

Memory Consolidation of Landmarks in Good Navigators

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ABSTRACT: Landmarks play an important role in successful navigation. To successfully find your way around an environment, navigationally relevant information needs to be stored and become available at later moments in time. Evidence from functional magnetic resonance imaging (fMRI) studies shows that the human parahippocampal gyrus encodes the navigational relevance of landmarks. In the present event-related fMRI experiment, we investigated memory consolidation of navigationally relevant landmarks in the medial temporal lobe after route learning. Sixteen right-handed volunteers viewed two film sequences through a virtual museum with objects placed at locations relevant (decision points) or irrelevant (nondecision points) for navigation. To investigate consolidation effects, one film sequence was seen in the evening before scanning, the other one was seen the following morning, directly before scanning. Event-related fMRI data were acquired during an object recognition task. Participants decided whether they had seen the objects in the previously shown films. After scanning, participants answered standardized questions about their navigational skills, and were divided into groups of good and bad navigators, based on their scores. An effect of memory consolidation was obtained in the hippocampus: Objects that were seen the evening before scanning (remote objects) elicited more activity than objects seen directly before scanning (recent objects). This increase in activity in bilateral hippocampus for remote objects was observed in good navigators only. In addition, a spatial-specific effect of memory consolidation for navigationally relevant objects was observed in the parahippocampal gyrus. Remote decision point objects induced increased activity as compared with recent decision point objects, again in good navigators only. The results provide initial evidence for a connection between memory consolidation and navigational ability that can provide a basis for successful navigation. © 2007 Wiley-Liss, Inc.

KEY WORDS: fMRI; object location memory; virtual environment; hippocampus; parahippocampal gyrus

INTRODUCTION

The medial temporal lobe including the hippocampus and the parahippocampal gyrus is involved in spatial tasks and spatial memory (e.g., O'Keefe and Nadel, 1978; Maguire et al., 1998; Burgess et al., 1999; Shelton and Gabrieli, 2002; Postma et al., 2004; Voermans et al., 2004; Henson, 2005). Previous functional magnetic resonance imaging (fMRI) evidence indicated that the human parahippocampal gyrus distinguishes

between landmarks placed at navigationally relevant and irrelevant locations (Janzen and van Turenhout, 2004). This neural representation of navigationally relevant information is automatically activated during recognition of landmarks in isolation and independent of attentional demands. In addition, this representation of navigational relevance is maintained over time (Janzen et al., 2007).

Performance in spatial tasks and the representation of spatial information is dependent on the navigational skill of a person. Recent fMRI studies (Hartley et al., 2003; Epstein et al., 2005) have shown differential neural activity for good and bad navigators. Epstein et al. (2005) showed stronger fMRI repetition effects for spatial scenes for good as compared with bad navigators. This finding indicates more efficient scene processing dependent on navigational skill. Hartley et al. (2003) found that good navigators activate the right hippocampus during navigation whereas poor navigators do not. Whether the representation of navigationally relevant objects varies as a function of navigational ability is so far unknown.

Wayfinding partly depends on successful storage of navigationally relevant information. An important factor that could play a role involves memory consolidation of spatial information. The topic of memory consolidation has intensively been studied through the last decades (for a review see Polster et al., 1991; Walker, 2005). These studies have implicated the medial temporal lobe to be crucially involved in declarative memory consolidation. More recent studies have focused on the role of sleep with its different sleep stages in memory consolidation (for an overview see Walker, 2005). However, there is no agreement about whether sleep is a requirement or of less importance, and whether dream stages or slow wave sleep is responsible for the strengthening of memories (Payne and Nadel, 2004; Peigneux et al., 2004; Walker, 2005). Recent investigations provide evidence that hippocampus-dependent memories (declarative memories) benefit from slow-wave sleep, whereas memories independent of the hippocampus (procedural memories or motor skill memories) gain from rapid eye movement sleep (e.g., Gais and Born, 2004; Born et al., 2006). The exact role of the hippocampus in memory consolidation is still a topic of debate (Nadel and Bohbot, 2001; Nadel and Moscovitch, 2001; Takashima et al., 2006). According to a system-level view, the hippocampus is initially involved in the retrieval of declarative memories. With time, a reor-

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ganization takes place that leads to a shift from the hippocampus to neocortical areas and makes memories independent of hippocampal functioning (e.g., Orban et al., 2006; Takashima et al., 2006; for an overview of lesion studies see Eichenbaum, 2000). Other studies provide evidence that spatial memories never become completely independent of the hippocampus (e.g., Nadel and Moscovitch, 2001; Moscovitch et al., 2005, 2006). This multiple trace theory was recently supported by a study of Maguire et al. (2006a) investigating a patient with a bilateral hippocampal lesion who had difficulties navigating through routes well known before the hippocampal damage (see Frankland and Bontempi, 2005 for an overview of consolidation theories).

These results suggest a specific connection between memory consolidation and spatial information in the hippocampus. In the present event-related fMRI experiment, we explicitly addressed the question of declarative memory consolidation after learning objects in a spatial environment. Furthermore, we examined whether memory consolidation of objects learned in a spatial environment varies as a function of navigational ability. Sixteen volunteers learned film sequences through a virtual museum with objects placed at locations relevant (decision points) or irrelevant (nondecision points) for navigation. To investigate consolidation effects, each participant learned one film sequence in the evening before scanning (remote objects), and the other one the following morning, directly before scanning (recent objects). Objects were placed at decision points (intersections) or nondecision points (simple turns). After the second study phase, event-related fMRI data of the whole brain were acquired during recognition of the objects in isolation. Participants decided whether they had seen the objects in the mazes or not. After scanning, participants answered standardized questions about their navigational skills in the Santa Barbara Sense of Direction (SBSOD) scale (Hegarty et al., 2002). On the basis of their scores, participants were divided into two equal groups of good and bad navigators.

