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Encoding and Retrieval of Landmark-Related Spatial Cues during Navigation: An fMRI Study

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ABSTRACT: To successfully navigate, humans can use different cues from their surroundings. Learning locations in an environment can be supported by parallel subsystems in the hippocampus and the striatum. We used fMRI to look at differences in the use of object-related spatial cues while 47 participants actively navigated in an open-field virtual environment. In each trial, participants navigated toward a target object. During encoding, three positional cues (columns) with directional cues (shadows) were available. During retrieval, the removed target had to be replaced while either two objects without shadows (objects trial) or one object with a shadow (shadow trial) were available. Participants were informed in blocks about which type of retrieval trial was most likely to occur, thereby modulating expectations of having to rely on a single landmark or on a configuration of landmarks. How the spatial learning systems in the hippocampus and caudate nucleus were involved in these landmark-based encoding and retrieval processes were investigated. Landmark configurations can create a geometry similar to boundaries in an environment. It was found that the hippocampus was involved in encoding when relying on configurations of landmarks, whereas the caudate nucleus was involved in encoding when relying on single landmarks. This might suggest that the observed hippocampal activation for configurations of objects is linked to a spatial representation observed with environmental boundaries. Retrieval based on configurations of landmarks activated regions associated with the spatial updation of object locations for reorientation. When only a single landmark was available during retrieval, regions associated with updating the location of oneself were activated. There was also evidence that good between-participant performance was predicted by right hippocampal activation. This study therefore sheds light on how the brain deals with changing demands on spatial processing related purely to landmarks. © 2014 Wiley Periodicals, Inc.

KEY WORDS: hippocampus; caudate nucleus; landmark; navigation; fMRI

INTRODUCTION

To find the way through their environment, humans can make use of different spatial cues. Positional cues, such as proximal landmarks, indicate one's exact location in an environment. On the contrary, directional cues inform people about their orientation in the environment. Directional information can be provided by distal landmarks (i.e., objects far from the observer). For example, humans can proficiently use information provided by the sun (Souman et al., 2009). This study focuses on how the brain encodes and retrieves locations based on different spatial cues (i.e., based on positional and direction information).

Configurations of proximal landmarks can provide a spatial frame of reference, relative to which other locations can be encoded and retrieved. Behavioral studies have shown that humans and other species are able to use such a configuration of identical objects to reorient and locate hidden objects (for a review, see Lew, 2011). Nevertheless, the geometry of spaces (such as the enclosing walls of a room) is the predominant frame of reference in spatial cognition, leading to the proposal of a "geometric module" (reviewed in Cheng and Newcombe, 2005). This is supported by a study showing that, when a boundary and a landmark were available during environmental learning, location memory was better when only the boundary was available during retrieval compared to when only the landmark was available (Doeller and Burgess, 2008). However, a recent study found that this so-called overshadowing effect of boundaries was eliminated with a sufficient number of regularly placed proximal landmarks (Mou and Zhou, 2012). Similarly, an array of objects placed in a regular layout (i.e., with an intrinsic axis) was found to facilitate reorientation comparable to the way enclosing walls do (Mou et al., 2006). These findings suggest configurations of objects can provide an allocentric frame of reference for humans.

Learning locations in an environment can be supported by parallel subsystems in the hippocampus and the striatum. The caudate nucleus, a region within the striatum, is associated with stimulus-response mapping relative to a landmark in a viewer-centered (e.g., turn left at the record store; Hartley et al., 2003) and a world-centered manner (e.g., walk 30 m south from

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the tree; Doeller et al., 2008). Similarly, rodent research has implicated the caudate nucleus when navigating using objects as beacons, that is, indicating a (nearby) target location (Packard and McGaugh, 1992; White and McDonald, 2002). Hippocampal place cells code allocentric (viewer-independent) space and have been found to be influenced by nearby boundaries (O'Keefe and Burgess, 1996). In an fMRI study in which participants learned locations either relative to a single landmark or relative to the boundary of the environment, the hippocampus was activated when subjects learned relative to the environmental boundary, whereas the caudate nucleus was activated when locations were learned relative to the landmark in the environment (Doeller et al., 2008). As we have seen, previous research showed that cellular representations of space have been found. However, it remains unclear how multiple object-based representations are remembered and retrieved in the absence of a boundary-based geometry. Finding an answer to this question in animal research has been difficult, because the environments containing the object configurations almost always contained walls, providing some geometric information (Lew, 2011). Here, we used a virtual environment (VE) that contained no boundaries to answer which brain regions are involved in the encoding and retrieval of specific object-related spatial cues, that is, based on positional and directional information. Specifically, we were interested in the encoding and retrieval based on a single positional cue with directional information compared to a configuration of positional cues. The expectation of availability of spatial cues during retrieval was manipulated in an allocentric working memory (WM) navigation task in an open field VE. To investigate this, we adapted a task previously used by Baumann et al. (2010). In this study, subjects first encoded the location of a target stimulus relative to three distinguishable columnar objects, providing positional information. Notably, an invisible sun cast shadows from these objects, providing subjects with directional information. During the retrieval phase, participants re-entered the environment from one of four locations and were provided with minimal information to reorient themselves: either two positional cues without directional information or one positional cue with directional information was provided. Based on this information, the removed target had to be replaced at its remembered location during encoding. The experiment was divided into blocks, which informed participants about which type of retrieval information was most likely to be available. This allowed us to determine which brain areas were involved in encoding based on which spatial cues participants expected during retrieval. During retrieval, we compared which areas were invoked when having to use expected and unexpected spatial cues. Furthermore, brain activity that predicted performance during encoding and retrieval was investigated.

This study investigates how the representations of discrete object locations and configurations of objects are supported by the hippocampal and striatal systems. In the absence of environmental boundaries, the locations of objects can be coded in two ways. The vector sum model (Cheng, 1988, 1989) proposes that each landmark's relation to a goal is stored in a separate vector. Given that the caudate nucleus is involved when locations have to be encoded relative to a single landmark (Doeller et al., 2008), this model predicts that the encoding and retrieval of several landmarks activates the caudate nucleus more compared to encoding and retrieving single landmarks. Alternatively, the configuration of objects could be encoded as a geometry. Given that configurations of objects can provide an allocentric frame of reference, the axes imagined in this way would serve as invisible boundaries coded by the hippocampus, which activates relative to the distance to boundaries in an environment (O'Keefe and Burgess, 1996; Bird et al., 2010).

MATERIALS AND METHODS

Participants

Fifty healthy right-handed adults participated in this study. Data from three participants were excluded due to structural abnormalities or large movement artifacts that significantly distorted the fMRI signal. Forty-seven participants were included in the final sample (29 males, mean age = 23.85, SD = 4.23). Participants received a monetary reward or course credits for their participation, and all gave informed consent according to institutional guidelines of the local ethics committee (CMO region Arnhem-Nijmegen, The Netherlands).

Navigation Task

Participants performed a navigation task in an open-field VE inspired by the VE in Baumann et al. (2010). The navigation task was created and administered in the Blender open source 3D package (The Blender Foundation Amsterdam, The Netherlands; www.blender.org). Participants moved through the environment with a four button keypad on their right hand, mapped from their index finger to their pinky: rotate left, move forward, rotate right, move backward, respectively. Each trial consisted of an encoding and retrieval phase in which participants had to navigate toward a target that was visible during encoding but hidden in retrieval (Fig. 1). In the encoding phase of the trial, participants entered an environment that contained three-colored columns and a target (a yellow pyramid). An implicit sun (not visible in the environment) cast a shadow off each column. The participants were instructed to navigate toward the target within a limited amount of time (10 seconds) and remember its location in the environment. Between encoding and retrieval, a blank screen was presented for 4 seconds. In the retrieval phase, participants re-entered the environment from one of four possible locations: the same starting location as in the encoding phase or a different location (shifted by 90°, 180°, or 270° with equal probability). The target was absent and participants were instructed to navigate to where they thought the target was during the encoding phase and confirmed its location with a button press with the index finger of their left hand. The retrieval phase had a time

