PERGAMON

Neuropsychologia 41 (2003) 863–876

NEUROPSYCHOLOGIA

www.elsevier.com/locate/neuropsychologia

Rapid publication

Nonconscious formation and reactivation of semantic associations by way of the medial temporal lobe

Katharina Henke [a,*], Christian R.A. Mondadori [a], Valerie Treyer [b], Roger M. Nitsch [a], Alfred Buck [b], Christoph Hock [a]

[a] *Division of Psychiatry Research, Psychiatric University Hospital, University of Zürich, Lenggstrasse 31, 8029 Zürich, Switzerland*
[b] *PET Center, Division of Nuclear Medicine, University Hospital Zürich, Rämistrasse 100, 8091 Zürich, Switzerland*

Received 10 July 2002; received in revised form 5 December 2002; accepted 10 January 2003

Abstract

A successful strategy to memorize unrelated items is to associate them semantically. This learning method is typical for declarative memory and depends on the medial temporal lobe (MTL). Yet, only a small fraction of perceived items emerge into conscious awareness and receive the status of representations in declarative memory. This functional magnetic resonance imaging (fMRI) study tackled the mnemonic fate of unrelated item pairs processed without conscious awareness. Stimuli consisted of a face and a written profession (experimental condition) or of a face (control condition) exposed very briefly between pattern masks. Although the participants were unaware of the stimuli, activity in the hippocampus and perirhinal cortex was changed in the experimental versus the control condition; perirhinal activity changes correlated with the reaction time measure of the later nonconscious retrieval. For retrieval, the previously presented faces were shown again, this time for conscious inspection. The task was to guess the professional category of each face. This task was to induce a nonconscious retrieval of previously formed face–profession associations. Remarkably, activity in the hippocampus and perirhinal cortex was enhanced when subjects were confronted with faces from the experimental versus the control condition. The degree of hippocampal and perirhinal activation changes correlated with the reaction time measure of nonconscious retrieval. Together, our findings suggest that new semantic associations can be formed and retrieved by way of the medial temporal lobe without awareness of the associations or its components at encoding or any awareness that one is remembering at retrieval.

Keywords: Memory; Hippocampus; Implicit; Masking; Subliminal; Functional magnetic resonance imaging

---

1. Introduction

We store a great amount of information within a short period of time by relating pieces of information in a meaningful way, thereby effectively reducing the number of chunks of information to be stored. Part of this associative learning proceeds intentionally—as when we try to memorize the names of people we meet at a party. In most situations, however, associative learning is incidental and takes place without conscious effort although we are aware of the encoding situation—as when we listen to an odd story a stranger tells at a party. The story is effortlessly linked to the stranger whom we will later remember as the ‘guy with the odd story’. Although much episodic learning occurs incidentally, i.e. without a conscious effort to learn, encoding is still usually accompanied by our conscious perception of the encoding situation. However, occasions may occur when an event is not only incidentally encoded but even without conscious awareness of the event itself. Such representations may remain nonconscious or may later surface to consciousness. Nonconsciously encoded information may consist of semantic and spatial associations and therefore has properties known to depend on the medial temporal lobe (MTL).

For intentional and incidental semantic associative learning it has been shown that the intact functioning of the hippocampal formation and rhinal cortices is necessary [87,88]. Moreover, functional neuroimaging revealed stronger hippocampal activations when primarily unrelated items were encoded via semantic associations than when they were encoded as isolated entities [33,34,46,51,56,76,77]. It is, however, unknown whether semantic associative learning and retrieval can at all occur without conscious awareness of both the encoding event and retrieval—and, if so, whether these nonconscious mnemonic operations involve structures of the medial temporal lobe such as the hippocampal

---

[*] Corresponding author. Tel.: +41-1-384-2619; fax: +41-1-384-2686.
E-mail address: henke@bli.unizh.ch (K. Henke).

0028-3932/03/$ – see front matter © 2003 Elsevier Science Ltd. All rights reserved.
doi:10.1016/S0028-3932(03)00035-6

formation and rhinal cortex. In a recent study [36], we have shown that bilateral hippocampal and right perirhinal activations accompanied the nonconscious retrieval of faces and face–word associations. The design of this first functional magnetic resonance imaging (fMRI) study, however, did not allow us to differentiate between memory for faces and memory for face–word associations. The objective of the present study was to clarify whether the nonconscious formation and retrieval of semantic face–word associations is possible and, if yes, whether nonconscious associative encoding and retrieval would activate MTL structures. To avoid the confounding effect of declarative memory, all learning material was presented very briefly between masks as in Henke et al. [36].

2. Methods

2.1. Participants

We examined 14 normally-sighted, right-handed men (age: 20–43, $M = 27.4$, S.D. $= 6.7$) with no current or past neurological or psychiatric diagnoses. Their handedness [6] and visual acuity [4] was tested prior to the fMRI experiment. Participants with a visual acuity of less than 1.0 were excluded from the study. Informed consent was obtained prior to the investigations. Participants were not informed that stimuli would be briefly flashed between masks until the end of the experiment. Our study protocol was approved by the local ethics committee for human studies.

3. Experimental design

3.1. Stimuli

Stimuli consisted of 48 black-and-white full frontal portraits of unknown bald individuals with neutral facial expressions and without paraphernalia [41]. Stimuli were digitized and degraded in contrast. Ten academic and 10 artistic professions were assigned in equal proportion to the faces. Professions were typed below the faces (Fig. 1B). The resulting face–profession combinations were of mean prototypicality, i.e. the appearance of the individuals was not indicative of their professions. This was shown in an earlier study with 17 participants whose uninformed guesses about the individuals' professional categories did not differ from chance [35]. These 48 face–word pairs were divided into 4 sets of 12 stimuli. Two sets were used for a practice trial and two sets for the fMRI experiment. The four sets were balanced across tasks to distribute stimulus generated effects. Forty black-and-white visual noise images were created for the masks (see Section 3.2 and Fig 1A and B). The fixation slide was black with a white cross placed at a location which corresponded to the midpoint between the eyes of the subsequently flashed stimulus faces.

3.2. Masking technique

Masking procedures interrupt the processing of the stimulus [44,68]. The pattern-masking paradigm of the present study has been adopted from Henke et al. [36]. In the Henke et al. [36] study, each stimulus (S) was consecutively flashed six times within 3 s for 17 ms, flanked by masks (M) which were presented for 183 ms, and preceded by a fixation cross (F) which was displayed for 233 ms, in the sequence F-M-S-M-M-S-M-F-M-S-M-M-S-M-F-M-S-M-M-S-M. In the present study, we increased the number of stimulus repetitions from 6 to 12 doubling the duration of one trial from 3 to 6 s (Fig. 1A). This increase in stimulation intensity was introduced to obtain a behavioral measure of nonconscious retrieval, namely reaction time differences between correct and incorrect answers. Retrieval accuracies and a structured interview administered following the fMRI experiment confirmed that participants were not aware of faces and words flashed between masks and could not distinguish between stimulus blocks of the experimental and control condition.

The computer driven stimulation (640 × 480 resolution, 60 Hz refresh rate, 8 bit color depth) was back-projected with a Sony LCD-projector (60 Hz refresh rate) on a screen standing in front of the scanner. We used the stimulus presentation program "Scope" which was written for the Microsoft Windows operating Systems Windows NT 4.0 (M. Dürsteler, University Hospital Zürich). Scope uses routines from the Microsoft Direct Draw SDK version 3.0 A to synchronize the stimulus change with the vertical retrace of the graphic card. The refresh rate of the computer's graphic card was 60 Hz. At this frequency, our LCD-projector synchronized itself to the graphic card's vertical retrace rate. The shortest presentation time which can be achieved is the time between two vertical retraces which is 16.67 ms with our equipment. The timing of the Scope program and the synchronization of the LCD-projector with the computer were examined using a Spectra Pritchard photometer directed to the projection screen. We observed the photometer's analog output together with Scope's flipping impulses on a digital oscilloscope while the program was running a sequence of alternating black-and-white images with a presentation time of 16.67 ms per image. The photometer's analog output and Scope's flipping impulses were found to be fully synchronized and presentation times were consistently 17 ms.

3.3. Behavioral tasks

3.3.1. Encoding

Twelve face–word combinations were presented between masks in the experimental condition and 12 faces alone were presented between masks in the control condition (Fig. 1B). The subjective percept of the stimulation sequence consisted of moving grains, regularly interrupted by a visual fixation cross. The instruction during the stimulation sequence was to remain attentive and to focus gaze on the fixation cross.

