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Cortical Analysis of Visual Context

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Summary

Objects in our environment tend to be grouped in typical contexts. How does the human brain analyze such associations between visual objects and their specific context? We addressed this question in four functional neuroimaging experiments and revealed the cortical mechanisms that are uniquely activated when people recognize highly contextual objects (e.g., a traffic light). Our findings indicate that a region in the parahippocampal cortex and a region in the retrosplenial cortex together comprise a system that mediates both spatial and nonspatial contextual processing. Interestingly, each of these regions has been identified in the past with two functions: the processing of spatial information and episodic memory. Attributing contextual analysis to these two areas, instead, provides a framework for bridging between previous reports.

Introduction

Visual objects in our environment tend to appear in specific and typical contexts. For example, a blender is expected to be found in a kitchen or on a shelf in an appliance store. Seeing a blender anywhere else will be surprising (Biederman et al., 1982). Such clustering of objects into groups that tend to appear together may explain why recognition of an object that is highly associated with a certain context facilitates the recognition of other objects that share the same context (Bar and Ullman, 1996; Biederman, 1981; Palmer, 1975). Is this clustering reflected in the cortical processing of contextual associations?

To address this question, we used functional magnetic resonance imaging (fMRI) and examined the cortical events taking place during the analysis of visual context. Specifically, we compared brain activity, as reflected by the fMRI signal, elicited during the perception of visual objects that are highly associated with a certain context (e.g., a hardhat) with the activity elicited by objects that are not associated with any unique context in particular (e.g., a fly).

This set of experiments further allowed us to answer a more general question about the role and processing of associations. Several regions in the brain, most often the hippocampus, the parahippocampal cortex, and the retrosplenial cortex, have been implicated as mediating two different functions: episodic memory (e.g., Ranganath and D'Esposito, 2001; Valenstein et al., 1987) and processing of place-related information (e.g., Aguirre et al., 1996; Maguire, 2001). The explanation that emerges from our findings, that parahippocampal and retrosplenial regions mediate contextual associations, provides a framework that bridges those seemingly unrelated interpretations.

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Context-Specific Cortical Processes

The goal of this first experiment was to compare cortical processing of highly contextual objects with the cortical processing of objects that have only a weak contextual association with other objects. A preliminary survey of 35 subjects was conducted to create a list of objects comprised of strong contextual association (Strong CA objects). Each of the Strong CA objects was rated to be the most typical object of a specific context (e.g., a supermarket cart for "supermarket," a microscope for "lab"). A second list contained weak contextual association (Weak CA) objects, which were defined in a separate survey with another group of 18 subjects as not being associated with any unique context in particular (e.g., a rope, a camera, a basket). Ideally, objects in this control list would not be associated with any context at all. However, objects in our environment do not appear in isolation but rather in multiobject settings, and it therefore seems impossible to generate a list of objects that cannot be associated with any context. Consequently, we selected objects that are very weakly associated with many possible contexts (e.g., a person, a generic container). The working assumption was that the recognition of a Strong CA object would immediately activate the information associated with its corresponding context, whereas Weak CA objects would not automatically elicit such contextual activation. This assumption is supported by established results of contextual priming (Biederman, 1981; Palmer, 1975) as well as by some of the results we report here. The stimuli in the subsequent fMRI experiment were photographs of objects from those Strong CA and Weak CA lists (Figure 1). We scanned six subjects in this first experiment. Their task was to press a response key as soon as they recognized what each object was, without having to name it.

Results and Discussion

Mean reaction time for recognizing the objects in each of the three conditions was statistically comparable [$F(2,105) = 0.272$; $p = 0.76$] (average reaction time for each condition: Strong $CA_B = 674$ ms; Strong $CA_I = 702$ ms; Weak CA = 684 ms). Comparing the fMRI signal elicited by the recognition of highly contextual objects (Strong CA) with the signal elicited by the recognition of Weak CA objects resulted in a map of bilateral cortical activation that concentrated in two main sites (Figure 2). The first and largest focus was in the posterior part of the parahippocampal cortex (PHC), straddling the collateral sulcus and the parahippocampal gyrus. The average Talairach coordinates of this PHC focus were (−24, −41, −4) in the left hemisphere, and it occupied 685 mm^2 of cortical surface where all voxels were differentially active at $p < 10^{-8}$. (For the sake of simplicity

Figure 1. Examples of Stimuli in the Different Conditions (Experiment 1)

Objects in the Weak CA condition were not associated strongly with any specific context. We used Strong CA objects "floating" in isolation (Strong CA$_I$) and Strong CA objects with some background (Strong CA$_B$). This third condition was used to study the possible effect of background on the facilitation of contextual activation. In selecting stimuli for all the experiments described here, special care was taken to guarantee that other than in their level of contextual association, objects in the Strong CA and Weak CA groups did not differ in any apparent dimension (e.g., physical properties, semantic attributes, function, etc.; see Supplemental Figure S1 at http://www.neuron.org/cgi/content/full/38/2/347/DC1 for a wide sample of the stimuli we used). The Strong CA and Weak CA objects were equally recognizable in terms of difficulty, as derived from reaction time (RT). RTs for Strong and Weak CA objects were also comparable in a separate behavioral experiment where participants named the objects aloud, thereby providing a better verification of compliance with the task. This RT compatibility is taken to reflect an equal combination of familiarity, typicality, name complexity, and all other factors that affect naming time. Furthermore, that the same results were obtained in all four experiments reported here, which used largely nonoverlapping sets of stimuli (and in some experiments completely different sets of objects altogether), increases the randomness of the stimuli in the Strong and Weak CA conditions, and therefore minimizes the chances that objects in the two groups will consistently differ in an additional dimension other than level of contextual association. For each participant, each object appeared in only one condition and was never repeated in another. Strong CA objects belonged each to a different context.

and given that the results were completely bilateral, only information about the left hemisphere is provided in detail.)

Interestingly, this parahippocampal focus of context-specific activation was located practically at the same coordinates as the site that has previously been reported to respond selectively to houses and other environmental landmarks (Aguirre et al., 1996), termed the parahippocampal place area (PPA) (Epstein and Kanwisher, 1998). The coordinates reported as reflecting the center of the PPA were (−28, −39, −6), and similar coordinates were reported in other studies (Aguirre et al., 1998; Levy et al., 2001). That context activated a cortical area implicated in processing place-related information raises important questions and may be interpreted in several ways, as elaborated later.

A second focus of activation was found in the retrosplenial cortex (Talairach coordinates: −15, −53, 9; occupying 332 mm^2 of cortical surface), immediately superior to the anterior calcarine sulcus. Not much is known about this region thus far, but it has often been implicated in processing various aspects of memory (Andreasen et al., 1995; Fink et al., 1996; Markowska et al., 1989; Valenstein et al., 1987) as well as spatial information (Cooper and Mizumori, 2001; Maguire, 2001; Vann and Aggleton, 2002). It has been occasionally reported to be active in studies of the PPA (Aguirre et al., 1996; O'Craven and Kanwisher, 2000).

Both of these foci were bilateral and consistent across all subjects (Figure 3). An additional site of significant differential activation in the comparison between Strong and Weak CA objects was found in the lateral occipital cortex (LO: −49, −72, 13). This focus, however, was pronounced in the condition where the contextual objects appeared with background (Strong CA$_B$) and may therefore reflect the differences in physical appearance and amount of visual information between Strong CA$_B$ and Weak CA, rather than a context-related difference in processing.

Figure 4 illustrates the corresponding change in fMRI signal as a function of condition. In both foci, the PHC and the retrosplenial, there was a clear effect of context: Strong CA objects elicited significantly higher signal change in those regions compared with Weak CA objects. In the PHC site, this effect was gradual in that it was higher for the Strong CA$_B$ compared with the Strong CA$_I$, although they were not significantly different from each other ($t_{10} = 1.701$), and both were significantly higher than the noncontextual objects ($t_{10} = 3.360$, $p < 0.004$ for Strong CA$_B$ versus Weak CA; $t_{10} = 2.729$, $p < 0.02$ for Strong CA$_I$ versus Weak CA). In the retrosplenial cortex site, on the other hand, signal increase for highly contextual objects was equivalent regardless of the presence of background. This result may indicate that processes in the PHC site are sensitive to visual appearance, in accordance with previous reports (Aguirre and D'Esposito, 1997; Schacter et al., 1997), whereas retrosplenial representations are more abstract and independent of exact physical properties. Consequently, it is proposed here that both the PHC and the retrosplenial cortex represent familiar associations, but with a different level of abstraction.