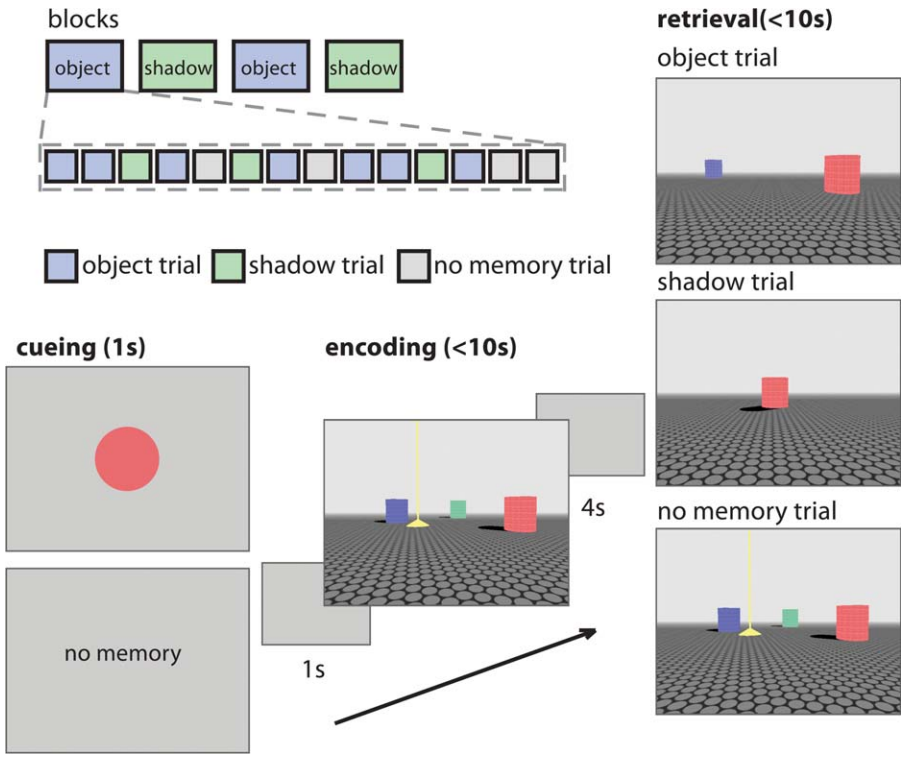

FIGURE 1. Experimental paradigm. During encoding, three object cues (columns in red, green and blue) and shadows were available. Participants were required to navigate to the target object, shown in yellow. Before each trial, participants received a color cue indicating which of the colored columns would be available during retrieval. During the retrieval part of the trial, either two objects without shadows (objects trial) or one object with a shadow (shadow trial) was available. Participants were instructed to move to the position where the now unavailable target was placed and confirm with a button press. In baseline trials, indicated at the cue phase, the target was also visible during retrieval. The experiment consisted of blocks, informing participants of which type of trial would be most likely to occur (70% expected trials, 30% unexpected trials). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

limit of 10 seconds. During the retrieval phase, objects that were present were in their original locations, but information that was previously available during the encoding phase was now missing. In objects trials, two of the previous three columns were available, but the directional information provided by the shadows was missing. In shadow trials, only one of the previous three columns was available, with directional information provided by a shadow. Note that, in both trial types, minimal information is provided to reorient within the environment. Further, we named our trials objects and shadow trials instead of positional and directional trials because positional information is necessarily provided in both trial types. In each trial, the location of the target and the columns were different to ensure that a unique spatial layout was encoded for every trial. There was an average delay of 5 seconds between trials, jittered between 4 and 6 seconds in steps of 0.5 seconds.

To investigate what the effect of expected spatial information was on encoding processes in the brain, the experiment was divided into blocks, informing participants about the type of spatial cues that was most likely to be available during the retrieval phase of trials. At the start of each block, participants were informed about the upcoming block type, stating either "objects block" or "shadow block," which remained on the screen until participants pressed a button to continue. Within each block, 70% of the ten experimental trials were expected (in accordance with the block type); the other three trials were unexpected, meaning that the unexpected spatial information was available during retrieval. Additionally, each block contained four "no memory" baseline trials, in which the target was still visible during the retrieval phase. The visually available spatial cues during retrieval in these trials matched the block type to strengthen the perception of the validity of the block types. In addition to the block instructions, at the start of each trial, participants were informed about which of the columns available during encoding would also be available during retrieval using a color cue. This cue was presented for 1 second, followed by a blank screen for 1 second, after which the encoding phase started. In objects trials, this cue informed about the identity of one of the two columns available during retrieval. In shadow trials, this cue informed about the single column with directional information that would later be available during retrieval. This was done to make the two trial types more equal in difficulty. Without these cues, in shadow trials, participants would have to remember directional information

on top of all column locations. This would render the memory requirements in objects trials a subset of those in shadow trials, thereby hampering the ability to distinguish between encoding processes for trial types in the brain. In baseline trials, the words "no memory" were presented instead of the cue at the beginning of the trial, informing participants that the target would be available during retrieval.

Before the sessions in the scanner, participants received training in the task. Before the training commenced, the task was explained on a laptop screen and several trials were performed until participants were familiar with the controls. Next, participants performed four training blocks inside a dummy MR scanner. This scanner resembles a real MR scanner but lacks the magnetic field and loud noise. This allowed participants to become proficient in performing the task in very similar circumstances as in the scanner. Four training blocks were administered, alternating between objects and shadow blocks. This alternation was continued in the real scanner sessions, with the first block type counterbalanced over subjects. The instructions combined with the training session lasted approximately 40 minutes. The scanning session was divided into two runs, each of which contained five blocks. This added up to 35 expected objects trials, 35 expected shadow trials, 15 unexpected objects trials, 15 unexpected shadow trials, 20 baseline objects trials, and 20 baseline shadow trials. In each trial, we recorded the absolute distance error (the distance in virtual meters between the target location and the response location indicated by the participant) as performance measure. Furthermore, duration (time in seconds it took participants to finish an encoding or retrieval phase), speed of movement (defined as the average traversed virtual meters per second), the signed rotation (the cumulative sum of angular rotations, with left rotations having a negative sign and right rotations a positive sign), and unsigned rotation (cumulative sum of angular rotations in both directions, representing the total amount of rotation).

Imaging Parameters

The data were acquired on a Siemens 3 Tesla MAGNETOM Trio MRI scanner (Siemens Medical system, Erlangen, Germany) using a 32-channel coil. A multi-echo echo-planar imaging (EPI) sequence was used to acquire 31 axial slices per functional volume (voxel size = 3 × 3 × 3 mm; repetition time (TR) = 2390 ms; TE = 9.4 ms, 21.2 ms, 33 ms, 45 ms, and 57 ms; flip angle = 90; field of view = 212 mm). This type of parallel acquisition sequence for functional images reduces motion and susceptibility artifacts (Poser et al., 2006). After the acquisition of functional images, a high-resolution anatomical scan was acquired (T1-weighted MPRAGE, voxel size = 1 × 1 × 1 mm, TR = 2300 ms, TE = 3.03 ms, 192 sagittal slices, 1 mm thick, FoV = 256 mm), accelerated with GRAPPA parallel imaging (Griswold et al., 2002).

Statistical Analysis

We analyzed average distance error, average time to complete encoding phases, and average time to complete retrieval phases as behavioral measures within 2 × 2 × 2 ANOVAs. For average distance error and average time to complete retrieval phases, this model contained the between-subject factor gender and two within-subject factors: cues available at retrieval (objects vs. shadow) and expectancy (expected vs. unexpected). For average time to complete the encoding phase of trials, the within-subject factors in the model were block type (objects vs. shadow) and expectancy (expected vs. unexpected).

The fMRI data were preprocessed and analyzed using SPM8 (www.fil.ion.ucl.ac.uk/spm). The first four images of each session were discarded to allow for T_1 equilibration. Then, the five echoes of the remaining images were realigned to correct for motion artifacts (estimation of the realignment parameters is done for the first echo and then copied to the other echoes). The weighting of echoes for this combination was calculated based on 26 volumes acquired before the actual experiment started and was dependent on the measure differential contrast to noise ratio (Poser et al., 2006). Data were subsequently spatially normalized and transformed into Montreal Neurological Institute space (resampled at voxel size 2 × 2 × 2 mm^3), as defined by the SPM8 EPI.nii template. Finally, the functional scans were spatially smoothed using a 3D isotropic Gaussian smoothing kernel (FWHM = 8 mm).