On the basis of previous evidence (e.g., Walker, 2005), we expect to find a main effect of memory consolidation in the hippocampus showing increased neural activity for remote as compared with recent objects. If memory consolidation supports successful wayfinding, we expect to find a specific effect of consolidation of navigationally relevant information. Given the previous evidence on the representation of navigationally relevant information, we expect this consolidation to occur in the parahippocampal gyrus. If an efficient connection exists between good navigational skills and memory consolidation, good navigators should show stronger effects of memory consolidation as compared with bad navigators.

MATERIALS AND METHODS

Participants

Sixteen healthy volunteers (eight females) gave informed written consent before participating in the experiment. All par-

ticipants were right-handed according to self-report. The mean age was 23.4 yr (range 20–30 yr). The study was approved by the CMO Committee on Research Involving Human Subjects (Region Arnhem-Nijmegen).

Design and Procedure

The experiment included two study sessions outside the scanner, and one scanning session. During study, participants viewed two film sequences through a virtual museum. One film sequence was seen the evening before scanning, the other one was seen the following morning. The delay between both films was 12 h for all participants. Participants were given the following standardized written instruction for the study phase: “You apply for a job in a museum that exhibits belongings of famous people. You will be guided through one section of the museum. The exhibits are placed on tables along the wall. Importantly, after training, you should be able to guide a children’s tour through the museum. Therefore, while you are watching the film sequences pay special attention to toys and things interesting for children.”

The architecture software (3D TraumhausDesigner 4.0, Data Becker GmbH) was used to create the film sequences through a virtual reality museum presented on a 1.60 GHz-M Pentium 4 personal computer with 512 MB of RAM and a 15.0 in. XGA LCD-Screen. The virtual museum consisted of two mazes of the same shape. In each maze, 72 three-dimensional, colored objects were placed on tables. In total 144 different objects were included in the mazes. In real world dimensions, each maze had a length of 279 feet and was 112 feet wide in relation to a simulated eye level of 5.6 feet. The two mazes were shown in separate film sequences, lasting 8.5 min each. The order in which the two film sequences were presented in the evening and the next morning was counterbalanced over participants.

Objects were placed at decision points (D-objects) or at nondecision points (ND-objects). Decision points were right angled intersections, nondecision points were simple right angled turns. Attended objects (toys) and non attended objects (nontoy) were equally assigned to decision and nondecision points. In the film sequences, a right or left turn was made both at decision and nondecision points. This way, the effects of motion were not confounded with those of navigational relevance. Participants had no control over the timing in the virtual environment to ensure that the amount of time spent at decision and nondecision points was matched (an object was visible on average 5 s in the visual focus and 11 s total).

Immediately after the second study session, fMRI time series were obtained while participants performed a simple object recognition task. In this recognition phase, participants were instructed to decide as accurately and as quickly as possible whether they had seen the object in the former film sequences by pressing either a yes or a no response key. Responses were given with the index and the middle finger of the right hand. A trial consisted of a fixation cross centered on the screen, followed by an object for 500 ms shown from a canonical perspective on a white background. Thus, during scanning, no maze-related

information was presented. The average interstimulus-interval was 4,000 ms, jittered between 3,000 and 5,000 ms in steps of 250 ms, counterbalanced over conditions. A total number of 252 stimuli were included in the recognition task. All stimuli were presented rapidly, in a randomly intermixed order to prevent participants from anticipating and changing strategies for the different event-types. The entire stimulus material consisted of eight sets of 18 objects each, belonging to the following event-types: remote D-objects toys, recent D-objects toys, remote ND-objects toys, recent ND-objects toys, remote D-objects nontoy, recent D-objects nontoy, remote ND-objects nontoy, and recent ND-objects nontoy. Three sets of 36 objects each were included as distractor objects: novel toys, novel nontoy, and scrambled objects. The scrambled objects were constructed from experimental objects using mosaic scrambling. Mean word frequency as well as frequency range was equal for all sets of objects.

After scanning, participants answered standardized questions about their navigational skills (SBSOD scale). On the basis of their scores, participants were divided into two equal groups of good and bad navigators.

Scanning Parameters

A 3 T MRI system (Siemens TRIO, Erlangen, Germany) was used to acquire functional images of the whole brain (455). Using a gradient-echo echo planar scanning sequence 36 axial slices were obtained for each participant (voxel-size $3 \times 3 \times 3$ mm³, TR = 2,290 ms, field of view = 192, TE = 30 ms, flip angle = 75°). All functional images were acquired in one run that lasted for 17 min. Following the acquisition of functional images, a high-resolution anatomical scan (T1-weighted MP-RAGE, 176 slices) was acquired.

Data Analysis

fMRI data were analyzed using BrainVoyager QX (Brain Innovation, Maastricht, The Netherlands). Functional images were corrected for motion and slice scan time acquisition. Data were temporally smoothed with a high pass filter removing low-frequency nonlinear drifts below 3 or fewer cycles per time course. Functional images were coregistered with the anatomical scan and transformed into Talairach coordinate space using the 9-parameter landmark method of Talairach and Tournoux (1988). Images were spatially smoothed with a FWHM Gaussian kernel of 6 mm.

