

# Parallel striatal and hippocampal systems for landmarks and boundaries in spatial memory

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**How the memory systems centered on the hippocampus and dorsal striatum interact to support behavior remains controversial. We used functional MRI while people learned the locations of objects by collecting and replacing them over multiple trials within a virtual environment comprising a landmark, a circular boundary, and distant cues for orientation. The relative location of landmark and boundary was occasionally changed, with specific objects paired with one or other cue, allowing dissociation of learning and performance relative to either cue. Right posterior hippocampal activation reflected learning and remembering of boundary-related locations, whereas right dorsal striatal activation reflected learning and remembering of landmark-related locations. Within the right hippocampus, anterior processing of environmental change (spatial novelty) was dissociated from posterior processing of location. Behavioral studies show that landmark-related learning obeys associative reinforcement, whereas boundary-related learning is incidental [Doeller CF, Burgess N (2008) *Proc Natl Acad Sci USA* 105:5909–5914]. The distinct incidental hippocampal processing of boundaries is suggestive of a “geometric module” or “cognitive map” and may explain the hippocampal support of incidental/observational learning in “declarative” or “episodic” memory versus the striatal support of trial-and-error learning in “procedural” memory. Finally, the hippocampal and striatal systems appear to combine “bottom-up,” simply influencing behavior proportional to their activations, without direct interaction, with “top-down” ventromedial prefrontal involvement when both are similarly active.**

cognitive map | functional MRI | incidental | learning | procedural

Memory is not a unitary process but rather consists of different systems relying on separate brain structures. Evidence for parallel “declarative,” “relational,” or “episodic” systems centered on the hippocampus and “procedural” systems centered on the dorsal striatum has been obtained in animals and humans (1–9). These systems are proposed to serve different functions: rapid acquisition of experience (supporting “episodic memory”) and slower cumulative trial-and-error acquisition of skills and habits, respectively (5, 9–12). Distinct processing by either system is seen particularly clearly in studies of spatial memory, with hippocampal-dependent learning of environmental layout (“place” or “locale” learning), and striatal-dependent learning of responses to individual stimuli (“response” or “taxon” learning) (2, 4, 13–15).

How these two systems act and interact to support learned behavior poses several important questions.

Do both systems simply learn over different time courses or is each biased to process specific types of stimuli? In the spatial domain, the rodent hippocampus has been identified with environment-centered representations of location, whereas the dorsal striatum has been associated with approach responses to a single landmark (2, 8, 13, 16–18). Consistent with this idea, the firing of hippocampal place cells is determined by the environmental boundary (19, 20) to a much greater extent than by discrete intramaze objects (21), whereas neuronal firing in the striatum reflects egocentric responses (22) and the stage of task (10).

How do the systems interact during learning? The hippocampal and striatal systems are often differentially involved in different

tasks (e.g., refs. 6 and 7), in different stages of the same task (initially hippocampal dependent, becoming striatal dependent with practice) (e.g., refs. 13 and 14), or in individuals with different strategies (e.g., refs. 15, 23, and 24). However, direct within-subjects investigation of the development and interaction of learning within both systems is not possible across different tasks or different subjects and is confounded by variation in novelty across different stages of the same task [e.g., hippocampal activation can result from novelty *per se* (25)].

Here, we seek to answer some of these questions in the context of human spatial memory. We designed a naturalistic task during which both memory systems are recruited in parallel, with similar time courses and task contingencies, and in which their relative involvement can be read out from behavior. This task allows fair, trial-by-trial, evaluation of: (i) differential involvement of neural systems, (ii) differences in the characteristics of learning in each system, and (iii) interactions between the two systems during learning or performance of a single task.

Our task was inspired by rat experiments in the Morris water-maze (17, 26), in which learning to find the submerged platform is hippocampal dependent (26), with the distance from the wall of the tank being a strong cue (27). However, if the platform is located at a constant distance and direction from an intramaze landmark and both landmark and platform are moved together within the tank between sessions, rats with hippocampal lesions outperform control rats at the beginning of each session (17). These results suggest that hippocampal processing concerns environmental geometry rather than intramaze landmarks, consistent with the place cell responses discussed above: control rats are biased toward the (incorrect) location predicted by the boundary in the previous session, whereas rats with hippocampal lesions follow the landmark alone. Finally, the definition of locations relative to the wall of the tank, or to the intramaze landmark, also requires orientational information that was provided by distal cues and presumably mediated by the head-direction system (ref. 28 and see ref. 29).

