Supplemental Data

A Single-Neuron Correlate of Change Detection and Change Blindness in the Human Medial Temporal Lobe

Leila Reddy, Rodrigo Quian Quiroga, Patrick Wilken, Christof Koch, and Itzhak Fried

Supplemental Results

Choice-Probability Analysis—"Behavior ROC"

To compute the choice probability, we conducted a receiver operating characteristic (ROC) analysis to determine the correlation between neuronal activity and the behavioral report of the subjects on a trial-by-trial basis. For this analysis, we estimated the probability of whether or not a change had occurred by comparing spike counts in the first and second display periods, as described for Figure 3. We then compared this estimate not with the actual stimulus (as in Figure 3), but with the subjects' behavioral report of a change, for each value of a sliding threshold. A "correct detection" or "false alarm" would be counted depending on whether the prediction from the spike counts matched the subjects' report of a change or not—irrespective of whether or not a change had actually occurred on the screen. The ROC curves for this analysis are shown in Figure S2A. As in Figure 3, the probability of correct detection is plotted against the probability of false alarms for each value of the threshold. The average area under the curves is 0.58 ± 0.01. The distribution of these values for all cells (Figure S2B) is significantly shifted to the right of 0.5 ($p < 0.001$).

The relationship between predicting changes in the stimulus (Figure 3) and predicting behavioral choice (Figure S2) is shown in Figure S4 for each cell. On average, the 29 medial-temporal-lobe neurons are significantly better at registering whether or not their preferred picture changed than at predicting the percept or the behavioral choice of the patient in this task, although the two types of predictions were significantly correlated (slope = 0.4, $p < 0.0001$, $r^2 = 0.5$).

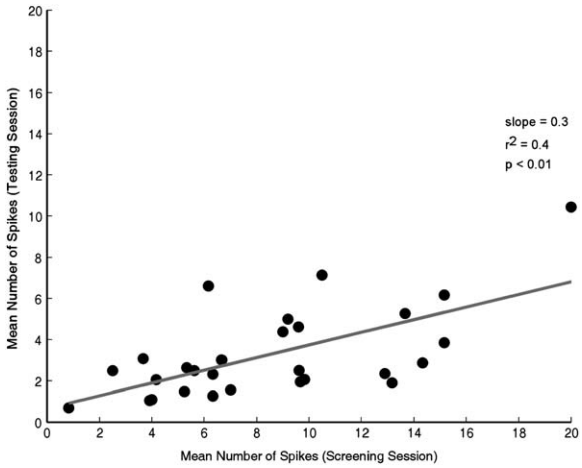

Figure S1. Comparison of Firing Activity in Change Detection and Screening Sessions for All 29 Cells

A significant decrease was observed in activity in the change-detection sessions. This can be explained by the fact that in the change-detection sessions, each preferred stimulus was presented peripherally along with three other stimuli known to drive the cell weakly, whereas in the screening session, a single image was foveally presented. On average, the response to the preferred stimulus during the change-detection sessions was 30% of the response during the screening session.

Supplemental Experimental Procedures

Behavioral Task

The timeline for one trial in the change-blindness paradigm is shown in Figure 1A. Each trial began with a fixation cross that was presented for a random interval between 1000 and 1200 ms. After the fixation cross, four images appeared on the screen for 1000 ms. The pictures were presented at four locations on a circle with a 6° radius. The midpoint of each picture was located on the circle; each picture subtended approximately 1.5°. A blank interval of 1.5 s (black screen) followed the first set of pictures, and then a second display of four pictures appeared for 1 s. In the second display period, the pictures occupied the same location as the previous set of pictures. In roughly half the trials, one of the four pictures was changed between the two display periods. Patients were instructed to report at the end of each trial whether they noticed a change or not by pressing the "Y" and "N" keys on the keyboard, respectively. The presentation times for the two display periods, as well as the interstimulus interval (ISI), were determined beforehand following extensive pilot studies on a nonclinical population (Caltech staff and students). In these pilot studies, six subjects were tested on this paradigm with ISI intervals of 100 and 1500 ms. Additionally, different display sizes (two, four, or six images) were tested. The performance of these subjects was determined with each of these parameters, and the current set of parameters was chosen because it resulted in a hit rate of above 0.70 on average.

The stimuli were presented to patients on a Macintosh G3 laptop computer. The laptop was placed on the patient's lap or a tray table about 60 cm in front of the patient, depending on the patient's preference.

During the experiment, patients were always instructed to fixate on the central fixation cross and to only covertly explore the pictures in each display period. Although we did not explicitly control for eye movements because of the difficulty involved with introducing the equipment into the clinical ward, there is evidence that suggests that eye movements do not influence neuronal responses in the MTL. In control experiments performed in the same hospital setting as our experiments, Kreiman and colleagues demonstrated that there was no modulation in firing rates of human MTL visually responsive cells as a result of eye movements [S1, S2]. These results are also compatible with electrophysiological reports in the monkey temporal lobe [S3, S4].