Statistical analyses were performed in the context of the general linear model, including 11 effects of interests and confounds. Event-related hemodynamic responses for each of the different event-types were modeled as delta functions convolved with a synthetic hemodynamic response function. Whole brain group analyses treating subjects as a fixed as well as a random factor were performed. Specific effects were tested by applying linear contrasts to the parameter estimates for each event as obtained in the random effects group analyses. The statistical threshold at the voxel level was set at $P < 0.001$, uncorrected for multiple comparisons. No unpredicted regions survived a

threshold of $P < 0.05$ corrected for whole brain volume in any of the analyses. To investigate fMRI responses separately for good and bad navigators, participants were divided into two equal groups of good and bad navigators based on their SBSOD scores. The ratio of male and female participants in the good and bad navigator groups was 5:3. The good navigator group included five female and three male participants and the bad navigator group included five male and three female participants. Mean SBSOD scores were 83.86 for good navigators (mean female score = 87.33, mean male score = 80.4), and the mean SBSOD score for the bad navigators was 62.0 (mean female score = 67.0, mean male score = 57.0).

Analyses of the fusiform gyrus and the parahippocampal gyrus were performed as follows: First, we functionally defined the regions by selecting all voxels showing an effect of toys vs. nontoy, and decision vs. nonddecision points in the whole brain group analysis. Then, we obtained the beta weights (i.e., the regression coefficients) as indexes of effect size for all voxels included in these regions of interest, separately for all individual subjects, for each of the event-types. Regionally averaged beta weights were analyzed in repeated-measurement ANOVAs including the within-factors delay, decision point, attention, and the between-subjects factor navigational skill. Specific effects were tested by applying *t*-contrasts to the regionally averaged beta weights obtained for the different event types.

A different type of method to identify regions of interest would be the use of an independent functional localizer task (e.g., a scene localizer as used by Epstein et al., 2005). The usefulness of such localizing scans in fMRI studies is a matter of debate (see the controversy discussed by Friston et al., 2006, Friston and Henson, 2006, Saxe et al., 2006).

To test for consolidation effects in the hippocampus, a region of interest analysis was performed as follows: We defined the right and the left hippocampus separately for each individual subject in the anatomical scans and obtained the beta weights out of these regions. The regionally averaged beta weights were used to calculate the effect of memory consolidation (beta weights of remote objects minus beta weights of recent objects). Participants' effect sizes were then correlated with their SBSOD scores.

RESULTS

Behavioral Results

Overall task performance was above chance level (68% correct). False positive responses for distractor items were 11.6% for the novel toys and 11.1% for the novel nontoy. Scrambled objects evoked 0.2% false positives. Accuracy data for the experimental items were entered in an analysis of variance (ANOVA) with the within-factors delay (remote objects and recent objects), decision point (D-objects and ND-objects), and attention (toys and nontoy) and the between-subjects-factor navigational skill (eight good navigators and eight bad navigators based on the SBSOD score). The data showed an effect of

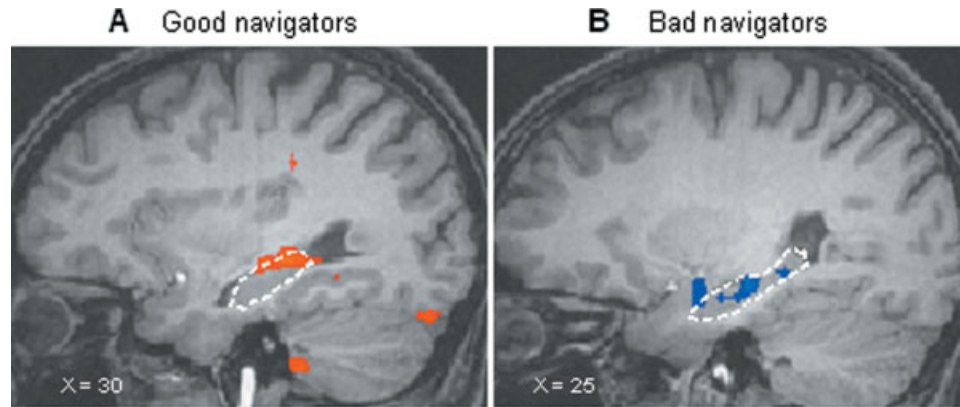


FIGURE 1. The effect of memory consolidation varies with navigational skill. **A:** Good navigators showed increased neural activity for remote as compared with recent objects in bilateral hippocampus (right: $x = 30$, $y = -28$, $z = -6$; 880 mm³; left: $x = -30$, $y = -34$, $z = -2$; 174 mm³). **B:** Bad navigators

showed decreased neural activity for remote as compared with recent objects in bilateral hippocampus (right hippocampus: $x = 25$, $y = -22$, $z = -9$; 478 mm³; left hippocampus: $x = -27$, $y = -25$, $z = -9$; 24 mm³). The statistical threshold was $P < 0.001$, uncorrected.

delay ($F(1,14) = 36.1$, $P < 0.001$). Remote objects evoked more errors (57.2%) than recent objects (44.9%; $t(15) = 5.93$, $P < 0.001$). No significant differences in error rates were observed for objects placed at decision (50.8%) and at nondecision points (51.3%). Error rates showed an effect of the attentional manipulation during study ($F(1,14) = 107.61$, $P < 0.001$). Error rates were lower for toys (39.3%) than for nontoy (62.8%; $t(15) = -10.73$, $P < 0.001$). The data showed an interaction between the factors decision point and attention ($F(1,14) = 5.57$, $P < 0.05$). This interaction reflected that an effect of decision point was observed for toys (D-object toys: 36.8%; ND-object toys: 41.8%; $t(15) = -2.06$, $P < 0.05$, one-tailed), but not for nontoy (D-object nontoy: 64.8%; ND-object nontoy 60.8%; $t(15) = 1.13$, $P = 0.14$). The data also showed an interaction between the factors delay, decision point and attention ($F(1,14) = 7.17$, $P < 0.05$), as well as an interaction between the factors delay, decision point, attention, and navigational skill ($F(1,14) = 6.34$, $P < 0.05$).

