisted of two words associated to either faces or positions. Participants had to decide whether these two words were associated with an identical face or an identical position or not. Depending on the number of learned associations (i.e., one or two), participants had to compare two (if both words were associated with only one stimulus), three (if one word was associated with one and the other with two stimuli) or four (if both words were associated with two stimuli) positions or faces, resulting in three levels of associative fan (1/1, 1/2, 2/2). Test probes were selected such that the factors stimulus type (face/position), level of fan (1/1, 1/2, 2/2) and type of response (yes/no) were completely crossed. In addition, a high-level baseline condition was introduced, in which two identical words were presented (“Fan0”). In this condition, participants were exposed to the same visual stimulation as in the other fan conditions, they also processed words associated with faces or positions during acquisition, and they were also required to give a response (which was always “yes”), but there was no need for genuine memory retrieval because the correct answer can be given just by visual comparison.

The 12 participants who had experienced a first retrieval phase with EEG recording 1 day after acquisition performed a second phase in the scanner between 5 and 53 days after the first one (depending on available scanner times; mean = 28 days). The protocol consisted of 36 trials for each fan and material combination and another 36 trials for the high-level baseline condition

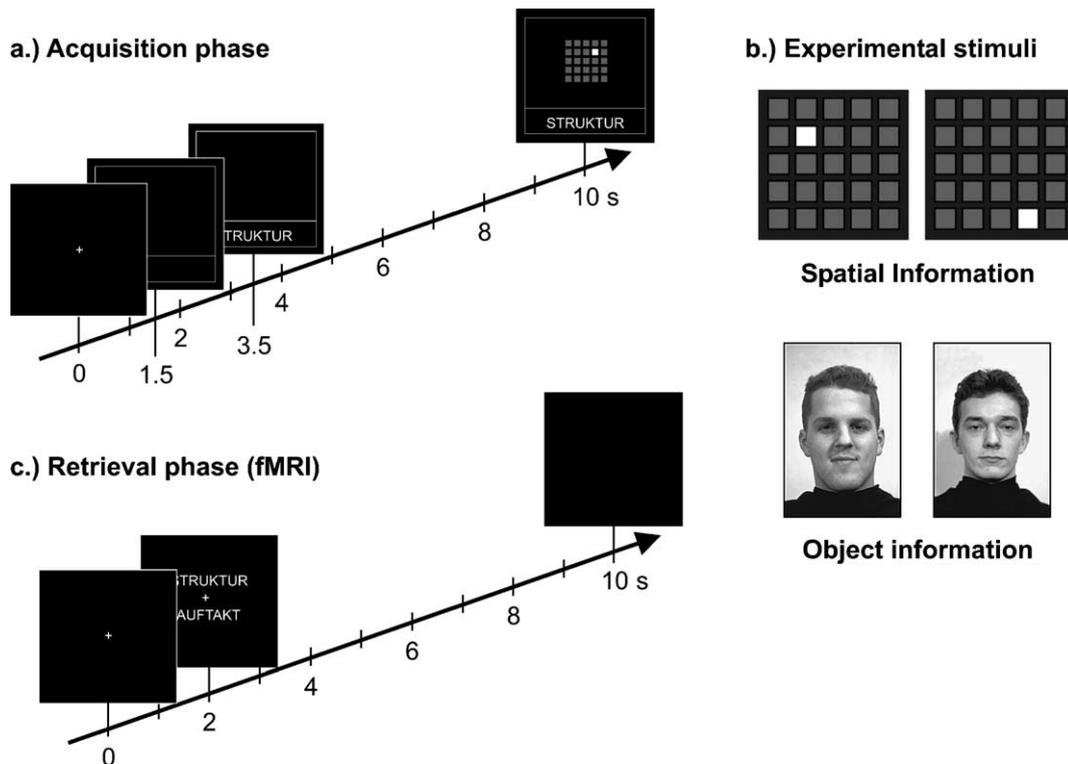


Fig. 1. Stimulus sequence of acquisition (a) and recall (c) trials. (b) Examples of faces and positions that had to be encoded during acquisition.

(i.e., 2 materials \times 3 levels of fan \times 36 + 36 baseline trials, in total 252). The trial order in the second retrieval phase was different from the one in the first retrieval phase. Due to the restriction of matching the number of trials in each experimental condition, the same word pairs were used for both retrieval phases. This could, in principle, have enabled participants to remember the answer to a certain word pair directly without a comparison of the associated stimuli. However, due to the long time periods between the first and second phase, participants reported to hardly remember the correct answer to more than a few word pairs. Furthermore, the obtained response times and error rates both showed a strong fan effect (see Results), which exactly parallels the results of the first retrieval phase¹ (Khader et al., *in press*) and which would not be present without a detailed comparison of the faces and positions associated to each word. The second group of 7 participants was scanned with the same protocol 1 day after learning, without an intervening EEG retrieval phase.

Trials of the *retrieval phase* consisted of a fixation cross which was followed (SOA = 2 s) by a word pair with one word above and one below the fixation cross. The words disappeared after 8 s followed by a blank screen which lasted for 4 s. Thus, each trial had a fixed duration of 14 s. Participants had to decide whether the words were linked to each other via an associated spatial position or a face. In the fMRI part, participants laid in the scanner in supine position with their head immobilized by a soft foam pillow during the whole experiment to minimize involuntary head movements. Additionally, headphones were used to dampen scanner noise. Participants had to press one of two buttons on an fMRI-compatible (fiber optic) response device to indicate a “yes” or “no” response. Mapping of the buttons to the response categories was varied systematically across participants. Stimuli were projected on a canvas the participants could see via mirrors mounted on the head coil. Participants responded as fast as possible, but accuracy was stressed in the instruction. The fMRI experiment consisted of 4 functional runs with 63 trials each. Between the second and third run, the anatomical reference volume was recorded. Participants laid in the scanner for approximately 1 h and 15 min.

fMRI data acquisition and analysis

Anatomical and functional imaging was performed with a 1.5 T MR scanner (Signa, GE Medical Systems). Functional BOLD images with 19 oblique slices covering the whole brain were acquired with a T2*-weighted EPI sequence (TR: 2 s, TE: 60 ms, flip angle = 80°, FOV: 240/240 mm, matrix: 64 \times 64, ascending slice acquisition, slice thickness: 5 mm, interslice gap: 1 mm, in-plane resolution: 3.75 \times 3.75 mm) using a standard quadrature head coil. Four functional time series were recorded, consisting of 441 volumes each. Anatomical whole-head images were acquired in

the same session from 124 axial slices (1.4 mm thick) using a spoiled gradient echo recalled acquisition sequence (SPGR; FOV = 240 \times 180 mm, TE/TR = 6.0 ms/33.0 ms, flip angle = 40°, 256 \times 192 acquisition matrix, in-plane resolution = 0.9375 \times 0.9375 mm).