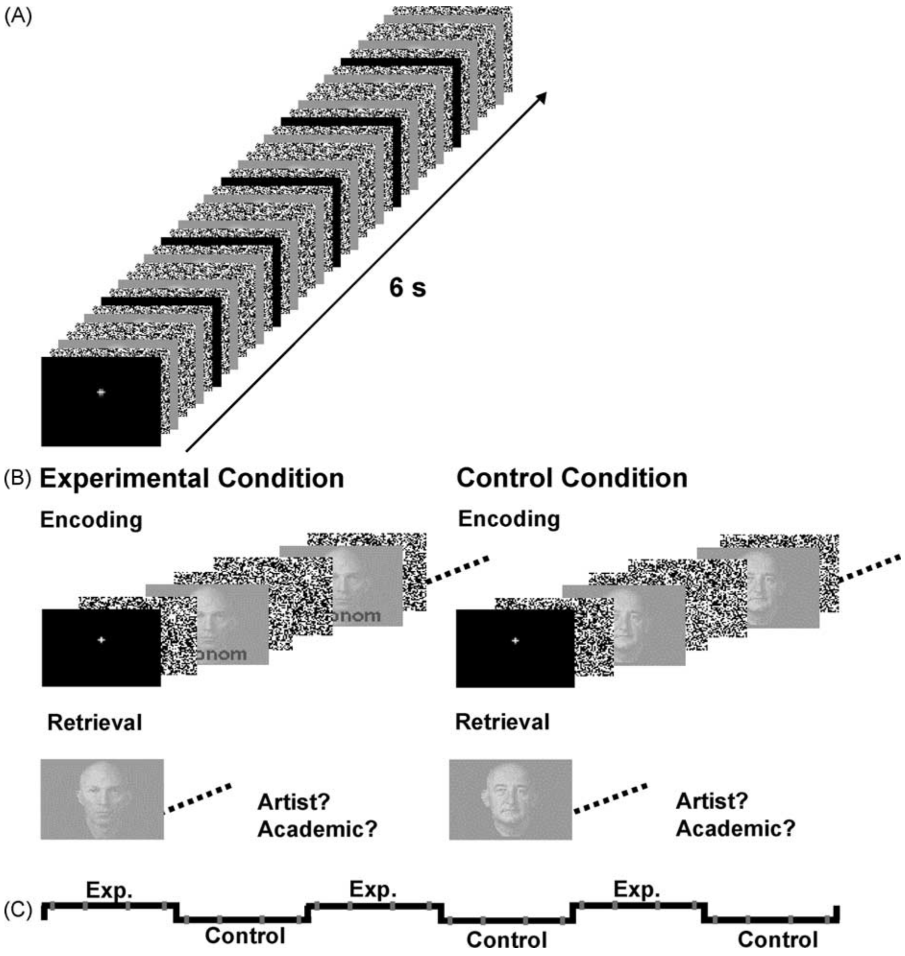

Fig. 1. Experimental design. (A) Presentation of one stimulus. Each stimulus was flashed 12 times for 17 ms flanked by pattern masks which were presented for 183 ms. A fixation cross was interjected six times for 233 ms. (B) There were two fMRI time-series, one for nonconscious encoding and one for nonconscious retrieval, each including an experimental and a control condition. Following the nonconscious encoding scan, the previously masked faces were presented again without masks. The instruction was to guess the professional category of each face. Faces are reproduced from the book "*Heads*" [41] by permission of A. Kayser. (C) Trials were blocked in both fMRI time-series. Four stimuli were presented in each of the three blocks per condition.

3.3.2. Retrieval

Three minutes following nonconscious encoding, a nonconscious reactivation of the memory traces for faces (both conditions) and face-associated occupational information (experimental condition) was induced. The previously masked faces from the experimental and the control condition were presented again, each only once for 5 s, all without words and without masks (Fig. 1B). In the experimental condition, the faces acted as cues to elicit the reactivation of previously formed face–profession associations. The task in both conditions was to guess the professional category of each individual—academic or artist—and to press one of two keys accordingly. The required translation from the profession (e.g. pianist) to the professional category (artist) was intended to reactivate established semantic rather than visual or phonological face–word associations in the experimental condition. Both accuracy and reaction time data were collected for later analysis, in particular to determine whether reaction times differ between correct and false answers in the experimental condition.

3.4. fMRI procedure

All images were acquired on a GE 1.5 T Signa MR scanner. Anatomical data were acquired in a 3D spoiled-gradient echo sequence with a matrix of 256×256 and a voxel size of $0.94\,\text{mm} \times 0.94\,\text{mm} \times 1.5\,\text{mm}$ ($\text{TR} = 40\,\text{ms}$, $\text{TE} = 8\,\text{ms}$, $\text{FA} = 40^\circ$, $\text{FOV} = 24 \times 24\,\text{cm}$, $\text{NEX} = 1$). Functional T2*-weighted images with a matrix size of 128×128 (voxel size $1.72\,\text{mm} \times 1.72\,\text{mm} \times 4\,\text{mm}$) were obtained with a whole-brain BOLD sensitive 2D-gradient echoplanar single shot pulse sequence (EPI) using an axial slice orientation (TR 4 s, flip angle 50°, TE 50 ms, 30 slices of 3 mm with 1 mm spacing).

fMRI data were collected in two time-series, one for encoding and one for retrieval, separated by 3 min. Trials were blocked with four trials per epoch (Fig. 1C). There were three epochs for the experimental condition and three epochs for the control condition in each time-series. An epoch lasted 24 s in the encoding scan and 20 s in the retrieval scan. The conditions alternated according to A-B-A-B-A-B for one half and B-A-B-A-B-A for the other half of the participants. The computer driven stimulation was back-projected with an LCD-projector onto a screen that subjects viewed through a mirror attached to the head coil. Following the fMRI experiment, participants' perceptual impressions were questioned and recorded by use of a structured interview. Finally, participants were fully debriefed.

3.5. *Analysis of imaging data*

3.5.1. *Data postprocessing*

Volumes were realigned to the first volume [24] (SPM99; see http://www.fil.ion.ucl.ac.uk/spm). A mean image was spatially normalized into stereotaxic space (standard EPI template SPM99) [25]. Data were then smoothed with an 8 mm (FWHM) isotropic Gaussian kernel.

3.5.2. *Group analysis*

Data analysis was calculated voxel by voxel modeling the conditions as stimulus functions—box car function convolved with a hemodynamic response function—applying the general linear model (SPM99; fixed effects model). The resulting within-subject effects of each subject were then further analyzed in a second level analysis (SPM99; random effects analysis) to obtain between-subjects effects. The second level analysis accounts for the variance of responses from subject to subject. It was also performed voxel by voxel and consisted of a one-sample *t*-test upon the computed contrast files of each single subject. The height threshold for this group analysis was set at $P = 0.005$ (uncorrected) with five voxels extent threshold. The locations of the resulting brain activations were a priori predicted on grounds of two earlier experiments with similar designs [35,36].

3.5.3. *Brain–behavior correlation*

The individual within-subject effects on which the group analysis was based (see Section 3.5.2) were used for correlations with the behavioral data acquired during the retrieval scan to examine whether MTL and other areas would change their activation level linearly with the behavioral measure. These correlations were computed for those comparisons which yielded significant activation changes in the MTL in the group contrasts. The behavioral measure used for correlation was each participant's mean reaction time difference between correct and false answers during the experimental condition of the retrieval scan. The correlations were computed using SPM99; the applied height threshold was $P = 0.005$ uncorrected, and the extent threshold was five voxels.

3.5.4. *Single subject analysis*

Single subject analyses were performed on the realigned and smoothed but not spatially normalized data from the retrieval scan for the precise anatomical localization of activation increases within the MTL during the experimental versus the control condition. Our functional data allowed for this analysis because it was collected nearly distortion-free. To this aim, individual contrasts were computed with SPM as described in Section 3.5.2 and coregistered with the individual 3D anatomical scans by use of the Pmod software (http://www.pmod.com) [53]. The height threshold for this intraindividual analysis of the MTL was set at $P = 0.05$ (uncorrected) with one voxel extent threshold. The locations of activations within the MTL were determined by two raters (K.H. and C.M.) who were relying on the descriptions of anatomical landmarks and subdivisions of the MTL by Insausti et al. [38] and Duvernoy [18].

4. Results

4.1. *Behavioral results*

4.1.1. *Retrieval performance*

The percentage of correctly guessed professional categories in the experimental condition ($M = 52.97\%$, S.D. $= 14.73\%$) did not differ from the percentage achieved in the control condition ($M = 55.36\%$, S.D. $= 9.27\%$; $t(13) = -0.5$, $P = 0.63$, two-tailed) where no occupational information was given during nonconscious encoding. Also, the reaction times (RT) in the experimental condition did not significantly differ from the reaction times in the control condition of the retrieval scan ($M_{\text{exp}} = 2246$ ms, S.D.$_{\text{exp}} = 510$ ms; $M_{\text{control}} = 2182$ ms, S.D.$_{\text{control}} = 470$ ms; $t(13) = 1.02$, $P = 0.34$, two-tailed).