Response times showed a trend effect of the attentional manipulation during study ($F(1,14) = 3.52$, $P = 0.08$). Response times were faster for toys than for nontoy (mean response latencies were 1,013 and 1,040 ms). No significant effect of delay, decision point, and navigational skill and no interaction between the factors were observed.

fMRI Results

Comparing fMRI responses with all objects included in the mazes with fMRI responses to a low-level-visual baseline (scrambled objects) revealed strong activity in bilateral occipito-temporal cortices. Additionally, increased activity was found in the bilateral parahippocampal gyrus, the bilateral middle frontal gyrus, the bilateral superior parietal lobe, and in the medial aspect of the frontal lobe.

To investigate main effects of memory consolidation in the hippocampus we compared fMRI responses for remote objects

with fMRI response for recent objects. No main effect of consolidation was observed in this region. To examine whether the absence of a consolidation effect was due to different results for good and bad navigators, we compared fMRI responses to remote objects with responses to recent objects separately for both groups of good and bad navigators. Good navigators showed increased neural activity for remote objects in bilateral hippocampus whereas bad navigators showed the opposite result (see Fig. 1). In addition, we performed a region of interest analysis separately for the right and left hippocampus (see Materials and Methods). Regionally averaged β -weights from the right and the left hippocampus were used to calculate the size of the consolidation effect (β -weights for remote objects minus the beta weights for recent objects). A significant correlation was obtained between the size of the consolidation effect and navigational skill in the right (Pearson's $r = 0.537$, $P = 0.016$) as well as in the left hippocampus (Pearson's $r = 0.489$, $P = 0.028$, one-tailed). Participants with a greater consolidation effect had a higher score on the SBSOD scale (see Fig. 2).

To investigate whether the differential effects for good and bad navigators were contaminated by differences in hippocampal size, we correlated the hippocampal volume with participants' score on the SBSOD scale. Better navigators could have larger hippocampi than poorer navigators and therefore produce larger neural responses. The right and left hippocampal volume was defined separately for each participant in the anatomical scans (see Materials and Methods). For each subject, hippocampal volume in mm³ was correlated with SBSOD score. No significant correlations were observed for the right hippocampus (Pearson's $r = -0.149$, $P = 0.581$) nor for the left hippocampus (Pearson's $r = -0.130$, $P = 0.631$).

To test whether the consolidation effect in the hippocampus reflects a retrieval difficulty rather than a pure consolidation effect in good navigators, hippocampal responses were obtained separately for correctly remembered and forgotten objects using the anatomically defined regions of interest (see Materials and

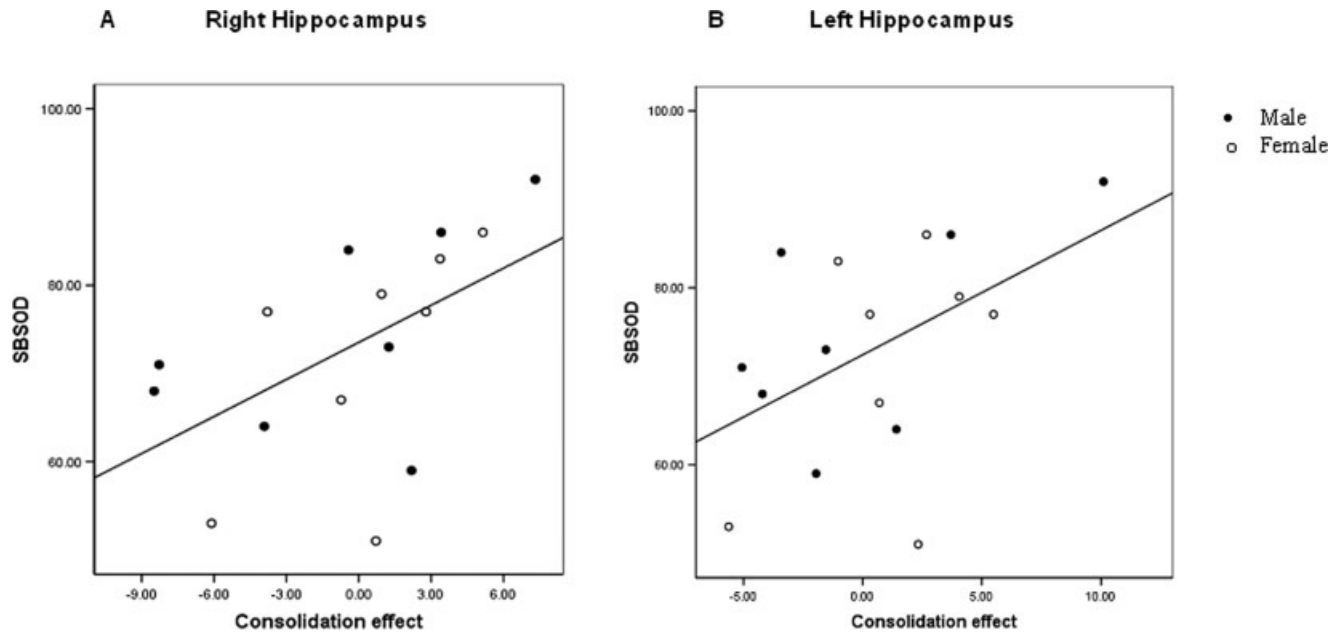


FIGURE 2. Correlation between subjects' SBSOD score and the size of the consolidation effect in the right (A) and the left (B) hippocampus.