Preprocessing and statistical analysis was performed with the BrainVoyager2000 software package (www.brainvoyager.com). The first four volumes of each run were discarded to allow for signal equilibration. After motion and slice scan time correction, temporal filtering (0.01 Hz high pass) and linear trend removal, the functional data were aligned with the anatomical reference from the same session, transformed into Talairach space (Talairach and Tournoux, 1988), spatially smoothed with a Gaussian kernel (FWHM = 6 mm) and z-standardized for each run. Voxelwise multi-subject multiple regression analysis was performed on the resulting time courses using a General Linear Model (GLM) with separate predictors for faces and positions at three levels of associative fan. To account for the fact that response times varied between approximately 1 and 8 s, the regressor functions were adjusted to the specific RTs associated with each trial (“RT-convolved HRF analysis”; see Christoff et al., 2001), that is, the length of the box-car predictor functions was set to 1, 2, 3 or 4 TRs, depending on whether the participants took less than 2 s, 2–4 s, 4–6 s or more than 6 s to respond. For statistical comparisons of experimental conditions, *t*-contrasts were computed for recalling faces vs. positions, as well as for the effects of associative fan for positions and faces (Fan0 < Fan1/1 < Fan1/2 < Fan2/2, with contrast coefficients $-3, -1, 1, 3$). To correct for multiple comparisons, statistical maps were thresholded at a Bonferroni-corrected level of $P < 0.05$. However, the number of voxels used for this correction was reduced to less than 50% of the total number of all voxels in Talairach space by deriving them from individual cortical sheet reconstructions based on the gray–white matter boundary of high-resolution T1-weighted structural recordings (Kriegeskorte and Göbel, 2001). Each voxel that was found to be part of the cortical gray matter of at least one subject was included in the Bonferroni correction, which resulted in *t*-values of more than 4.82 for each contrast. For a better overall view of the cortical topography of brain activations, the statistical maps were projected on a slightly inflated cortex reconstruction (Kriegeskorte and Göbel, 2001) of one subject, on which concave curvature (i.e., sulci) appears in dark and convex curvature (i.e., gyri) in light gray (see Figs. 3–5).

Finally, group random effect analyses were performed on functionally defined regions of interest (ROIs) to test whether the mean of the individual participants’ *t*-values was reliably different from zero. ROIs were defined by selecting all contiguous significantly active voxels in each contrast of interest. Time series data were averaged across all voxels within each of these ROIs and submitted to across-subject random effect analyses (Ranganath and D’Esposito, 2001). Effects were considered substantial when their significance level was below $P < 0.05$.

Results

Behavioral data

Mean percentage of accurate judgments and response times are shown in Fig. 2. Overall accuracy was high and varied between 80 and 93% over participants (mean = 87.9%, SD = 4.9%). An ANOVA with factors stimulus type (face/position) and level of

¹ The behavioral data of the EEG retrieval phase showed significant fan effects with respect to response times (positions: 3164 ms (Fan1/1), 4168 ms (Fan1/2), 4806 ms (Fan2/2), faces: 3171 ms (Fan1/1), 4118 ms (Fan1/2), 5003 ms (Fan2/2)) and accuracy (positions: 96% correct response (Fan1/1), 92% (Fan1/2), 86% (Fan2/2), faces: 97% (Fan1/1), 87% (Fan1/2), 82% (Fan2/2)). In the corresponding statistical analyses, only the main effect of fan was found to be significant. Post hoc tests revealed that response times and error rates increased significantly with increasing fan for both types of stimuli (for more details on the EEG retrieval phase, see Khader et al., *in press*).

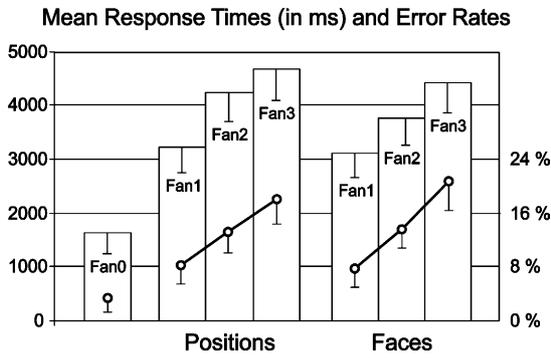


Fig. 2. Mean percentage of accurate judgments and response times in ms (with corresponding standard errors) for different stimulus types (faces/positions) and levels of associative fan (0, 1/1, 1/2, 2/2, labeled Fan0, Fan1, Fan2 and Fan3 in the figure). Accuracy decreased significantly with increasing fan for both positions and faces, whereas response times increased significantly with increasing fan.

associative fan (1/1, 1/2, 2/2), computed with data from 11 participants (data of one participant had to be discarded due to an equipment error), revealed only a significant main effect of fan level, $F(2,20) = 24.91, P < .0001, \epsilon(H - F) = .852$. Post hoc t tests showed that accuracy decreased significantly with increasing fan (cf. Fig. 2). Furthermore, two additional t tests revealed that in condition “Fan0” participants were significantly more accurate than in both “Fan1/1” conditions. The error rates of the second group of participants, which were scanned 1 day after the learning session, showed the same pattern (Fan0 = 3.57%; positions: Fan1/1 = 15.13%, Fan1/2 = 21.43, Fan2/2 = 30.56%; faces: Fan1/1 = 11.11%, Fan1/2 = 18.65%, Fan2/2 = 23.81%). Accordingly, only the main effect of fan level was significant, $F(2,12) = 22.95, P < .0001, \epsilon(H - F) = 1$. Post hoc t tests showed that accuracy decreased significantly with increasing fan. Furthermore, responses in condition “Fan0” were significantly more accurate than in condition “Fan1/1” for positions, whereas for faces there was only a tendency towards more accurate responses in the “Fan0” condition ($P < .11$).

Response times also strongly followed the parametric variation of fan size (cf. Fig. 2). An ANOVA with factors of stimulus type and

fan size (data from incorrect responses and outliers (RT < 500 ms or RT > 2.5 SD for each subject and experimental condition) were discarded prior to statistical analysis) revealed significant main effects of fan level, $F(2,20) = 57.99, P < .0001, \epsilon(H - F) = .619$, and stimulus type, $F(1,10) = 9.97, P < .0102$, indicating that RT increased significantly with increasing fan and that recalling positions took generally longer than recalling faces. Furthermore, condition “Fan0” showed significantly shorter response times than both “Fan1/1” conditions. The response times of the second group of participants (Fan0 = 913 ms; positions: Fan1/1 = 2969 ms, Fan1/2 = 3513 ms, Fan2/2 = 4177 ms; faces: Fan1/1 = 2758 ms, Fan1/2 = 3258 ms, Fan2/2 = 4046 ms) also showed a main effect of fan level, $F(2,12) = 19.63, P < .0014, \epsilon(H - F) = .669$, but no effect of stimulus type. Post hoc t tests indicated that RT increased significantly with increasing fan. Furthermore, condition “Fan0” showed significantly shorter response times than both “Fan1/1” conditions.

fMRI data

To contrast brain areas that are more involved in memory retrieval of faces compared to positions and vice versa, a t -contrast was computed for recalling faces vs. positions independent of fan size (see Fig. 3). Compared to faces, remembering positions bilaterally activated an extended cluster of posterior cortical areas ranging from the parastriate cortex (BA18, cuneus) and the middle and superior occipital gyrus up to the inferior and superior parietal lobes. Strong activations were also observed in the left and right precentral gyrus. Additionally, smaller clusters of active voxels were found in the left parahippocampal gyrus, the left dorsolateral prefrontal cortex (BA46) and the left and right inferior/middle temporal lobe.

Except the dorsolateral prefrontal cortex and the parahippocampal gyrus, all significant clusters were bilateral with more active voxels in the right hemisphere (see Table 1). In contrast, face recall more strongly activated areas in the left hemisphere, i.e., the left inferior frontal gyrus (BA45) and two areas in the left middle temporal gyrus (one reaching up into the angular gyrus), as well as the left and right striate and parastriate cortex including parts of BA17, BA18 and the posterior portion of the left fusiform gyrus.