However, within the experimental condition, RT were significantly longer for false than correct selections of professional categories ($M_{\text{correct}} = 2184$ ms, S.D.$_{\text{correct}} = 519$ ms; $M_{\text{false}} = 2321$ ms, S.D.$_{\text{false}} = 488$ ms; $t(13) = 2.24$, $P = 0.04$, two-tailed; Fig. 2A). Importantly, RT for correct and false selections did not differ in the control condition ($M_{\text{correct}} = 2202$ ms, S.D.$_{\text{correct}} = 486$ ms; $M_{\text{false}} = 2166$ ms, S.D.$_{\text{false}} = 517$ ms; $t(13) = -0.42$, $P = 0.68$, two-tailed). Interestingly, we found a similar RT difference in another group of eight subjects who consciously encoded and retrieved the same number of face–word combinations (Fig. 2B; $M_{\text{correct}} = 2436$ ms, S.D.$_{\text{correct}} = 81$ ms; $M_{\text{false}} = 3052$ ms, S.D.$_{\text{false}} = 225$ ms; $t(6) = 2.68$, $P = 0.04$, two-tailed).

4.1.2. *Subjective perception*

Following the fMRI experiment, participants underwent a structured interview and a step-by-step debriefing. All participants reported having perceived only the fixation cross and the moving black-and-white grains of the masks. When participants were informed about briefly flashed face–word stimuli and their appearance and location on the screen, one participant mentioned to have briefly seen an 'alien', yet at a different screen location than the locations where our stimuli appeared. Three participants claimed to have perceived moving shapes other than faces or words which were formed by the changing arrangements of the black-and-white dots of the masks. Thus, four participants mentioned observations

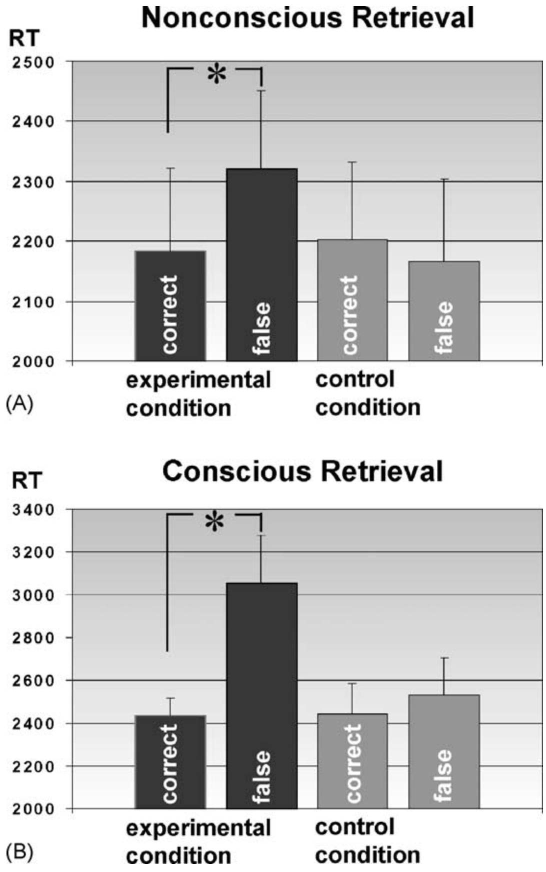

Fig. 2. Reaction times during retrieval. Displayed are group means and standard error of means. (A) Reaction times in the experimental but not the control condition were significantly longer when participants selected false than correct professional categories for the presented faces. (B) The same pattern of reaction times emerged in eight further subjects who consciously encoded and retrieved the face–word pairs (experimental conditions) or the faces (control conditions). Asterisks indicate a significant difference between RT for correct and false answers at $P < 0.05$, two-tailed.

which were elicited by certain arrangements of the rapidly changing configurations of black-and-white grains contained in the masks. None had perceived aspects of the actual face and word stimuli. Therefore, we concluded that stimuli had been presented below the subjective awareness threshold [7].

4.2. Imaging results

4.2.1. Nonconscious encoding

The group comparison between the experimental (face–word pairs) and the control (faces alone) condition of the nonconscious encoding scan isolates activity which underlies nonconscious word analyses and associating words with faces. This comparison revealed activations in a network of structures which have been identified in neuroimaging studies of reading. An activation focus was located in the same area of the left fusiform gyrus that has been identified as the 'visual word form area' [10] (their location −42, −57, −6; our location −44, −60, −20) (Table 1). Further activation foci were located in the left lingual gyrus and the left cuneus. The angular gyrus was activated in the right instead of the expected left hemisphere. The same was true for activations in the inferior frontal gyrus, Brodmann area (BA) 44/45, and the middle (BA 21) and superior (BA 22) temporal gyri of the right rather than the left hemisphere (Table 1). Additional right hemisphere activations were found in the middle frontal gyrus (BA 8, 9), the left superior parietal lobule (BA 7), the right inferior parietal lobule (BA 40), and bilateral precentral gyrus and central sulcus. Finally, we located activation foci in the anterior and posterior cingulate gyrus.

The most significant difference was, however, revealed by reversing the contrast, i.e. comparing the control (faces alone) versus the experimental condition (face–word pairs). The most significant activation change was located in the right hippocampal formation and adjacent perirhinal cortex ($T = 5.8$; Table 1, Fig. 3A). Two further voxel clusters were located in the left hippocampal formation. A large activation spread from the right cerebellum into the right lingual gyrus (BA 37). The posterior part of the left middle temporal gyrus (BA 37) and the left temporal insula also exhibited activation changes. Further activation changes were present in the right posterior lingual gyrus (BA 17 and 18).

4.2.2. Nonconscious retrieval

The group comparison between the experimental and the control condition of the nonconscious retrieval scan isolates activity which solely underlies the process of nonconsciously searching for and retrieving face–profession associations. If no associations had been formed, this comparison should not yield significant results.

This comparison revealed many activation foci in a wide network of bilateral temporo-frontal and some posterior structures (Table 2). The strongest activation was located in a large area enclosing the left superior temporal gyrus and the adjacent supramarginal gyrus. Further left temporal foci were located in the temporal pole and the posterior part of the middle temporal gyrus. The right temporal lobe contained four activation peaks. One activation comprised the anterior hippocampal formation and the adjacent perirhinal cortex ($T = 4.12$; Fig. 3B). A second perirhinal focus was located 1 cm posterior to this first one ($T = 3.52$; Fig. 3B). A third and fourth right temporal focus were found in the middle and superior temporal gyri.

Within the frontal lobes there was a very large band of strong activation extending from BA 11 of the right orbital gyrus to BA 10 of the right superior frontal gyrus and stretching medially to the anterior cingulate gyrus (BA 24). Three further right frontal activation sites were located in BA 9. Homotopic areas in BA 9–11 of the left frontal lobe were coactivated. A large activation spread from the left BA 9 into BA 8. There was further left frontal activation in the inferior frontal gyrus, Broca's area, BA 44/45, and in the middle/superior frontal gyrus, BA 6.

In the posterior part of the brain, a strong activation included the left middle occipital gyrus (BA 17, 18, 37). A

Table 1
Encoding contrasts: maxima of regions

Region of activation	L/R	Brodmann area	Coordinates for maxima voxel			Number of voxels	*T*
			X	*Y*	*Z*		
Experimental–control							
Posterior cingulate	R	23	6	−28	40	42	5.45
Anterior cingulate	R	24	12	38	16	21	4.74
Anterior cingulate	L	24	−14	40	16	7	4.05
Precentral g	R	4	38	−16	40	6	4.28
Pre-/postcentral g	R	4/3	42	−22	60	47	3.85
Pre-/postcentral g	R	4/3	48	−22	28	21	5.39
Precentral g	L	4	−24	−32	56	28	4.21
Precentral g	L	4	−32	−6	60	10	3.65
Superior parietal l	L	7	−28	−56	56	21	4.51
Superior parietal l	L	7	−26	−64	48	9	4.01
Inferior parietal l	R	40	46	−26	36	21	3.79
Angular g	R	39	50	−72	20	8	3.85
Fusiform g	L	37	−44	−60	−20	7	3.59
Lingual g	L	18	−12	−86	−12	12	4.03
Cuneus	L	18	−6	−82	28	29	4.07
Inferior frontal g	R	44/45	50	18	12	36	4.16
Middle frontal g	R	8	36	24	44	25	4.74
Middle frontal g	R	9	36	48	32	25	4.54
Middle temporal g	R	21	52	−14	−24	12	4.11
Middle temporal g	R	21	64	−38	−16	14	3.63
Superior temporal g	R	22	62	−32	8	10	3.66
Control–experimental							
Hipp/perirhinal	R		36	−16	−20	25	5.8
Cerebellum/lingual g	R	37	10	−46	−24	68	5.44
Temporal insula	L		−34	−8	8	8	4.54
Lingual g	R	17/18	16	−68	−8	34	4.26
Hipp	L		−16	−30	−8	7	4.2
Hipp	L		−34	−26	−12	7	3.93
Middle temporal g	L	37	−54	−58	−4	8	3.62

$P = 0.005$ uncorrected, five voxels extent threshold. L, left; R, right; l, lobule; g, gyrus; hipp, hippocampal formation.

second activation focus comprised the right retrosplenial cortex of BA 29. A third focus covered part of the right angular gyrus. Parietal areas 7 were bilaterally activated. We also located significant activation in the right putamen.