These results demonstrate that the perception of individual, highly contextual objects in isolation is sufficient to elicit robust context-specific activation in the PHC as well as in the retrosplenial cortex. A separate experiment of contextual associations, which otherwise addressed independent issues, resulted in similar activation pattern. In this other experiment (Experiment 2), rather than presenting "key" objects, each of which was strongly associated with a different and unique context, we presented blocks of pictures in which all objects shared the same context (Figure 5A, top). Twelve subjects participated in this experiment. Unlike Experiment 1, where stimuli where presented for 1700 ms each, stimuli here were presented for a duration of 400 ms only. Contextually related objects, compared with control objects that were not contextually related to each other, elicited activation in the same PHC and retrosplenial sites as in Experiment 1 (Figure 5B).

Houses can be seen as highly contextual objects, and we therefore decided to test directly whether activity for houses, previously used to define the PPA, may be explained as contextual activation. This follow-up experiment (Experiment 3; see Experimental Procedures) demonstrated that the activation pattern obtained for contextual objects in isolation was statistically equivalent to this elicited by pictures of individual houses, both in the PHC ($t_{16} = -1.229$ in Experiment 3 and $t_{13} = -.043$ when compared with Strong CA$_I$ from Experiment 1) and the retrosplenial sites ($t_{16} = -0.227$). The same two foci

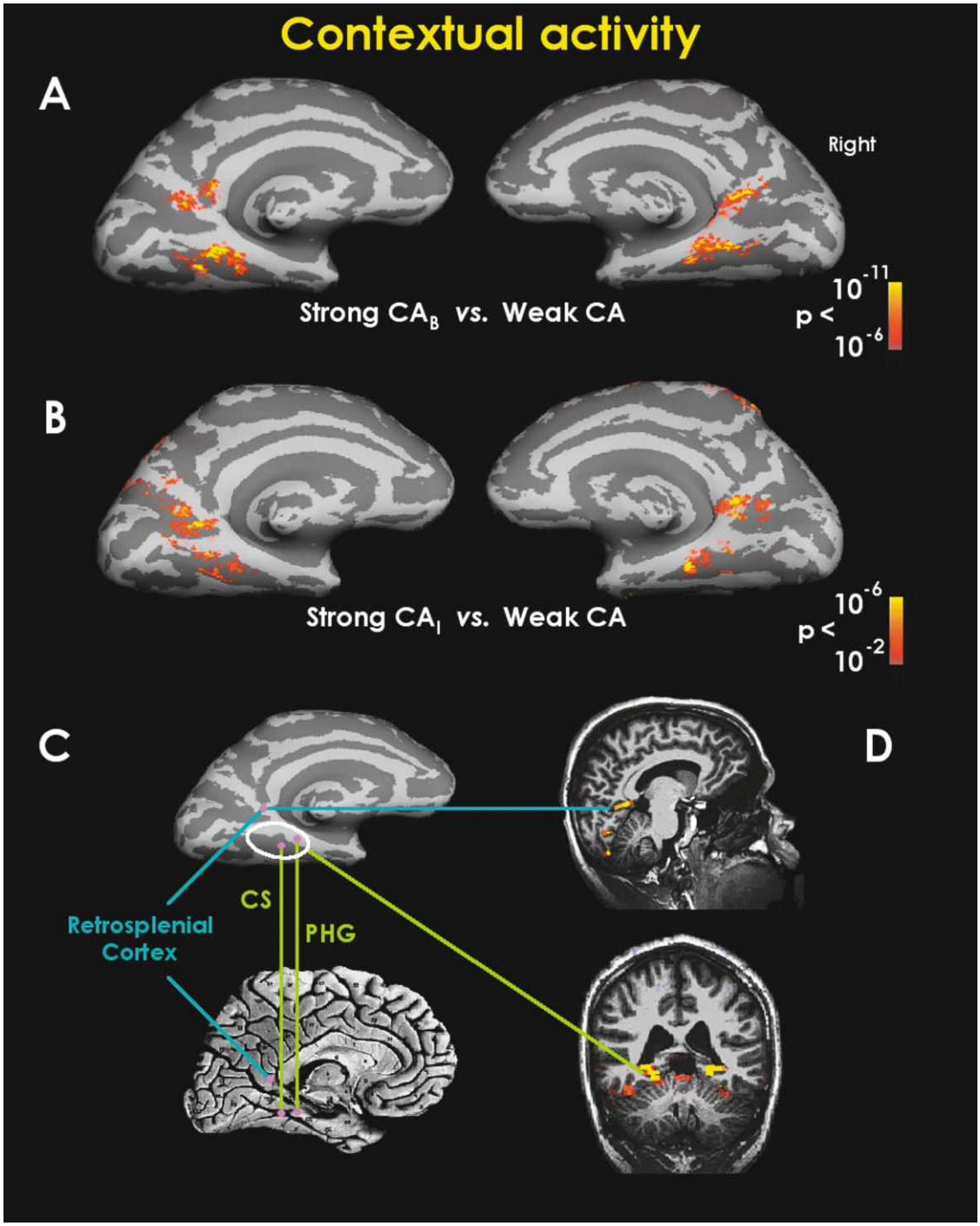

Figure 2. Statistical Activation Maps Representing the Difference between Perceiving Highly Contextual Objects and Perceiving Objects That Are Not Associated with a Unique Context

(A) Highly contextual objects that were presented with background (Strong CA_B) versus weak contextual association objects (Weak CA). The activity was averaged across all six participants and Bonferroni corrected for multiple comparisons. This is a medial view, with the left hemisphere on the left and right hemisphere on the right. Context-specific activation was consistently observed in the parahippocampal and retrosplenial cortices.

(B) Highly contextual objects in isolation (Strong CA_I) versus Weak CA objects.

(C) The brain was inflated to expose the sulci, and the result is a smooth surface. Gyri from the original brain are shown in light gray and sulci in dark gray. Here we provide anatomical context by comparing an inflated left hemisphere with a picture of a real (but different) left hemisphere. PHG, parahippocampal gyrus; CS, collateral sulcus; together referred to here as the paraphippocampal cortex (PHC).

(D) Sagittal and coronal views in a single subject (MD) of the same comparison depicted in the group average in (A).

All statistical maps presented here are bidirectional in that they were designed to detect both positive and negative contrasts. Therefore, the lack of blue-colored voxels implies that, under these conditions, there were no significant voxels where Weak CA objects elicited significantly higher fMRI signal than Strong CA objects. Furthermore, note that in all experimental conditions, subjects viewed similarly looking color photographs of meaningful, everyday common objects that were equally recognizable. Consequently, activation due to low-level processes was subtracted out, and the differential activation maps shown here presumably represent only processes that are related to level of contextual association.