Statistical analyses were performed in the context of the general linear model. The time series of each condition (expected objects encoding, expected shadow encoding, no memory encoding in objects blocks, no memory encoding in shadow blocks, expected objects retrieval, expected shadow retrieval, unexpected objects retrieval, unexpected shadow retrieval, no memory retrieval in objects blocks, no memory retrieval in shadow blocks) was convolved with a canonical hemodynamic response function (HRF) and used as a regressor in the SPM first-level model. To account for trial-by-trial differences in movement in the VE (speed of movement, signed and unsigned rotation), we modeled these effects over all trials in a run. To this end, a model was created per run for each subject, collapsing all encoding and retrieval trials into a single condition. For each trial in this model, the average speed, signed and unsigned rotation were modeled as parametric modulators. These were convolved with the HRF and the resulting three parametric modulation regressors were included in the first-level statistical models per run. Events were time-locked when the subjects first entered the environment in the encoding and retrieval phase of each trial and were modeled for the entire period in that phase. Block instructions, trial cues, and missed trials were also modeled. In addition, six realignment parameters were entered as effects of no interest. Statistical analysis included high-pass filtering (cutoff, 128 seconds) to remove low-frequency confounds such as scanner drifts and correction for serial correlations using an autoregressive AR(1) model.

To compare brain activity during encoding when expecting to have to rely on positional cues (in objects blocks) with that when expecting a single positional and a directional cue (in shadow blocks), we created linear contrasts of encoding in expected objects trials minus encoding in expected shadow trials, which were entered into a one-sample *t*-test on the second

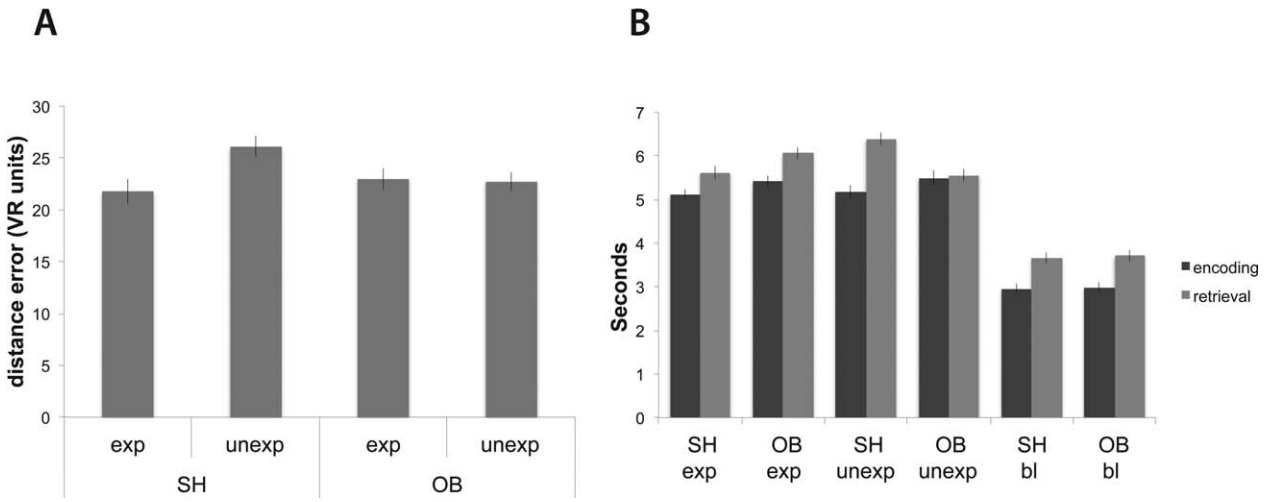

FIGURE 2. Behavioral performance. (A) Absolute distance error (the distance in virtual meters between the target location and the response location indicated by the participant) for expected and unexpected shadow and objects trials. (B) Time to finish encoding and retrieval phases for shadow and objects trials for expected, unexpected and baseline trials. OB = objects, SH = shadow, exp = expected, unexp = unexpected, bl = baseline.

level. To compare brain activity during retrieval, the activity during experimental conditions was compared against the corresponding baseline condition on the first level. These contrast images were subsequently entered into paired *t*-tests to compare activations between experimental conditions. Because we observed main effects of gender in our behavioral analysis, we added gender as a covariate of no interest in our second-level main effect models.

To assess the brain regions that correlated with performance on a trial-by-trial basis, we added regressors in which the HRFs for each trial within each experimental condition was parametrically modulated by the absolute distance error on that trial. These regressors were created separately for the encoding and retrieval phases of each condition (expected objects, unexpected objects, expected shadow, unexpected shadow), similar to previous studies (Wolbers et al., 2007; Baumann et al., 2010). These effects were tested by entering the first-level linear contrast estimates in second-level one-sample *t*-tests. In the whole brain search, the results of the random effects analyses were thresholded at $P < 0.001$ (uncorrected) and statistical inference was performed at the cluster level ($P < 0.05$), correcting for multiple comparisons over the search volume (the whole brain). Next to regions that predicted within-subject performance within a condition, we also looked at regions that predicted between-subject performance within our experimental conditions. To investigate these effects, we performed second-level multiple regression analyses on the contrast estimates for the encoding and retrieval phases for each experimental condition. The average distance error for the condition being modeled was entered for each subject as covariate of interest to investigate which regions were predictive of low or high performance. Given the performance difference between males and females, we did not include gender as a covariate of interest in this model.

Based on previous literature focusing on object-based active spatial navigation (Iaria et al., 2003; Janzen and van Turennout, 2004; Doeller et al., 2008; Baumann et al., 2010; Wegman and Janzen, 2011), we targeted the hippocampus, parahippocampal gyrus, and caudate nucleus as regions of interest (ROIs). We created masks for each hemisphere in these regions based on the automated anatomical labeling library (Tzourio-Mazoyer et al., 2002). For all ROI analyses, an intensity threshold necessary to determine the cluster-level threshold was set at $P < 0.001$, uncorrected. Statistical inference ($P < 0.05$) was performed at the cluster level, correcting for multiple comparisons over the search volume using small volume correction, which corrects for a reduced search region based on the size of the region under investigation.

RESULTS

Behavioral Results

We analyzed the behavioral data with $2 \times 2 \times 2$ ANOVAs (see Methods). The results for our performance measure, average distance error, are presented in Figure 2A. The average distance error was higher for females than for males ($F(1,45) = 24.2$, $P < 0.001$). We also observed a main effect of expectancy ($F(1,45) = 5.29$, $P = 0.026$), showing that participants performed worse on unexpected trials. The main effect of the cue available during retrieval was not significant ($F(1,45) = 0.8$, $P = 0.376$). An interaction effect between the

TABLE 1.

Brain Regions Showing Significant Activations Compared to Corresponding Baseline Conditions

Contrast	Region	*k*	*x*	*y*	*z*	Peak *t* score
encoding objects > baseline	bil inf/mid occipital gyrus, inf/sup parietal cortex, precuneus, post cingulate, RSC, inf temporal cortex, fusiform gyrus, medial frontal cortex, SMA, middle frontal gyrus, caudate nucleus, thalamus, R hippocampus, R parahippocampal gyrus	34140***	32	−70	32	11.58^^
	l Cerebellum	269*	−8	−54	−20	4.59
	r Hippocampus	14+	38	−34	−10	4.34^
	r Parahippocampal gyrus	27+	36	−38	−18	4.5^
encoding shadows > baseline						
	bil inf/mid occipital gyrus, inf/sup parietal cortex, precuneus, post cingulate, RSC, inf temporal cortex, fusiform gyrus, medial frontal cortex, SMA, middle frontal gyrus, caudate nucleus, thalamus	25946***	−10	−60	48	9.95^^
	r Middle frontal gyrus	353*	50	32	32	4.96
retrieval expected objects > baseline						
	bil precuneus, inf/sup parietal cortex, middle occipital gyrus, posterior cingulate, R supramarginal gyrus	10103***	2	−62	52	16^^
	r Mid/sup frontal gyrus	6295***	20	4	56	15.42^^
	r Mid/inf frontal gyrus	627***	46	30	32	6.97^^
	r Insula	246*	−32	22	−2	6.06^^
	l Middle frontal gyrus	313*	−28	52	12	4.98
	r Caudate nucleus	174+	18	4	22	7.7^
	l Caudate nucleus	150+	−16	−2	24	6.56^
retrieval expected shadows > baseline						
	bil precuneus, inf/sup parietal cortex, middle occipital gyrus, posterior cingulate, R angular gyrus	7392***	6	−68	58	12.94^^
	r Mid/sup frontal gyrus	828***	28	2	58	9.26^^
	l Mid/sup frontal gyrus	2292***	−23	2	54	7.22^^
	r Mid frontal gyrus	341**	46	36	32	5.74^^
	r Thalamus/caudate nucleus	424**	24	−30	12	5.69^^
	r Insula/inf Orbitofrontal	215*	28	28	−2	5.46^^
	l Insula	230*	−32	22	0	5.29
	r Caudate nucleus	100+	18	−18	20	4.84^
	l Caudate nucleus	64+	−18	4	24	4.73^

***$P < 0.001$ at the cluster level, **$P < 0.01$ at the cluster level, *$P < 0.05$ at the cluster level, +$P < 0.05$ small volume corrected, ^^$P < 0.05$ FWE-corrected for the whole brain at the voxel level, ^$P < 0.05$ FWE-corrected within the ROI at the voxel level.

cue available during retrieval and expectancy was also observed ($F(1,45) = 12.98$, $P < 0.01$). This interaction reflects a significantly higher error for unexpected shadow trials than for expected shadow trials ($t_{46} = 3.286$, $P < 0.002$), whereas the difference between unexpected objects trials is not significantly different from expected objects trials ($t_{46} = 0.353$, $P = 0.726$). All other interactions were not significant (all $P > 0.1$).

