Neurons in the human hippocampus and amygdala respond to both low- and high-level image properties

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low- and high-level image properties. J Neurophysiol 105: 2874 –2884, 2011. First published April 6, 2011; doi:10.1152/jn.00977.2010.—A large number of studies have demonstrated that structures within the medial temporal lobe, such as the hippocampus, are intimately involved in declarative memory for objects and people. Although these items are abstractions of the visual scene, specific visual details can change the speed and accuracy of their recall. By recording from 415 neurons in the hippocampus and amygdala of human epilepsy patients as they viewed images drawn from 10 image categories, we showed that the firing rates of 8% of these neurons encode image illuminance and contrast, low-level properties not directly pertinent to task performance, whereas in 7% of the neurons, firing rates encode the category of the item depicted in the image, a high-level property pertinent to the task. This simultaneous representation of high- and low-level image properties within the same brain areas may serve to bind separate aspects of visual objects into a coherent percept and allow episodic details of objects to influence mnemonic performance.

human single neuron; image illuminance and contrast; multilevel representation

Although it is clear that the hippocampus is required for the formation of new memories of a declarative nature (Squire and Zola 1996; Cohen et al. 1999; Squire 2004), its broader role in memory retrieval and in forming associations among different aspects of our experience remains unclear (Squire 2004). One theory is that the hippocampus is only required for the initial acquisition and consolidation of memory and not critical for later retrieval (Squire et al. 1984; Teyler and DiScenna 1986). In contrast, recent studies have shown that the fMRI BOLD signal within the hippocampus changes even when distant memories of details are retrieved (Nadel et al. 2000) and that recall of such details for remote memories is impaired by hippocampal damage (Pascalis et al. 2009).

Prior single neuron recordings in human epilepsy patients have suggested that neural representations within the medial temporal lobe are highly abstracted representations of the visual scene (Heit et al. 1988; Quiroga et al. 2005), a view consistent with the position of the hippocampus near the end of the ventral stream of visual processing (Felleman and Van Essen 1991) and at the top of a hierarchy of associational areas (Lavenex and Amaral 2000). Nonetheless, the performance of human observers in a variety of memory tasks has shown that the details of a scene, incidental to correct task performance, can materially change the speed and accuracy of recall (Paller et al. 1993; Church and Schacter 1994; Goldinger 1996), which suggests that representation of such episodic details is connected with mnemonic, and potentially more abstract, representations within the medial temporal lobe.

To better understand how such details are represented in the human hippocampus and other medial temporal lobe structures, we examined how the firing of the fundamental computational units of the brain, single neurons, reflect basic image properties as subjects perform a simple image categorization task (whether an image contains a human face or not) that does not explicitly depend on these basic image properties.

MATERIALS AND METHODS

Task

Visual stimuli were presented to participants using a laptop computer (Apple Computer, Cupertino, CA) placed in front of the participant sitting in the hospital bed. Each image occupied a square 0.1 m on each side. At a distance of ~0.6 m, this area subtends 9.6° of the visual arc. Response button presses were collected from a trackball with large buttons (ExpertMouse, Kensington, Redwood Shores, CA) to increase participant comfort and provide isolation from the laptop switching power supply. For experiment 1 (E1), images were presented for 600 or 1000 ms (same for all trials in one experiment), and subjects could press the button as soon as they had made a decision; an 800-ms interval with a blank screen followed the button press. The righthand button was used to indicate a face. For experiment 2 (E2), images were presented for 1,000 ms, button presses were prompted by the presentation of a question mark on the screen after the image disappeared, and all button presses before the end of image presentation were ignored. Participants had up to 800 ms to respond and normally pressed the left button with the thumb of the left hand and the right button with the thumb of the right hand. The button used to indicate a face was randomly assigned to the left or right button for each experiment. A randomly chosen interval between 400 and 800 ms followed the button press and the start of the next image. Each image was shown six times, and the order was randomized. For all experiments, stimulus presentation, timing, response collection, and synchronization with the neural recordings were performed using a JAVA (Sun Microsystems, Santa Clara, CA) program framework (PsychGameFramework) developed by our laboratory.