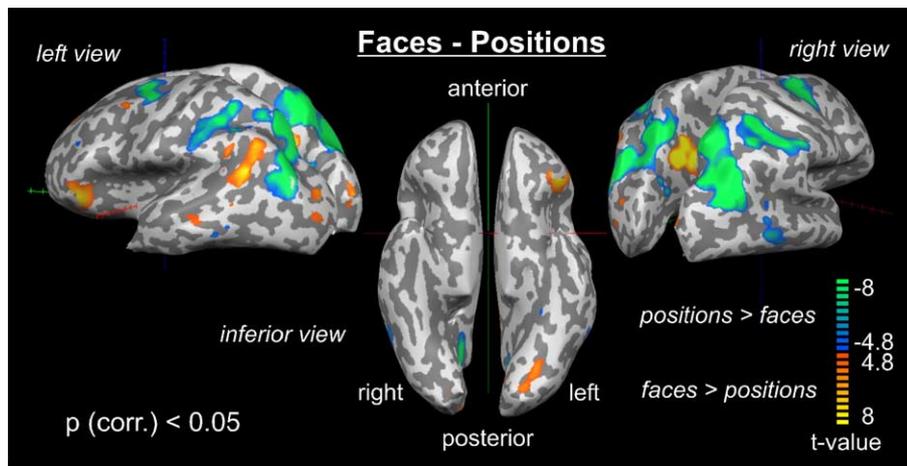


Fig. 3. fMRI contrast of recalling positions (blue to green) vs. faces (red to yellow), independent of the number of to-be-retrieved associations ($P < 0.05$, Bonferroni-corrected). Activations are projected on the partially inflated cortex reconstruction of one participant and shown from three different orientations (left, inferior and right view).

Table 1

Location (region, BA and center of gravity in Talairach coordinates), peak *t*-value and number of significantly activated voxels of brain areas differentiating retrieval of positions and faces (*P* corrected < 0.05)

Region	BA	x	y	z	t	Voxels
<i>Positions > Faces</i>						
L precentral gyrus	6	-25	-6	54	10.94	4635
R precentral gyrus	6	23	-4	52	12.09	7055
L inferior parietal lobe	40	-44	-45	44	9.70	7918
R inferior parietal lobe	40	38	-44	46	13.30	11,887
L superior parietal lobe/precuneus	7	-14	-70	43	13.62	10,777
R superior parietal lobe/precuneus	7	14	-67	45	15.04	15445
L superior/middle occipital gyrus	19	-30	-76	22	13.16	6007
R superior/middle occipital gyrus	19	31	-71	25	16.70	9824
L parastriate cortex (cuneus)	18	-20	-65	18	9.84	3785
R parastriate cortex (cuneus)	18	18	-56	17	13.17	6592
L inferior temporal gyrus	37	-53	-56	-8	7.59	536
R inferior/middle temporal gyrus	37	48	-53	-1	7.24	2428
L middle frontal gyrus	46	-42	31	33	5.50	390
R middle frontal gyrus	6	45	4	32	6.19	650
L parahippocampal gyrus	35	-31	-39	-8	5.27	47
<i>Faces > Positions</i>						
L striate/parastriate cortex	17/18	-17	-87	3	6.50	1674
R striate/parastriate cortex	17/18	12	-87	5	7.04	481
L posterior fusiform gyrus	19	-18	-74	-11	6.47	2695
L middle temporal/angular gyrus	39	-47	-62	25	8.63	5804
L middle temporal gyrus	21	-54	-36	0	5.34	338
L middle frontal gyrus	6	-38	10	51	5.94	1130
L inferior frontal gyrus	45	-40	23	2	8.00	2621
L posterior cingulate gyrus	31	-3	-53	26	13.10	8704
L superior frontal gyrus	9	-7	50	36	7.27	5792

Additionally, strong activity clusters were found in the left posterior cingulate cortex and the left superior medial frontal lobe. A smaller cluster was found in the left middle frontal gyrus.

All reported activation clusters of the “faces vs. positions” contrast, except the left middle temporal gyrus for “faces > positions”, which reached marginal significance (*P* < 0.1), also proved to be significant in the ROI random effect analyses.

The corresponding analysis of the second group of 7 participants revealed virtually identical activations. For both positions and faces, all areas that proved to be significant in the sample of 12 subjects also lighted up here, but now all activations (except the middle frontal gyrus for faces) lighted up in the left and right hemisphere, that is, there were additional activations in the right parahippocampal gyrus (*x* = 26, *y* = -38, *z* = -7, no. of active voxels = 584, max. *t*-value = 8.60) and dorsolateral prefrontal cortex (47/4/27, 132, 5.92) for positions and in the right inferior frontal (50/23/19, 810, 7.69), middle temporal (49/-32/11, 3246, 6.95) and angular gyrus (47/-58/28, 3293, 7.94) for faces. Consistent with the previous analysis with 12 participants, all additional activations had more active voxels in the left hemisphere.

In a second analysis, we wanted to find out which areas respond parametrically to the fan variation, i.e., the number of associations to be recalled from long-term memory. Therefore, fan contrasts ($0 < 1/1 < 1/2 < 2/2$) were computed for recalling positions and faces revealing brain areas that show a linear increase in activation with increasing associative fan. Fig. 4 shows a superposition map of the contrasts for positions (dark to light green) and faces (red to yellow). What is obvious from Fig. 4 is that there is only a partial overlap of regions that respond to

the fan variation for positions and faces and that these regions correspond only in part to those found for faces and positions in general (see above). First, there are regions that exhibit similar increases in activity with increasing fan for *both* positions and faces, i.e., the left inferior frontal gyrus (BA44), the left medial frontal cortex (pre-SMA) and the left inferior precentral/middle frontal gyrus (frontal eye field). Second, there are areas that respond more strongly to faces than positions or vice versa. The superposition map in Fig. 4 shows that for positions these areas consist of an extended posterior bilateral cluster (including the superior parietal lobe, the superior occipital gyrus and a posterior part of the precuneus), as well as the left and right precentral gyrus, whereas more activity for faces was found only in the left posterior cingulate cortex. This has additionally been illustrated in Fig. 4 by plots of event-related BOLD signals (averaged to cue onset) from the right precentral gyrus (top, right) and the left posterior cingulate cortex (bottom, left), showing a gradual increase of the hemodynamic response with increasing fan, which is much more pronounced for positions in the right precentral gyrus and for faces in the posterior cingulate cortex (Table 2).

All reported activation clusters of the fan contrasts for faces and positions, except the right superior occipital/superior parietal lobe for positions, also proved to be significant in the subsequent ROI random effect analyses, demonstrating high inter-individual consistency of the fan effects. To further strengthen this claim, we additionally computed single-subject GLMs (including the experimental predictors as well as one level confound predictor for each study run). As can be seen in Table 3 and in the upper part of Fig. 5 (showing fan contrast superposition maps for individual participants), the BOLD fan effects (i.e., contrasts of Fan2/2 > 1/2 > 1/1 > 0) for positions and faces in the main foci of activation could be reliably observed across participants (participants 1 to 12 in Table 3).

For both positions and faces, all areas described above that proved to be significant in the sample of 12 participants also showed up in the corresponding analysis of the second group of 7 participants. Consistent with the analysis of the first group, those areas which showed an asymmetrical activation, i.e., more activity for faces or positions, exhibited the same asymmetry in the analysis of the second group. As can be seen in Table 3 (right part) and in the lower part of Fig. 5, the BOLD fan effects for positions and faces in the main foci of activation could be reliably observed across participants (participants A to G in Table 3).