Methods). Beta weights were obtained for all event types and entered in ANOVAs including the within-factors object retrieval (correctly remembered and forgotten objects), decision point (D-objects and ND-objects), and attention (toys and nontoy). Navigational skill (good navigators and bad navigators) was included as a between-subject factor. Separate ANOVAs were run for recent and remote objects in the left and the right hippocampus. No significant effects were observed. Results showed no main effect of object retrieval for remote objects (RH: $F(1,14) = 3.21$, $P = 0.1$; LH: $F(1,14) = 1.84$, $P = 0.2$) nor for recent objects (RH: $F(1,14) = 1.63$, $P = 0.2$; LH: $F(1,14) = 1.29$, $P = 0.3$). No interaction was obtained between object retrieval and navigational skill for remote objects (RH: $F(1,14) = 0.63$, $P = 0.4$; LH: $F(1,14) = 0.12$, $P = 0.7$) nor for recent objects (RH: $F(1,14) = 0.87$, $P = 0.4$; LH: $F(1,14) = 2.95$, $P = 0.1$).

In addition to general object consolidation in the hippocampus, for good navigators we observed a specific consolidation effect for navigationally relevant objects only in the parahippocampal gyrus. Remote decision point objects induced increased neural activity in the parahippocampal gyrus as compared with recent decision point objects (right: $t(8) = 6.44$, $P < 0.001$; left: $t(8) = 4.87$, $P < 0.01$; see Figure 3). An ANOVA of the regionally averaged β -weights was performed separately for the right and the left parahippocampal gyrus. This analysis showed a significant interaction between delay and decision point ($F(1,7) = 10.55$; $P < 0.05$) in the right parahippocampal gyrus (see Fig. 3).

To investigate effects of navigational relevance, we compared fMRI responses with D-objects with responses to ND-objects. This contrast revealed an increase in activity in the left ($x = -27$, $y = -41$, $z = -8$; volume: 9 mm^3) and the right para-

hippocampal gyrus ($x = 23$, $y = -45$, $z = -8$; volume: 1 mm^3) for D-objects. An ANOVA of the regionally averaged β -weights was performed separately for the right and the left parahippocampal gyrus. Besides a main effect of decision point, a main effect of attention was observed ($F(1,14) = 12.85$; $P < 0.01$) showing decreased activity for toys as compared with nontoy (3.57 mean β -weight for toys; 4.29 mean β -weight for nontoy) in the left parahippocampal gyrus. Importantly, no interaction between decision point and attention was obtained.

To test for effects of attention we compared event-related fMRI responses to toys with those to nontoy and observed increased activity in the right fusiform gyrus ($x = 37$, $y = -44$, $z = -16$; volume: 833 mm^3). An analysis of the averaged β -weights obtained for all voxels in this region did not show main effects of the factors delay, decision point or the between-subjects factor navigational skill and no interaction between the factors.

DISCUSSION

In the present event-related fMRI study, we investigated memory consolidation of objects previously learned in a spatial environment and addressed the question whether consolidation effects vary as a function of navigational relevance and navigational skill. Participants learned routes with navigationally relevant and irrelevant objects the evening before scanning (remote objects) and a different set of objects the next morning directly before scanning (recent objects). To control for effects of attention, participants were instructed to pay special attention to toys during route learning. In the fMRI scanner they