Images and Illuminance/Contrast Normalization

The two basic image properties studied here were image exit illuminance [measured as the mean pixel intensity value (ranging
from 0–255]) and image contrast (measured as the SD of the pixel intensity values). The sets of images that have typically been used in the categorization task during human single neuron recordings contain a natural variation of image illuminance and contrast since they have been gathered from a variety of sources on the World Wide Web (Kreiman et al. 2000a), and these two properties covary with image category. To study the effects of this covariation on neural responses, we used two experimental strategies.

In E1, we examined the responses of medial temporal lobe neurons to the presentation of images that had image illuminance and contrast covarying in a natural way with the category of the image (e.g., images of tools often have a bright background). The images, kindly provided by G. Kreiman, were drawn from six or seven categories [chosen from animals, cars, buildings, faces, famous people, indoor scenes, objects, outdoor scenes, spatial patterns, and tools (per Kreiman et al. 2000a)], where the illuminance and contrast remained as the images collected from the World Wide Web (Fig. 1). All color images were converted to grayscale. Figure 2 shows the distribution of illuminance and contrast for these images in 10 possible categories (solid line for E1).

For E2, images for the four categories of animals, buildings, outdoor scenes, and tools were gathered from pages on the World Wide Web that contained the images and had no copyright or licensing restrictions. Images of faces were taken from the Psychological Image Collection at Stirling, UK (http://pics.psych.stir.ac.uk/), specifically the Nottingham scans, and were half male and half female. The distribution of the illuminance and contrast (characterized as the mean and SD, ignoring higher-order moments) was first computed for each category of image. Each image within the category then had both the mean and SD of its pixel intensity values moved toward the mean values for the category to which it belonged by an amount designed to make the distribution of the image illuminance and contrast equal for all categories up to the second-order moments of the distribution [using the program ImageJ (Abramoff et al. 2004)].

Each image was examined after this adjustment, and, in some cases, manual changes were required to achieve a reasonable visual appearance, such as replacing the white background of the tools with a patterned background of the mean intensity. After such manual adjustments, another round of adjustment of pixel intensities was performed to ensure equal distributions (up to the second-order moment) of both image illuminance and contrast across all categories.

Filtering and event detection. Possible action potentials (waveform events) were detected by filtering twice (forward and backward, acausally) with a 24th-order digital IIR bandpass filter, 300–3,000 Hz, with a −100-dB stop band and −12-dB notches at 1, 2, and 3 kHz.

All patient participants had drug-resistant epilepsy requiring the implantation of depth electrodes (Ad-Tech Medical, Racine, WI) for clinical evaluation and consideration of possible surgical resection of their seizure focus. This implantation was performed stereotactically (Medtronic StealthStation), and the position was confirmed by co-registering the postoperative computed tomography or MRI (using the Statistical Parametric Mapping toolkit, http://www.fil.ion.ucl.ac.uk/spm/) to the preoperative structural MRI. This procedure localizes the tips of the microwires to within ±2 mm. Consent to include the patient in the research protocol and implant microwires was obtained in accordance with the Declaration of Helsinki, and the protocol approved by St. Joseph’s Hospital and Medical Center or the University of California–Los Angeles Institutional Review Board. Bundles of nine 38-μm-diameter platinum-iridium microwires (California Fine Wire, Grover Beach, CA) were introduced through a lumen within the clinical intraparenchymal electrode during surgery. The implantation sites were chosen according to clinical criteria, which limits the potential recording sites. In almost all cases, however, this included the hippocampus and amygdala, bilaterally.

Microwire Implantation

The extracellular potentials corresponding to single neuron activity (SUA) were recorded from the tips of the microwires. At each site, the potential difference between eight of the microwires was recorded relative to a ninth microwire in the same bundle using a headstage amplifier of custom design. This amplifier provides a 400× gain and was connected to signal conditioning electronics and analog-to-digital converters (model DT9834, Data Translation, Marlborough, MA) via a 1-m tether cable. Each signal channel was preconditioned with a highpass filter (0.5-Hz corner) followed by a 10-kHz antialiasing filter and a computer-controlled 1–16× adjustable gain amplifier (custom-designed signal conditioning board). The conditioned signal was digitized at 29,412 Hz with 16-bit resolution. For E1, recordings were performed using a Neuralynx (Bozeman, MT) Lynx-8 amplifier.