The reversed contrast (control versus experimental condition) yielded only one area of significant activation change located in the left cerebellum.

4.2.3. *Nonconscious retrieval: single subject analysis*

The precise anatomical loci of MTL activations resulting from the comparison between the experimental and the control condition of the retrieval scan were determined in each of the 14 participants. Eleven of the 14 participants exhibited significant MTL activations (Fig. 4, Table 3). Eight participants activated the hippocampus (CA regions, dentate gyrus), four the subicular structures (parasubiculum, presubiculum, subiculum), seven the entorhinal cortex, eight the perirhinal cortex, and seven the parahippocampal cortex [18,38]. Half of these activation spots were located in the left MTL.

4.2.4. *Correlation fMRI–behavior*

For the two comparisons which yielded significant activation changes within the MTL in the group statistics, we correlated each participant's individual fMRI contrast with his mean RT difference between correct and false answers during the retrieval scan to examine the relation between fMRI signal changes and the behavioral measure of retrieval. The two contrasts of interest are: (1) the control versus the experimental condition of the encoding scan and (2) the experimental versus the control condition of the retrieval scan.

(1) *Encoding*: The same right perirhinal area which exhibited a significant activation change in the group contrast (control versus experimental condition) at coordinate position 36, −16, −20, and 36, −8, −24 (subcluster) linearly changed its activity with participants' RT differences (peak at 30, −4, −24; $r = 0.8$) (Fig. 3C). The same was true for a region in BA 17 in the right lingual gyrus ($r = 0.78$) and BA 37 in the right posterior inferior temporal lobe ($r = 0.84$). Significant correlations

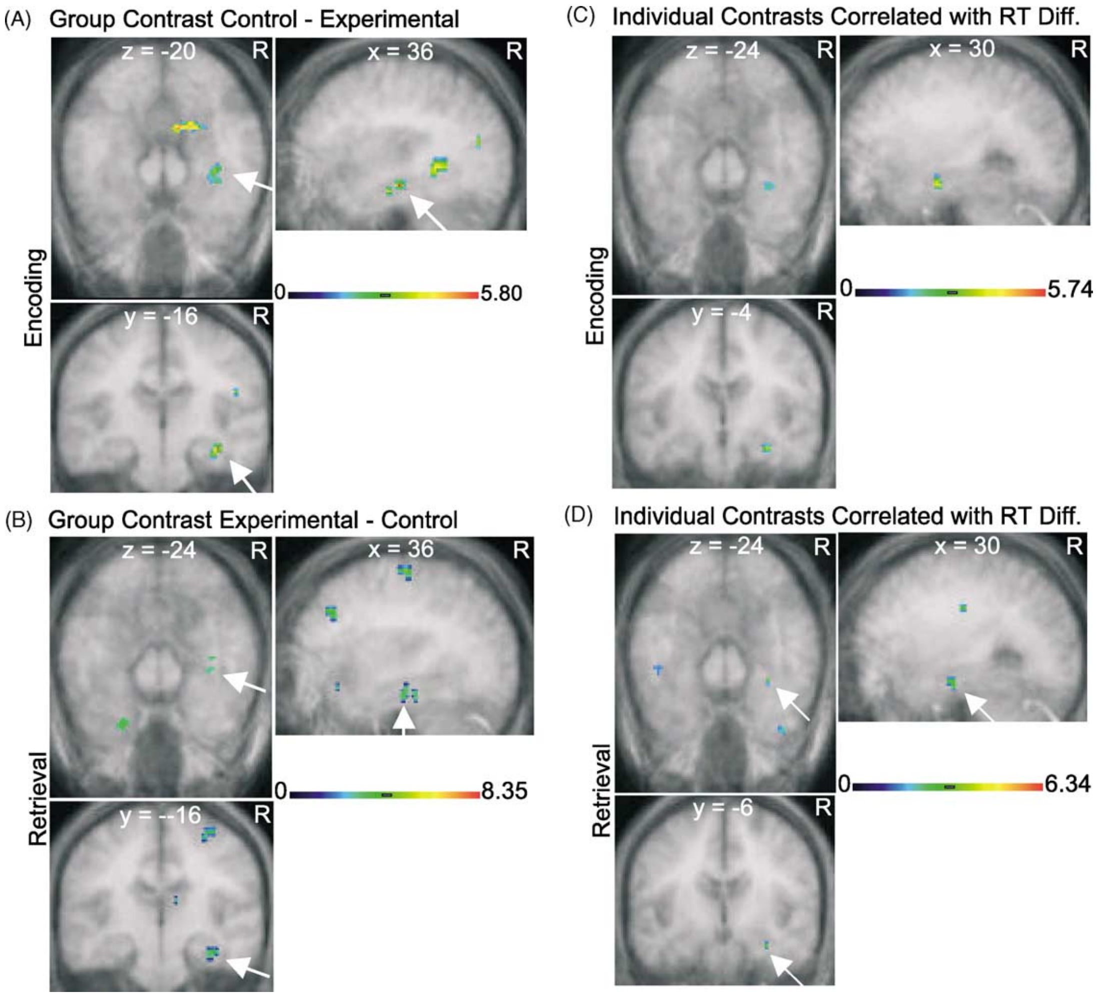

Fig. 3. Results in the right perirhinal cortex from the group contrasts (A and B) and from the correlations of the individual contrasts with mean RT differences between correct and false answers (C and D). (A) fMRI results from the group comparison between the control and the experimental condition of the encoding scan. (B) fMRI results from the group comparison between the experimental and the control condition of the retrieval scan. (C) Correlation between the 14 participants' encoding contrasts (control–experimental condition) and their mean RT differences between correct and false answers during retrieval. (D) Correlation between the 14 participants' retrieval contrasts (experimental–control condition) and their mean RT differences between correct and false answers during retrieval. FMRI data are coregistered with the 14 participants' spatially normalized (SPM99) mean brain. Activation differences and correlation strengths are expressed in color-coded T values; the values to the right of the color bars represent the most significant results of these whole-brain analyses. The height threshold for the group contrasts in (A and B) is $T = 3.01$ ($P = 0.005$) and for the correlations in (C and D) $T = 3.05$ ($P = 0.005$). Extent thresholds are five voxels in (A–D). The locations of significant results are displayed in the three dimensions, arrows point to the voxel clusters in the right perirhinal region (reference points for sections). Slice positions (x, y, z) are indicated by SPM coordinates for the standard brain from the Montreal Neurological Institute (MNI). R, right side of the brain; Diff., difference.

with behavior were also found for bilateral areas in the superior temporal gyrus (BA 42; $r_{\text{left}} = 0.76$; $r_{\text{right}} = 0.76$) and for an area in the right anterior middle temporal gyrus (BA 21; $r = 0.76$). The most significant ($r = 0.86$) linear activation change was located in the right inferior frontal gyrus (BA 44)—an area that did not exhibit significant activation change in the group contrast.

(2) *Retrieval*: As observed for encoding, the area in the right perirhinal cortex which exhibited a significant activation change in the group contrast (experimental versus control condition; peak at 36, −16, −24) also displayed a linear activity increase associated with participants' RT differences (peak at 30, −6, −24; $r = 0.70$; Fig. 3D). Remarkably, activity in the head of the left hippocampal formation was also correlated with behavior (peak at −16, −10, −20; $r = 0.71$) although activation changes in this region did not reach significance in the group contrast. There were several additional areas which significantly changed their activities both in the group contrast and in relation to behavior: visual areas in the left middle (BA 18; $r = 0.88$) and bilateral superior occipital gyri (BA 19; $r_{\text{left}} = 0.81$; $r_{\text{right}} = 0.79$), areas in the left (BA 39; $r = 0.74$) and right (BA 22: $r = 0.72$; BA 39: $r = 0.70$) superior temporal gyri, the

Table 2
Retrieval contrasts: maxima of regions

Region of activation	L/R	Brodmann area	Coordinates for maxima voxel			Number of voxels	*T*
			X	*Y*	*Z*		
Experimental–control							
Hipp/perirhinal	R		36	−16	−24	16	4.12
Perirhinal	R		34	−26	−24	5	3.52
Middle temporal g	R	21	50	−10	−24	6	3.57
Superior temporal g	R	22	66	−26	0	6	3.49
Middle temporal g	L	37	−36	−62	4	18	4.67
Temporal pole	L	38	−24	22	−28	12	3.71
Superior temporal g/supramarginal g	L	22/39/40	−60	−56	20	70	8.35
Inferior frontal g	L	44/45	−52	16	8	5	3.25
Middle/superior frontal g	L	8/9	−34	32	36	118	5.58
Superior frontal g	L	10	−18	44	8	33	5.25
Superior frontal g	L	9	−18	60	28	13	4.26
Middle/superior frontal g	L	6	−26	6	40	54	5.09
Orbital g	L	11	−18	44	−16	89	5.00
Orbital g/superior frontal g/medial frontal g/anterior cingulate g	R	11/10/24	24	46	−8	270	7.02
Middle frontal g	R	9	34	36	32	27	4.29
Superior frontal g	R	9	26	48	32	18	3.63
Superior frontal g	R	9	22	42	40	14	4.1
Middle occipital g	L	18/37/17	−30	−76	16	57	6.26
Retrosplenial cortex	R	29	14	−44	0	52	4.82
Precuneus	R	7	16	−60	36	8	4.5
Putamen	R		28	0	−4	13	4.45
Angular g	R	39	48	−72	32	32	4.25
Superior parietal l	R	7	18	−48	72	28	4.06
Precentral g	R	4	34	−20	60	29	4.83
Control–experimental							
Cerebellum	L		−16	−78	−24	24	4.27

$P = 0.005$ uncorrected, five voxels extent threshold. L, left; R, right; l, lobule; g, gyrus; hipp, hippocampal formation.