The times to complete the encoding phases of trials are presented in Figure 2B. The analysis revealed a main effect of gender ($F(1,45) = 4.958$, $P = 0.031$), where females ($M = 4.919$ s, SE = 0.215 s) completed the encoding phases faster than males ($M = 5.529$ s, SE = 0.17 s) did. A main effect of block was also observed ($F(1,45) = 11.108$, $P = 0.002$), where participants completed encoding phases in shadow blocks ($M = 5.088$ s, SE = 0.138) faster than in objects blocks ($M = 5.36$ s, SE = 0.148 s). No other main effects or interactions were observed in the time it took participants to complete the encoding phase of trials.

The times to complete the retrieval phases of trial are presented in Figure 2B. An ANOVA for the time it took participants to complete the retrieval parts of trials revealed a main effect of cue ($F(1,45) = 46.814$, $P < 0.001$), where objects trials ($M = 6.225$ s, SE = 0.138 s) were completed slower than shadow trials ($M = 5.642$ s, SE = 0.145 s). An interaction between gender and cue available during retrieval was significant ($F(1,45) = 8.956$, $P = 0.004$). Exploring this interaction further,

TABLE 2.

Brain Regions Showing Significant Activations in Expected Encoding Contrasts

Contrast	Region	*k*	*x*	*y*	*z*	Peak *t* score
Encoding: expected objects > expected shadow	Left superior occipital cortex	273**	−12	−100	22	5.81^^
	Left hippocampus	51+	−32	−40	−2	5.41^
	Right hippocampus	11+	36	−30	−8	3.61
Encoding: expected shadow > expected objects	Bilateral middle/anterior cingulate cortex	302**	0	10	30	5.12
	Bilateral thalamus/caudate nucleus	433***	−8	−16	18	4.94
	Right insula/inferior frontal gyrus	294**	30	22	4	4.64
	Right caudate nucleus	64+	10	12	14	4.72^
	Left caudate nucleus	10+	−12	−8	16	3.61

***$P < 0.001$ at the cluster level, **$P < 0.01$ at the cluster level, *$P < 0.05$ at the cluster level, +$P < 0.05$ small volume corrected, ^^$P < 0.05$ FWE-corrected for the whole brain at the voxel level, ^$P < 0.05$ FWE-corrected within the ROI at the voxel level.

we found that both males and females took longer to finish retrieval parts in objects trials, but that this effect was stronger for males (t_{28}=7.80, $P < 0.001$) than for females ($t_{17} = 2.53$, $P = 0.022$). A significant interaction between cue and expectancy was also observed ($F(1,45) = 13.958$, $P = 0.001$). Within the objects trials, unexpected trials were completed slower than expected trials ($t_{46} = 3.828$, $P < 0.001$), whereas this effect was not observed within the shadow trials ($t_{46} = -0.513$, $P = 0.61$).

Neuroimaging Results

General Effects of Encoding and Retrieval

First, we compared activity during experimental trials with activity during the corresponding baseline conditions. For the objects encoding trials, we observed whole-brain significant activations in clusters in the occipital, parietal, temporal, and frontal lobes, as well as the caudate nucleus and the thalamus (Table 1, Supporting Figure S1A). In our ROIs, we found significant clusters in the right hippocampus and the right parahippocampal gyrus. For the shadow encoding trials, the observed whole-brain significant activations were very similar to those observed during objects encoding trials (Table 1, Supporting Figure S1A). For expected objects retrieval trials versus baseline, whole-brain significant activations were found in clusters extending to parietal, occipital, and frontal lobes. In our ROIs, we observed significant activations in the left and right caudate nucleus (Table 1, Supporting Figure S1B). When comparing expected shadow retrieval trials to the corresponding baseline, we found similar activations in parietal, occipital, and frontal lobes as well as in the thalamus/caudate nucleus. In our ROIs, we observed significant activations in the left and right caudate nucleus (Table 1, Supporting Figure S1B).

Effects of Spatial Cues

To investigate which regions contributed to encoding the target location based on expected information to be available during retrieval, we directly compared brain responses during encoding phases of trials in object blocks with that of trials in shadow blocks. This comparison revealed significant activations in left superior occipital gyrus and bilateral hippocampus (see Table 2, Fig. 3B). A contrast between encoding phases of trials in shadow blocks with that in object blocks revealed stronger activation in bilateral middle/anterior cingulate cortex, bilateral thalamus, bilateral caudate nucleus, and the right insula/IFG (Table 2, Fig. 3A).

To reveal brain activity related to retrieving spatial locations based on different spatial cues, we first compared trials in which the expected information was present. Comparing expected retrieval parts of objects trials with that of shadow trials revealed bilateral precuneus extending into right inferior/superior parietal lobule and angular gyrus, left inferior/superior parietal lobule and angular gyrus, right middle/inferior frontal gyrus, left interior frontal/precentral gyrus, and a region spanning left middle and superior frontal gyrus (Table 3, Fig. 4B). This contrast showed no significant activation in bilateral hippocampus, as was seen during encoding. The contrast comparing expected retrieval parts of shadow trials with that of objects trials revealed bilateral insula/operculum, bilateral central regions including precentral and postcentral gyrus, medial prefrontal cortex (mPFC)/anterior cingulate cortex, as well as bilateral visual regions (Table 3, Fig. 4A). The corresponding encoding contrast also activates bilateral insula, but the insular regions activated during retrieval are more posterior (Table 3, Fig. 4A). The observed caudate activation during encoding was not observed during retrieval.

Effects of Expectancy

To investigate how the brain deals with unexpected spatial cues during retrieval, we compared the unexpected retrieval conditions with the corresponding expected retrieval conditions. Unexpected objects trials compared to expected objects trials activated clusters in the left superior frontal gyrus (Table 4). Expected compared to unexpected objects trials did not reveal any significant activations. Comparing unexpected to expected shadow retrieval trials revealed numerous clusters in the

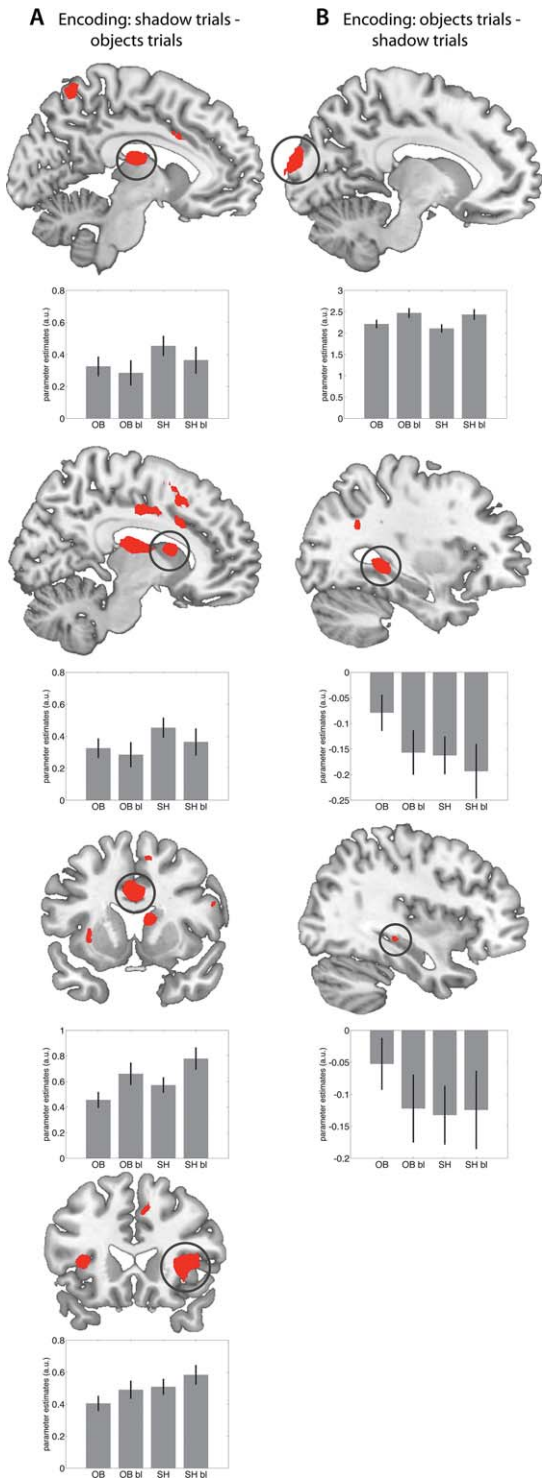

FIGURE 3. Direct comparisons between encoding in objects and shadow blocks. (A) Regions activated more strongly during encoding of shadow trials compared to objects trials. (B) Regions activated more strongly during encoding of objects trials compared to shadow trials. Graphs indicate parameter estimates for experimental and corresponding baseline conditions. Bars represent means (±SEM). OB = objects, SH = shadow, bl = baseline. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