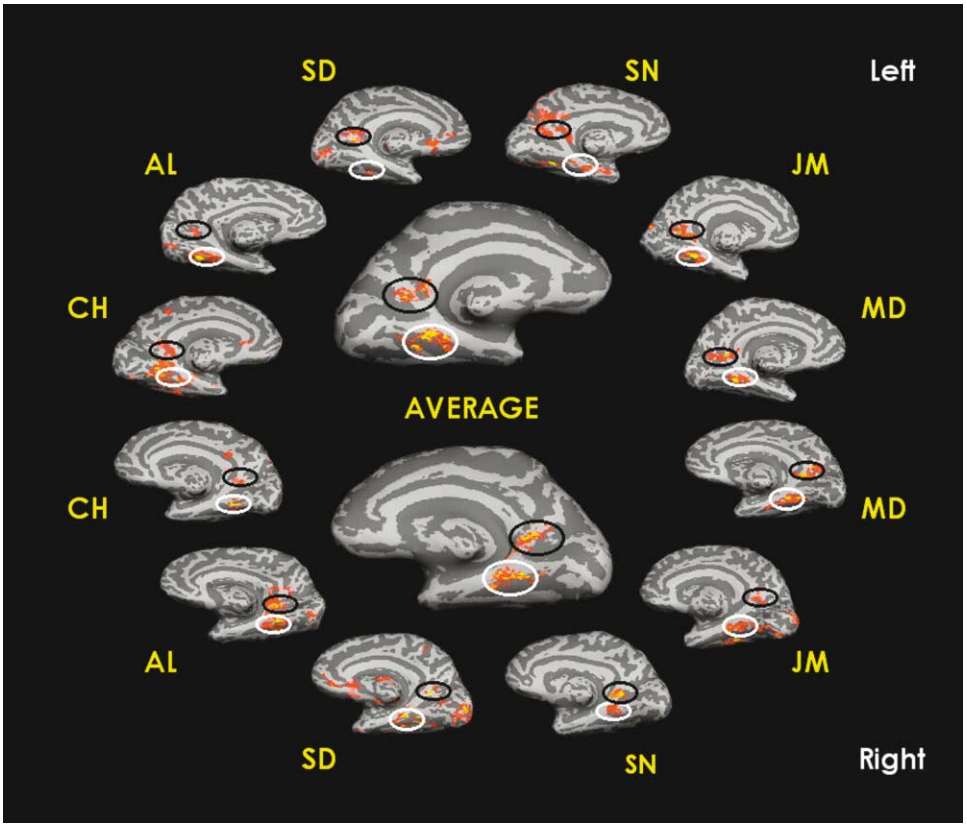

Figure 3. Statistical Activation Maps Reflecting the Difference between Perceiving Strong CA_B Objects and Weak CA Objects in Each of the Individual Participants

The PHC focus is circled in white and the retrosplenial focus in black.

were also differentially active for indoor and outdoor complete scenes.

Figure 6 summarizes this experiment and compares its results with those of Experiment 1. All contextual conditions, with no exception, elicited significant differential activation in the retrosplenial and PHC foci. Note the additional negative (blue) voxels in the comparison between houses and Weak CA objects. We propose that this activation, which is confined mainly to occipital visual areas, is the result of the many perceptual and conceptual differences between the esoteric blocks of houses and the visually and semantically diverse objects in the Weak CA condition. This comparison verifies the similarity between the previously reported PPA and the PHC site we obtained here, and it further supports our proposed reinterpretation of the role of this region within the PHC as more closely related to contextual processing.

Contexts, Places, or Both?

Given that the PHC and retrosplenial foci we obtained have previously been associated with the perception of

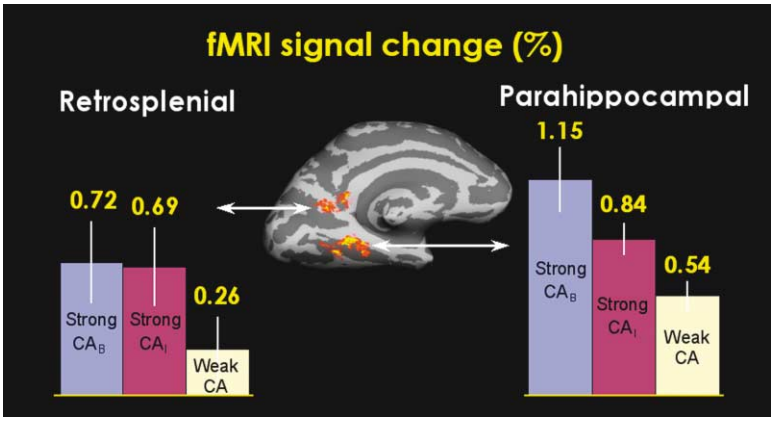

Figure 4. Average Percent Signal Change at the Two Foci That Were Activated in the Comparison between Strong and Weak Contextual Association (CA) Objects

This is a random-effect analysis between all six subjects. Throughout the paper, percent signal change is calculated in comparison with the fixation baseline condition, and error bars represent a single standard error.

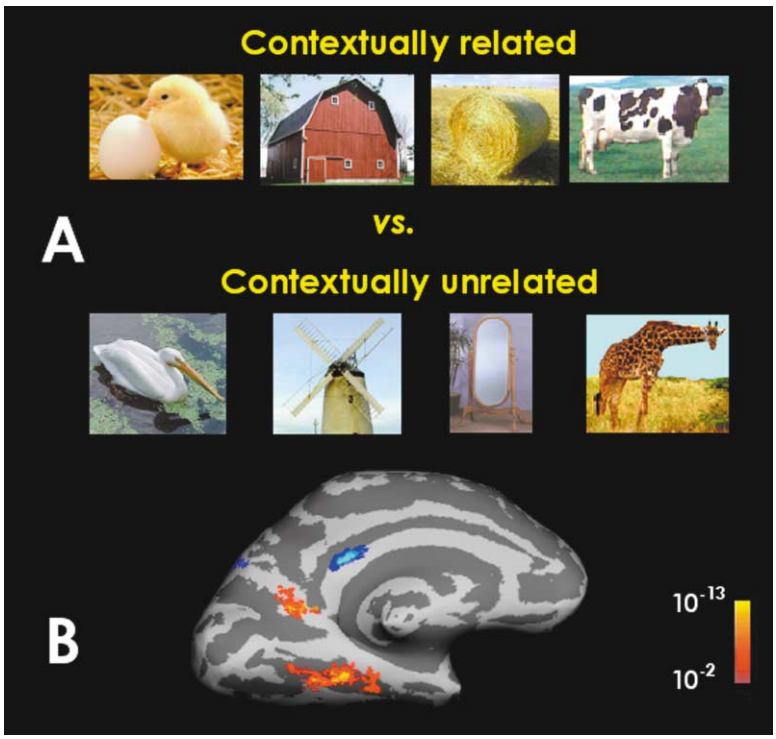

Figure 5. Similar Results with a Different Design (Experiment 2)

(A) Examples of some of the objects presented in a single contextually related block (top) where all 12 subjects shared the same context, and of objects presented in the control, contextually unrelated blocks (bottom). We used five different contexts: farm, office, bathroom, garden, and water sports.

(B) Contextually related objects elicited differential activation in the PHC and in the retrosplenial cortex. The same sites were activated by individual, highly contextual objects in Experiment 1. The activity was averaged across all 12 participants and Bonferroni corrected for multiple comparisons.

places, there are two alternative interpretations for their role. First, consider the relation between visual contexts and places. All the objects we used were part of contexts that were also highly associated with specific places. For example, a hardhat is associated with a construction site, an oven with a kitchen, a roulette wheel with a casino, etc. Therefore, it may be conceivable that perceiving the contexts indirectly activated the corresponding places and, consequently, elicited cortical activation in a region that has been associated with the perception of places (PPA) and the retrosplenial cortex. To the best of our knowledge, such indirect cortical activation of place information by individual, nonlandmark objects has not been reported before. (The PHC has nevertheless been shown to be activated when people imagine specific, previously studied places and landmarks [O'Craven and Kanwisher, 2000], demonstrating that the physical presentation of an actual stimulus is not essential for activating this region.)

An alternative interpretation is that the PHC and retrosplenial foci mediate the representation and processing of familiar contextual associations in general, rather than places per se. Indeed, in many cases, sets of associations implicitly or explicitly correspond to places. However, what is proposed here is that the PHC and retrosplenial processes are not limited to place-related information, but they also involve nonspatial object associations (e.g., romance, music, crime) where sets of objects that typically share the same context are associated with each other, but not necessarily with a specific place or specific spatial relations.

To distinguish between these two alternatives—"place" activation by contextual objects versus contextual activation by place-related stimuli—we designed an experiment that compared the cortical activation elicited by spatial, place-specific contexts with the activation elicited by nonspatial contexts (Experiment 4; Figure 7A). If the activation in the PHC and retrosplenial sites mediates solely the processing of place-related information, one would expect to see no significant differential activation in these foci for nonspatial associations.

We initially conducted this experiment with identical instructions to those of Experiment 1, where participants were simply required to recognize each picture. Under these conditions, only the objects in the *spatial* condition elicited significant differential activation in the PHC and in the retrosplenial cortex. This result may suggest that the PHC and retrosplenial sites process only place-related contexts. Alternatively, this result may indicate that while spatial contexts are activated automatically during object recognition, nonspatial contexts are activated only when the task requires so explicitly. Consequently, we modified the experiment such that subjects became aware of the two possible context types, spatial and nonspatial, and were required to recognize the actual contexts rather than the objects.