Table 3
Retrieval contrast: activated MTL regions

	Participants															
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	*T*1	*T*2
MTL regions																
L hipp				×					×	×	×				4	**8**
R hipp	×		×			×						×			4	
L subiculum										×					1	**4**
R subiculum	×					×						×			3	
L entorhinal				×		×					×				3	**7**
R entorhinal	×	×			×	×							×		5	
L perirhinal			×	×		×			×	×	×	×			7	**8**
R perirhinal					×	×				×		×			4	
L parahipp	×		×			×				×	×				5	**7**
R parahipp	×		×			×						×	×		5	

L, left; R, right; *T*1, total of participants who activated the region in the left or right hemisphere; *T*2, total of subjects who activated the region in either hemisphere.

left middle temporal gyrus (BA 21; $r = 0.74$) and right temporal pole (BA 38; $r = 0.79$), the left inferior frontal gyrus (BA 47; $r = 0.71$), the left anterior cingulate gyrus (BA 24; $r = 0.79$), the left orbital gyrus (BA 11; $r = 0.70$), and the right middle frontal gyrus (BA 10; $r = 0.77$).

5. Discussion

In the present fMRI experiment, we studied the processing of masked face–profession pairs and the subsequent nonconscious reactivation of face-associated occupational information.

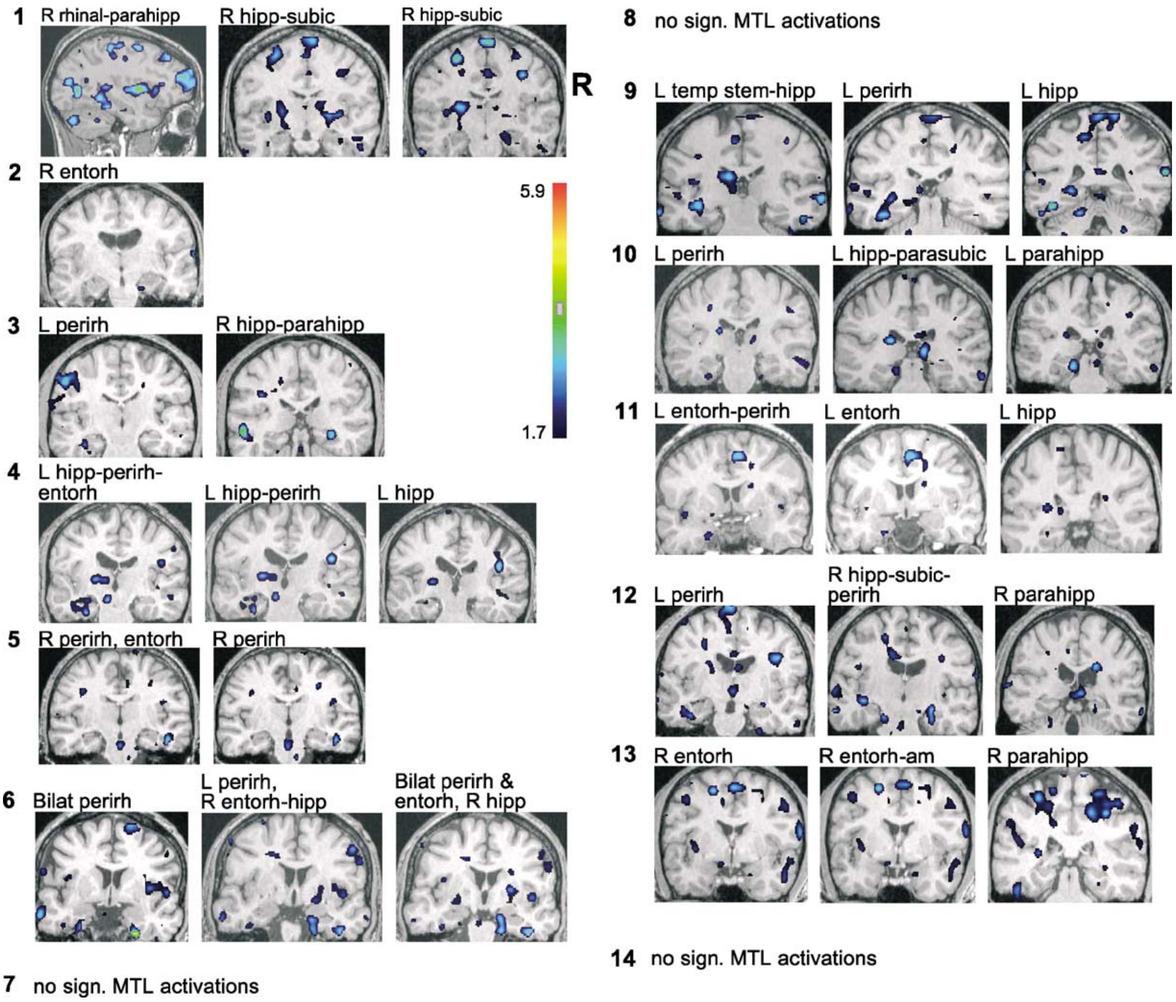

Fig. 4. Single-subject analysis of MTL activations during retrieval. Non-normalized functional and anatomical data are presented for each participant (#1–14) who exhibited activation differences within the MTL as a result of the retrieval contrast. Activation differences are illustrated with a common color code for T values between 1.7 (height threshold, $P = 0.05$) and 5.9 (largest difference reached). The location of the displayed MTL activations is indicated above each image. R, right hemisphere; L, left hemisphere; Bilat, bilateral; hipp, hippocampus (CA fields and dentate gyrus); parahipp, parahippocampal cortex; subic, subiculum; parasubic, parasubiculum; entorh, entorhinal cortex; perirh, perirhinal cortex; temp, temporal; am, amygdala; sign., significant; MTL, medial temporal lobe.

5.1. *Encoding*

The encoding contrast (masked face–word pairs versus masked faces) revealed multiple activation foci in a network of structures that have been found activated during conscious word reading [2,14–16,22,23,39,65,66,70]. The strength and extent of neural activity in response to the masked words was clearly smaller than that reported for conscious reading, a phenomenon which is known from masking studies [14,31,36,44,68]. Dehaene et al. [14] have reported cerebral activation evoked by masked words in a subset of structures typically activated by conscious reading, namely left extrastriate cortex, a left fusiform area that has been identified as the 'visual word form area' [10], and left precentral sulcus. These brain areas were also activated by the masked words in the present study. We found additional activation foci within structures implicated in the reading process, such as the left lingual gyrus [2,70], the left cuneus [65,66] and the right instead of the expected left angular gyrus known to mediate written word processing [16,39,66]. An unexpected right lateralization was also found for activations in the inferior frontal gyrus and in the middle and superior temporal gyri—areas with a putative role in semantic word analyses [15,22,23,39,65,67]. These activations hint at a nonconscious word analysis up to the semantic level, adding evidence that meaning can be nonconsciously extracted from masked words [7,13,14,30,43,60].

The right hemisphere instead of left hemisphere dominant activations may correspond to the known right hemisphere preference for face processing weighting the right hemisphere processing system during the formation of face–word associations [42,48,74] or they may be due to the nonconscious nature of stimulus processing. The latter interpretation receives support by a study [57] in which a significant neural response was elicited in the right, but not left, amygdala to masked presentations of a conditioned angry face. Unmasked presentations of the same angry face produced enhanced neural activity in the left, but not right, amygdala. These results indicate that this neural response is lateralized according to the subjects' level of awareness of the stimuli.

Interestingly, the reversed contrast (masked faces versus masked face–word pairs) yielded significant activation changes in the right hippocampal–perirhinal area and the left hippocampal formation among others. The individual right perirhinal activation changes correlated with the participants' behavioral measure of the later retrieval. It is noteworthy that exactly the same perirhinal voxel cluster, which exhibited this signal reduction in the experimental compared to the control condition of encoding, was later exhibiting a signal enhancement during the nonconscious retrieval of face–profession associations compared to the control condition. Because conscious encoding of associations has typically been found to produce more medial temporal activation than conscious non-associative encoding, the observed signal reduction during the experimental compared to the control condition of encoding seems paradoxical. In the following, we offer a possible explanation for this apparent discrepancy.