following regions: middle occipital cortex, inferior parietal cortex, inferior/middle/superior frontal gyrus, middle cingulum, precuneus, inferior/middle temporal cortex, orbitofrontal cortex, and temporal pole. When comparing expected to unexpected shadow trials, a cluster overlapping with the right putamen, the pallidum and the caudate nucleus was activated (Table 4).

Effects of Spatial Cues during Unexpected Trials

We also compared the effect of available spatial cues during unexpected retrieval conditions by comparing the unexpected retrieval conditions with each other. When comparing unexpected objects retrieval periods (when shadow cues were expected to be available) with unexpected shadow retrieval periods, we found the precuneus activated. The bilateral caudate nucleus was activated as well, unlike in expected objects retrieval (Table 5, Fig. 5B). Stronger activation during unexpected shadow retrieval compared to unexpected objects retrieval revealed the left insula/operculum, which was also activated in the expected shadow contrast. Additionally, the left occipital gyrus and the mPFC/anterior cingulate gyrus were activated, both of which were also observed in the expected shadow contrast (Table 5, Fig. 5A).

Interaction Effects of Spatial Cues and Expectancy

Apart from the main effects of spatial cues and expectancy during retrieval trials, we investigated the interaction between the two factors. Comparing the effect of expectancy (unexpected–expected trials) during objects trials with the expectancy effect during shadow trials, the left and right caudate nuclei were activated within our ROIs (Table 6, Fig. 6B). The expectancy effect in shadow trials was stronger than for objects in the right angular gyrus and the precuneus (Table 6, Fig. 6A).

Effects of Performance

When we investigated activation predicting within-subject performance, we found an inconsistent pattern of regions. In some conditions, errors between trials were positively or negatively predicted by activity in several central, parietal, occipital, and cerebellar regions, the right angular gyrus and a small cluster in the left caudate nucleus (Supporting Table S1).

When we investigated between-subject activation that predicted performance, we found a cluster in the right hippocampus for which the activation significantly correlated with performance on that condition for encoding of expected objects trials and expected shadow trials and retrieval of expected shadow trials. Retrieval for expected objects trials showed a trend in the right hippocampus (Table 7, Fig. 7). However, only the association between performance and right hippocampal activation during encoding of expected objects trials showed a significantly stronger association than that between performance and activation in the observed right hippocampal cluster during the corresponding baseline condition (Table 7). No

TABLE 3.

Brain Regions Showing Significant Activations in Expected Retrieval Contrasts

Contrast	Region	*k*	*x*	*y*	*z*	Peak *t* score
Retrieval: expected objects > expected shadows	Bilateral precuneus/right inf/sup parietal lobule/angular gyrus	3715***	2	−60	42	9.41^^
	Right middle/inferior frontal gyrus	1280***	50	26	32	6.12^^
	Left inf frontal/precentral gyrus	1009***	−34	−62	38	5.62^^
	Left inf/sup parietal lobule/angular gyrus	1609***	−38	−64	36	5.61^^
	Left middle/superior frontal gyrus	378**	−28	62	8	4.35
Retrieval: expected shadows > expected objects	Right inf occipital/temporal gyrus	946***	−36	−90	−4	5.57^^
	Right postcentral/supramarginal gyrus	310**	58	−16	34	4.84
	Left precentral/postcentral gyrus	239*	−30	−40	66	4.54
	Left inf occipital/temporal gyrus	1006***	44	−70	−8	4.53
	Right insula/operculum	437**	40	6	0	4.35
	Medial PFC/anterior cingulate gyrus	271*	2	46	14	4.3
	Left insula/operculum/postcentral gyrus	454**	−60	−16	24	4.2

***$P < 0.001$ at the cluster level, **$P < 0.01$ at the cluster level, *$P < 0.05$ at the cluster level, +$P < 0.05$ small volume corrected, ^^$P < 0.05$ FWE-corrected for the whole brain at the voxel level, ^$P < 0.05$ FWE-corrected within the ROI at the voxel level.

regions were found in all encoding and retrieval contrasts that predicted within-subject performance effects.

Effects of Strategy and Spatial Cue Bias

The effects of the factors mentioned above could also interact. For instance, participants could adopt different strategies to solve the task at hand. Given that the block instructions are only informative for 70% of trials, a participant who wants to be perfect on the task could always try to remember all spatial cues. On the contrary, participants that adapt their strategy according to the block instructions will be significantly impaired in unexpected trials. To look into this we computed a switch cost value, which was defined as the degree to which they adapted their strategy according to the block instructions. Additionally, because of a strategy or implicit preference, participants might exhibit a bias toward one of the spatial cue types. Therefore, a measure of bias toward local or global trials was defined as the difference between expected trials in global and local blocks. This can be thought of as being independent of switch cost, because regardless of whether participants switched or not according to block instructions, this difference expresses how well participants performed in expected trials of the different block types. To investigate these effects on the neural level, we divided participants according to these factors into four groups. When comparing encoding of expected objects trials versus baseline, we did not observe differences between the groups. For expected shadow trials versus baseline, we observed a difference between groups with a shadow and those with an objects bias in the right frontal gyrus and in our ROIs in the left hippocampus and the right parahippocampal gyrus. In the comparison between encoding of expected objects trials and expected shadow trials, we observed effects in the right inferior temporal lobe and the right hippocampus, which were both more activated in high compared to low switchers. In the retrieval contrasts for both expected objects and shadow trials versus baseline, we did not observe significant group differences, neither in the direct comparison between expected objects and shadow trials. However, when comparing retrieval during unexpected objects trials versus retrieval during unexpected shadow trials, we found that people with a shadow bias activated the right middle cingulum more than people with an objects bias. For the same contrast, we found a positive switching*spatial cue bias interaction in the right caudate nucleus. See Supporting Information (Supporting Materials & Methods and Supporting Table S2) for more information on this division and results. In summary, although we observed some differences in neural activation between these groups of participants, the effects on the neural processes under investigation were small.

DISCUSSION

In the present event-related fMRI study, we used an allocentric WM task to determine the brain structures involved in encoding and retrieving location information based on different object-based spatial cues. During encoding phases of trials, participants learned a target location in the presence of three landmarks (positional cues). From each of the landmarks, a shadow was cast on the ground (directional cues). During subsequent retrieval, only two landmarks (objects trial) or one landmark with a shadow (shadow trial) were available and participants had to replace the target. Participants were informed in blocks about which type of retrieval trial was most likely to occur, thereby modulating expectations of having to rely on a single landmark or on a configuration of landmarks.