Data Analysis

Filtering and event detection. Possible action potentials were detected by filtering twice (forward and backward, acausally) with a 24th-order digital IIR bandpass filter, 300–3,000 Hz, with a −100-dB stop band and −12-dB notches at 1, 2, and 3 kHz.
followed by a two-sided threshold detector (threshold = 2.8 times each channel’s SD) to identify event times. The original signal was then highpass filtered (100 Hz, single-pole Butterworth, applied causally) to capture event waveform shape in windows of 32 samples (1.1 ms) with the absolute peak value aligned at the ninth sample.

Event characterization. Because more than one neuron may be recorded near any given electrode, event windows were grouped into several clusters of events of similar waveform shape. This clustering was performed using the open-source clustering program KlustaKwik (Klustakwik.sf.net), which is a modified implementation of the Classification Expectation-Maximization clustering algorithm (Celeux and Govaert 1995).

Each cluster of waveform events was examined for three criteria to determine if it represented well-isolated single neuron activity: 1) the cluster had to have evidence in the waveform of an initial sharp voltage deflection followed by a slower opposite deflection, 2) an interspike interval histogram for the cluster had to show no more than 5% of events occurring within 3 ms of another event (such a “dead time” is expected for SUA because of the neuronal refractory period), and 3) there had to be no peak in the power spectral density of spike times at a power line harmonic frequency that exceeded 30% over the average power level with 3 Hz of this frequency.

Single unit response calculation. The exact nature of the representation of objects by single neurons within the human medial temporal lobe is presently unknown and subject to considerable debate (Bowers 2009). In principle, the representations that are meaningful to downstream neurons can only be known if the connectivity to and actions of those downstream neurons are known. Nonetheless, as a rough measure, most previous reports have used one, or a sequence, of tests of a statistic computed from an absolute measure of firing rate in a fixed interval time interval after the stimulus onset, a measure of the firing rate in this interval relative to its baseline, or a combination of these (Heit et al. 1988; Kreiman et al. 2000a; Quiroga et al. 2005; Viskontas et al. 2006; Rutishauser et al. 2006; Steinmetz 2009). As one view of these representations, the absolute response on each trial was defined as the total number of firings of the cluster within 200–1000 ms after image presentation (ending at the termination of the image presentation). We then tested for significant effects of image illuminance and contrast as well as image category on the absolute response using ANOVA (Kleinbaum et al. 2007).

Testing for effects of factors. More specifically, the responses for each cluster were fit with three nested generalized linear models (GLM) with normal error terms (Kleinbaum et al. 2007). Model 1 (M1) contained only a constant term and thus no effect of image

Fig. 2. A and B: distribution of illuminance (A) and contrast (B) for each category of image in E1 (solid line) and E2 (dashed line). The vertical gray line shows the mean value for the images used in E2. Illuminance distribution was smoothed by a Gaussian kernel with SD = 2; contrast distribution was smoothed by a Gaussian kernel with SD = 3.
illuminance, contrast, or category. Model 2 (M2) contained a constant term and image illuminance and contrast separately and interacting as independent variables. Model 3 (M3) contained a constant term, image illuminance and contrast separately and interacting, and image category as independent variables. The significance of adding each term was tested with nested ANOVA using the F-ratio statistic. As an additional test to compare with previously observed category-selective visual responses, a model with a constant term and image category [model 4 (M4)] was constructed and compared with M1. The construction of these tests and computation of P-values were performed using the R statistics package (R Development Core Team; http://www.R-project.org).

To account for the number of clusters whose responses were being statistically tested and multiple testing, we compared the number of clusters where the null hypothesis would be rejected at the 0.05 level with the number that would be expected by chance given a binomial distribution (P_{binom}). To determine whether the number of clusters with a significant effect of one factor, such as image illuminance and contrast, is independent of another factor, such as brain area or image category, we use Fisher’s exact test to test for independence between the fractions of the total number of clusters that had a significant effect of each factor (Lindgren 1993).