Both *spatial* and *nonspatial* contexts elicited significant differential activation in the PHC and the retrosplenial cortex (Figure 7B), supporting our hypothesis that the PHC and retrosplenial sites mediate the general analysis of contextual associations, and not only of place-related information.

There are several reasons to believe that the activation elicited by the nonspatial contexts is indeed a result of activating the corresponding nonspatial associations, and not merely a relatively weak activation of spatial associations. First, after scanning, subjects filled a debriefing questionnaire designed to ensure that they have indeed recognized the contexts correctly. Second, the PHC and the retrosplenial were not significantly acti-

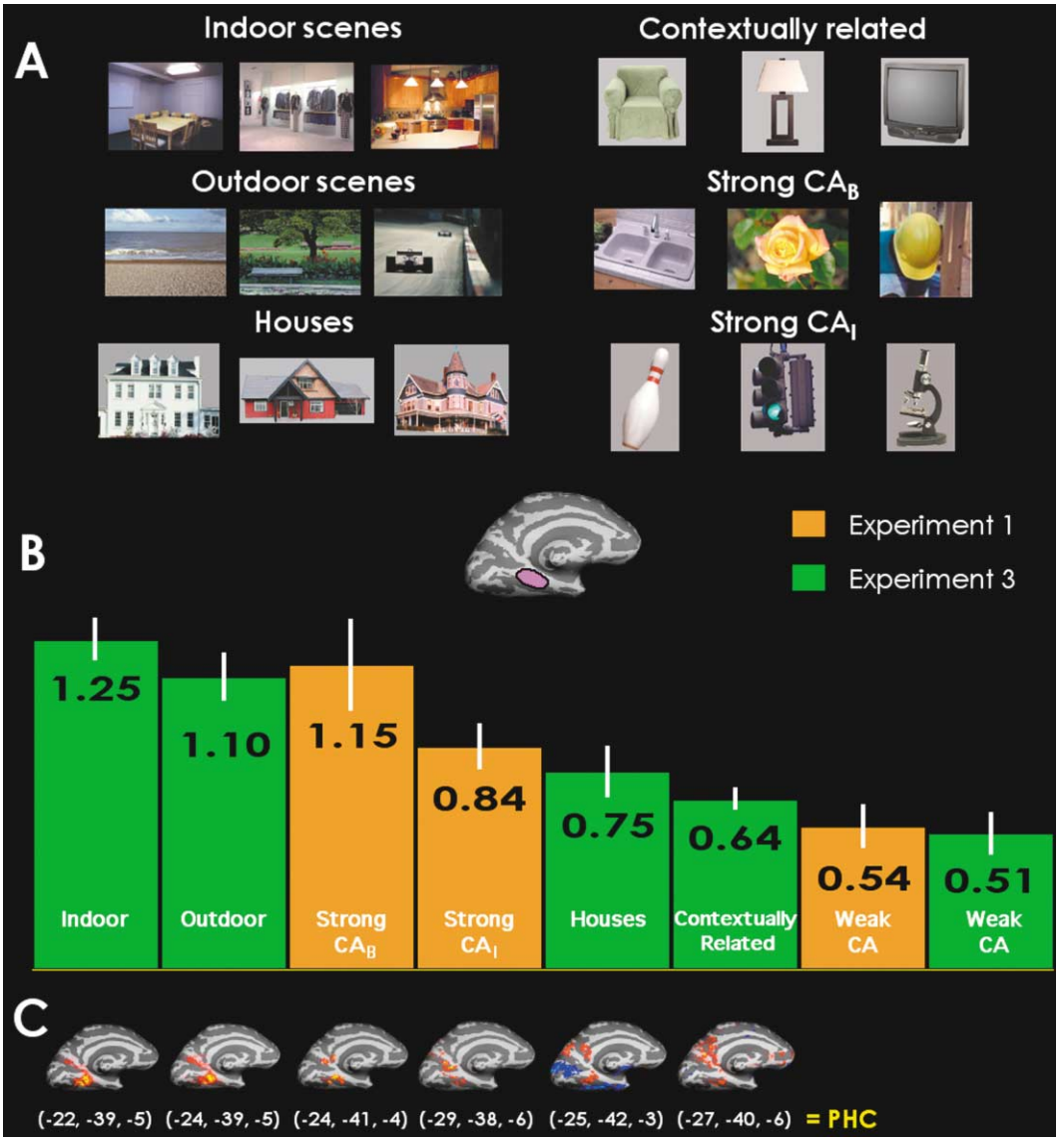

Figure 6. The Relative Cortical Activation Elicited by Scenes, Houses, and Individual Objects (Experiments 3 and 1)

(A) Examples of stimuli. The conditions in Experiment 3 included indoor and outdoor scenes, pictures of houses, contextually related objects in isolation (similar to the contextually related condition in Experiment 2, but with a different set of stimuli and without background information), and weak contextual objects (Weak CA; see Supplemental Figure S1 at http://www.neuron.org/cgi/content/full/38/2/347/DC1). As described earlier, the conditions in Experiment 1 included Strong CA objects in isolation (Strong CA_I), Strong CA objects with background (Strong CA_B), and Weak CA objects. The pictures in the two experiments were different, and different groups of subjects participated in both.

(B) A random-effect analysis of percent fMRI signal change as a function of condition, within the identical PHC region of interest derived from Experiment 1 (shown here in purple). This ROI encompasses the previously defined PPA. As can be seen, the highest activation was elicited by complete scenes, as well as by individual objects presented with minimal background (Strong CA_B). Houses and contextual objects in isolation (both in the contextually related and Strong CA_I conditions) elicited a statistically equivalent signal within this PHC region of interest, which was significantly higher than that elicited by Weak CA objects ($t_{16} = 2.327$; $p < 0.017$ for houses versus Weak CA and $t_{16} = 1.874$; $p < 0.05$ for contextually related versus Weak CA).

(C) The corresponding statistical activation maps obtained when we compared each of the conditions with the relevant Weak CA condition (the different maps have different significance thresholds, all of which are at least significant with $p < 0.01$).

vated in the nonspatial condition of the initial version of this experiment, where subjects were not required to extract the context explicitly, although they were significantly active in the spatial condition. Finally, the spatial and nonspatial contexts elicited activation that concentrated in different, nonoverlapping subregions of the PHC, and we therefore analyzed them separately (Figure 7C). As can be seen, the spatial contexts resulted in a stronger fMRI signal in a relatively posterior part of the PHC focus, whereas the nonspatial contexts elicited signal that peaked in a more anterior part of this focus.

This specific result suggests that the representation of associations in the PHC is organized along a hierarchy of spatial specificity, where posterior representations

are relatively more spatially specific, whereas the anterior representations are relatively more abstract. It is interesting that the location of the posterior ROI, which was more active for spatial contexts, reflects more closely the previously defined PPA than the anterior ROI. Furthermore, when the PHC region activated by houses in Experiment 3 was projected as a ROI and analyzed in the data obtained in the present experiment, spatial contexts indeed elicited in this ROI activation that was significantly higher than that elicited by nonspatial contexts ($t_{12} = 2.101$; $p < 0.03$) and by Weak CA objects ($t_{12} = 4.329$; $p < 0.0005$).

In the retrosplenial cortex, both spatial and nonspatial contexts elicited a statistically equivalent activation level (Figure 7D), which was significantly higher than that elicited by Weak CA objects ($p < 0.005$). In other words, whereas spatial and nonspatial contexts activated different subparts of the PHC, they activated the same retrosplenial locus regardless of the relative magnitude of their spatial component.

In addition to activating the retrosplenial and PHC sites as did the previous three experiments, contextual conditions in the present experiment activated occipital visual areas. Two factors might have contributed to the presence of this activation. First, of the four experiments reported here, this is the only experiment where the control stimuli happen to have been homogenous in their largely black-and-white appearance. Therefore, the occipital differential activation may reflect the difference between the visually diverse contextual objects and the gray-looking control images. Although this difference was a nonintentional aspect of the design, it helped reveal which cortical areas are active when the objects in the two conditions differ also in visual properties, in addition to their main difference in level of contextual association. Second, the task here was different than in the previous experiments in that subjects were required to identify the context rather than recognize the objects. Future research may be required to determine whether any aspect of the observations we report here is a result of this difference in task requirements.