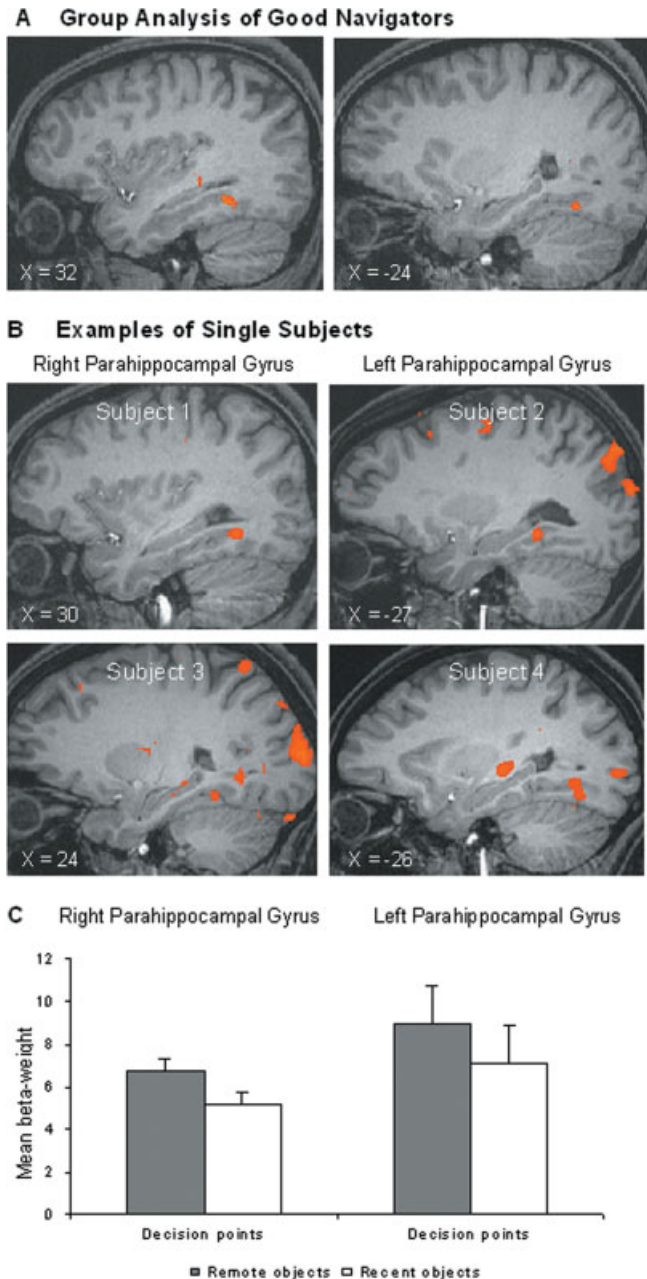


FIGURE 3. Remote versus recent decision point objects in good navigators. **A:** Remote decision point objects induced increased activity in the right parahippocampal gyrus ($x = 32$, $y = -43$, $z = -10$; 54 mm^3) as well as in the left parahippocampal gyrus ($x = -23$, $y = -52$, $z = -9$; 20 mm^3). The statistical threshold was $P < 0.001$, uncorrected. **B:** Examples of remote versus recent decision-point object effects in single subjects: Locations of peak activity in the parahippocampal gyrus were for subject 1 ($x = 30$, $y = -49$, $z = -7$; 48 mm^3), for subject 2 ($x = -27$, $y = -42$, $z = -9$; 320 mm^3), for subject 3 ($x = 24$, $y = -44$, $z = -11$; 25 mm^3), and for subject 4 ($x = -26$, $y = -58$, $z = -7$; 160 mm^3). The statistical threshold for single subject analysis was $P < 0.01$, uncorrected. **C:** Regionally averaged β -weights for the right and the left parahippocampal gyrus showing increased activity for remote as compared with recent decision-point objects in good navigators. Bars indicate standard errors across participants.

performed a simple object recognition task with the previously learned and new objects randomly intermixed. Afterwards, they answered a questionnaire about their navigational skills.

Replicating results from previous studies (Janzen and van Turennout, 2004; Janzen et al., 2007), the data show that the parahippocampal gyrus selectively responds to the navigational relevance of an objects location whereas the right fusiform gyrus responds to previously attended objects. In line with the previous data, no interaction between the factors navigational relevance and attention was observed, indicating a dissociation between both effects. The parahippocampal place area (PPA) is a functional part of the parahippocampal gyrus that is involved in scene processing (e.g., Epstein and Kanwisher, 1998). Epstein et al. (2005) suggests that scene representations within the PPA are more efficient in good navigators than in bad navigators stressing that activity in this area varies as a function of navigational skill. Our previous and present data (Janzen and van Turennout, 2004; Janzen et al., 2007) show that the parahippocampal gyrus not only responds to scenes but also to single objects that have previously been viewed in a navigationally relevant context. The coordinates of peak activity in the posterior part of the parahippocampal gyrus in the present as well as in our previous studies (Janzen and van Turennout, 2004; Janzen et al., 2007) are close to the coordinates reported for the PPA (e.g., Epstein and Kanwisher, 1998; Epstein et al., 2005). This emphasizes the involvement of the posterior part of the parahippocampal gyrus in spatial representations and its variation as a function of navigational skill. Future research is necessary to examine the precise role of different parts of the parahippocampal gyrus for successful wayfinding.

The fMRI data show a main effect of memory consolidation in bilateral hippocampus that varied with participants' navigational skill. Increased activity for remote as compared with recent objects was observed in bilateral hippocampus for the group of good navigators only. Bad navigators showed the opposite result (Fig. 1). Interestingly, rather than two distinct groups of good and bad navigators, a linear relationship between the size of the consolidation effect and the participants' score in the SBSOD scale was observed (see Fig. 2). These data indicate that memory consolidation in the hippocampus is linked to good navigational skills. The better the navigational skill, the greater the consolidation effect in the hippocampus. Since no systematic differences in hippocampal volume were observed between good and bad navigators, the effect cannot be explained by greater hippocampal volume in good navigators.

Alternatively, the consolidation effect in good navigators could be explained by increased retrieval difficulty for remote versus recent objects. Remote objects could generally be processed in a way that they are more difficult to remember than recent objects. However, our fMRI results showed that hippocampal responses to remote and recent objects were not affected by successful object retrieval. In addition, no interaction was observed between navigational ability and object retrieval indicating that differences in hippocampal activity between good and bad navigators could not solely be explained

by successful object retrieval. From this, we conclude that the differential hippocampal activity for remote as compared with recent objects in good navigators are more likely to reflect memory consolidation rather than retrieval difficulty.