Contour plots of responses. Because the illuminance and contrast of the images are drawn from a continuous distribution (cf. Fig. 2), the responses of any given cluster to images as a function of illuminance or contrast will lie in a response versus illuminance or contrast plane. Given the large number of trials showing images within an interval of illuminance or contrast, we computed the density of the responses in this plane with a Gaussian smoothing kernel, rather than using a scatterplot of the points, because the points overlap. To illustrate this density, we plot the contour lines of the smoothed density. The total volume under the surface thus depicted was normalized to 1 as a density. This representation also allowed us to plot the effect of illuminance or contrast in M2 as a line superimposed on the contour plot.

RESULTS

Neuron Responses When Image Illuminance and Contrast Covaried With Category

In E1, we examined the responses of medial temporal lobe neurons to the presentation of images that had image illuminance and contrast covarying in a natural way with the category of the image. Figure 3A shows an example of a response of a neuron in the hippocampus to eight images presented during this experiment.

E1 was performed by 5 subjects (3 men and 2 women; 5 right-handed subject) in 12 experimental sessions during which we recorded 24 clusters of SUA and 188 clusters of multiunit activity (MUA) in the hippocampus and amygdala combined. The ANOVA for category-selective visual responses using a GLM (M4 vs. M1) found 3 of 24 (12%) clusters of SUA and 23 of 188 (12%) clusters of MUA had significant category-

Fig. 3. Neural activity during the performance of E1 and E2. A: activity of a cluster in the right hippocampus during the performance of eight trials in E1. The vertical axis shows the average firing rate [in spikes/s (sp/s) smoothed with a Gaussian kernel (SD = 100 ms)]. The horizontal axis shows time since beginning of experiment. The vertical tick marks on the horizontal axis show times of cluster firing. The horizontal bars shows times of presentation of the image shown above the bar. Images were drawn from the categories of animals, tools, and outdoor scenes. Responses for animals (trials) occurred in the intensity shown in Fig. 5B near coordinate (120,4). B: activity of a cluster in the right hippocampus during the performance of eight trials in E2. Axes, smoothing, and lines are as in A. Images were drawn from categories of animals, tools, and outdoor scenes. Responses for both tools in trials occurred in the intense point shown in Fig. 7B near coordinate (65,3).
When the nested models of neural activity were compared, the proportion of units with significant responses failed to differ significantly between SUA and MUA ($P = 1.0$ for a test of M2 vs. M1, Fisher’s exact test), so, in agreement with other recent reports (Quiroga et al. 2005; Mormann et al. 2008), we combine and label these as clusters of neural activity for further statistical testing. To account for the number of clusters whose responses were being statistically tested and multiple testing, we compared the number of clusters where the null hypothesis would be rejected at the 0.05 level with the number that would be expected by chance given a binomial distribution.

Using nested models of neural activity in E1, the addition of illuminance and contrast improved the fit ($P < 0.05$, M2 vs. M1) in $9\%$ of clusters of neural activity in the amygdala ($P_{\text{binom}} = 0.051$), and in $10\%$ of clusters in the hippocampus ($P_{\text{binom}} = 0.028$).

Figure 4 shows the cumulative distribution of the $P$ values for these clusters as well as the number that were significant ($P < 0.05$) and the probability of obtaining that number by chance. The addition of image category improved the fit ($P < 0.05$, M3 vs. M2) for $13\%$ of clusters in the amygdala ($P_{\text{binom}} = 2 \times 10^{-4}$) and $8\%$ of clusters in the hippocampus ($P_{\text{binom}} = 0.14$). For this experiment, the difference between the fraction of clusters with significant effects in the amygdala and hippocampus was not significant ($P = 0.81$, M2 vs. M1, and $P = 0.27$, M3 vs. M2, Fisher’s exact test); when these brain areas were combined, the fraction of clusters with a significant effect for M2 versus M1 ($9\%$) was highly significant ($P_{\text{binom}} = 0.0051$), as was the fraction of clusters with a significant effect for M3 versus M2 ($11\%$, $P_{\text{binom}} = 1.8 \times 10^{-2}$).