Discussion

The theory of a dorsal and ventral visual pathway (e.g., Mishkin et al., 1983) predicts that objects and positions are processed perceptually in topographically distinct neural subsystems. Based on models of distributed cortical memory representations (Damasio, 1989; McClelland et al., 1995; Rösler and Heil, 2003), we hypothesized a corresponding dissociation of the long-term memory representations of faces and spatial positions. Accordingly, we found clear topographical dissociations of event-related brain activations when faces and positions were retrieved from long-term memory. As expected, a main effect of stimulus type was evident. Recalling positions more strongly activated an extended cluster of dorsal pathway visual areas reaching bilaterally from the parastriate cortex and the middle and superior occipital gyrus up to the inferior and superior parietal lobes. This result supports the

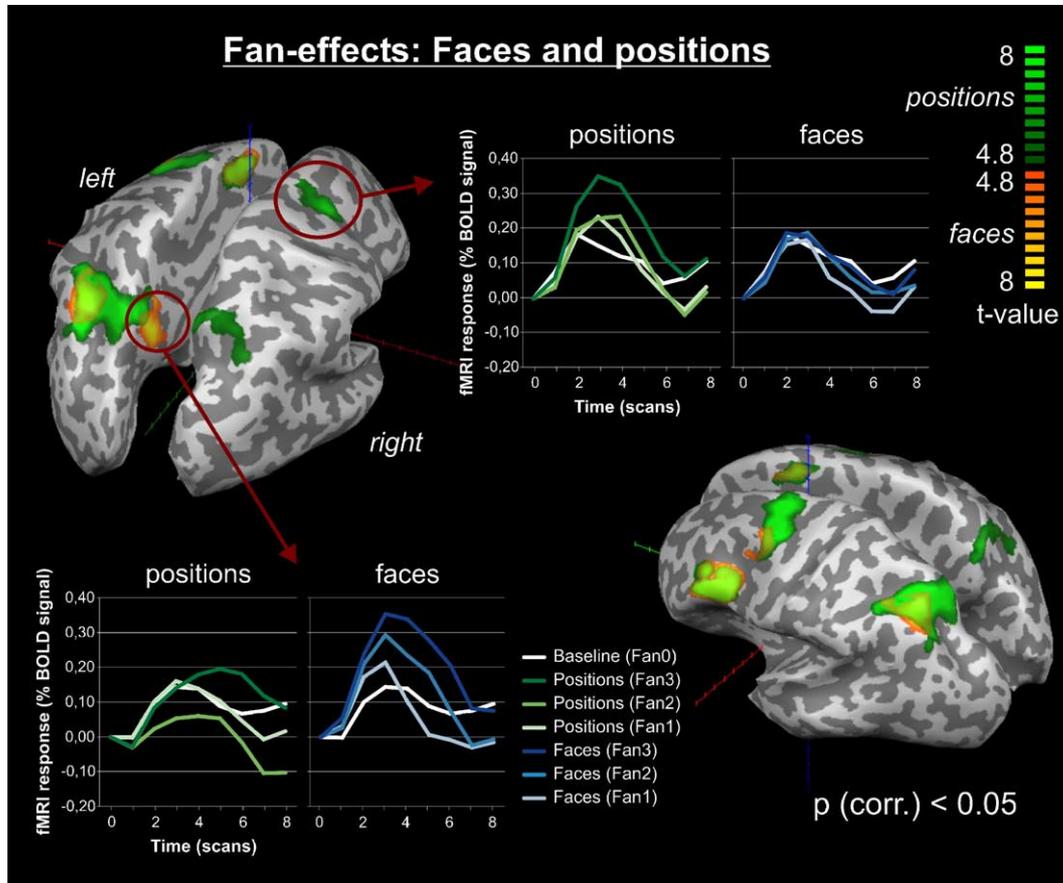


Fig. 4. Superposition of the fMRI fan contrasts (Fan2/2 > Fan1/2 > Fan 1/1 > Fan0, P corrected < 0.05) for recalling faces (red–yellow) and positions (dark green–light green), revealing brain areas that show a linear increase in activation with increasing associative fan. Beside are illustrative sample plots of event-related BOLD signals (averaged to cue onset) from two brain areas (right precentral gyrus and posterior cingulate cortex) for the different levels of associative fan, (0, 1/1, 1/2, 2/2, labeled 0, 1, 2 and 3 in the figure), showing a gradual increase with increasing fan during retrieval of positions and faces.

claim that areas of the dorsal pathway which are involved in the perceptual processing of spatial information also play a significant role during retrieval from long-term memory.

In contrast to the strong dorsal pathway activations for positions, recalling faces activated, albeit much less pronounced,

more ventral cortical regions, i.e., the left and right striate and parastriate cortex and the left posterior fusiform gyrus (cf. Fig. 3). Together with the more dorsal activations for positions, this pattern of results supports the notion that material-specific cortical long-term representations of positions and faces become re-activated in

Table 2

Location (region, BA and center of gravity in Talairach coordinates), peak t -value and number of significantly activated voxels of brain areas showing a linear increase in activation with increasing associative fan (P corrected < 0.05)

Region	BA	x	y	z	t	Voxels
<i>Positions</i>						
L superior parietal lobe/precuneus/superior occipital gyrus	7/19	-22	-66	41	11.07	15,756
R superior parietal lobe/superior occipital gyrus	7/19	16	-68	45	6.93	4025
L precentral gyrus	6	-27	-5	53	11.02	6558
R precentral gyrus	6	24	-3	53	7.76	2464
L medial frontal gyrus (pre-SMA)	6/32	-3	8	50	9.96	6832
L inferior frontal gyrus	44	-44	12	31	11.46	7602
<i>Faces</i>						
L posterior cingulate gyrus/parietal cuneus	31/7	-5	-61	29	8.86	4374
L superior parietal lobe/superior occipital gyrus	7/19	-30	-65	39	9.35	4976
L precentral/middle frontal gyrus	6	-35	-2	56	7.45	1904
L medial frontal gyrus (pre-SMA)	6/32	-4	10	50	9.32	5726
L inferior frontal gyrus	44	-42	11	32	12.25	9138

Table 3

Consistency of the BOLD fan effects (contrast of Fan2/2 > Fan1/2 > Fan 1/1 > Fan0) across participants (participants 1 to 12 performed an EEG retrieval phase prior to the fMRI experiment, whereas the additional participants A to G were scanned 1 day after acquisition without an intervening EEG phase)

Region	BA	1	2	3	4	5	6	7	8	9	10	11	12	A	B	C	D	E	F	G
<i>Positions</i>																				
L sup. parietal lobe/precuneus/sup. occipital gyrus	7/19	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
R sup. parietal lobe/sup. occipital gyrus	7/19	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
L precentral gyrus	6	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
R precentral gyrus	6	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
L medial frontal gyrus	6/32	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
L inf. frontal gyrus	44	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
<i>Faces</i>																				
L posterior cingulate gyrus/parietal cuneus	31/7				*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
L sup. parietal lobe/sup. occipital gyrus	7/19	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
L precentral/mid. frontal gyrus	6	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
L medial frontal gyrus	6/32	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
L inferior frontal gyrus	44	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*

Asterisks indicate whether the participant showed significantly activated voxels (single-subject-GLM, P uncorrected < 0.001, five or more contiguous voxels, unsmoothed data) in brain areas for which a linear increase in activation with increasing associative fan was found with the multi-subject-GLM.

at least some of those areas which are relevant for their initial perceptual processing (e.g., Mishkin et al., 1983; Ungerleider and Mishkin, 1982) and working memory maintenance (Belger et al., 1998; D'Esposito et al., 2000; Haxby et al., 2001; Postle and D'Esposito, 1999; Postle et al., 2000). The activation in the fusiform gyrus was found to be small compared to the strong parietal activity. However, there are several reasons for why the ventral activity was smaller than originally expected. First, the fusiform gyrus is anatomically small compared to the inferior and superior parietal lobes. Nevertheless, all ventral activations for faces, albeit small, were statistically reliable with the initial analysis and also in the subsequent ROI random effect analysis. Therefore, these activations must be considered as reliable brain responses to face recall. Second, the ventral stream areas are located close to air-filled skull compartments and apertures. This leads, compared to, e.g., the dorsal regions in the parietal lobe, to higher susceptibility artifacts in the measured BOLD signal and therefore to lower signal-to-noise ratios, making statistical testing in these areas more conservative.