We created an object-location memory task, in which some objects maintained a fixed location relative to the environmental boundary, whereas others maintained a fixed location relative to a single intramaze landmark. Functional MRI (fMRI) was used to examine the neural bases of learning and remembering the locations of the objects. Participants explored a first-person perspective virtual reality arena, navigating through it by pressing buttons to move the viewpoint. The arena was bounded by a circular wall, contained a single landmark, and was surrounded by distant cues for orientation. During initial exploration participants encountered four objects in different locations. On each subsequent trial they

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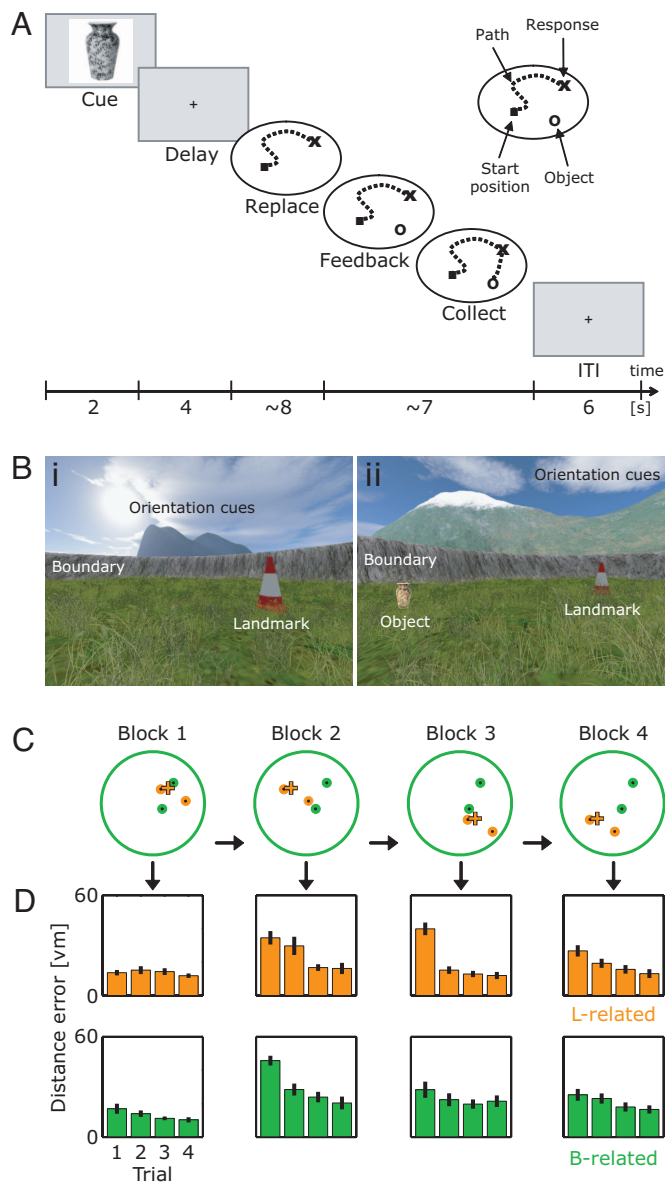
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**Fig. 1.** Virtual reality task and behavior. (A) Trial structure (after initial collection of objects). Participants replace the cued object after a short delay phase and received feedback (object appears in correct location immediately after the response and is collected). (B) Virtual arena from the participant's perspective [replace phase (i) and feedback phase (ii); different viewpoints] showing the intramaze landmark (traffic cone), the boundary (circular wall), the extramaze orientation cues (mountains, which were projected at infinity), and one object (vase). (C) Participants learned four object-locations over four blocks, the landmark (orange +) and boundary (green circle) moving relative to each other at the start of each block (columns). Two objects were paired with the landmark (orange dots), and two objects were paired with the boundary (green dots). (D) Participants learned the associations to landmark and boundary within and across blocks 2–4 at similar rates. Neither learning nor performance differed significantly between landmark-related and boundary-related objects. Bars show the “distance error” of the response location from the correct location for each trial, averaged over the two objects paired with each cue, in virtual meters (vm). Error bars show SEM; ITI, intertrial interval.

saw a picture of an object on a blank background (the cue phase) and indicated its location within the arena by navigating to it from a variable start location and making a button-press response (the replace phase), the object then appeared in its correct location and was collected (the feedback phase; see Fig. 1A and B). The replace

phase reflects memory retrieval, whereas spatial learning occurs during the feedback phase. Each set of 16 trials (four per experimental object) comprised a block, with four blocks in total. Critically, the landmark and boundary were moved relative to each other between blocks, with two objects maintaining their location relative to the boundary and two relative to the landmark (Fig. 1C).