The number of neurons that had a significant improvement in the fit when image illuminance and contrast were added (M2 vs. M1) and were further improved by the addition of image category (M3 vs. M2) was quite small: four neuron in the amygdala and zero neurons in the hippocampus. As noted above, the number of clusters with a significant improvement in fit when image category was added as an independent variable relative to no effects (M4 vs. M1) was 26 clusters of a total of 212 clusters of SUA and MUA combined in the hippocampus and amygdala. Summarizing these tests, the numbers of clusters in the hippocampus and amygdala combined with each of the effects are shown in Table 1. These numbers are consistent with the effects of image illuminance and contrast and image category being represented in separate groups of neurons during E1 and with the fraction of neurons with these effects being equal. Fisher’s exact test failed to reject with $P = 0.51$. Assuming that these are independent groups of neurons, the power for detecting a difference at least as large as 0.1 between the fraction of neurons with a significant effect of image illuminance and contrast and the fraction with a significant effect of image category was 0.8 (Erdfelder et al. 1996) (post hoc calculation of power given $\alpha$ and sample and effect sizes).

A separate model examining the effect of image illuminance and contrast as main effects (with no interaction between them) showed similar numbers of clusters with significant effects of illuminance or contrast. To illustrate the effects of illuminance on cluster responses, Fig. 5 shows the density of responses for two clusters as a function of image illuminance and the trend selective responses, in agreement with previous reports (Kreiman et al. 2000a; Steinmetz 2009).

![Figure 4](http://jn.physiology.org/)

**Fig. 4.** Distribution of $P$ values for the comparison of models of responses to images with natural covariation of image illuminance and contrast with category (E1). A: the amygdala. Triangles show the distribution of $P$ values for the comparison of the model with illuminance and contrast, separately and interacting, to a model with a constant response to images [model 2 (M2) vs. model 1 (M1)]. Plus signs show the distribution of $P$ values for the comparison of the model with illuminance and contrast interacting plus category to the model with illuminance and contrast, separately and interacting [model 3 (M3) vs. M2]. The dotted line shows the expected theoretical distribution. Numbers of clusters with a significant response ($P < 0.05$) are shown; numbers in parentheses are the fractions of total clusters. B: the hippocampus. Symbols and numbering are same as for the amygdala in A.

<table>
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<th>Significant Effect of Illuminance and Contrast (Model 2 Versus Model 1)</th>
<th>No</th>
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<td>172</td>
<td>20</td>
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<td>Yes</td>
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line for the effect of image illuminance on response. The cluster shown in Fig. 5A responds to image illuminance with a trend producing a 40% change for the variation in image illuminance used here.

**Neuron Responses When the Variation of Illuminance and Contrast Was Equal Across Categories**

To further understand the relationship between the responses to image low- and high-level properties, we performed E2, where we manipulated the illuminance and contrast of images from five categories and adjusted them to produce equal distributions of illuminance and contrast in each category (Fig. 2, solid lines). In E2, the effects of image illuminance and contrast can appear independently of any effect of a high-level property, such as image category.

E2 was performed for 7 sessions by 4 subjects (1 man and 3 women, 4 right-handed subjects), yielding recordings from 59 clusters of neural activity in the amygdala and 144 clusters of neural activity in the hippocampus.

Figure 6 shows the cumulative distribution of P values for the two tests of the nested models in both the amygdala and hippocampus. Given the number of clusters recorded in this
experiment, the fraction of clusters with significant effects of image illuminance and contrast interacting or image category were not significantly different between the amygdala and hippocampus ($P = 0.10$, M2 vs. M1, and $P = 0.36$, M3 vs. M2, Fisher’s exact test), and the results with these brain areas were combined. For this experiment, 8% of clusters had a significant improvement in fit when image illuminance and contrast were added to the model ($P_{\text{binom}} = 0.027$, M2 vs. M1). This number was significantly larger than would be expected by chance. Only 7% of clusters had an improved fit when category was added as a term ($P_{\text{binom}} = 0.14$, M3 vs. M2), which was not significant, although it may reflect the limited number of clusters recorded. The number of clusters where the addition of image illuminance and contrast significantly improved the fit (M2 vs. M1) and were also improved by the addition image category (M3 vs. M2) was only three clusters. Table 2 shows the results of these tests, which are again consistent with the notion that the effects of image illuminance and contrast and image category appear independently among these clusters and that the proportions are equal ($P = 0.10$, Fisher’s exact test). Assuming the effects are independent, the power to detect a difference of 0.1 in the proportion of clusters with a significant effect of image illuminance and contrast or image category was 0.83.