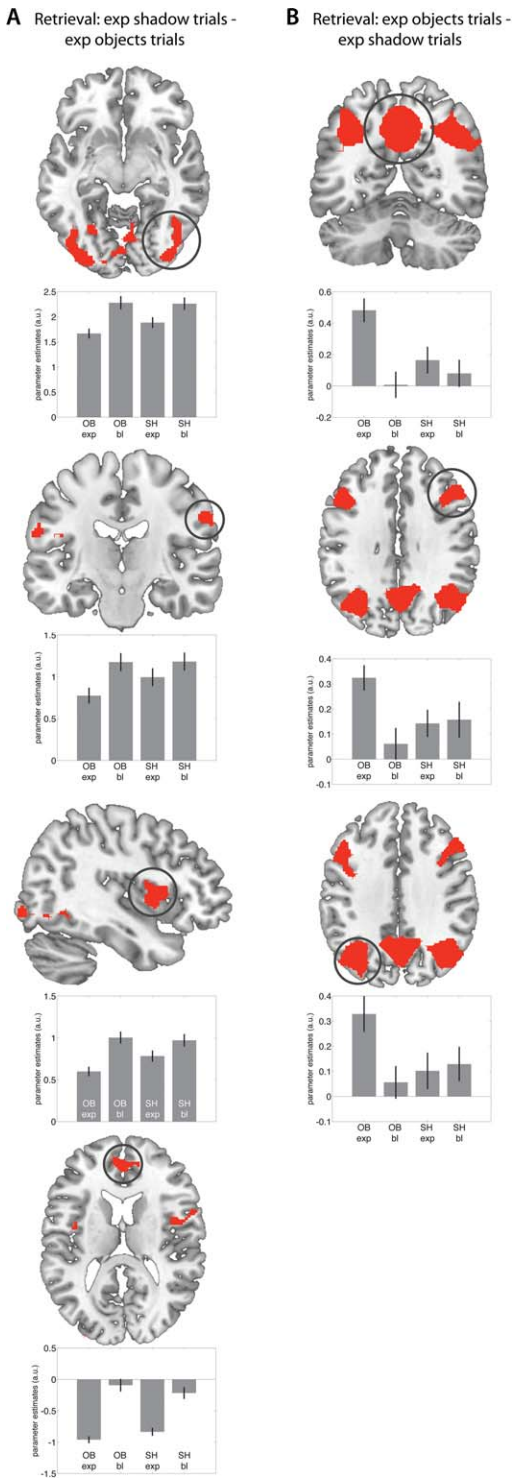

FIGURE 4. Comparisons between retrieval in expected objects and shadow blocks. (A) Regions activated more strongly during retrieval of expected shadow trials compared to expected objects trials. (B) Regions activated more strongly during expected retrieval of objects trials compared to expected shadow trials. Graphs indicate parameter estimates for experimental and corresponding baseline conditions. Bars represent means (±SEM). OB = objects, SH = shadow, exp = expected, bl = baseline. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Effects of Spatial Cues

Effects of Spatial Cues in the Hippocampus and Caudate Nucleus

The bilateral hippocampus was involved in encoding of objects trials, that is, when participants expected a configuration of landmarks. The hippocampus is well established in the literature on allocentric representations for navigation (O'Keefe and Nadel, 1978; Hartley et al., 2003; Iaria et al., 2003; Doeller et al., 2008). Place cells in the rat as well as in the human hippocampus represent the location of an animal or person within an environment (O'Keefe and Nadel, 1978; Ekstrom et al., 2003). Landmarks can influence place cell firing when they are close to the perceived background or seen as distal landmarks (see Jeffery, 2007, for a review). In contrast, place cell firing is not controlled by a configuration of proximal objects within an environment (Cressant et al., 1997). Human behavioral studies have suggested that configurations of objects can serve as an allocentric frame of reference (Mou et al., 2006; Li et al., 2012; Mou and Zhou, 2012). Nevertheless, encoding relative to geometric boundaries seems to be superior to encoding relative to landmarks (Cheng and Newcombe, 2005). For instance, encoding of geometric boundaries normally overshadows encoding relative to landmarks when both are available during encoding. As a result, larger errors are made when the boundaries are missing during retrieval compared to when the landmarks are missing (Doeller and Burgess, 2008). However, with an increasing number of landmarks, the boundary superiority effect disappeared (Mou and Zhou, 2012). These findings suggest that landmark configurations can serve as a geometry similar to boundaries. Hippocampal place fields have been found that were determined by the distance to a boundary in an allocentric direction (O'Keefe and Burgess, 1996). It has been proposed that the hippocampus is provided with information about distances and angles to extended surfaces by so-called boundary vector cells (BVCs; O'Keefe and Burgess, 1996; Hartley et al., 2000). The BVC model predicts that inputs from these cells are necessary for stable place cell firing, which was supported by findings in rodents by Barry et al. (2006). Support for the BVC model in humans comes from an fMRI study showing increased hippocampal activity with an increased number of imagined boundaries (Bird et al., 2010). In that study, five objects were to be imagined either horizontally, functioning as boundaries, or vertically, functioning as landmarks. The increased hippocampal activation with more boundaries was therefore simultaneously a decrease with the number of imagined landmarks. A possible explanation for this observation is that boundaries (here lying objects) provide a clearer geometry than vertical objects that function as landmarks. Another explanation would be that lying objects simply provide more reference points (in the horizontal plane) than vertical objects (landmarks). A very recent study provides support for this possibility, by showing the existence of landmark vector cells in the hippocampus; place cells that showed a functional equivalence to boundary cells for landmarks, responding

TABLE 4.

Brain Regions Showing Significant Activations in Unexpected Compared to Expected Retrieval Contrasts

Contrast	Region	*k*	*x*	*y*	*z*	Peak *t* score
Retrieval in unexpected objects trials > expected objects trials	Left superior frontal gyrus	344**	−16	60	14	4.54
	Left superior frontal gyrus	215*	−20	38	44	4.33
Retrieval in expected objects trials > unexpected objects trials	no significant clusters					
Retrieval in unexpected shadow trials > expected shadow trials	Right middle occipital gyrus	2477***	48	−66	28	7.66^^
	Left inferior parietal cortex	2182***	−34	−76	50	7.4^^
	Bilateral superior frontal gyrus/anterior cingulate cortex/middle cingulum/orbitofrontal cortex	7391***	30	64	10	7.32^^
	Bilateral precuneus/posterior cingulate cortex	4146***	8	−62	34	7.16^^
	Right inferior/middle temporal cortex	1217***	54	−28	−12	6.47^^
	Right inferior orbitofrontal cortex/superior temporal pole	353**	34	20	−26	5.79^^
	Left inferior/middle/superior frontal cortex	1443***	−50	22	40	5.7^^
	Left inferior orbitofrontal cortex/superior temporal pole	248*	−34	20	−20	5.19
	Left inferior/middle temporal cortex	739***	−62	−34	−10	5
Retrieval in expected shadow trials > unexpected shadow trials	Right putamen/pallidum/caudate	145*	20	8	−2	4.48

***$P < 0.001$ at the cluster level, **$P < 0.01$ at the cluster level, *$P < 0.05$ at the cluster level, +$P < 0.05$ small volume corrected, ^^$P < 0.05$ FWE-corrected for the whole brain at the voxel level, ^$P < 0.05$ FWE-corrected within the ROI at the voxel level.

to a point rather than a line in horizontal space (Deshmukh and Knierim, 2013). Therefore, regardless of whether participants in our study imagined boundaries, the observed hippocampal activation most likely reflects encoding a geometry formed by the configuration of objects, which is qualitatively different from encoding locations relative to single landmarks in the caudate nucleus.

The stronger activation of the hippocampus in objects trials than in shadow trials could simply be related to the number of object locations that have to be kept in WM. Participants could focus on only a single landmark during shadow encoding trials, ignoring the others. Arguing against this possibility, we did not observe a statistically significant performance difference between expected and unexpected objects trials. This indicates that, when expecting a shadow retrieval trial, participants also encoded the positions of all landmarks at least to the degree to be able to use them for reorientation. Furthermore, a recent meta-analysis (Rottschy et al., 2012) did not reveal WM load-dependent effects in the hippocampus. In a VE study in which object locations had to be tracked in an egocentric way, the hippocampus also did not show increased activity with an increased number of object locations to be tracked in WM (Wolbers et al., 2008). Combined, it is unlikely that the observed effects in the hippocampus are due to WM load.

TABLE 5.

Brain Regions Showing Significant Activations in Unexpected Retrieval Contrasts

Contrast	Region	*k*	*x*	*y*	*z*	Peak *t* score
Retrieval: unexpected objects > unexpected shadows	Bilateral precuneus	702***	−4	−56	46	5.69^^
	Left caudate nucleus	35+	−14	2	16	3.94^
	Right caudate nucleus	14+	14	14	10	3.77^
Retrieval: unexpected shadows > unexpected objects	Left operculum/insula	417**	−38	−26	24	5.81^^
	Left occipital gyrus	341**	−36	−90	−4	5.05
	medial PFC/anterior cingulate gyrus	1033***	12	50	12	4.68

***$P < 0.001$ at the cluster level, **$P < 0.01$ at the cluster level, *$P < 0.05$ at the cluster level, +$P < 0.05$ small volume corrected, ^^$P < 0.05$ FWE-corrected for the whole brain at the voxel level, ^$P < 0.05$ FWE-corrected within the ROI at the voxel level.