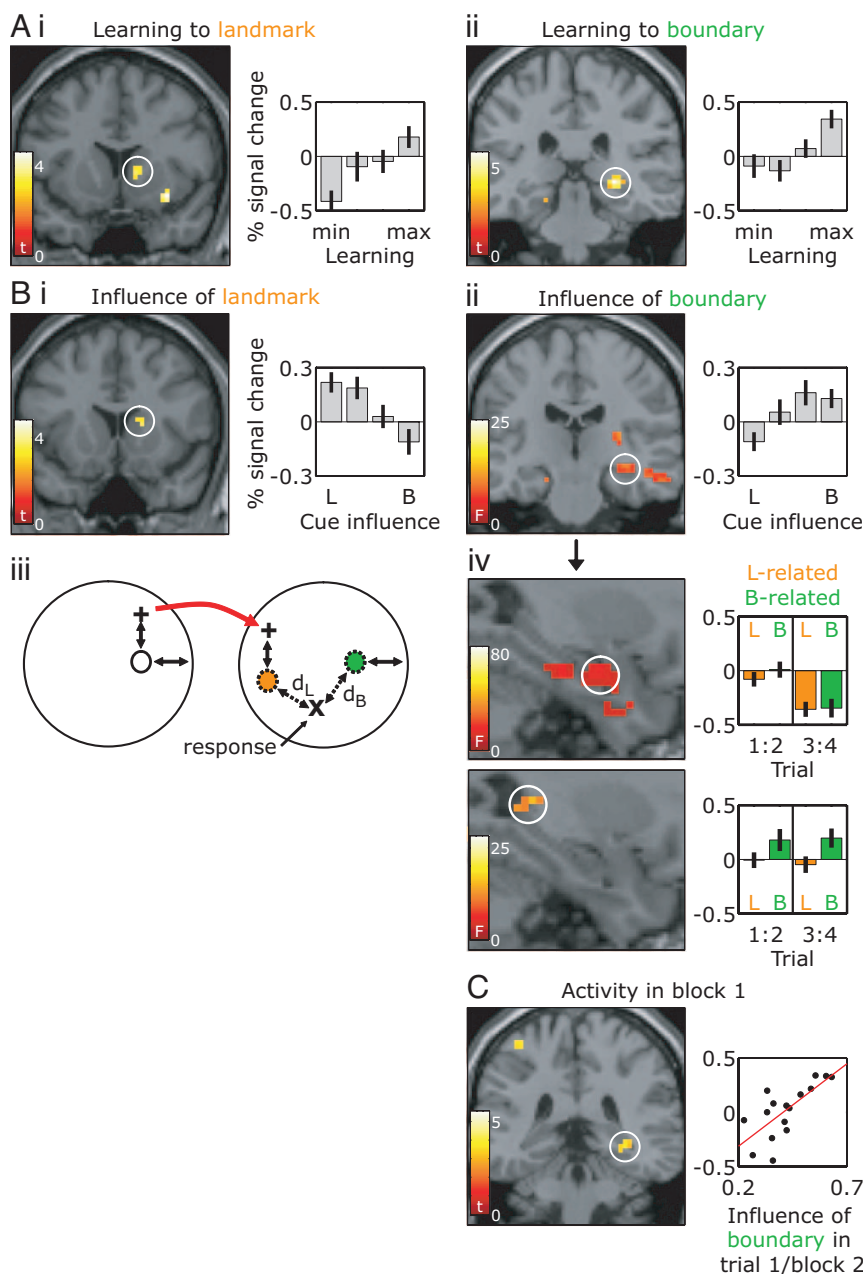
Within each block, participants gradually learned the relationships between object locations and landmark or boundary by using the feedback provided. Performance was measured as the proximity of the response location to the correct location, whereas learning during the feedback phase was measured as the improvement in performance on the next trial with the same object. The relative influence of boundary versus landmark on responding in blocks 2–4 was measured as the relative proximity of the response location to the locations predicted by either cue. Both cues played functionally equivalent roles in the task and were not distinguished in the instructions. The distant orientation cues were projected at infinity so that they could be used for orientation but not location. In separate behavioral studies we formally tested the associative characteristics of learning of locations relative to the landmark or boundary within this paradigm (30).