During masking, participants were processing information at two levels, the conscious and the nonconscious level. At the conscious level, they concentrated on the fixation crosses and observed the changing configurations of black-and-white grains contained in the masks. We found that this task alone, with no stimuli flashed between masks, enhanced the activity in the hippocampal area and in the neocortex when contrasted with a simple perceptual task (see also [50]), either because of the automatic encoding of the configurations of the black-and-white grains or because of the encoding of concurrent spontaneous thoughts or day dreams [78]. At the nonconscious level, participants encoded the briefly presented stimuli. Consequently, the hippocampal neurons engaged in the continuous conscious encoding of configurations and thoughts or in the discontinuous processing of the masked items. We assume that a larger number of hippocampal neurons turned from conscious to nonconscious encoding if a face plus a word was flashed than if only a face alone was flashed. The BOLD signal in the hippocampal area was less enhanced in response to masked face–word pairs compared to masked faces because the firing of the hippocampal neurons to masked stimuli was presumably interrupted by the masks [44,68]. This interruption may have decreased the local blood-oxygen level [1] compared to the uninterrupted firing in response to the conscious encoding of configurations and thoughts. Thus, the larger the number of neurons which turned from the non-interrupted conscious to the interrupted nonconscious processing, the smaller the corresponding BOLD effect. We have observed this sign reversal in a further fMRI study [12] and in a positron emission tomography (PET) study [35] but not in our first fMRI study [36] on the encoding of masked stimuli.

5.2. Retrieval

Selection accuracies in the forced-choice task between the two professional categories were not different from chance in both the experimental and the control condition confirming that the masked presentations were below the awareness threshold. Yet, the reaction latencies for the selections of professional categories indicated that semantic face–profession associations had been formed during encoding. Reaction latencies were significantly longer for false than correct choices in the experimental (professions had been presented between masks) but not the control condition (no professions had been presented). This effect was also apparent in subjects who consciously encoded and retrieved face–profession associations and, more generally, is an ubiquitous phenomenon in recall and two-alternative forced-choice tests [17,59,61,62], and has also been observed with indirect measures of memory [71]. In stem completion priming for example [26,73], the correct completion of stems of studied words is faster than the incorrect completion of stems of studied words. Our difference in reaction latencies between correct and false trials, by analogy with stem completion priming, could be regarded as a measure of implicit memory. This distinction between correct and false trials may reflect a successful retrieval of face-associated occupational information in correct trials, search processes in false trials, or an interference between a first conscious guess and conflicting nonconscious information in false trials. In any case, reaction latencies in correct differed from reaction latencies in false answers with reference to the professional category of the occupations that had been presented with the faces between masks. Therefore, some occupational information must have been acquired with the faces during the encoding scan. This face-associated occupational information appears to have been reactivated during the retrieval scan—yet, without influencing the conscious selections (i.e. selection accuracies). If this were a standard priming experiment, then reaction times for the whole set of studied faces from the experimental and the control condition would have been compared, and evidence of priming claimed if the experimental faces produced faster reaction times. Our subjects' overall reaction time differences between the associative condition and the face only condition did not yield significance. It should be considered that face priming was present in both the experimental and the control condition and that neither the profession labels presented for encoding nor the corresponding professional categories were presented during the retrieval task. Therefore, no simple reprocessing of the verbal occupational information was possible. Instead, the faces were presented alone as cues to elicit, together with the instruction, a cued nonconscious retrieval of the previously formed face–profession associations. Because this is a new task it is unknown whether the cued nonconscious retrieval increases or decreases reaction times compared to face priming alone. A pilot study (unpublished) and the current data showed that the reaction times for incorrect guesses are longer than those for correct guesses but this difference was not big enough to increase the overall reaction times significantly in the experimental over the control condition.

The imaging data support our interpretation in terms of a reactivation of face-associated semantic information. The difference between the reaction times to correct and false answers in the experimental condition of the retrieval scan correlated with neural activity in brain structures related to successful memory retrieval. We found significant correlations between reaction time differences and activity in the right perirhinal cortex and the left hippocampal formation. The degree of activity in these regions has previously been related to successful retrieval from episodic memory [8,29,32,63,80]. We also found an association in bilateral superior temporal areas, in the left middle temporal gyrus and the left inferior prefrontal cortex—structures known to mediate the retrieval of semantics [11,27,37,40,81,85,86] and structures which had been activated during the conscious retrieval of face–profession combinations [36]. Moreover, activity in the right middle frontal gyrus (BA 10) increased with RT difference—an area whose activity has been found to correlate with the maintenance of an ‘episodic memory retrieval mode’ defined as a necessary condition for remembering past experiences [47]. We recognize that this correlation is difficult to interpret because about half of the responses contributing to each participant’s BOLD response were the slower incorrect guesses. Therefore and to be comparable with typical priming studies, we also correlated fMRI signal changes with each participant’s overall reaction time differences between the experimental and the control condition of the retrieval scan. This correlation also yielded significant results in the right rhinal cortex (16, −4, −28), bilateral anterior superior temporal gyri and the fronto-polar cortex (BA 10).

Several areas where the correlations with reaction time differences failed to reach significance were activated in the experimental compared to the control condition, namely the left frontal BA 6, bilateral BA 9 in the superior frontal gyri, the right parietal BA 7, BA 40 in the left supramarginal gyrus and BA 29 in the retrosplenial cortex. The retrospenial cortex is crucial for episodic memory [28,49,52,75] and, in the monkey brain, is heavily interconnected with the mid-dorsolateral part of the prefrontal cortex and with the MTL [58]. Interestingly, these additional activation sites in areas 6, 7, 9, and 40, as well as several of the sites with RT-correlated activity, were also obtained in two studies that tested for the conscious retrieval of face-associated verbal information [9,64].

We conclude that occupational information associated with the faces was nonconsciously reactivated. Remarkably, the reactivation of nonconscious face-associated information induced activity increases in a network which has been found to mediate the retrieval from episodic memory. Contrary to what could be expected from the ‘repetition suppression’ seen in priming following conscious or nonconscious study [14], we found neither neocortical nor medial temporal activity decreases during the experimental versus the control condition of retrieval. The absence of ‘repetition suppression’ and the presence of activity increases in a network known to mediate episodic memory both suggest that this form of implicit memory is different from priming.

Our results correspond to those of Elliott and Dolan [20] who found activations in brain structures otherwise activated during episodic memory, in a context in which there was no subjective recognition of stimuli. Processing objectively novel compared to familiar (because of previous masked presentation) Japanese ideograms enhanced activity within the right parahippocampal gyrus, left mediodorsal thalamus, left fusiform gyrus (BA 19), left superior temporal gyrus (BA 38), and right cuneus (BA 19). This effect was task-independent, i.e. it occurred both during forced choice judgments on the basis of preference (which of two stimuli is more pleasant to look at?) and explicit memory (which of two stimuli had been seen between masks?). One interpretation is that activity decreased with familiar versus novel ideograms because of ‘repetition suppression’. Alternatively, activation in these regions reflected a response to stimulus novelty implying that the processing of stimulus novelty is independent of subjective awareness. Beauregard et al. [3] found a significant increase rather than decrease [14,20] of blood flow in the right hippocampal formation during the reprocessing of single words that had been presented between masks compared to words that had not been presented. Their task induces priming effects which are primarily perceptual and not conceptual. Contrary to the found preservation of perceptual single word priming in many patients with medial temporal damage and amnesia, Beauregard et al. [3] suggest that the right anterior hippocampal formation is involved in perceptual word priming. The direction and the locus of the hippocampal activity changes were strikingly similar in their and the present study although the nonconscious retrieval operations were clearly different between the two studies.

5.3. Medial temporal activations

The components of the MTL—hippocampus, perirhinal, entorhinal, and parahippocampal cortex [5,19,54,55]—and even the subcomponents of the hippocampus (CA1, CA3) [45,69] appear to segregate with respect to their contributions to memory. A precise anatomical localization of MTL activations may further our understanding of the functional organization of MTL structures. Towards this end, we localized MTL activations resulting from the individual retrieval contrasts on the basis of the realigned and smoothed individual anatomical brain scans. Some caution is warranted with the localization of the activation peaks because the data were smoothed with an 8 mm isotropic Gaussian kernel. Eleven of the 14 participants exhibited significant MTL activations with an equal distribution across the MTL: 8 participants activated the hippocampus (CA regions, dentate gyrus), 7 the entorhinal, 8 the perirhinal, and 7 the parahippocampal cortex. Given that the primate hippocampus is linked to association cortices by way of the perirhinal and parahippocampal cortices and through the entorhinal cortex [79,82–84] and considering that these related MTL structures must work in concert for learning to be effective [21], our finding of an equal distribution of activations in the MTL is less surprising. This does not imply that the hippocampus and its neighboring structures mediate the same form of memory but may simply indicate that the information flow between MTL areas is important for hippocampus-dependent memory processes.