To summarize, this fourth experiment indicates that the PHC and the retrosplenial mediate the processing of both spatial and nonspatial associations.

Contextual Associations as a Bridge between Episodic Memory and Spatial Representations

More than in any other process, the PHC has been repeatedly implicated in two different functions: processing of spatial information (Aguirre et al., 1998; Epstein and Kanwisher, 1998; Mellet et al., 2000) and facilitating the formation of episodic memory (Brewer et al., 1998; Davachi et al., 2003; Mishkin et al., 1998; Ranganath and D'Esposito, 2001; Schacter and Wagner, 1999; Squire and Zola, 1996; Wagner et al., 1998). The PHC and the retrosplenial cortex are reciprocally connected to each other (Suzuki and Amaral, 1994). Like the PHC, the retrosplenial cortex has most often been implicated in both spatial analysis (Cooper and Mizumori, 2001; Maguire, 2001; Vann and Aggleton, 2002) and episodic memory (Andreasen et al., 1995; Bowers et al., 1988; Maeshima et al., 2001; Markowska et al., 1989; Valenstein et al., 1987; Wiggs et al., 1999). Assigning two different and seemingly unrelated functions to the same cortical regions may appear conflicting at first. The present proposal that the PHC and the retrosplenial cortex mediate processing of contextual associations, however, provides a framework for bridging these sets of findings. Both spatial information and episodic memories rely on familiar associations. Consequently, a reasonable explanation for why studies of episodic memory as well as studies related to navigation activate similar regions is that they both entail the activation of familiar associations, which, as suggested here, is mediated by the PHC and the retrosplenial cortex. (A related account was developed independently with regard to the hippocampal "place versus memory" debate [Eichenbaum, 2001; Hirsh, 1974; Redish, 2001]. In addition, an alternative explanation for why the hippocampus is active in spatial as well as nonspatial tasks has been proposed, according to which structures that represent spatial information and structures that represent nonspatial information are both intertwined within the hippocampus [Hampson et al., 1999; Wood et al., 1999].)

It is not argued that the PHC is the main circuitry subserving episodic memory. This function is attributed more generally to the hippocampus (Aggleton and Brown, 1999; Davachi and Wagner, 2002; Eichenbaum et al., 1996; Vargha-Khadem et al., 1997). With its suggested role in associative processing, the parahippocampal cortex may project to the hippocampus essential input for processing autobiographical memories and familiar episodes. Along these lines, the PHC represents general associative knowledge built through experience (e.g., "which objects tend to appear in *a* kitchen"), and a later stage at the hippocampus represents episodic instances of this knowledge (e.g., "which objects appear in *my* kitchen") (Buckner, 2000). Our findings with regard to the hippocampus support this hypothesis; while the objects elicited hippocampal activation when compared with fixation baseline, there was no significant hippocampal activation when we compared the perception of highly contextual objects with the perception of Weak CA objects. The same comparisons have nevertheless elicited significant activation in the PHC. These results suggest that the objects in both conditions have elicited a comparable amount of personal episodic memories, which subsequently were subtracted out and hence showed no significant differential activation in the hippocampus. Because the objects in the two groups differed in the amount and strength of general contextual associations, however, they activated the PHC regardless of the participants' autobiographic experience with those specific objects.

That the PHC generally mediates associative processing is supported by reports from multiple disciplines. For example, associations between nonrelated objects (e.g., monkey-umbrella) activate a similar region in the parahippocampal gyrus and collateral sulcus as we observed here (Henke et al., 1997; Rombouts et al., 1997). In addition, associative encoding, but not match-to-sample of visual scenes, activates the parahippocampal gyrus (Montaldi et al., 1998). A final example from the visual domain is a recent study of associative and recognition memory, where object-color associations elicited significantly more parahippocampal acti-

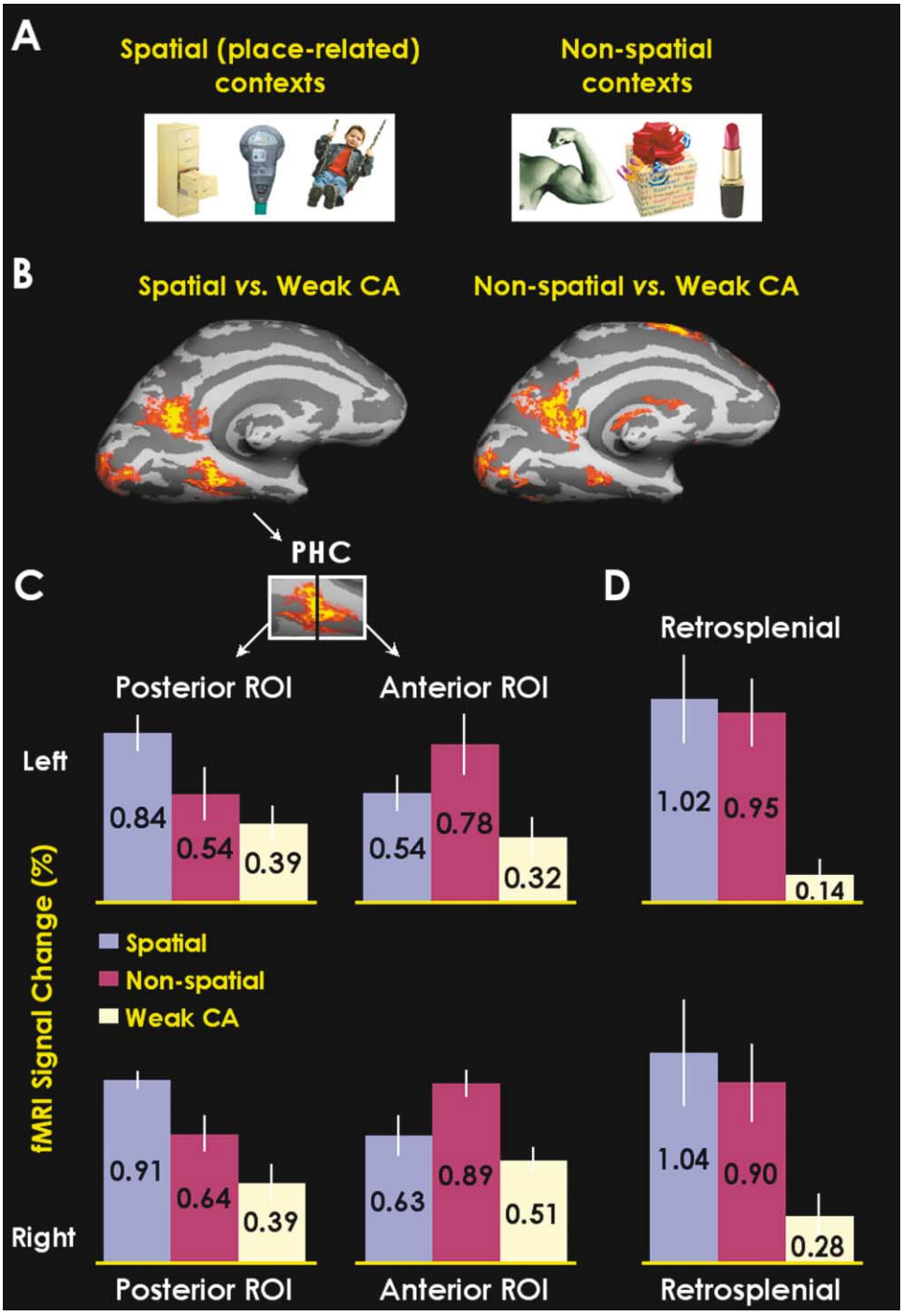

Figure 7. Spatial versus Nonspatial Context (Experiment 4)

(A) Objects in the *spatial* condition were associated with place-specific contexts such as office, street, and playground. Objects in the *nonspatial* condition conveyed contexts such as strength, birthday, and cosmetics. The nonspatial contexts were not strongly associated with specific places, but they were nevertheless strongly associated with typical sets of objects. Average reaction time for recognizing spatial contexts was 805 ms and for recognizing the nonspatial context was 875 ms. That they were not significantly different from each other ($t_{10} = -1.221$) indicates that there was no difference in difficulty between extracting spatial and nonspatial contexts. Both these contextual conditions were compared with a third condition, not depicted here, of Weak CA control objects.