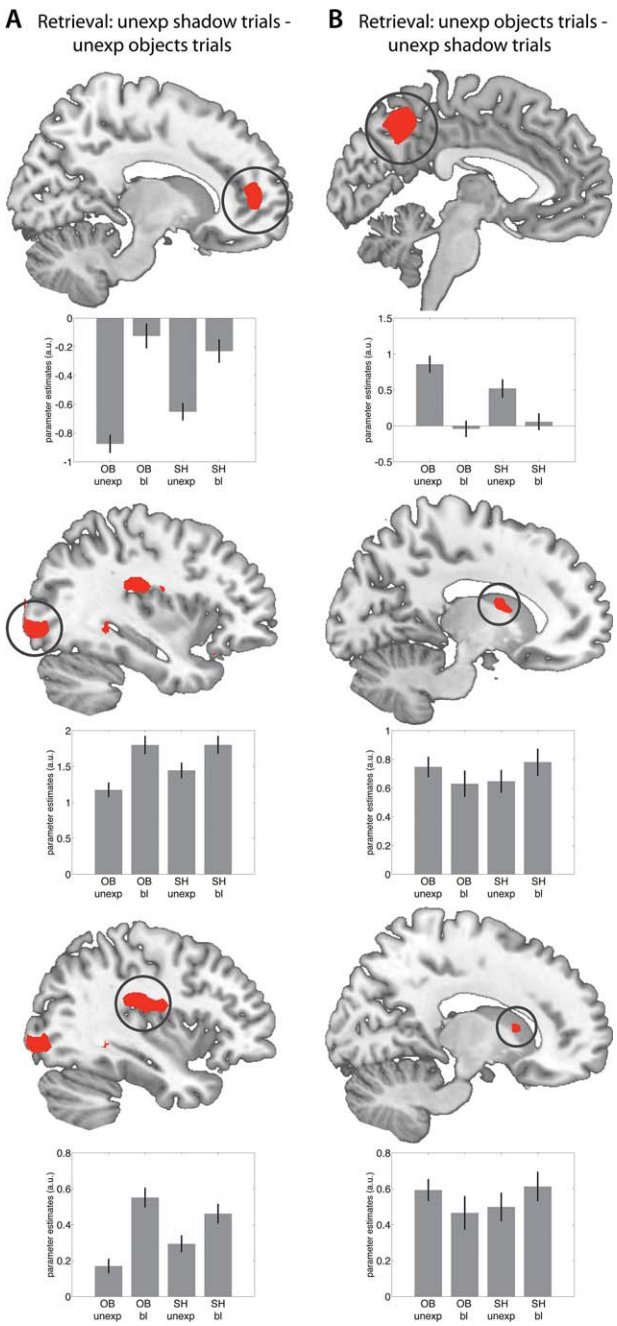

FIGURE 5. Comparisons between retrieval in unexpected objects and shadow blocks. (A) Regions activated more strongly during retrieval of unexpected shadow trials compared to unexpected objects trials. (B) Regions activated more strongly during unexpected retrieval of objects trials compared to unexpected shadow trials. Graphs indicate parameter estimates for experimental and corresponding baseline conditions. Bars represent means (±SEM). OB = objects, SH = shadow, unexp = unexpected, bl = baseline. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

During expected encoding phases of shadow trials, participants expected to have only a single positional cue accompanied by directional information available during retrieval. Comparing the neural activation of this condition to when several positional cues were expected to be available (objects trials) resulted in bilateral caudate nucleus activation. Activation of the caudate nucleus when participants rely more on single objects is consistent with its role in stimulus-response mapping associated with landmarks, which was also observed in an allocentric task (e.g., to walk 50 m south of a column (Hartley et al., 2003; Doeller et al., 2008). Rodent research has shown caudate nucleus involvement when navigating using objects as beacons, that is, indicating a (nearby) target location (McDonald and White, 1994; Packard and McGaugh, 1996). This process is independent of the hippocampus, as a lesion in this area left this kind of learning intact (Pearce et al., 1998). In bounded environments, the BVC model and the vector sum model (Cheng, 1988, 1989), which assumes landmark-goal vectors encoding, can both explain behavioral findings when the boundaries are seen as landmarks. However, our results show that when only landmark objects are available, the neural systems underlying this encoding are different. Our results are therefore in line with an account in which the hippocampus represents multiple landmark locations as a geometry formed by their configuration, whereas the caudate stores separate landmark-goal vectors to a goal.

In contrast to our predictions, we did not observe differences in hippocampal or caudate nucleus involvement between expected objects and shadow trials during retrieval. Instead, the observed differential activation in parietal, central, and frontal (including insular) regions during expected retrieval trials seems to reflect reorientation processes rather than memory processes, as discussed below. In line with the findings of Baumann et al. (2010), the caudate nucleus was activated compared to baseline in both conditions, whereas the hippocampus was not. This shows that the caudate nucleus is involved to the same degree when retrieving based on a single expected landmark and when target-landmark vectors need to be computed from a memory representation of the landmark configuration.

Effects of Spatial Cues in the Rest of the Brain

Although we had no specific hypotheses regarding other brain regions involved in retrieving locations with respect to different spatial cues, we interpret the different activations during expected objects and shadow trials during retrieval as reflecting imagined rotation of objects in the environment and imagined updating one's own location. When we compared expected objects with expected shadow trials during retrieval, the bilateral precuneus, bilateral parietal cortex, and central and frontal regions were activated. Precuneus activation has been found for tasks in which perspective taking was required (Shelton and Gabrieli, 2002; Vogeley et al., 2004) and in imagining both rotations of one's own viewpoint as well as of objects in a scene (Lambrey et al., 2012). Furthermore, the precuneus, superior parietal lobe, and precentral regions activations overlap with a network that showed increased activation with more objects having to be tracked during self-motion in a VE (Wolbers et al., 2008). This suggests that allocentric retrieval of several positional cues during objects trials in this study

TABLE 6.

*Brain Regions Showing Significant Spatial Cue*Expectancy Interactions in Retrieval Contrasts*

Contrast	Region	k	x	y	z	Peak t score
Retrieval: Spatial cue*Expectancy interaction: (unexp − exp OB) − (unexp − exp SH)	R Caudate	77++	16	16	8	4.18^
	L Caudate	20+	−18	18	4	3.70^
Retrieval: Spatial cue*Expectancy interaction: (unexp − exp SH) − (unexp − exp OB)	R angular	970***	50	−64	28	5.1
	bil precuneus	247*	0	−58	38	4.31

***$P < 0.001$ at the cluster level, **$P < 0.01$ at the cluster level, *$P < 0.05$ at the cluster level, +$P < 0.05$ small volume corrected, ^^$P < 0.05$ FWE-corrected for the whole brain at the voxel level, ^$P < 0.05$ FWE-corrected within the ROI at the voxel level.

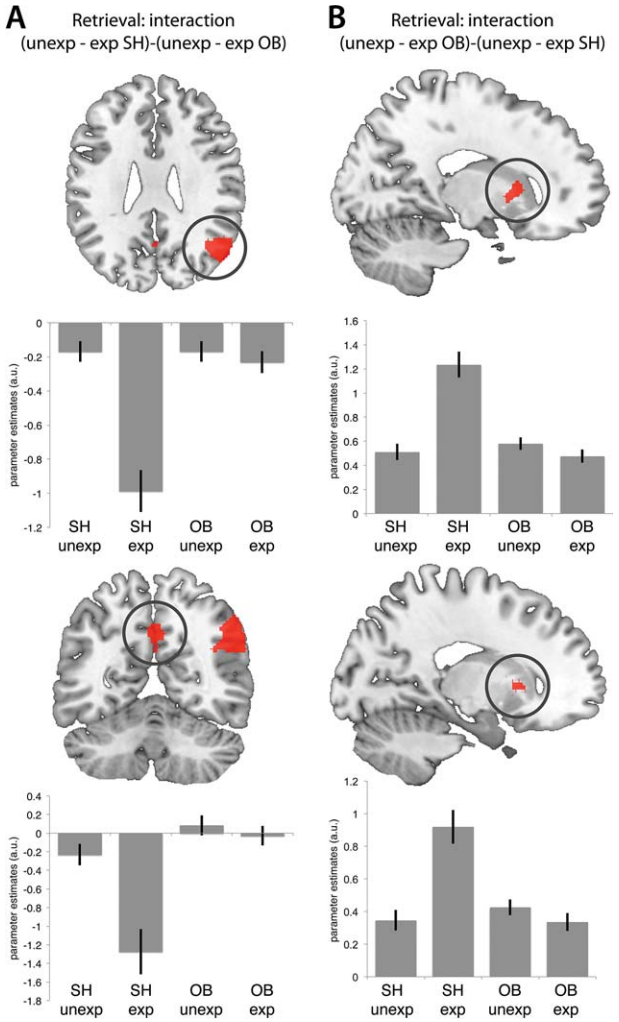

FIGURE 6. Interaction effects of spatial cues and expectancy during retrieval. (A) Regions activated more strongly in the interaction (unexpected–expected shadow trials)–(unexpected–expected objects trials). (B) Regions activated more strongly in the interaction (unexpected–expected objects trials)–(unexpected–expected shadow trials). Graphs indicate parameter estimates for experimental conditions. Bars represent means (±SEM). OB = objects, SH = shadow, unexp = unexpected, exp = expected. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