Apart from these anatomical and technical explanations, there are also some conceptual reasons for why the fusiform activation was small compared to other face-related activations in this experiment. It is conceivable that some perceptual features of the faces are consolidated not only by means of a visual-imagery code, but also via verbal mediators which activate left anterior areas (i.e., Broca's area). This would explain the strong left frontal activity in BA44 found during face recall (cf. Figs. 3 and 4). Haxby et al. (1996) also found left frontal activity when comparing an intentional face encoding task with an incidental face-matching task and attributed this effect to the use of verbal encoding processes during intentional encoding. On the other hand, our participants consistently reported that, even if they had tried to encode some of the facial features by verbalization, the comparison during retrieval was made mainly on the basis of a recalled visual analog image. To clarify whether the left anterior activation is related to a verbal mediating strategy, an additional experiment is currently run (Khader et al., in preparation) in which objects have to be learned which are different exemplars of highly similar objects and therefore much harder to encode by direct naming than faces (i.e., pictures of different cups).

A related point is that the faces could have been encoded more as "persons" than as faces. This is supported by the posterior cingulate cortex activation, which was also found for emotional words compared to neutral words (Maddock et al., 2003), during the evaluation of emotional salience during episodic memory retrieval (Maddock, 1999) and during name-cued retrieval of autobiographical memories of familiar persons (Maddock et al., 2001). The latter finding suggests that the posterior cingulate activations play a role in coding "person familiarity" (Shah et al., 2001). The results of the present study clearly support this claim. Our participants reported to have encoded the faces not only as abstract images, but also as "persons" they came across again and again during the acquisition phase. Therefore, face encoding may not only have established face–word, but also face–person associations, and the gradual activation of these associations during recall could be reflected by the parametric increase in posterior cingulate activation with fan size. Furthermore, the faces surely had more affective salience compared to the abstract positions coded by dark and bright squares.

Compared to faces, recalling positions also activated the parahippocampal gyrus. This activation was small too (cf. Table 1 and Fig. 3), but nevertheless reliable in the fixed and the random effect analyses. The parahippocampal cortex receives strong afferent projections from dorsal stream areas (Mishkin et al., 1997; Suzuki and Amaral, 1994) and thus seems to be the major source of spatial information transmitted to the hippocampus (Mair et al., 2003). Furthermore, it was found to be involved in long-term coding of associative relationships (Düzel et al., 2003; Vargha-Khadem et al., 1997; Yonelinas et al., 2001). Our finding of more activity in this area when recalling positions suggests that it is also involved in long-term memory retrieval of spatial associative relationships. The prominent role of the parahippocampal cortex in spatial memory has also been substantiated by other neuroimaging studies with humans (Bellgowan et al., 2003; Maguire et al., 1998) and with lesion studies in monkeys (Malkova and Mishkin, 2003; Parkinson et al., 1988). Along with the finding that face recall elicited more activity in the left posterior fusiform gyrus, this also supports the notion that material-specific areas in the temporal cortex that are assumed to be involved in the processing of objects and places (i.e., the fusiform face area (FFA; Kanwisher et al., 1997; O'Craven and Kanwisher,

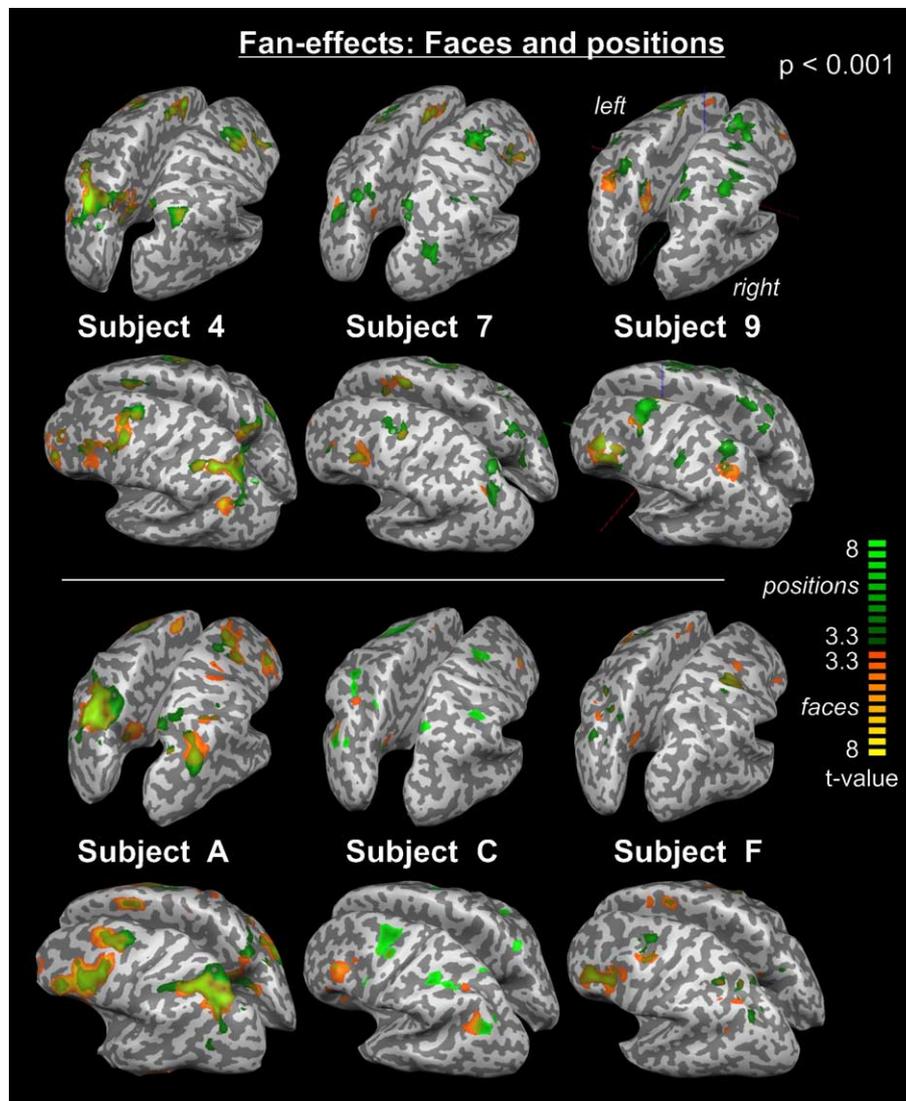


Fig. 5. Subject-specific superposition maps of the fMRI fan contrasts (Fan2/2 > Fan1/2 > Fan 1/1 > Fan0, P uncorrected < 0.001) for recalling faces and positions, substantiating the consistency of the BOLD fan effects across participants and showing that the main foci of activation found in the multi-subject-analysis (see Fig. 4) can be reliably observed across participants. Top row: three participants from the sample with a first retrieval test with EEG recording; bottom row: three participants from the sample without the intervening EEG recording phase.

2000; Puce et al., 1995) and the parahippocampal place area (PPA; Aguirre et al., 1998; Epstein and Kanwisher, 1998; O'Craven and Kanwisher, 2000) also play a material-specific role during the retrieval of object vs. spatial information.

In addition to the posterior differences along the dorsal and ventral visual pathways, recalling faces and positions also revealed differences in the left prefrontal cortex, with stronger activity for positions in the left dorsolateral prefrontal cortex (DLPFC, BA46) and for faces in the left ventrolateral prefrontal cortex (VLPFC, BA45). This dissociation is in accordance with the notion of a material-specific fragmentation of the prefrontal cortex, with object information being maintained and processed in the VLPFC and spatial information in the DLPFC (Banich et al., 2000; Levy and Goldman-Rakic, 2000). To give the correct answer, the participants had to recall the cued stimuli from long-term memory and had to compare them before being able to give the correct answer. The present study supports the claim that these processes draw on material-specific subdivisions of the prefrontal cortex.