(B) Statistical activation maps for the different context types compared with controls ($p < 0.0001$ for *spatial* and $p < 0.01$ for *nonspatial* versus Weak CA). The activity was averaged across all seven participants and Bonferroni corrected for multiple comparisons.

(C) fMRI percent signal change as a function of condition, in both the posterior and anterior nonoverlapping parts of the PHC focus (top, left hemisphere; bottom, right hemisphere). For demonstration purposes, the division of the PHC region of interest (ROI) into posterior and anterior parts is illustrated here by a straight vertical line on the average activation map. The specific analysis, however, was conducted on the individual activation maps, and the actual shape of these subdivisions naturally varied between subjects. The average extent of the posterior ROI was thirteen $3.125 \times 3.125 \times 3$ mm^3 voxels and it centered on $-26, -41, -6$. The average extent of the anterior ROI was eleven $3.125 \times$

vation than old/new object judgments (Yonelinas et al., 2001). Associations between items other than visual objects have also been shown to elicit differential parahippocampal activation (although not always at the exact parahippocampal locations we have observed here). For example, associations between abstract nouns (e.g., *hint-illusion*) (Henke et al., 1999; Jackson et al., 2002) or even associations between novel odors in rats (Bunsey and Eichenbaum, 1993; Wood et al., 1999) seem to rely on the parahippocampal cortex.

Conclusions

An important open question is what exact aspect of contextual associations is represented and processed in the PHC and the retrosplenial cortex. It seems safe to assume that a highly contextual object does not merely activate in these foci the actual visual representations of the objects that share its context, because object representations have been shown to be stored elsewhere in the visual cortex (e.g., Bar et al., 2001; Grill-Spector et al., 2001; Ishai et al., 1999; Kanwisher et al., 1997; Kosslyn et al., 1995; Malach et al., 2002; Martin et al., 1996). Therefore, it is possible that the PHC and the retrosplenial cortex analyze long-term associations rather than participate in object perception per se.

One alternative is that these representations have the form of "schemata" (Hock et al., 1978; Mandler and Johnson, 1976) or "context frames" (Bar and Ullman, 1996), containing information about frequent members of each context and the typical relations between them. Consequently, the activation elicited by a highly contextual object may reflect the triggering of relevant expectations (Kutas and Federmeier, 2000) and information on what other associated representations need to be activated or primed. Future studies will be necessary to characterize the exact role of the PHC and retrosplenial sites in associative representation and processing.

In summary, the set of experiments we report here revealed that visual context consistently activates an area in the parahippocampal cortex and an area in the retrosplenial cortex. The proposal that emerges from these findings is that these two regions process familiar associations that provide a critical basis both for episodic memories and for finding our way around.

Experimental Procedures

Subjects

A total of 34 subjects participated in this study: six in Experiment 1, twelve in Experiment 2, nine in Experiment 3, and seven in Experiment 4 (four males in each; age range 19–34). All subjects had normal or corrected-to-normal vision. None were aware of the purpose of the experiment. Informed written consent was obtained from each subject prior to the scanning session. All procedures were approved by Massachusetts General Hospital Human Studies Protocol number 2000P-000949.

Stimuli, Design, and Procedure

The pictures were color photographs of everyday objects, 9.2° in their largest dimension, presented on a gray background. The image presentations and response collection were controlled by a Macintosh Power Mac G4, with a resolution of 1024 × 768 pixels and a refresh rate of 75 Hz, and by the PsyScope experimental software (Macwhinney et al., 1997). In Experiment 1, there were three different conditions: Strong CA_B, Strong CA_I, and Weak CA. In Experiment 4 there were three different conditions: Spatial, Nonspatial, and WCA. In both experiments, each subject had 30 practice trials prior to functional scanning with images that were not presented again in the experiment. Each stimulus was present on the screen for 1700 ms and was therefore readily recognizable. Each condition included 40 different pictures that were presented three times. Each block consisted of ten consecutive presentations of different pictures from a specific experimental condition, appearing in a random order. The total block duration was 20 s. Blocks of experimental images were separated by 20 s intervals of rest during which a fixation dot was presented. Each experimental condition was presented in 12 blocks, and there were 30 fixation blocks. All blocks were homogeneously distributed across six consecutive scans. In Experiment 1, instructions required subjects to press a button as soon as they recognized

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3.125 × 3 mm^3 voxels and it centered on −30, −35, −9. In the posterior PHC, spatial contexts elicited a signal that was significantly higher than this elicited by Weak CA objects ($t_{10} = 4.389$; $p < 0.0007$ in the left hemisphere), whereas the signal increase elicited by the nonspatial contexts in this region failed to reach significance ($t_{10} = 1.321$). In the anterior PHC, on the other hand, the nonspatial contexts elicited a signal that was significantly higher than this elicited by Weak CA objects ($t_{10} = 2.039$; $p < 0.04$), whereas the spatial contexts failed to reach a significant difference in this anterior PHC region ($t_{10} = 1.464$). As can be seen in the lowest panel, exactly the same trend was obtained also in the right hemisphere.

The specific posterior/anterior analysis was post hoc and the ROIs were defined on functional data. Because this result is central to our interpretation of the role of the PHC and the retrosplenial cortex, we performed three additional analyses, examining the same issue using different methods. First, we redefined the PHC posterior/anterior sections based on anatomical information only. In other words, for each subject, we split the parahippocampal gyrus and collateral sulcus in half, creating equal posterior and anterior parts and using those halves as the two ROIs in the analysis. The results of this anatomically based analysis confirmed our previous finding in that spatial contexts activated the posterior part significantly higher, and the nonspatial contexts activated the anterior part significantly higher [a significant interaction between posterior/anterior and spatial/nonspatial: $F(2,102) = 3.10$; $p < 0.05$].

In a second analysis, we split the data in two such that, for each subject, half the data was used for defining the ROIs and the second half of the data was used to perform the statistical analyses (i.e., crossvalidation). The total experiment consisted of six scanning runs; therefore, three runs were included in each half of the analysis. Half A consisted of runs 1, 4, and 6, and Half B consisted of runs 2, 3, and 5. The split was balanced such that each half contained presentations of all the pictures used. The ROIs were first defined based on the activation pattern elicited by Half A and analyzed on Half B, and then, in a complementary analysis, Half B was used for defining the ROIs and Half A for the analysis. We averaged the outcome of both tests. This analysis, too, resulted in a significant interaction between posterior/anterior and spatial/nonspatial [$F(2,282) = 3.974$; $p < 0.02$].

Finally, in a third analysis, we used the functional activation map of one subject to define the posterior and anterior PHC ROIs and subsequently performed the ROI analysis on the data of the remaining six subjects. We repeated this analysis seven times, using a different individual each time, and eventually averaging the outcome of all seven parts. This last analysis also resulted in a significant interaction between location (posterior/anterior) and condition (spatial/nonspatial) [$F(2,246) = 4.187$; $p < 0.017$]. Taken together, these additional analyses provide critical support for the dissociation we report, where posterior PHC is more active for spatial contexts and anterior PHC is more active for nonspatial contexts.

(D) fMRI percent signal change as a function of condition in the retrosplenial cortex. Error bars represent a single standard error.

the image presented to them. In Experiment 4, during contextual blocks, subjects' task was to press the button when they recognized the context that each object represented. In the Weak CA blocks, subjects had to press a button as soon as they recognized the object.

In Experiment 2, there were 20 blocks of contextually related objects (four for each of the five main categories). Half of the pictures in this experiment were with and half were without background, in both contextual and control conditions. Each block consisted of 12 presentations of pictures. Each picture was presented for 400 ms with a 1600 ms interstimulus interval. There were 119 different pictures in the contextually related category and 119 pictures in the control condition.