## Results

**Behavioral Results.** Performance in block 1, in which both cues indicate the same location for each object, was noticeably better than in blocks 2–4, in which the relative movement of landmark and boundary causes the two cues to indicate different locations. In blocks 2–4, participants' responses were influenced by both cues when replacing objects formally paired with either, with performance corresponding closely to the relative influence of the correct cue (explaining 83.3% of the variance, in blocks 2–4,  $P < 0.001$ ) [see Fig. 1D and supporting information (SI) Fig. S1]. Improving performance indicated that participants learned the associations to landmark or boundary within ( $F_{3,45} = 84.85$ ,  $P < 0.001$ ) and across ( $F_{2,30} = 8.07$ ,  $P < 0.01$ ) blocks 2–4. Neither performance levels (overall:  $F_{1,15} = 3.51$ ;  $P > 0.08$ ; block 1:  $F_{1,15} < 1$ ) or their rate of improvement (within-block:  $F_{3,45} = 2.12$ ,  $P > 0.1$ ; across-block:  $F_{2,30} < 1$ ) differed significantly between boundary-related and landmark-related objects. Debriefing after the experiment indicated that the majority of subjects were aware of the association of each object to either cue (see SI Text).

**Imaging Results.** fMRI data were fitted by a general linear model containing separate regressors for the cue phase, the replace phase, and the feedback phases of boundary-related and landmark-related objects (one regressor for each object type in the feedback phase). To model variations in activation across boundary-related feedback phases that might reflect learning about the boundary, we included a copy of the boundary-related feedback-phase regressor whose amplitudes were parametrically modulated by the amount learned in each trial. A similar parametric modulation of the landmark-related feedback-phase regressor was included to capture landmark-related learning. To model variations in activation across replace phases according to the relative influence of boundary versus landmark on behavior in that trial, we included a parametric modulation of the replace-phase regressor by the relative influence of boundary versus landmark on the replacement location (see Fig. S2). Finally, we included parametric modulations of the feedback-phase and replace-phase regressors by time-within-block (exponential decay across trials 1–4 for each object) to capture any effects of novelty-within-block that might otherwise confound apparent effects of learning or the influence of either cue. The resulting coefficients were analyzed across participants using SPM2, with regions showing significant effects (threshold  $P = 0.001$ , uncorrected) being referred to as activations below. See Methods and SI Text for details.

During the feedback phase of blocks 2–4, learning of landmark-related locations corresponded to increased activation of the right



**Fig. 2.** Distinct neural bases support learning relative to landmark or boundary in right dorsal striatum and right posterior hippocampus, respectively, and independent of a right anterior hippocampal response to spatial novelty. (A) Extent of learning during the feedback phase (performance increase in next trial with that object in blocks 2–4) corresponds to activation of right dorsal striatum for landmark-related objects [peaked in head of caudate: Montreal Neurological Institute (MNI) coordinates 12/12/3] (i) and right posterior hippocampus for boundary-related objects (27/–30/–3) (ii). (B) After relative movement of landmark and boundary (i.e., in blocks 2–4), we measured the relative influence of boundary versus landmark on replacement location as  $d_L/(d_L + d_B)$ , where  $d_L$  is the distance of the response from the location predicted by the landmark and  $d_B$  is the distance from the location predicted by the boundary (see iii). (i) Replacement of objects relative to the landmark corresponds to activation of right dorsal striatum (peaked in head of caudate: 18/15/9). (ii) Activity in the right hippocampus (33/–21/–9) reflected the influence of the boundary combined with an effect of trial-within block. (iv) Dissociation of novelty and boundary processing along the long axis of right hippocampus. An object-type (landmark-related vs. boundary-related)  $\times$  trial-within-block (1–2 vs. 3–4) ANOVA revealed independent main effects of trial anteriorly [36/–9/–21 (Upper)] and object-type posteriorly [30/–39/3 (Lower)]. Both images are shown at  $x = 30$ . (Left) Plots show fMRI activation on aligned SPM structural template (coronal sections; sagittal sections in Biv). (Right) Bar plots show mean percentage fMRI signal change ( $\pm$  SEM) in feedback or replace phase (y axis), binned by the measure of learning, influence of cue, or trial (x axis). (C) (Left) Activity in right posterior hippocampus (33/–36/–6) in block 1 predicts each participant's bias toward using the boundary in the first trial of block 2. (Right) Percentage signal change in block 1 versus the influence of the boundary in trial 1 of block 2, averaged over the four objects. Each dot represents one participant. This activation reflects overshadowing of the landmark by the boundary in block 1 (see ref. 30). For display purposes, images are thresholded at  $P < 0.005$  in A–C or  $P < 0.00025$  in Biv, uncorrected.