To illustrate the effects of contrast on cluster responses, Fig. 7 shows the density of responses for two clusters as a function of image contrast and the trend line for the effect of image illuminance on response. The cluster shown in Fig. 7A responds to image contrast with a trend producing a 40% change for the variation in image contrast used here.

**Comparison of Neuron Responses When Illuminance and Contrast Either Covaried or Did Not Covary With Image Category**

If we take the $P$ value of the test for an effect of image illuminance and contrast (M2 vs. M1) as a measure of the strength of this effect for a given cluster, we can compare the distribution of such strengths between E1, where image illuminance and contrast varied naturally with category, and E2, where the distribution of illuminance and contrast was equal (to second-order moments) across categories. Figure 8 shows the distribution of the $P$ values for the two experiments at the more significant end of the range of $P$ values for the hippocampus and amygdala combined. A Kolmogorov-Smirnov test for a difference between these two distributions failed to show a significant difference ($P = 0.29$).

In contrast, when we compared the $P$ values for a test of the effects of image category (M4 vs. M1, i.e., image category plus a constant vs. constant alone) between E1 and E2, we found a highly significance difference in the distribution of the $P$ values in these experiments ($P = 7.9 \times 10^{-5}$, Kolmogorov-Smirnov test). Figure 9 shows these $P$ values and that the number of

| Significant Effect of Illuminance and Contrast (Model 2 Versus Model 1) |
|--------------------------|----------|----------|
| No                      | Yes      |
| 175                     | 11       |

Table 2. Number of clusters in the hippocampus and amygdala with significant effects of image illuminance and contrast or image category during experiment 2

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**Table 2.** Number of clusters in the hippocampus and amygdala with significant effects of image illuminance and contrast or image category during experiment 2

| Significant effect of the addition of category (model 3 versus model 2) |
|-------------------------------------------------|---------|---------|
| No                                              | 175     | 11      |
| Yes                                             | 14      | 3       |
clusters with a significant effect of image category was significantly reduced in E2, when the distribution of image illumination and contrast was equal across categories (to second-order moments).

DISCUSSION

Taken together, the results from these two experiments show that there are neurons in the human medial temporal lobe that respond to image illumination and contrast as well as neurons that respond to image category (Kreiman et al. 2000a; Steinmetz 2009), and these are likely separate populations of neurons. The sum of the fraction of neurons responding to image illumination and contrast in E2, 8%, and fraction responding to image category, 7%, are nearly equal to the previously reported values for responses to image category, which were in the range 15–20% (Kreiman et al. 2000a; Steinmetz 2009). Since these prior experiments used images with illumination and contrast covarying with image category, as in E1 here, it is likely that the responses of neurons within the human medial temporal lobe during this type of experiment can be dissected into two components, reflecting different levels of abstraction of the visual scene.

Fig. 7. Neural activity as a function of image contrast during E2 for two clusters in the right hippocampus. Shown is a contour plot of responses to images at a particular rate (vertical axis: responses (in spikes/s), smoothed with a Gaussian kernel (SD = 4) in this direction) versus contrast of the image (horizontal axis: SD of pixel intensity; kernel (SD = 1) in this direction). The solid lines show the trend lines for contrast in the model (M2).
One notable item is that the task used here, object categorization, does not explicitly require memory. This task was chosen due to its widespread use in a variety of previous human microwire recording experiments (Kreiman et al. 2000a; Kreiman et al. 2000b; Quiroga et al. 2005; Quiroga et al. 2008). This task does, however, require identifying the category to which a depicted object belongs, a form of semantic nondeclarative memory.