Besides the observed main effect of material type, we also found a monotonic increase of BOLD signal amplitude with increasing associative fan of the to-be-remembered stimuli during retrieval of faces and positions in various brain regions (cf. Figs. 4 and 5), indicating that the activity level of stimulus-specific cell assemblies increased with the number of accessed representations. Accordingly, response times and error rates were found to be a function of the number of associative links fanning out from a given memory representation for both positions and faces (cf. Fig. 2). As with the general comparison of stimulus type, the places where activity increased parametrically with increasing fan also dissociated topographically for positions and faces (cf. Figs. 4 and 5). For positions, those areas consisted of the left and right superior parietal lobe, the left and right precentral gyrus (including the frontal eye fields), the left inferior frontal cortex and the medial frontal cortex (pre-SMA). Because the superior parietal lobes as well as the precentral gyri also showed up in the general contrast, with more activity during the recall of positions, we are safe to

conclude that these areas play a crucial role in storing, recalling and comparing the memory representations of spatial information. Interestingly, both superior parietal lobes showed more activity for positions, whereas fan size affected the BOLD signal much more on the left side. Therefore, while both parietal lobes seem to be involved in the retrieval of spatial information, especially the left parietal lobe seems to be responsible for the activation of long-term representations.

The fan contrast for recalling faces revealed activity in the left inferior frontal cortex and pre-SMA, as well as the left posterior cingulate cortex, superior parietal lobe and frontal eye field. The left inferior frontal and posterior cingulate cortex were also found to exhibit strong activity in general contrast with positions, and therefore we conclude that these areas play an important role in storing, recalling and comparing the memory representations of faces (see discussion below). Interestingly, the left superior parietal lobe was also activated, even if not as much as for positions. This indicates that recalling faces also involves the parietal cortex to some extent, which is in accordance with studies who found that successful episodic memory retrieval of newly learned faces activates the left parietal cortex (Clark et al., 1998; Leube et al., 2003; Leveroni et al., 2000).

Although hemispheric asymmetry of brain processes had not been the core issue of the present study, the obtained results should be discussed in the light of recent studies on mental imagery, suggesting that mental imagery processes, compared to perceptual processes, recruit predominantly left hemispheric brain regions (Farah, 1995; Ishai et al., 2000). In our study, two contrasts were of interest, the overall comparison of recalling faces vs. positions and the corresponding fan effects. In the overall comparison of stimulus type, clusters revealing more activation for positions were all distributed bilaterally with usually more active voxels in the right hemisphere. The only exceptions were the parahippocampal and prefrontal cortex. In contrast, more activation was found in the left hemisphere for faces, i.e., in the inferior frontal, middle temporal and posterior fusiform gyrus. The only exception of a bilateral activation for faces concerned the striate/parastriate cortex. The same pattern of a more bilateral activation for positions and a more left lateralized activation for faces was also observed in the fan contrasts. Here, however, the fan effect proved as significant for both materials predominantly in the left hemisphere. Taken together, the hemispheric differences are not consistent in that they would support the claim of a specialized role of the left or right hemisphere for visual imagery.

On the other hand, some brain areas were activated in our study that correspond to the content-unspecific fronto-parietal “attention/imagery network” proposed in recent studies of mental imagery (i.e., Ishai et al., 2000, 2002; Mechelli et al., 2004). However, in contrast to these studies, the present data provide more evidence for a content-dependent rather than a content-independent involvement of the fronto-parietal network, with a stronger reliance on parietal regions for positions and a stronger reliance on left frontal regions for faces.

At present, we can only speculate about the underlying causes of the observed hemispheric asymmetries. The finding that face recall showed a more pronounced left-sided activity compared to positions could be due to stronger reliance on visual details vs. absolute positions. Furthermore, as noted previously, some perceptual features of the faces could have been consolidated, not only by means of a visual code, but also via verbal descriptors which activate predominantly left hemispheric brain

regions. This is in accordance with studies by Kosslyn et al. (1995), who found the left hemisphere to be more involved when stored descriptions are used to arrange parts of a mental image, whereas the right hemisphere is more involved in storing analog spatial information.

The previous findings from mental imagery studies relate to an important functional distinction between activation of long-term representations on the one hand and possible peri-retrieval processes on the other hand. Our retrieval task comprised the activation of long-term representations, as well as subsequent maintenance and comparison processes. However, we think that the material-specific activations in the present study are primarily due to different topographies of long-term memory representations. First, the kind of retrieval cue was the same for both types of material, and in a pilot study, we had varied systematically the visual complexity of the stimuli. By adjusting the visual similarity of the faces and the size of the position matrices, we ensured that our participants learned both types of association equally well. Accordingly, the error rates during the overlearning phase revealed no effect of stimulus type neither at the beginning nor during the course of the overlearning phase. Therefore, it is unlikely that the observed topographic differences during retrieval are due to differences in the complexity of the mental images that had to be generated. Second, although the overall contrast which compared retrieval of faces and positions, irrespective of the fan level, could indeed be contaminated by material-specific control processes, this argument is difficult to apply to the material-specific fan effects. In these contrasts, the control processes should be of the same quality for small and large fan conditions of one material, and in this respect, they should not be detected by the statistical analysis. Thus, we conclude that differences in control processes alone cannot explain the topographical differences observed in the present experiment.

It is important to relate the obtained fMRI findings to the corresponding EEG results of the first retrieval phase (see Khader et al., *in press*) because the participants were tested twice, and therefore the second retrieval phase could, in principle, rely on altered cognitive processes compared to the initial retrieval phase. However, there is strong support for the conclusion that the very same retrieval processes were triggered in both the EEG and the fMRI session and that in both situations fully consolidated permanent representations were activated. The present study was explicitly designed to activate fully consolidated information, in contrast to studies in which retrieval was tested after a brief and most likely incomplete learning/consolidation phase. To ensure that each and every participant had fully consolidated the material and that all were tested on the same performance level, we had employed an extensive overlearning procedure before the first retrieval test took place, and furthermore we had inserted a refreshing overlearning phase before the next retrieval test took place with fMRI recordings (see Materials and methods section). The initial overlearning procedure (which took about 1 to 2 h of extensive training) ensured that all participants had full access to all associations. At the end of this training, each participant committed less than 5% of retrieval errors with this rather complex associative material. As noted in the Materials and methods section, participants had to work through training sets once more prior to the fMRI scan until they had reached the same overlearning criterion again. In contrast to the initial overlearning phase, the second one took about 15–30 min only, which clearly shows that it was essentially an updating of permanently stored

information rather than a complete re-acquisition of associations. This is also strongly supported by the very rapidly decreasing number of errors during the course of updating that could be observed irrespective of the time that had passed between the EEG and the fMRI retrieval session. Furthermore, there is also direct empirical evidence for the notion that all participants retrieved permanently stored and fully consolidated representations from LTM and that this was the case in both retrieval sessions. The level of fan affected response times and error rates equivalently in both experimental phases and for both types of stimuli (Khader et al., *in press*). Furthermore, the EEG data showed pronounced fan effects for both faces and positions, which were similar to the observed BOLD signal changes in the present study and which showed clear topographic differences depending on stimulus type. We think that this indicates high commonality of the two retrieval phases and it also stresses that our retrieval situation is different to that created in the majority of memory retrieval studies in which only weakly consolidated material was tested. Finally, to explicitly control for the possibility that our participants could have been not naive with respect to the retrieval task because of the previous EEG retrieval session, we scanned seven additional participants who entered the scanner immediately 1 day after learning without an intervening retrieval phase and without a fresh-up procedure prior to the fMRI experiment. As outlined in the Results section, the brain activations observed in these participants did not differ substantially from the activations obtained with the 12 participants who had encountered an intervening EEG retrieval phase. To conclude, there is much evidence for our argument that each participant retrieved permanently stored and fully consolidated memory representations from LTM and that this was the case with as well as without an intervening EEG retrieval phase which might have caused a reconsolidation of the material.