dorsal striatum (peaked in the caudate), whereas learning of boundary-related locations corresponded to activation of the right posterior hippocampus. Higher activation corresponded to greater performance increase in the next trial with the same object, as

indicated by significant positive coefficients for the respective parametric modulations in the two brain regions. See Fig. 2A and Table S1 for details, including activations in nonhypothesized areas. Thus boundary-related learning and landmark-related learning

appear to be supported by distinct neural systems in the right posterior hippocampus and dorsal striatum, respectively.

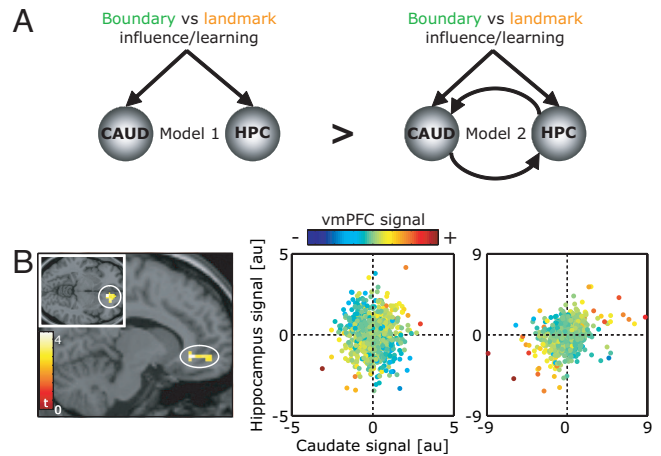
During the replace phases in blocks 2–4, the influence of the landmark on response locations corresponded to activity in the right dorsal striatum (peaked in the caudate head), as indicated by a significant coefficient for the replace-phase regressor parametrically modulated by the influence of the landmark versus the boundary (Fig. 2*Bi*). We did not observe a response in the hippocampus simply reflecting the influence of the boundary. Rather, activity in the right hippocampus reflected the influence of the boundary combined with an effect of trial-within block (Fig. 2*Bii*, as indicated by an *F* test assessing the joint effect of the influence of the boundary and the decay of activation across trial-within-block, see *Methods* and Fig. S2 for details). A follow-up object-type (landmark-related vs. boundary-related)  $\times$  trial-within-block (trials 1–2 vs. 3–4) ANOVA revealed a posterior–anterior dissociation within the right hippocampus during the replace phase: a posterior response to boundary-related relative to landmark-related objects and an anterior response to spatial novelty (decaying within blocks after a new landmark/boundary configuration had been introduced; Fig. 2*Biv*). Additional parametric analyses showed that this within-block anterior right hippocampal response to novelty was independent of the object's association to landmark or boundary, specific to the replace phase and specific to spatial change, not occurring in block 1 (before any change) or across blocks (see *SI Text* for details).

In addition to concurrent effects of boundary-related learning or memory, an individual's bias toward using the boundary to replace objects when boundary and landmark are first moved relative to each other (i.e., at the start of block 2) was predicted by their right posterior hippocampal activation during the replace phase of block 1 (Fig. 2*C*), as indicated by a significant across-subject correlation between bias and hippocampal activity. This finding corresponds to overshadowing of learning to the landmark by learning to the boundary in block 1: the higher the posterior hippocampal activity during block 1, the greater the influence of the boundary on responding at the start of block 2 (see ref. 30 for the corresponding behavioral experiment).