These findings confirm and extend our previous result of bilateral hippocampal and right perirhinal activations during nonconscious retrieval processes [36]. The design of this first fMRI study [36], however, did not allow us to distinguish between the contribution from nonconscious face retrieval and from nonconscious face–profession retrieval to brain activation—particularly MTL activation. The present study clarifies that the reactivation of semantic associations alone is sufficient to increase MTL activity. This is in line with evidence from patients with severe hippocampal damage who exhibited impaired nonconscious semantic associative learning [26,71,72,73]. These lesion data and our fMRI findings suggest a role of the MTL in both conscious and nonconscious semantic associative learning/retrieval. These findings have theoretical implications because they suggest the existence of an additional class of nondeclarative memory—a class that is dependent on the hippocampal formation and rhinal cortex. It remains to be shown in how far this class of nonconscious memories shares characteristics with episodic memory.

Acknowledgements

We thank Dominique J.-F. de Quervain, Adrian Schwaninger, Barbara Küpfer, Nadia Degonda, Guillén Fernández, Bernd Krause, Alex Gamma, Max Dürsteler, Kirsten I. Taylor and the anonymous reviewers for their help and comments, and Alex Kayser for granting us the permission to use and reproduce his “*Heads*”. V.T. was supported by Swiss National Science Foundation Grant 32862769.00.

References

[1] Iadecola C. The neural basis of functional brain imaging signals. Trends in Neurosciences 2002;25:621–5.

[2] Beauregard M, Chertkow H, Bub D, Murtha S, Dixon R, Evans A. The neural substrate for concrete, abstract, and emotional word lexica: a positron emission tomography study. Journal of Cognitive Neuroscience 1997;9:441–61.

[3] Beauregard M, Gold D, Evans AC, Chertkow H. A role for the hippocampal formation in implicit memory: a 3D PET study. NeuroReport 1998;9:1867–73.

[4] Birkhäuser R. Near-vision test cards. Basel: Birkhäuser Press; 1995.

[5] Brown MW, Aggleton JP. Recognition memory: what are the roles of the perirhinal cortex and hippocampus? Nature Reviews in Neurosciences 2001;2:51–61.

[6] Chapman LJ, Chapman JP. The measurement of handedness. Brain and Cognition 1987;6:175–83.

[7] Cheesman J, Merikle PM. Priming with and without awareness. Perception & Psychophysics 1984;36:387–95.

[8] Cameron KA, Yashar S, Wilson CL, Fried I. Human hippocampal neurons predict how well word pairs will be remembered. Neuron 2001;30:289–98.

[9] Campanella S, Joassin F, Rossion B, De Volder A, Bruyer R, Crommelinck M. Association of the distinct visual representations of faces and names: a PET activation study. NeuroImage 2001;14:873–82.

[10] Cohen L, Dehaene S, Naccache L, Lehéricy S, Dehaene-Lambertz G, Hénaff M-A, et al. The visual word form area. Brain 2000;123:291–307.

[11] Demb JB, Desmond JE, Wagner AD, Vaidya CJ, Glover GH, Gabrieli JDE. Semantic encoding and retrieval in the left inferior prefrontal cortex: a functional MRI study of task difficulty and process specificity. Journal of Neuroscience 1995;15:5870–8.

[12] Degonda NM, Schmidt C, Jaermann T, Boesiger P, Nitsch RM, Hock C, et al. Nonconscious impacts conscious semantic associative encoding by way of the hippocampus. Program no. 620.3 2002 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience; 2002 [Online].

[13] Dehaene S, Naccache L, Le Clerc HG, Koechlin E, Mueller M, Dehaene-Lambertz G, et al. Imaging unconscious semantic priming. Nature 1998;395:597–600.

[14] Dehaene S, Naccache L, Cohen L, Le Bihan D, Mangin J-F, Poline J-B, et al. Cerebral mechanisms of word masking and unconscious repetition priming. Nature Neuroscience 2001;4:752–8.

[15] Démonet J-F, Chollet F, Ramsay S, Cardebat D, Nespoulous J-L, Wise R, et al. The anatomy of phonological and semantic processing in normal subjects. Brain 1992;115:1753–68.

[16] Démonet J-F, Price C, Wise R, Frackowiak RSJ. Differential activation of right and left posterior sylvian regions by semantic and phonological tasks: a positron emission tomography study in normal human subjects. Neuroscience Letters 1994;182:25–8.

[17] Diller DE, Nobel PA, Shiffrin RM. An ARC-REM model for accuracy and response time in recognition and recall. Journal of Experimental Psychology: Learning Memory and Cognition 2001;27:414–35.

[18] Duvernoy HM. The human hippocampus. Berlin: Springer; 1998.

[19] Eldridge LL, Knowlton BJ, Furmanski CS, Bookheimer SY, Engel SA. Remembering episodes: a selective role for the hippocampus during retrieval. Nature Neuroscience 2000;3:1149–52.

[20] Elliott R, Dolan RJ. Neural response during preference and memory judgments for subliminally presented stimuli: a functional neuroimaging study. Journal of Neuroscience 1998;18:4697–704.

[21] Fell J, Klaver P, Lehnertz K, Grunwald T, Schaller C, Elger CE, et al. Human memory formation is accompanied by rhinal–hippocampal coupling and decoupling. Nature Neuroscience 2001;4:1259–64.

[22] Fiez JA, Petersen SE. Neuroimaging studies of word reading. Proceedings of the National Academy of Sciences of the United States of America 1998;95:914–21.

[23] Fiez JA, Balota DA, Raichle ME, Petersen SE. Effects of lexicality, frequency, and spelling-to-sound consistency on the functional anatomy of reading. Neuron 1999;24:205–18.

[24] Friston KJ, Ashburner J, Poline JB, Frith CD, Heather JD, Frackowiak RSJ. Spatial registration and normalisation of images. Human Brain Mapping 1995;2:165–89.

[25] Friston KJ, Holmes AP, Poline JB, Grasby PJ, Williams SCR, Frackowiak RSJ, et al. Analysis of fMRI time-series revisited. NeuroImage 1995;2:45–53.

[26] Gabrieli JDE. Cognitive neuroscience of human memory. Annual Review of Psychology 1998;49:87–115.

[27] Gabrieli JDE, Desmond JE, Demb JB, Wagner AD, Stone MV, Vaidya CJ, et al. Functional magnetic resonance imaging of semantic memory processes in the frontal lobes. Psychological Science 1996;7:278–83.

[28] Gainotti G, Almonti S, Di Betta AM, Silveri MK. Retrograde amnesia in a patient with retrospenial tumour. Neurocase 1998;4:519–26.

[29] Grasby PM, Frith CD, Friston K, Frackowiak RSJ, Dolan RJ. Activation of the human hippocampal formation during auditory–verbal long-term memory function. Neuroscience Letters 1993;163:185–8.

[30] Greenwald AG, Draine SC, Abrams RL. Three cognitive markers of unconscious semantic activation. Science 1996;273:1699–702.

[31] Grill-Spector K, Kushnir T, Hendler T, Malach R. The dynamics of object-selective activation correlate with recognition performance in humans. Nature Neuroscience 2000;3:837–43.

[32] Gur RC, Ragland JD, Mozley LH, Mozley PD, Smith R, Alavi A, et al. Lateralized changes in regional cerebral blood flow during performance of verbal and facial recognition tasks: correlations with performance and effort. Brain and Cognition 1997;33:388–414.

[33] Henke K, Buck A, Weber B, Wieser HG. Human hippocampus establishes associations in memory. Hippocampus 1997;7:249–56.

[34] Henke K, Weber B, Kneifel S, Wieser HG, Buck A. Human hippocampus associates information in memory. Proceedings of the National Academy of Sciences of the United States of America 1999;96:5884–9.

[35] Henke K, Turi Nagy E, Berthold T, Weber B, Buck A. $H_2{}^{15}O$ PET imaging of conscious and unconscious encoding/retrieval of semantic associations. Society for Neuroscience Abstracts 1999;25:647.

[36] Henke K, Treyer V, Turi Nagy E, Kneifel S, Dürsteler M, Nitsch RM, et al. Active hippocampus during nonconscious memories. Consciousness and Cognition, in press.

[37] Hodges JR, Patterson K, Oxbury S, Funnell E. Semantic dementia. Brain 1992;115:1783–806.

[38] Insausti R, Juottonen K, Soininen H, Insausti AM, Partanen K, Vainio P, et al. MR volumetric analysis of the human entorhinal, perirhinal, and temporopolar cortices. American Journal of Neuroradiology 1998;19:659–71.

[39] Kang AM, Constable RT, Gore JC, Avrutin S. An event-related fMRI study of implicit phrase-level syntactic and semantic processing. NeuroImage 1999;10:555–61.

[40] Kapur S, Rose R, Liddle PF, Zipursky RB, Brown GM, Stuss D, et al. The role of the left prefrontal cortex in verbal processing: semantic processing or willed action? NeuroReport 1994;5:2193–6.