The role of the medial temporal lobe structures, including the hippocampus, in tasks not involving declarative memory remains uncertain (Baxter 2009; Suzuki 2009; Suzuki and Baxter 2009). Whereas early reports from patients with medial temporal lobe damage indicated that perception was intact (Milner et al. 1968), as was confirmed in a lesion study of nonhuman primates (Correll and Scoville 1965), more recent work with patients with selective damage to medial temporal lobe structures, such as the perirhinal cortex, have suggested a perceptual role for medial temporal lobe structures (Lee et al. 2005b) as well as a role for the hippocampus in perceiving the spatial layout of virtual scenes (Lee et al. 2005a; Graham et al. 2006; Murray et al. 2007) (although also see Hamann and Squire 1997; Holdstock et al. 2000; Shrager et al. 2006). The results presented here show that hippocampal neurons respond to both image category and low-level image properties, even when these are not involved in a declaration about a memory, suggesting a broader role of the hippocampus in tasks not involving memory, such as categorization and perception.

There are important methodological differences between these studies that are useful to consider. The results of lesion studies speak to the brain areas that must be present to perform a task, whereas single neuron recordings provide a view of the activity of neurons in the intact brain. Such activity may be not required to perform a task but may nonetheless be an integral part of the mechanisms used in the intact human brain, while

Both components are simultaneously represented by the firing of neurons within the hippocampus and amygdala as images are viewed. The first component is a response to a combination of image illuminance and contrast, and there are a significant fraction of neurons in the hippocampus and amygdala where the responses are best explained by the independent variables of illuminance and contrast, rather than image category. The second component is a response to the category, and there are a significant fraction of neurons where the response is significantly better explained by including image category. With natural covariation of image illuminance and contrast among image categories (E1), the representation of category appears in a roughly equal number of clusters as the representation of illuminance and contrast and appears independent of it (11% vs. 9%). The relative balance of these two components is likely affected by image properties not captured by our analysis of image illuminance, contrast, and category here, which may explain the differences in the fractions of neurons with responses to each factor in E1 and E2.

Although the effect of image illuminance and contrast on neural activity in medial temporal lobe structures is surprising, assuming views of the hippocampus either at the far end of the ventral stream of visual processing (Felleman and Van Essen 1991), representing the most abstract binding associations in the medial temporal lobe (Shimamura and Wickens 2009) or representing the configural aspects of a scene (Bussey and Saksida 2007), it is nonetheless true that the illuminance and contrast of a visual scene are ecologically very pertinent cues, with a bright object, for example, often being of considerable behavioral importance. Interestingly, in one report (Lee et al. 2005b), patients with hippocampal damage were impaired in discriminating outdoor scenes that may have differed in image contrast, which would be consistent with the results reported here.
other mechanisms may come into use after damage to a brain area. (While the brains of epileptics are not completely normal and are often being treated with anti-epileptic medication, prior comparisons in the laboratory between the side containing the seizure onset zone and the opposite side, which is less affected by disease, suggests that such factors do not affect the neural responses to the presentation of visual stimuli.) To better understand the functional role of these hippocampal responses, we are currently developing experiments that vary both the type of memory required and level of image property needed to correctly perform the tasks.

Since neither of the present experiments presented multiple images or views of specific objects, we cannot directly compare the responses to image illuminance, contrast, and category with previously reported responses to individual persons or objects (Quiroga et al. 2005). In the two experiments reported here, we did not observe a significant number of neurons responding to individual images that were single views of an object shown six times (at either the $P < 0.05$ or $P < 0.01$ levels). Given the frequency of both previously reported object invariant (5%) responses as well as the illuminance/contrast (9%) and category-selective (11%) responses reported here, it is possible that all such responses are present independently within the human medial temporal lobe. An experiment presenting multiple views of the same objects with controlled variation of image illuminance and contrast would help to understand the relationship between these multiple levels of representation within the human medial temporal lobe.

Taken together, previous descriptions of category-selective responses (Kreiman et al. 2000a) and the results reported here show that the activity of neurons within the human medial temporal lobe reflects both abstracted and basic properties of the visual scene. Although such dual representations of different visual properties within a brain area have been observed previously, these have involved properties of comparable levels of abstraction, such as color and form (Seymour et al. 2009). Such separate representations of aspects of a visual scene must be bound together in the perception of objects as a whole (Whitney 2009) and interact to affect perception and recollection, as evidenced in behavioral performance (Palmeri et al. 1993; Church and Schacter 1994; Goldinger 1996). The results reported here show that neurons within the medial temporal lobe represent multiple levels of abstraction of the visual scene and are thus well positioned to bind these representations into coherent percepts for further action and recollection.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

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