How do the hippocampal and striatal systems interact to control behavior? Do they compete via mutual inhibition, or does activation in each independently signal suitability for behavioral control? We used dynamic causal modeling (31) to test for direct interaction between hippocampal and caudate activity during the feedback and replacement phases of blocks 2–4. In model 1, activation in hippocampus or caudate simply reflects learning relative to (during the feedback phase) or influence of (during the replace phase) boundary or landmark respectively. Model 2 allows, in addition, direct interaction between activity in the two regions. Bayesian model selection favored the simpler, independent, model in all participants during both phases (Bayes factor 6.94 during replacement, 7.17 during feedback; see *SI Text* and Fig. 3*A*). Thus the two systems appear to operate independently in parallel. However, ventromedial prefrontal activity correlated with temporary fluctuations in the covariance of hippocampal and caudate activation during the replace phase. Prefrontal activity increased when hippocampus and caudate were similarly activated or deactivated (positive covariance), whereas prefrontal activity decreased whenever hippocampal and caudate activity had negative covariance. Thus ventromedial prefrontal cortex may mediate between the conflicting behavioral responses indicated by both systems when similarly active (see Fig. 3*B* and *SI Text*). No such correlation was found during the feedback phase, when learning can occur in parallel.

## Discussion

Our findings strongly support the idea of parallel memory systems centered on the hippocampus and dorsal striatum (1–9). Our paradigm provides a sensitive means of detecting the relative involvement of the two systems on a trial-by-trial basis and allows



**Fig. 3.** Dorsal striatum and hippocampus independently influence behavior according to their activation, with ventromedial prefrontal involvement when both are similarly active. (A) Alternative models of the activity in caudate and hippocampus during replacement and feedback phases. (Left) Model 1: inputs solely reflecting behavior (influence of boundary versus landmark during replacement; learning about boundary versus landmark during feedback). (Right) Model 2: additional inputs reflecting the influence of activity in the other structure. Bayesian model selection favors model 1, indicating that caudate and hippocampal activity reflect the influence of landmark and boundary on replacement location and learning, but do not interact directly. (B) (Left) Activity in ventromedial prefrontal cortex [12/33/–6; shown on sagittal section; (Inset) axial section] correlates with fluctuations in covariance between hippocampal and caudate activity, increasing whenever they are similarly activated or deactivated. (Center and Right) Mean-corrected prefrontal activity during object-replacements plotted as color against mean-corrected hippocampal and caudate activity for two representative subjects. au, arbitrary units. For display purposes, the statistical image is thresholded at  $P < 0.005$ , uncorrected.

their distinct functional characteristics to be examined. Differential activity in the hippocampus and caudate corresponded to the acquisition and expression of information about locations derived from environmental boundaries or landmarks, respectively.

Our behavioral experiments (30) indicate that the striatal landmark-related learning obeys associative reinforcement with a single prediction-error signal (32, 33), whereas the hippocampal boundary-related learning appears to be incidental, occurring independent of error. Thus the two systems' distinct roles may result from differences in the learning rule implemented by each and not necessarily differences in learning rate. Our results provide well controlled confirmation of some previous theories of hippocampal function (1–3) and are consistent with studies in animals (34–36) and humans (37–39) showing that striatal activity follows the predictions of reinforcement learning, and with observations that striatal dysfunction impairs feedback-based learning (compared to observational learning) (6, 40).

The apparent specialization of the right posterior hippocampus in memory for spatial locations is consistent with a specifically spatial role for this region in humans (41) and with spatial specialization of the dorsal portion of the rat hippocampus (corresponding to the posterior human hippocampus) where a higher precision coding of spatial location (42) is found and where lesions have a greater impact on spatial memory (43). The additional specialization for representations of location relative to environmental boundaries is consistent with the dependence of place cell firing on boundaries (19, 20) and with apparent specialization of the human hippocampus for processing environmental geometry rather than other aspects of visual scenes (44).