The efficient connection of memory consolidation and navigational skill is consistent with findings that show a better representation of places and views in good navigators (Epstein et al., 2005). In line with our findings Hartley et al. (2003) found that good navigators showed greater hippocampal activity during wayfinding than poor navigators. A very recent study by Moffat et al. (2006) showed a correlation between navigational performance and the volumes of the caudate nucleus and the hippocampus. Better navigational performance was associated with larger volume of these areas (see also Maguire et al., 2000). Recently, Maguire et al. (2006b) found that London taxi drivers who navigate around the city on different routes had greater midposterior hippocampal gray matter volume as compared with London bus drivers who follow a constrained set of routes. Together, these findings show that greater spatial ability and spatial knowledge is associated with hippocampal functioning. Our data support this relationship between hippocampal functioning and spatial skill. In addition, our results suggest that memory consolidation in the hippocampus might be one of the underlying mechanisms supporting efficient navigation.

In addition to general consolidation effects, we observed a specific consolidation effect of navigationally relevant landmarks in good navigators only (Fig. 3). Remote decision point objects induced increased activity in bilateral parahippocampal gyrus as compared with decision point objects seen directly before scanning. Good navigators not only show consolidation effects in the hippocampus but additionally make use of the parahippocampal gyrus for consolidation of navigationally relevant information. The combination of a general effect of consolidation supported by the hippocampus and a more spatial-specific consolidation effect in the parahippocampal gyrus provides evidence for a functional role of memory consolidation in spatial navigation. The parahippocampal gyrus is highly interconnected with the hippocampus and reports into the hippocampus through the perirhinal and entorhinal cortex (e.g., Hargreaves et al., 2005). Whether better navigational ability is supported by a more efficient connection between the parahippocampal gyrus and the hippocampus needs to be investigated in future research.

The behavioral results from our study do not show differences between good and bad navigators. This result can be explained by the simple object recognition task that can be solved without the explicit need of spatial knowledge. The accuracy data showed that remote objects evoked more errors than recent objects. This finding excludes the possibility that increased activity in the hippocampus and parahippocampal gyrus for remote as compared with recent objects can be explained by explicit recognition of the objects. Consistent with this finding, previous results (Janzen and van Turennout, 2004) showed that the neural representation in the parahippocampal gyrus occurs even without explicit memory of having seen the object before.

From the present study, no hard conclusions can be drawn on whether the observed effects of consolidation provide support for the theory of system-level consolidation (e.g., Bayley et al., 2005; Takashima et al., 2006) or the multiple trace theory (Moscovitch et al., 2005, 2006). It is possible that for a system-level consolidation mechanism the delay of 12 h is not sufficient to provoke a shift from hippocampal to neocortical areas. However, Takashima et al. (2006) reported a shift from hippocampal to medial prefrontal cortex already within the first 24 h after learning. Further investigations are necessary to precisely analyze the time course of system-level consolidation. A recent study by Maguire et al. (2006a) supports the multiple trace theory with showing that a patient with a bilateral hippocampal lesion relies on hippocampal functioning for successful navigation through all parts of a former well known city. However, the patient was able to navigate on the main roads only. Further support for the multiple trace theory and in line with our findings of stronger consolidation effects in bilateral hippocampus for good navigators is provided by a study by Bosshardt et al. (2005). The researchers found that good learners of word pairs showed increased hippocampal activity from a one day lag up to a one month lag between learning and memory retrieval. This finding shows a connection between memory consolidation in the hippocampus and good learning abilities. This is in line with the present data showing a correlation between memory consolidation and navigational skill.

In conclusion, our results provide initial evidence for a linkage between the navigational relevance of objects, a person's navigational skill and memory consolidation. Further investigations are required to provide more detailed evidence on the neural mechanisms mediating such a linkage. The presence of general memory consolidation in the hippocampus in combination with spatial-specific consolidation in the parahippocampal gyrus could support efficient pathfinding in good navigators. The direct relation between memory consolidation of navigationally relevant information and spatial skill could support a highly specific neural wayfinding mechanism in good navigators.

REFERENCES

- Bayley PJ, Gold JJ, Hopkins RO, Squire LR. 2005. The neuroanatomy of remote memory. *Neuron* 46:799–810.
- Born J, Rasch B, Gais S. 2006. Sleep to remember. *Neuroscientist* 12:410–424.
- Bosshardt S, Degonda N, Schmidt CF, Boesiger P, Nitsch RM, Hock C, Henke K. 2005. One month of human memory consolidation enhances retrieval-related hippocampal activity. *Hippocampus* 15:1026–1040.
- Burgess N, Jeffery KJ, O'Keefe J. 1999. *The Hippocampal and Parietal Foundations of Spatial Cognition*. Oxford: Oxford University Press.
- Eichenbaum H. 2000. A cortical-hippocampal system for declarative memory. *Nat Rev Neurosci* 1:41–50.
- Epstein RA, Kanwisher N. 1998. Cortical representation of the local visual environment. *Nature* 392:598–601.
- Epstein RA, Higgins JS, Thompson-Schill SL. 2005. Learning places from views: Variation in scene processing as a function of experience and navigational ability. *J Cogn Neurosci* 17:73–83.