A major interpretational advantage of the present study is that all topographic differences between faces and positions cannot be attributed to differences in retrieval cue processing because the retrieval of faces and spatial positions were both triggered by the same kind of stimulus, i.e., words. Here, it has been clearly necessary to access permanently stored representations by intentionally scanning an associative structure of stimulus representations. The difficulty of this scanning procedure was a priori defined and thus well controlled by parametric manipulation.

Taken together, the findings of the present study support the model of material-specific cortical cell assemblies for episodic memories (Damasio, 1989; McClelland et al., 1995) by demonstrating that it also applies to the long-term memories of faces and positions. The brain activation results have shown that stored representations of faces and positions are, in correspondence with their topographic dissociation during perceptual processing, also permanently represented in material-specific cortical cell assemblies.

Acknowledgments

This work was supported by Grant FOR254/2-1,2 of the German Research Foundation (DFG) assigned to FR. We thank Siegfried Sporer for kindly providing stimulus material and Martin Heil and Kerstin Jost, as well as two anonymous reviewers for valuable comments and helpful discussions.

References

- Aguirre, G.K., Zarahn, E., D'Esposito, M., 1998. An area within human ventral cortex sensitive to "building" stimuli: evidence and implications. *Neuron* 21 (2), 373–383.
- Anderson, J.R., 1974. Retrieval of propositional information from long-term memory. *Cogn. Psychol.* 6, 451–474.
- Banich, M.T., Milham, M.P., Atchley, R., Cohen, N.J., Webb, A., Wszalek, T., Kramer, A.F., Liang, Z.P., Wright, A., Shenker, J., Magin, R., 2000. fMRI studies of Stroop tasks reveal unique roles of anterior and posterior brain systems in attentional selection. *J. Cogn. Neurosci.* 12 (6), 988–1000.
- Belger, A., Puce, A., Krystal, J.H., Gore, J.C., Goldman-Rakic, P., McCarthy, G., 1998. Dissociation of mnemonic and perceptual processes during spatial and nonspatial working memory using fMRI. *Hum. Brain Mapp.* 6 (1), 14–32.
- Bellgowan, P.S.F., Buffalo, E.A., Bodurka, J., Martin, A., 2003. High resolution imaging of the anterior medial temporal lobe during object and spatial memory. *Soc. Neurosci.* 556.1 (Abstr.).
- Christoff, K., Prabhakaran, V., Dorfman, J., Zhao, Z., Kroger, J.K., Holyoak, K.J., Gabrieli, J.D., 2001. Rostrolateral prefrontal cortex involvement in relational integration during reasoning. *Neuroimage* 14 (5), 1136–1149.
- Clark, V.P., Maisog, J.M., Haxby, J.V., 1998. An fMRI study of face perception and memory using random stimulus sequences. *J. Neurophysiol.* 79 (6), 3257–3265.
- Damasio, A.R., 1989. Time-locked multiregional retroactivation: a system-level proposal for the neuronal substrates of recall and recognition. *Cognition* 33, 25–62.
- Desimone, R., Albright, T.D., Gross, C.G., Bruce, C., 1984. Stimulus-selective properties of inferior temporal neurons in the macaque. *J. Neurosci.* 4 (8), 2051–2062.
- D'Esposito, M., Postle, B.R., Rypma, B., 2000. Prefrontal cortical contributions to working memory: evidence from event-related fMRI studies. *Exp. Brain Res.* 133, 3–11.
- Düzel, E., Habib, R., Rotte, M., Guderian, S., Tulving, E., Heinze, H.J., 2003. Human hippocampal and parahippocampal activity during visual associative recognition memory for spatial and nonspatial stimulus configurations. *J. Neurosci.* 23 (28), 9439–9444.
- Epstein, R., Kanwisher, N., 1998. A cortical representation of the local visual environment. *Nature* 392 (6676), 598–601.
- Farah, M.J., 1995. Current issues in the neuropsychology of image generation. *Neuropsychologia* 33 (11), 1455–1471.
- Felleman, D.J., Van Essen, D., 1991. Distributed hierarchical processing in the primate cerebral cortex. *Cereb. Cortex* 1, 1–47.
- Funahashi, S., Bruce, C.J., Goldman-Rakic, P.S., 1989. Mnemonic coding of visual space in the monkey's dorsolateral prefrontal cortex. *J. Neurophysiol.* 61, 331–349.
- Haxby, J.V., Ungerleider, L.G., Horwitz, B., Maisog, J.M., Rapoport, S.I., Grady, C.L., 1996. Face encoding and recognition in the human brain. *Proc. Natl. Acad. Sci. U. S. A.* 93 (2), 922–927.
- Haxby, J.V., Gobbini, M.I., Furey, M.L., Ishai, A., Schouten, J.L., Pietrini, P., 2001. Distributed and overlapping representations of faces and objects in ventral temporal cortex. *Science* 293, 2425–2430.
- Henson, R.N., Goshen-Gottstein, Y., Ganel, T., Otten, L.J., Quayle, A., Rugg, M.D., 2003. Electrophysiological and haemodynamic correlates of face perception, recognition and priming. *Cereb. Cortex* 13 (7), 793–805.
- Ishai, A., Ungerleider, L.G., Haxby, J.V., 2000. Distributed neural systems for the generation of visual images. *Neuron* 28 (3), 979–990.
- Ishai, A., Haxby, J.V., Ungerleider, L.G., 2002. Visual imagery of famous faces: effects of memory and attention revealed by fMRI. *Neuroimage* 17 (4), 1729–1741.
- Kanwisher, N., McDermott, J., Chun, M.M., 1997. The fusiform face area: a module in human extrastriate cortex specialized for face perception. *J. Neurosci.* 17 (11), 4302–4311.
- Khader, P., Heil, M., Rösler, F., *in press*. Material-specific long-term