The processing of environmental boundaries by a specific neural system with a specific type of learning rule is reminiscent of the idea of a dedicated geometric module (45, 46) for processing the surface geometry of the local environment, albeit for determining location

rather than orientation. It also supports a specific role for the hippocampus in incidental learning of spatial layout (2) and emphasizes the importance of boundaries in this process. Consequently, environmental boundaries may have a privileged role in the hippocampal contribution of spatial context to episodic memory (2). More generally, the different types of learning may explain the two systems' differential roles in memory. Striatum-dependent learning controlled by a single error signal may underlie procedural memory and other forms of learning by trial and error (5, 10), whereas incidental hippocampal-dependent learning may be more appropriate for maintenance of a flexible mental model (9), mediating representation (47) or cognitive map (2, 48), and for efficient encoding of experience into episodic memory (5, 49) (see also ref. 30).

The anterior hippocampal response to spatial novelty agrees with findings in rodents that hippocampal lesions disrupt the exploration of changes to spatial layout (e.g., ref. 50) and that place cell activity is modulated by spatial, but not nonspatial, novelty (51). Our results suggest that, in the rat, the ventral hippocampus might be the primary source of this novelty signal. In humans, a recent fMRI study (52) found anterior hippocampal activity to correlate with the formation of a survey representation of a new virtual reality (VR) environment, possibly reflecting incorporation of new landmark information into a boundary-based representation. Our results are also consistent with numerous fMRI studies showing an anterior hippocampal novelty response (e.g., ref. 25). Interestingly, the posterior parahippocampal cortex responded to both spatial novelty and processing of the boundary, consistent with its role in representing spatial scenes (53).

What distinguishes a landmark from a boundary in terms of ability to activate the two systems? We cannot be sure, but place cell firing appears to reflect a matching of distances to the nearest obstacle in all directions around the rat (19, 20). Thus, the influence of a given object on the hippocampal representation of location might be simply proportional to the horizontal angle subtended by it at the participant, with extended obstacles having a greater influence than discrete ones. However, our results are not explained by previous findings of striatal versus hippocampal processing of proximal versus distal cues (4, 8, 16). We used a variety of object locations so as to include boundary-related objects initially nearer to the landmark and landmark-related objects initially nearer to the boundary. Conversely, the proximal–distal dissociation may reflect differences in the type of processing required rather than the distance of the cue from the goal *per se*. Distal cues are important for orientation [via the head-direction system (28)], and tasks that test memory for location relative to a boundary often also require orientation, whereas tasks involving a proximal cue actually at the goal location can be solved by a simple association (cue approach) and do not require orientation. In our task, navigation relative to landmark or boundary both require orientation and neither can be solved by cue approach.

How did the two systems interact to support behavior within a single task? When put into conflict, each system's influence on behavior corresponded to its activation level, without direct activation-based competition between systems. Thus a system's suitability to control behavior may be signaled bottom-up by its activation. This interpretation would be consistent with effects of locally injected anesthetic in biasing behavior to follow a hippocampal place strategy when injected into the striatum and to follow a striatal response strategy when injected into the hippocampus (13). In addition, top-down ventromedial prefrontal mediation may be required when both systems are similarly active (54, 55). More generally, the effect of having two independent systems may appear competitive or cooperative according to the situation (7, 8, 13, 24, 56). Overall, our paradigm appears to be highly sensitive to the relative activation of the two systems, and so may provide a useful indicator of damage, e.g., in Huntington's (24) or Alzheimer's (23) diseases.

In conclusion, our findings, together with behavioral experiments using the same paradigm (30), indicate that learning locations relative to an intramaze landmark is supported by the dorsal striatum and obeys associative reinforcement, whereas learning locations relative to a boundary is supported by the right posterior hippocampus and is incidental. Both types of learning occur in parallel within the same task and do not reflect differences in the time course of learning, performance levels, instructions, or in the proximity, salience, or novelty of stimuli that would otherwise confound identification of the characteristics of the two systems. Indeed, spatial novelty produced anterior hippocampal activation unrelated to the boundary-related learning in posterior hippocampus. Finally, the two systems appear to influence behavior proportionally to their activation, with ventromedial prefrontal involvement when both are similarly active.

## Methods

**Participants.** Sixteen male participants (aged 20–31, mean age 23.8 years) gave written consent and were paid for participating, as approved by the local Research Ethics Committee. All were right-handed with normal or corrected-to-normal vision and reported to be in good health with no history of neurological disease. All had experience of playing first-person perspective video games.