- Frankland PW, Bontempi B. 2005. The organization of recent and remote memories. *Nat Rev Neurosci* 6:119–130.
- Friston KJ, Henson RN. 2006. Commentary on: Divide and conquer, a defence of functional localisers. *NeuroImage* 30:1097–1099.
- Friston KJ, Rotshtein P, Geng JJ, Sterzer P, Henson RN. 2006. A critique of functional localisers. *NeuroImage* 30:1077–1087.
- Gais S, Born J. 2004. Declarative memory consolidation: Mechanisms acting during human sleep. *Learn Mem* 11:679–685.
- Hargreaves EL, Rao G, Lee I, Knierim JJ. 2005. Major dissociation between medial and lateral entorhinal input to dorsal hippocampus. *Science* 308:1792–1794.
- Hartley T, Maguire EA, Spiers HJ, Burgess N. 2003. The well-worn route and the path less traveled: Distinct neural bases of route following and wayfinding in humans. *Neuron* 37:877–888.
- Hegarty M, Richardson AE, Montello DR, Lovelace K, Ilavani S. 2002. Development of a self-report measure of environmental spatial ability. *Intelligence* 30:425–447.
- Henson R. 2005. A mini-review of fMRI studies of human medial temporal lobe activity associated with recognition memory. *Q J Exp Psychol B* 58:340–60.
- Janzen G, van Turenout M. 2004. Selective neural representation of objects relevant for navigation. *Nat Neurosci* 7:673–677.
- Janzen G, Wagensveld B, van Turenout M. 2007. Neural representation of navigational relevance is rapidly induced and long-lasting. *Cereb Cortex* 17:975–981.
- Maguire EA, Burgess N, Donnett JG, Frackowiak RS, Frith CD, O'Keefe J. 1998. Knowing where and getting there: A human navigation network. *Science* 280:921–924.
- Maguire EA, Gadian DG, Johnsrude IS, Good CD, Ashburner J, Frackowiak RSJ, Frith CD. 2000. Navigation-related structural change in the hippocampi of taxi drivers. *Proc Natl Acad Sci USA* 97:4398–4403.
- Maguire EA, Nannery R, Spiers HJ. 2006a. Navigation around London by a taxi driver with bilateral hippocampal lesions. *Brain* 129:2894–2907.
- Maguire EA, Woollett K, Spiers HJ. 2006b. London taxi drivers and bus drivers: A structural MRI, neuropsychological analysis. *Hippocampus* 16:1091–1101.
- Moffat SD, Kennedy KM, Rodrigue KM, Raz N. 2007. Extrahippocampal contributions to age differences in human spatial navigation. *Cereb Cortex* 17:1274–1282.
- Moscovitch M, Rosenbaum RS, Gilboa A, Addis DR, Westmacott R, Grady C, McAndrews MP, Levine B, Black S, Winocur G, Nadel L. 2005. Functional neuroanatomy of remote episodic, semantic and spatial memory: a unified account based on multiple trace theory. *J Anat* 207:35–66.
- Moscovitch M, Nadel L, Winocur G, Gilboa A, Rosenbaum RS. 2006. The cognitive neuroscience of remote episodic and semantic and spatial memory. *Curr Opin Neurobiol* 16:179–190.
- Nadel L, Moscovitch M. 2001. The hippocampal complex and long-term memory revisited. *Trends Cogn Sci* 5:228–230.
- Nadel L, Bohbot V. 2001. Consolidation of memory. *Hippocampus* 11:56–60.
- O'Keefe J, Nadel L. 1978. *The Hippocampus as a Cognitive Map*. Oxford: Oxford University Press.
- Orban P, Rauchs G, Baeteu E, Degueldre C, Luxen A, Maquet P, Peigneux P. 2006. Sleep after spatial learning promotes covert reorganization of brain activity. *Proc Natl Acad Sci USA* 103:7124–7129.
- Payne JD, Nadel L. 2004. Sleep, dreams, and memory consolidation: The role of the stress hormone cortisol. *Learn Mem* 11:671–8.
- Peigneux P, Laureys S, Fuchs S, Collette F, Perrin F, Reggers J, Phillips C, Degueldre C, Del Fioe G, Aerts J, Luxen A, Maquet P. 2004. Are spatial memories strengthened in the human hippocampus during slow wave sleep? *Neuron* 44:535–45.
- Polster MR, Nadel L, Schacter DL. 1991. Cognitive neurosciences analysis of memory: A historical perspective. *J Cogn Neurosci* 3:95–116.
- Postma A, Kessels RPC, van Asselen M. 2004. Neuropsychology of object-location-memory. In: Allen G, editor. *Human Spatial Memory: Remembering Where*. Mahwah, NJ: LEA. pp 143–160.
- Saxe R, Brett M, Kanwisher N. 2006. Divide and conquer: A defense of functional localizers. *NeuroImage* 30:1088–1096.
- Shelton AL, Gabrieli JD. 2002. Neural correlates of encoding space from route and survey perspectives. *J Neurosci* 22:2711–2717.
- Takashima A, Petersson KM, Rutters F, Tendolkar I, Jensen O, Zwarts MJ, McNaughton BL, Fernandez G. 2006. Declarative memory consolidation in humans: A prospective functional magnetic resonance imaging study. *Proc Natl Acad Sci USA* 103:756–761.
- Talairach J, Tournoux P. 1988. *A Co-Planar Stereotaxic Atlas of the Human Brain*. New York: Thieme Medical Publishers.
- Voermans NC, Petersson KM, Daudey L, Weber B, Van Spaendonck KP, Kremer HP, Fernandez G. 2004. Interaction between the human hippocampus and the caudate nucleus during route recognition. *Neuron* 43:427–435.
- Walker MP. 2005. A refined model of sleep and the time course of memory formation. *Behav Brain Sci* 28:51–64; discussion 64–104.