- memory representations of faces and spatial positions: evidence from slow event-related brain potentials. *Neuropsychologia*.
- Khader, P., Knoth, K., Bien, S., and Rösler, F., in preparation. Converging EEG and fMRI evidence for content-specific activation during associative long-term memory encoding and retrieval.
- Kosslyn, S.M., Maljkovic, V., Hamilton, S.E., Horwitz, G., Thompson, W.L., 1995. Two types of image generation: evidence for left and right hemisphere processes. *Neuropsychologia* 33 (11), 1485–1510.
- Kriegeskorte, N., Göbel, R., 2001. An efficient algorithm for topologically correct segmentation of the cortical sheet in anatomical MR volumes. *Neuroimage* 14 (2), 329–346.
- Leube, D.T., Erb, M., Grodd, W., Bartels, M., Kircher, T.T., 2003. Successful episodic memory retrieval of newly learned faces activates a left fronto-parietal network. *Cogn. Brain Res.* 18 (1), 937–1001.
- Leveroni, C.L., Seidenberg, M., Mayer, A.R., Mead, L.A., Binder, J.R., Rao, S.M., 2000. Neural systems underlying the recognition of familiar and newly learned faces. *J. Neurosci.* 20 (2), 878–886.
- Levy, R., Goldman-Rakic, P.S., 2000. Segregation of working memory functions within the dorsolateral prefrontal cortex. *Exp. Brain Res.* 133 (1), 23–32.
- Livingstone, M.S., Hubel, D.H., 1988. Segregation of form, color, movement, and depth: anatomy, physiology, and perception. *Science* 240, 740–749.
- Maddock, R.J., 1999. The retrosplenial cortex and emotion: new insights from functional neuroimaging of the human brain. *Trends Neurosci.* 22 (7), 310–316.
- Maddock, R.J., Garrett, A.S., Buonocore, M.H., 2001. Remembering familiar people: the posterior cingulate cortex and autobiographical memory retrieval. *Neuroscience* 104 (3), 667–676.
- Maddock, R.J., Garrett, A.S., Buonocore, M.H., 2003. Posterior cingulate cortex activation by emotional words: fMRI evidence from a valence decision task. *Hum. Brain Mapp.* 18 (1), 30–41.
- Maguire, E.A., Frith, C.D., Burgess, N., Donnett, J.G., O'Keefe, J., 1998. Knowing where things are parahippocampal involvement in encoding object locations in virtual large-scale space. *J. Cogn. Neurosci.* 10 (1), 61–76.
- Mair, R.G., Burk, J.A., Porter, M.C., 2003. Impairment of radial maze delayed nonmatching after lesions of anterior thalamus and parahippocampal cortex. *Behav. Neurosci.* 117 (3), 596–605.
- Malkova, L., Mishkin, M., 2003. One-trial memory for object–place associations after separate lesions of hippocampus and posterior parahippocampal region in the monkey. *J. Neurosci.* 23 (5), 1956–1965.
- McClelland, J.L., McNaughton, B.L., O'Reilly, R.C., 1995. Why there are complementary learning systems in the hippocampus and neocortex: insights from the successes and failures of connectionist models of learning and memory. *Psychol. Rev.* 102, 419–457.
- Mechelli, A., Price, C.J., Friston, K.J., Ishai, A., 2004. Where bottom–up meets top–down: neuronal interactions during perception and imagery. *Cereb. Cortex* 14 (11), 1256–1265.
- Miller, E.K., Li, L., Desimone, R., 1993. Activity of neurons in anterior inferior temporal cortex during a short-term memory task. *J. Neurosci.* 13 (4), 1460–1478.
- Mishkin, M., Ungerleider, L.G., Macko, K.A., 1983. Object vision and spatial vision: two cortical pathways. *Trends Neurosci.* 6, 414–417.
- Mishkin, M., Suzuki, W.A., Gadian, D.G., Vargha-Khadem, F., 1997. Hierarchical organization of cognitive memory. *Philos. Trans. R Soc. London, Ser. B, Biol. Sci.* 352 (1360), 1461–1467.
- Miyashita, Y., Chang, H.S., 1998. Neuronal correlate of pictorial short-term memory in the primate temporal cortex. *Nature* 331 (6151), 68–70.
- O'Craven, K.M., Kanwisher, N., 2000. Mental imagery of faces and places activates corresponding stimulus-specific brain regions. *J. Cogn. Neurosci.* 12 (6), 1013–1023.
- O'Reilly, R.C., Rudy, J.W., 2001. Conjunctive representations in learning and memory: principles of cortical and hippocampal function. *Psychol. Rev.* 108 (2), 311–345.
- Parkinson, J.K., Murray, E.A., Mishkin, M., 1988. A selective mnemonic role for the hippocampus in monkeys: memory for the location of objects. *J. Neurosci.* 8 (11), 4159–4167.
- Pesaran, B., Pezaris, J.S., Sahani, M., Mitra, P.P., Andersen, R.A., 2002. Temporal structure in neuronal activity during working memory in macaque parietal cortex. *Nat. Neurosci.* 5 (8), 805–811.
- Pohl, W., 1973. Dissociation of spatial discrimination deficits following frontal and parietal lesions in monkeys. *J. Comp. Physiol. Psychol.* 82, 227–239.
- Postle, B.R., D'Esposito, M., 1999. “What”–Then–“Where” in visual working memory: an event-related fMRI study. *J. Cogn. Neurosci.* 11 (6), 585–597.
- Postle, B.R., Berger, J.S., Taich, A.M., D'Esposito, M., 2000. Activity in human frontal cortex associated with spatial working memory and saccadic behavior. *J. Cogn. Neurosci.* 12 (Suppl. 2), 2–14.
- Puce, A., Allison, T., Gore, J.C., McCarthy, G., 1995. Face-sensitive regions in human extrastriate cortex studied by functional MRI. *J. Neurophysiol.* 74 (3), 1192–1199.
- Ranganath, C., D'Esposito, M., 2001. Medial temporal lobe activity associated with active maintenance of novel information. *Neuron* 31, 865–873.
- Ranganath, C., Cohen, M.X., Dam, C., D'Esposito, M., 2004. Inferior temporal, prefrontal, and hippocampal contributions to visual working memory maintenance and associative memory retrieval. *J. Neurosci.* 24 (16), 3917–3925.
- Rösler, F., Heil, M., 2003. The principle of code-specific memory representations. In: Kluwe, R.H., Lüer, G., Rösler, F. (Eds.), *Principles of Learning and Memory*. Birkhäuser, Basel, pp. 71–92.
- Shah, N.J., Marshall, J.C., Zafiris, O., Schwab, A., Zilles, K., Markowitsch, H.J., Fink, G.R., 2001. The neural correlates of person familiarity. A functional magnetic resonance imaging study with clinical implications. *Brain* 124 (4), 804–815.
- Smith, E.E., Jonides, J., Koeppel, R.A., 1996. Dissociating verbal and spatial working memory using PET. *Cereb. Cortex* 6, 11–20.
- Sporer, S.L., 1999. The own-race bias in Germany: testing the contact hypothesis with Turks and Germans. Paper Presented at the 4th European Conference on Psychology and Law of the American Psychology-Law Association and the European Psychology-Law Association in Dublin, Ireland.
- Squire, L.R., 1992. Memory and hippocampus: a synthesis from findings with rats, monkeys, and humans. *Psychol. Rev.* 99, 195–231.
- Squire, L.R., Alvarez, P., 1995. Retrograde amnesia and memory consolidation: a neurobiological perspective. *Curr. Opin. Neurobiol.* 5, 169–177.
- Suzuki, W.A., Amaral, D.G., 1994. Perirhinal and parahippocampal cortices of the macaque monkey: cortical afferents. *J. Comp. Neurol.* 350 (4), 497–533.
- Talairach, J., Tournoux, P., 1988. *Co-Planar Stereotactic Atlas of the Human Brain*. Georg Thieme Verlag, Stuttgart.
- Ungerleider, L.G., Mishkin, M., 1982. Two cortical visual systems. In: Ingle, D.J., Goodale, M.A., Mansfield, R.J. (Eds.), *Analysis of Visual Behavior*. MIT Press, Cambridge, MA, pp. 549–580.
- Vaidya, C.J., Zhao, M., Desmond, J.E., Gabrieli, J.D., 2002. Evidence for cortical encoding specificity in episodic memory: memory-induced reactivation of picture processing areas. *Neuropsychologia* 40 (12), 2136–2143.
- Vargha-Khadem, F., Gadian, D.G., Watkins, K.E., Connelly, A., Van Paesschen, W., Mishkin, M., 1997. Differential effects of early hippocampal pathology on episodic and semantic memory. *Science* 277, 376–380.
- Yonelinas, A.P., Hopfinger, J.B., Buonocore, M.H., Kroll, N.E., Baynes, K., 2001. Hippocampal, parahippocampal and occipital–temporal contributions to associative and item recognition memory: an fMRI study. *NeuroReport* 12 (2), 359–363.