**Virtual Reality Environment.** We used UnrealEngine2 Runtime software (Epic Games) to present a first-person perspective view of a grassy plane surrounded by a circular cliff with a background of mountains, clouds, and the sun (created by using Terragen; Planetside Software) projected at infinity, to provide orientation but not location within the arena. A traffic cone was used as an intramaze landmark. Both the boundary (cliff) and landmark (cone) were rotationally symmetric, leaving the distal cues as the main source of orientation. Participants moved the viewpoint by using their right hand to operate keys to move forward and turn left or right. The viewpoint is  $\approx 2$  virtual meters above ground, the boundary is  $\approx 180$  virtual meters in diameter, and the virtual heading and location were recorded every 100 ms. Participants practiced in an unrelated virtual environment before performing the experiment (see *SI Text*).

**Stimuli, Task, and Trial Structure.** Participants initially familiarized themselves with the arena by exploring for 2–3 min. Next, everyday objects were presented sequentially (once each) within the arena; participants collected the objects by running over them and were instructed to remember their locations. At the beginning of each subsequent trial, a picture of an object was presented on a blank background for 2 s (the cue phase), followed by a variable delay period (fixation cross; 2–6 s; mean 4 s). Participants then started at a random position within the arena and had to move to where they thought the cued object had been (the replace phase; mean duration 8.32 s). After participants had indicated their response by a button press, feedback was provided, i.e., the object appeared in its correct position and participants collected it by running over it (the feedback phase; mean duration 6.59 s). Participants could use the feedback phase to (re)learn the object positions. A fixation cross was then presented for a variable intertrial interval (2–10 s; mean 6 s), before the start of the next trial.

**Details of Procedure and Design.** Participants performed four blocks. Each block comprised 16 trials with the four experimental objects (four trials each) in pseudorandom order. Trials with one control object were interspersed with regular trials (see *SI Text*). The landmark and boundary were moved relative to each other between blocks, with two experimental objects maintaining a fixed position relative to the landmark and two relative to the boundary (see Fig. 1C). There were four arena configurations, with the landmark roughly in the middle of the northeast, southeast, southwest, and northwest sectors of the arena, as defined by the distal cues. Arena configuration to block assignment was counterbalanced across participants. There were four initial object positions in block 1, which were assigned to landmark- or boundary-related objects, counterbalanced across participants, such that one object of each type was close to the landmark in block 1 (and one of each type distant from it).

**Characterizing the Relative Influence of Either Cue on Replace Location.** For blocks 2–4, we attempted to quantify the relative influence of either cue on each response location. In a pilot study, we noticed that incorrect responses tended to be clustered around locations previously associated with the incorrect cue: either during block 1 or during the immediately preceding block. Accordingly, we calculated the relative influence of boundary versus landmark in blocks 2–4 as  $d_l/(d_l + d_b)$ , where  $d_l$  is the distance of the response from the location predicted

by the landmark and  $d_B$  is the distance from the location predicted by the boundary. This measure varies between 0 (using the landmark) and 1 (using the boundary). On the basis of our pilot data the incorrect cue potentially predicts two different locations in blocks 3 and 4 (reflecting the object's positions relative to it in the preceding block and in block 1): we used whichever was closest to the response location. This measure was used to create a parametric regressor for analysis of fMRI data in the replace phase (see Fig. S2).

**Acquisition and Analysis of fMRI Time Series.** Functional images were acquired on a 3T scanner and analyzed by using SPM2, including standard preprocessing procedures. fMRI time series were modeled by a general linear model including regressors for the cue, replace, and feedback phases, and parametric modulations of these regressors reflecting trial-by-trial behavioral measures and time of trial within block. We also modeled effects related to VR movements by including parametric modulations of the replace- and feedback-phase regressors by speed and signed and unsigned rotation following ref. 14. All regressors were con-

volved with the SPM hemodynamic response function. Data were high-pass filtered (cut-off period = 128 s). Coefficients for each regressor were estimated for each participant by a least-mean-squares fit of the model to the time series. Linear contrasts of coefficients for each participant were entered into a second-level random-effects analysis. Based on our strong *a priori* hypotheses with respect to the hippocampus and striatum we have chosen an uncorrected statistical threshold of  $P = 0.001$ . Nonhypothesized activations outside of the hippocampus and striatum are reported in Table S1. Coordinates of brain regions are reported in MNI space. See *SI Text* for details.

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