[41] Kayser A. Heads. New York: Abbeville Press; 1984.

[42] Kelley WM, Miezin FM, McDermott KB, Buckner RL, Raichle ME, Cohen NJ, et al. Hemispheric specialization in human dorsal frontal cortex and medial temporal lobe for verbal and nonverbal memory encoding. Neuron 1998;20:927–36.

[43] Kiefer M, Spitzer M. Time course of conscious and unconscious semantic brain activation. NeuroReport 2000;11:2401–7.

[44] Kovács G, Vogels R, Orban GA. Cortical correlate of pattern backward masking. Proceedings of the National Academy of Sciences of the United States of America 1995;92:5587–91.

[45] Lee I, Kesner RP. Differential contribution of NMDA receptors in hippocampal subregions to spatial working memory. Nature Neuroscience 2002;5:162–8.

[46] Lepage M, Habib R, Cormier H, Houle S, McIntosh AR. Neural correlates of semantic associative encoding in episodic memory. Cognitive Brain Research 2000;9:271–80.

[47] Lepage M, Ghaffar O, Nyberg L, Tulving E. Prefrontal cortex and episodic memory retrieval mode. Proceedings of the National Academy of Sciences of the United States of America 2000;97: 506–11.

[48] Leube DT, Erb M, Grodd W, Bartels M, Kircher TTJ. Differential activation in parahippocampal and prefrontal cortex during word and face encoding tasks. NeuroReport 2001;12:2773–7.

[49] Maguire EA. The retrospenial contribution to human navigation: a review of lesion and neuroimaging findings. Scandinavian Journal of Psychology 2001;42:225–38.

[50] Martin A. Automatic activation of the medial temporal lobe during encoding: lateralized influences of meaning and novelty. Hippocampus 1999;9:62–70.

[51] Mayes AR, Gooding PA, Hunkin NM, Nunn JA, Gregory LJ, Brammer MJ, et al. Storage of verbal associations is sufficient to activate the left medial temporal lobe. Behavioural Neurology 1998;11:163–72.

[52] McDonald CR, Crosson B, Valenstein E, Bowers D. Verbal encoding deficits in a patient with a left retrosplenial lesion. Neurocase 2001;7:407–17.

[53] Mikolajczyk K, Szabatin M, Rudnicki P, Grodzki M, Burger C. A JAVA environment for medical image data analysis: initial application for brain PET quantitation. Medical Informatics (London) 1998;23:207–14.

[54] Mishkin M, Suzuki W, Gadian DG, Vargha-Khadem F. Hierarchical organization of cognitive memory. Philosophical Transactions of the Royal Society of London Series B: Biological Sciences 1997;352:1461–7.

[55] Mishkin M, Vargha-Khadem F, Gadian DG. Amnesia and the organization of the hippocampal system. Hippocampus 1998;8: 212–6.

[56] Montaldi D, Mayes AR, Barnes A, Pirie H, Hadley DM, Patterson J, et al. Associative encoding of pictures activates the medial temporal lobes. Human Brain Mapping 1998;6:85–104.

[57] Morris JS, Öhman A, Dolan RJ. Conscious and unconscious emotional learning in the human amygdala. Nature 1998;393:467–70.

[58] Morris R, Petrides M, Pandya DN. Architecture and connections of retrospenial area 30 in the rhesus monkey (*Macaca mulatta*). European Journal of Neuroscience 1999;11:2506–18.

[59] Murdock BB, Dufty PO. Strength theory and recognition memory. Journal of Experimental Psychology 1972;94:284–90.

[60] Naccache L, Dehaene S. Unconscious semantic priming extends to novel unseen stimuli. Cognition 2001;80:223–37.

[61] Nobel PA, Shiffrin RM. Retrieval processes in recognition and cued recall. Journal of Experimental Psychology: Learning Memory and Cognition 2001;27:384–413.

[62] Norman DA, Wickelgren WA. Strength theory of decision rules and latency in retrieval from short-term memory. Journal of Mathematical Psychology 1969;6:192–208.

[63] Nyberg L, McIntosh AR, Houle S, Nilsson L-G, Tulving E. Activation of medial temporal structures during episodic memory retrieval. Nature 1996;380:715–7.

[64] Paller KA, Ranganath C, LaBar KS, Parrish TB, Gitelmann DR, Bozic VS, et al. Neural correlates of memory for faces: hemodynamic and electrophysiological differences between retrieval success and retrieval effort. Society for Neuroscience Abstracts 1999;25:648.

[65] Price CJ, Wise RJS, Frackowiak RSJ. Demonstrating the implicit processing of visually presented words and pseudowords. Cerebral Cortex 1996;6:62–70.

[66] Price CJ, Moore CJ, Humphreys GW, Wise RJS. Segregating semantic from phonological processes during reading. Journal of Cognitive Neuroscience 1997;9:727–33.

[67] Pugh KR, Shaywitz BA, Shaywitz SE, Constable RT, Skudlarski P, Fulbright RK, et al. Cerebral organization of component processes in reading. Brain 1996;119:1221–38.

[68] Rolls ET, Tovee MJ. Processing speed in the cerebral cortex and the neurophysiology of visual masking. Proceedings of the Royal Society of London Series B: Biological Sciences 1994;257:9–15.

[69] Roozendaal B, Phillips RG, Power AE, Brooke SM, Sapolsky RM, McGaugh JL. Memory retrieval impairment induced by hippocampal CA3 lesions is blocked by adrenocortical suppression. Nature Neuroscience 2001;4:1169–71.

[70] Roskies AL, Fiez JA, Balota DA, Raichle ME, Petersen SE. Task-dependent modulation of regions in the left inferior frontal

cortex during semantic processing. Journal of Cognitive Neuroscience 2001;13:829–43.

[71] Savage GR, Saling MM, Davis CW, Berkovic SF. Direct and indirect measures of verbal relational memory following anterior temporal lobectomy. Neuropsychologia 2002;40:302–16.

[72] Schacter DL. Implicit expressions of memory in organic amnesia: learning of new facts and associations. Human Neurobiology 1987;6:107–18.

[73] Schacter DL, Buckner RL. Priming and the brain. Neuron 1998;20: 185–95.

[74] Sergent J, Ohta S, Macdonald B. Functional neuroanatomy of face and object processing. Brain 1992;115:15–36.

[75] Shah NJ, Marshall JC, Zafiris O, Schwab A, Zilles K, Markowitsch HJ, et al. The neural correlate of person familiarity. A functional magnetic resonance imaging study with clinical implications. Brain 2001;124:804–15.

[76] Small SA, Nava AS, Perera GM, DeLaPaz R, Mayeux R, Stern Y. Circuit mechanisms underlying memory encoding and retrieval in the long axis of the hippocampal formation. Nature Neuroscience 2001;4:442–9.

[77] Sperling RA, Bates JF, Cocchiarella AJ, Schacter DL, Rosen BR, Albert MS. Encoding novel face–name associations: a functional MRI study. Human Brain Mapping 2001;14:129–39.

[78] Stark CEL, Squire LR. When zero is not zero: the problem of ambiguous baseline conditions in fMRI. Proceedings of the National Academy of Sciences of the United States of America 2001;98:12760–6.

[79] Suzuki WA, Amaral DG. Perirhinal and parahippocampal cortices of the macaque monkey: cortical afferents. Journal of Comparative Neurology 1994;350:497–533.

[80] Tulving E, Habib R, Nyberg L, Lepage M, McIntosh AR. Positron emission tomography correlations in and beyond medial temporal lobes. Hippocampus 1999;9:71–82.

[81] Vandenberghe R, Price C, Wise R, Josephs O, Frackowiak RSJ. Functional anatomy of a common semantic system for words and pictures. Nature 1996;383:254–6.

[82] Van Hoesen GW, Pandya DN. Some connections of the entorhinal (area 28) and perirhinal (area 35) cortices of the rhesus monkey. 1. Temporal lobe afferents. Brain Research 1975;95:1–24.

[83] Van Hoesen GW, Pandya DN. Some connections of the entorhinal (area 28) and perirhinal (area 35) cortices of the rhesus monkey. 3. Efferent connections. Brain Research 1975;95:39–59.

[84] Van Hoesen GW, Pandya DN, Butters N. Some connections of the entorhinal (area 28) and perirhinal (area 35) cortices of the rhesus monkey. 2. Frontal lobe afferents. Brain Research 1975;95:25–38.

[85] Wagner AD, Koutstaal W, Maril A, Schacter DL, Buckner RL. Task-specific repetition priming in left inferior prefrontal cortex. Cerebral Cortex 2000;10:1176–84.

[86] Warrington EK. The selective impairment of semantic memory. Quarterly Journal of Experimental Psychology 1975;27:635–57.

[87] Warrington EK, Weiskrantz L. Amnesia: a disconnection syndrome? Neuropsychologia 1982;20:233–48.

[88] Winocur G, Weiskrantz L. An investigation of paired-associate learning in amnesic patients. Neuropsychologia 1976;14:97–110.