requires more imagined viewpoint movements than retrieval in the shadow trials does. The parietal activation we observed overlapped bilaterally with the intraparietal sulcus, which was found to be activated more strongly for the rotation of objects in an environment than the rotation of the self within that environment (Keehner et al., 2006; Lambrey et al., 2012). The activation of this region during retrieval, but not during encoding, therefore seems to reflect the imagined updation of object locations in the environment with respect to the viewer in order to reorient.

Comparing expected shadow encoding to expected objects encoding phases revealed activation in the right insula, middle cingulate cortex, and thalamus. The insula was found to be activated during mental navigation (Ghaëm et al., 1997), indicating the vestibular system's involvement in virtual movement. Furthermore, the insula activated stronger when precise spatial relations needed to maintained in memory compared to maintenance of more qualitative relations (van der Ham et al., 2009). The insula regions activated during both encoding and retrieval overlap with those found in Lambrey et al. (2012) for the contrast of imagined rotation of the self compared to imagined rotation of objects in the environment. Note that our interpretation of these activations can only reflect imagined updating, as our brain results are corrected for between-trial differences in movement in the VE. Therefore, although this interpretation is post hoc and speculative, the parietal findings for rotation of objects and insula findings for self-rotation in earlier studies nevertheless form a striking parallel with our retrieval results.

Effects of Spatial Cue-Expectancy

Although we did not have a specific hypothesis about the effects, we were interested in how expectancy and spatial cues interacted during retrieval. We found interaction effects in the caudate nucleus, the precuneus, and the angular gyrus. In contrast to the expected conditions during encoding, the caudate nucleus was not activated in the contrasts between the expected retrieval conditions. Instead, it seems that this region is less

TABLE 7.

Brain Regions Showing Between-Subject Correlations with Performance

Contrast	Region	*k*	*x*	*y*	*z*	Peak *t* score	Steiger's Z: experimental condition vs. corresponding baseline
Encoding: negative linear correlation with normal objects error during normal objects trials	Right hippocampus	11+	40	−18	−14	3.65^	−2.70 ($P = 0.007$)
Encoding: negative linear correlation with normal shadow error during normal shadow trials	Right hippocampus	9+	42	−20	−14	3.55^	−1.27 ($P = 0.204$)
Retrieval negative linear correlation with normal objects error during normal objects trials	Right hippocampus	4ns	42	−16	−16	3.45	−0.81 ($P = 0.417$)
Retrieval negative linear correlation with normal shadow error during normal shadow trials	Medial prefrontal cortex	259*	−14	42	0	5.11	
	Left cerebellum	363**	−20	−42	−26	4.34	
	Right hippocampus	12+	42	−18	−14	4.24^	−1.18 ($P = 0.237$)

***$P < 0.001$ at the cluster level, **$P < 0.01$ at the cluster level, *$P < 0.05$ at the cluster level, +$P \leq 0.05$ small volume corrected, ^^$P < 0.05$ FWE-corrected for the whole brain at the voxel level, ^$P < 0.05$ FWE-corrected within the ROI at the voxel level.

involved in unexpected shadow trials compared to the other retrieval conditions: it was activated less compared to unexpected objects trials and compared to expected shadow trials. Given our interpretation of the role of the caudate in storing separate landmark-goal vectors in a stimulus-response manner during encoding, these results suggest that this information is simply not available during the unexpected shadow trials, because it was not encoded.

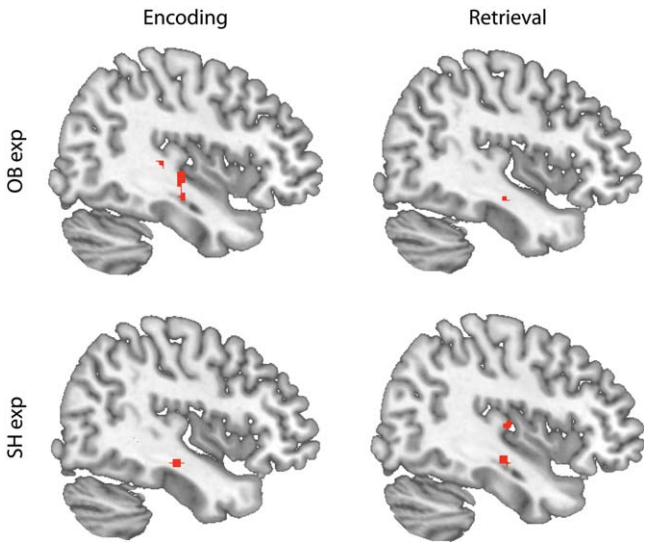

FIGURE 7. Between-subject performance-related areas in the right hippocampus predicting lower absolute distance error for encoding and retrieval phases in expected (exp) objects (OB) and shadow (SH) conditions. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

An interaction in the opposite direction was observed in the precuneus and angular gyrus. The precuneus was found to be involved when objects trials are expectedly or unexpectedly encountered: it was more activated in both expected and unexpected objects retrieval conditions compared to expected and unexpected shadows, respectively. Also, it was more invoked during unexpected compared to expected shadow trials. These results are in line with the abovementioned interpretation that the precuneus is involved in the imagined updating of stored object locations in the environment during memory retrieval.

Effects of Performance

Contrasting findings in previous navigation studies (Hartley et al., 2003; Baumann et al., 2010), we did not observe consistent regions that predicted within-subject performance over trials in any of our conditions. Our study differs from these virtual navigation studies in one important way. In our study, the type of cues and (in the case of objects trials) which specific cues would be available during retrieval was not completely certain. Therefore, encoding strategies that depend on the efficient reliance on specific brain regions, which would be successful in the real world, will often have failed in our experiment.

Between-subject performance was predicted by activation in the right hippocampus during the encoding phases of expected objects and shadow trials and during the retrieval of expected shadow trials. In contrast, while predicting better performance

during the retrieval phase of expected objects trials, we only observed a trend in a cluster in the right hippocampus. These findings are in line with previous studies that showed a between-subject correlation with better navigational performance in the hippocampus (Maguire et al., 1998; Hartley et al., 2003). However, in the right hippocampus, only the encoding of objects trials showed a significantly greater correlation with performance than did the corresponding baseline condition. This could indicate that the observed performance correlations in the right hippocampus in the other conditions might be explained by processes not specific to memory, such as effort. However, a previous study using the same task found correlations with better navigational performance in both the medial temporal lobe (parahippocampal gyrus) and striatum (caudate nucleus and putamen; Baumann et al., 2010). It might indeed be expected that, given the explicit shifting of reliance on different spatial cues in our task, the regions that show correlations with better task performance would be task-dependent. Nevertheless, given the uncertainty of the available spatial cues during retrieval, it might be that better navigators always rely on a cognitive map strategy, that is, depend on the hippocampal representation.

Summary

In summary, these results indicate that humans are able to flexibly encode location information based on expected spatial cues during retrieval. The hippocampus was involved in encoding when relying on the configurations of objects, whereas the caudate nucleus was involved when relying on a single landmark during encoding. Our findings are in line with an account where the hippocampus encodes geometries formed by configuration of landmarks, similar to processing boundaries. In contrast, the caudate nucleus stores separate landmark-goal vectors in a stimulus-response manner. During retrieval, regions associated with reorienting oneself relative to objects were activated when a single landmark was available. When two landmarks were available, regions associated with the mental rotation of objects relative to the self were activated. Finally, we found evidence for hippocampus activation predicting participant performance. By showing different involvement of striatal and hippocampal spatial memory systems during encoding, this study sheds light on how the brain deals with changing demands on spatial processing related purely to landmarks.

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