In Experiment 3 there were five different conditions: Weak CA, contextually related objects in isolation, Houses, Indoor Scenes, and Outdoor Scenes. There were a total of 100 different pictures in each condition, except for Weak CA, which had a total of 60 different pictures. Each block of pictures consisted of ten consecutive picture presentations (five different pictures presented twice in a random order). The contextually related blocks contained five different objects sharing the same context. Each experimental block contained pictures from a single experimental condition (e.g., Houses). Each picture was presented for 1700 ms with a 300 ms interstimulus interval. The experiment consisted of nine consecutive scans. The experimental blocks and the fixation blocks were homogeneously distributed within each scan. The subjects' task was to press a button as soon as they recognized the image presented to them.

Imaging Details

Subjects were scanned in a 3T Siemens Allegra magnetic resonance (MR) scanner, using a gradient-echo echo-planar pulse sequence. Stimuli were back projected (LCD projector, Notevision6) onto a translucent screen that subjects viewed through a mirror mounted on the head coil. A custom-designed magnet-compatible panel of four keys was used for subjects' responses. Head motion was minimized using pillows and cushions around the head and a forehead strap. MR images were acquired using a custom-built head coil. MR slices were oriented approximately 10° axially, 3 mm thick with 1 mm gap, and with an in-plane resolution of 3.125 mm. In Experiments 1 and 4, each scan lasted 3 min 48 s, during which 3630 images were acquired (110 images per slice; 33 slices). In Experiment 2, each scan lasted for 5 min and 40 s, during which 5478 images were acquired (166 images per slice; 33 slices). In Experiment 3, each scan lasted for 5 min and 48 s, during which 5610 images were acquired (170 images per slice; 33 slices).

For each subject, a series of conventional structural images was first collected to provide detailed anatomical information. Then, a series of functional images was collected (TR = 2 s, TE = 25 ms, flip angle = 90°) to provide both anatomical and functional images sensitive to the BOLD contrast. The entire session, including both structural and functional sequences, lasted between 1 and 1.5 hr.

Statistical Analysis

The methods used here are similar to and detailed in Bar et al. (2001). Data from individual fMRI runs were first motion corrected using AFNI motion correction algorithm in which all images were aligned to the first image of the first functional run. The data were then spatially smoothed using a Gaussian full-width half-max (fwhm) of 5 mm. The intensities for all runs were globally rescaled such that the in-brain mean intensity was 1000. Signal intensity for each condition was then computed and averaged throughout all the runs. The estimated hemodynamic response was defined by a γ function of 2.25 s hemodynamic delay and 1.25 s dispersion. To account for intrinsic serial correlation in the fMRI data within subjects, we used a global autocorrelation function that computes a whitening filter (Burock and Dale, 2000). The data were then tested for statistical significance and activation maps were constructed for comparisons of the different conditions (t tests).

Cortical Surface-Based Analysis

Once all trials were averaged, the mean and variance volumes were resampled onto the cortical surface for each subject. Each hemisphere was then morphed into a sphere in the following manner. First, each cortical hemisphere was morphed into a metrically optimal spherical surface. The pattern of cortical folds was then represented as a function on a unit sphere. Next, each individual subject's spherical representation was aligned with an average folding pattern constructed from a large number of individuals aligned previously. This alignment was accomplished by maximizing the correlation between the individual and the group, while prohibiting changes in the surface topology and simultaneously penalizing excessive metric distortion (Fischl et al., 1999).

Region of Interest (ROI) Analysis

The voxels chosen for an ROI were constrained both functionally and structurally. The structural constraint was based on hand labeling of the PHC for each subject. The functional constraint was based on the voxels that were activated by any component of the task as revealed by the main effect (all versus fixation contrast), with a threshold of $p < 0.01$. Only voxels that elicited signal change in a positive direction when compared with baseline were included for analysis. All the voxels that met those constraints were averaged together, and contrasts of interest (COIs) were then computed on the resulting time courses. The COIs were not biased by the functional constraint because the contrast used in the functional constraint did not favor one condition or set of conditions over another. In defining the ROIs for Experiment 3, we used the functional activation in the PHC and the retrosplenial cortex from Experiment 1 to choose the voxels to be included in each ROI. Once defined, the appropriate ROI was then projected to each of the individual subjects for the necessary computations. In defining the separate posterior and anterior ROIs for each individual in Experiment 4, we split the PHC activation to posterior and anterior nonoverlapping regions. Although this division into posterior and anterior parts was arbitrary, it stemmed from a consistent trend we noticed in activation maps of the individual subjects. See caption of Figure 7 for details on several additional methods we used to divide the PHC ROI.

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References

Aggleton, J.P., and Brown, M.W. (1999). Episodic memory, amnesia, and the hippocampal-anterior thalamic axis. Behav. Brain Sci. *22*, 425–444; discussion 444–489.

Aguirre, G., and D'Esposito, M. (1997). Environmental knowledge is subserved by separable dorsal/ventral neural areas. J. Neurosci. *17*, 2512–2518.

Aguirre, G.K., Detre, J.A., Alsop, D.C., and D'Esposito, M. (1996). The parahippocampus subserves topographical learning in man. Cereb. Cortex *6*, 823–829.

Aguirre, G.K., Zarahn, E., and D'Esposito, M. (1998). An area within human ventral cortex sensitive to "building" stimuli: evidence and implications. Neuron *21*, 373–383.

Andreasen, N.C., O'Leary, D.S., Cizadlo, T., Arndt, S., Rezai, K., Watkins, G.L., Ponto, L.L., and Hichwa, R.D. (1995). Remembering the past: two facets of episodic memory explored with positron emission tomography. Am. J. Psychiatry *152*, 1576–1585.

Bar, M., and Ullman, S. (1996). Spatial context in recognition. Perception *25*, 343–352.

Bar, M., Tootell, R., Schacter, D., Greve, D., Fischl, B., Mendola, J., Rosen, B., and Dale, A. (2001). Cortical mechanisms of explicit visual object recognition. Neuron *29*, 529–535.

Biederman, I. (1981). On the semantic of a glance at a scene. In Perceptual Organization, M. Kubovy and J.R. Pomerantz, eds. (Hillsdale, NJ: Erlbaum), pp. 213–253.

Biederman, I., Mezzanotte, R.J., and Rabinowitz, J.C. (1982). Scene perception: detecting and judging objects undergoing relational violations. Cognit. Psychol. *14*, 143–177.

Bowers, D., Verfaellie, M., Valenstein, E., and Heilman, K.M. (1988). Impaired acquisition of temporal information in retrosplenial amnesia. Brain Cogn. *8*, 47–66.

Brewer, J.B., Zhao, Z., Desmond, J.E., Glover, G.H., and Gabrieli, J.D. (1998). Making memories: brain activity that predicts how well visual experience will be remembered. Science *281*, 1185–1187.

Buckner, R.L. (2000). Neural origins of 'I remember'. Nat. Neurosci. *3*, 1068–1069.

Bunsey, M., and Eichenbaum, H. (1993). Critical role of the parahippocampal region for paired-associate learning in rats. Behav. Neurosci. *107*, 740–747.

Burock, M.A., and Dale, A.M. (2000). Estimation and detection of event-related fMRI signals with temporally correlated noise: a statistically efficient and unbiased approach. Hum. Brain Mapp. *11*, 249–260.

Cooper, B.G., and Mizumori, S.J. (2001). Temporary inactivation of the retrosplenial cortex causes a transient reorganization of spatial coding in the hippocampus. J. Neurosci. *21*, 3986–4001.

Davachi, L., and Wagner, A. (2002). Hippocampal contributions to episodic encoding: insights from relational and item-based learning. J. Neurophysiol. *88*, 982–990.

Davachi, L., Mitchell, J., and Wagner, A. (2003). Multiple routes to memory: distinct medial temporal lobe processes build item and source memories. Proc. Natl. Acad. Sci. USA *100*, 2157–2162.

Eichenbaum, H. (2001). The hippocampus and declarative memory: cognitive mechanisms and neural codes. Behav. Brain Res. *127*, 199–207.

Eichenbaum, H., Schoenbaum, G., Young, B., and Bunsey, M. (1996). Functional organization of the hippocampal memory system. Proc. Natl. Acad. Sci. USA *93*, 13500–13507.

Epstein, R., and Kanwisher, N. (1998). A cortical representation of the local visual environment. Nature *392*, 598–601.

Fink, G.R., Markowitsch, H.J., Reinkemeier, M., Bruckbauer, T., Kessler, J., and Heiss, W.D. (1996). Cerebral representation of one's own past: neural networks involved in autobiographical memory. J. Neurosci. *16*, 4275–4282.

Fischl, B., Sereno, M.I., Tootell, R.B., and Dale, A.M. (1999). High-resolution intersubject averaging and a coordinate system for the cortical surface. Hum. Brain Mapp. *8*, 272–284.

Grill-Spector, K., Kourtzi, Z., and Kanwisher, N. (2001). The lateral occipital complex and its role in object recognition. Vision Res. *41*, 1409–1422.

Hampson, R.E., Simeral, J.D., and Deadwyler, S.A. (1999). Distribution of spatial and nonspatial information in dorsal hippocampus. Nature *402*, 610–614.

Henke, K., Buck, A., Weber, B., and Wieser, H.G. (1997). Human hippocampus establishes associations in memory. Hippocampus *7*, 249–256.

Henke, K., Weber, B., Kneifel, S., Wieser, H.G., and Buck, A. (1999). Human hippocampus associates information in memory. Proc. Natl. Acad. Sci. USA *96*, 5884–5889.

Hirsh, R. (1974). The hippocampus and contextual retrieval of information from memory: a theory. Behav. Biol. *12*, 421–444.

Hock, H.S., Romanski, L., Galie, A., and Williams, C.S. (1978). Real-world schemata and scene recognition in adults and children. Mem. Cognit. *6*, 423–431.

Ishai, A., Ungerleider, L.G., Martin, A., Schouten, J.L., and Haxby, J.V. (1999). Distributed representation of objects in the human ventral visual pathway. Proc. Natl. Acad. Sci. USA *96*, 9379–9384.

Jackson, O., Dobbins, I.G., and Schacter, D.L. (2002). The ties that bind: an event-related fMRI study of associative encoding. Poster session presented at the annual meeting of the Cognitive Neuroscience Society, San Francisco.

Kanwisher, N., Woods, R.P., Iacoboni, M., and Mazziotta, J.C. (1997). A locus in human extrastriate cortex for visual shape analysis. J. Cogn. Neurosci. *9*, 133–142.

Kosslyn, S.M., Alpert, N.M., and Thompson, W.L. (1995). Identifying objects at different levels of hierarchy: a positron emission tomography study. Hum. Brain Mapp. *3*, 107–132.

Kutas, M., and Federmeier, K.D. (2000). Electrophysiology reveals semantic memory use in language comprehension. Trends Cogn. Sci. *4*, 463–470.

Levy, I., Hasson, U., Avidan, G., Hendler, T., and Malach, R. (2001). Center-periphery organization of human object areas. Nat. Neurosci. *4*, 533–539.

Macwhinney, B., Cohen, J., and Provost, J. (1997). The PsyScope experiment-building system. Spat. Vis. *11*, 99–101.

Maeshima, S., Ozaki, F., Masuo, O., Yamaga, H., Okita, R., and Moriwaki, H. (2001). Memory impairment and spatial disorientation following a left retrosplenial lesion. J. Clin. Neurosci. *8*, 450–451.

Maguire, E.A. (2001). The retrosplenial contribution to human navigation: a review of lesion and neuroimaging findings. Scand. J. Psychol. *42*, 225–238.

Malach, R., Levy, I., and Hasson, U. (2002). The topography of high-order human object areas. Trends Cogn. Sci. *6*, 176–184.

Mandler, J.M., and Johnson, N.S. (1976). Some of the thousand words a picture is worth. J. Exp. Psychol. Hum. Learn. *2*, 529–540.

Markowska, A.L., Olton, D.S., Murray, E.A., and Gaffan, D. (1989). A comparative analysis of the role of fornix and cingulate cortex in memory: rats. Exp. Brain Res. *74*, 187–201.

Martin, A., Wiggs, C.L., Ungerleider, L.G., and Haxby, J.V. (1996). Neural correlates of category-specific knowledge. Nature *379*, 649–652.

Mellet, E., Briscogne, S., Tzourio-Mazoyer, N., Ghaem, O., Petit, L., Zago, L., Etard, O., Berthoz, A., Mazoyer, B., and Denis, M. (2000). Neural correlates of topographic mental exploration: the impact of route versus survey perspective learning. Neuroimage *12*, 588–600.

Mishkin, M., Vargha-Khadem, F., and Gadian, D.G. (1998). Amnesia and the organization of the hippocampal system. Hippocampus *8*, 212–216.

Montaldi, D., Mayes, A.R., Barnes, A., Pirie, H., Hadley, D.M., Patterson, J., and Wyper, D.J. (1998). Associative encoding of pictures activates the medial temporal lobes. Hum. Brain Mapp. *6*, 85–104.

O'Craven, K.M., and Kanwisher, N. (2000). Mental imagery of faces and places activates corresponding stiimulus-specific brain regions. J. Cogn. Neurosci. *12*, 1013–1023.

Palmer, S.E. (1975). The effects of contextual scenes on the identification of objects. Mem. Cognit. *3*, 519–526.

Ranganath, C., and D'Esposito, M. (2001). Medial temporal lobe activity associated with active maintenance of novel information. Neuron *31*, 865–873.

Redish, A.D. (2001). The hippocampal debate: are we asking the right questions? Behav. Brain Res. *127*, 81–98.

Rombouts, S.A., Machielsen, W.C., Witter, M.P., Barkhof, F., Lindeboom, J., and Scheltens, P. (1997). Visual association encoding activates the medial temporal lobe: a functional magnetic resonance imaging study. Hippocampus *7*, 594–601.

Schacter, D.L., and Wagner, A.D. (1999). Medial temporal lobe activations in fMRI and PET studies of episodic encoding and retrieval. Hippocampus *9*, 7–24.

Schacter, D.L., Uecker, A., Reiman, E., Yun, L.S., Bandy, D., Chen, K., Cooper, L.A., and Curran, T. (1997). Effects of size and orientation change on hippocampal activation during episodic recognition: a PET study. Neuroreport *8*, 3993–3998.

Squire, L.R., and Zola, S.M. (1996). Structure and function of declarative and nondeclarative memory systems. Proc. Natl. Acad. Sci. USA *93*, 13515–13522.

Suzuki, W.A., and Amaral, D.G. (1994). Perirhinal and parahippocam-

pal cortices of the macaque monkey: cortical afferents. J. Comp. Neurol. *350*, 497–533.

Valenstein, E., Bowers, D., Verfaellie, M., Heilman, K.M., Day, A., and Watson, R.T. (1987). Retrosplenial amnesia. Brain *110*, 1631–1646.

Vann, S.D., and Aggleton, J.P. (2002). Extensive cytotoxic lesions of the rat retrosplenial cortex reveal consistent deficits on tasks that tax allocentric spatial memory. Behav. Neurosci. *116*, 85–94.

Vargha-Khadem, F., Gadian, D.G., Watkins, K.E., Connelly, A., Van Paesschen, W., and Mishkin, M. (1997). Differential effects of early hippocampal pathology on episodic and semantic memory. Science *277*, 376–380.

Wagner, A.D., Schacter, D.L., Rotte, M., Koutstaal, W., Maril, A., Dale, A.M., Rosen, B.R., and Buckner, R.L. (1998). Building memories: remembering and forgetting of verbal experiences as predicted by brain activity. Science *281*, 1188–1191.

Wiggs, C.L., Weisberg, J., and Martin, A. (1999). Neural correlates of semantic and episodic memory retrieval. Neuropsychologia *37*, 103–118.

Wood, E.R., Dudchenko, P.A., and Eichenbaum, H. (1999). The global record of memory in hippocampal neuronal activity. Nature *397*, 613–616.

Yonelinas, A.P., Hopfinger, J.B., Buonocore, M.H., Kroll, N.E., and Baynes, K. (2001). Hippocampal, parahippocampal and occipital-temporal contributions to associative and item recognition memory: an fMRI study. Neuroreport *12*, 359–363.