Stimulus Presentations and Trial Types

In our experimental set-up, on each testing day, we performed a screening session in which patients were shown a large number of images (average 94). Each image (1.5°) was shown by itself, for 1 s at fixation, and was repeated six times in pseudorandom order. The data obtained from the screening session were then rapidly analyzed offline to determine which stimuli elicited visual responses in our neuronal population [S5]. For the change-detection experiment, on the basis of the results of these screening sessions, sets of preferred (usually, only one) and nonpreferred (4 to 8 on average) stimuli were selected for each targeted cell.

Because of time constraints, there was a limitation in the number of preferred pictures we could select for each session. Given the 30 min recording session on average, and taking the length of

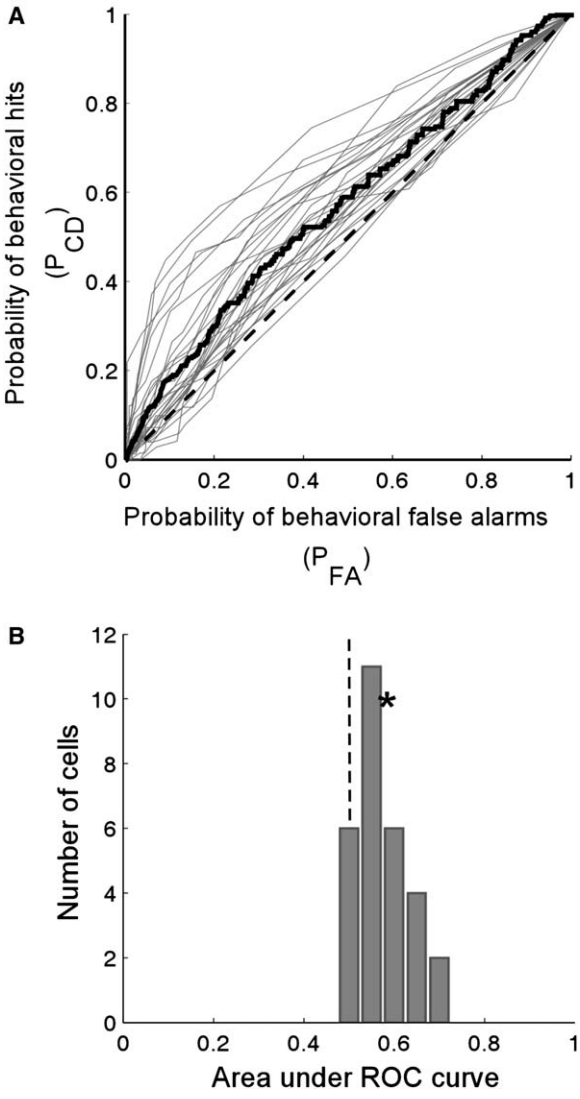

Figure S2. Predicting Behavioral Choice—ROC analysis.

(A) The probability of predicting behavioral choice correctly, P_{CD} ("correct detection"), is plotted against the probability of incorrect predictions ("false alarms," P_{FA}). The dashed line indicates chance performance ($P_{CD} = P_{FA}$). The different lines show the result of this calculation for each cell. The solid black line is the average ROC curve.

(B) The distribution of the area under the curve for each cell. The histogram is significantly shifted to the right of 0.5, indicating that the 29 cells can predict behavioral choice above chance on a trial-by-trial basis ($p < 0.001$). The mean area is marked by a * and equals 0.58 ± 0.01.

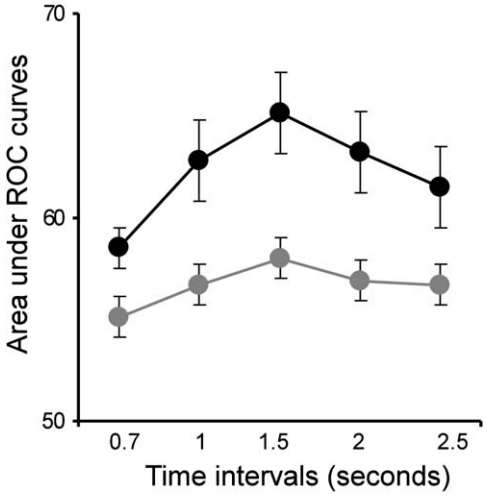

Figure S3. Comparison of the Area under the Stimulus and Behavior ROC Curves

ROC curves for predicting the stimulus (black line) and behavior (gray line) were computed over different time intervals. Each point on the graph corresponds to the ROC area when computed between 300 ms following stimulus onset and X for five different values of X (shown on the *x* axis). A two-factor ANOVA showed a significant main effect for the type of ROC analysis (i.e., stimulus ROC versus behavior ROC), [$F(1,280) = 35.4$, $p < 0.00001$] and a significant main effect for the time interval [$F(4,280) = 2.7$, $p = 0.03$], implying that the optimal time window for analysis was the same for both types of ROC. The interaction effect was not significant [$F(4,280) = 0.4$, $p = 0.8$]. The ROC data reported in this paper were computed over 300–1500 ms, which is optimal for both stimulus and behavior predictions.

each trial into account, we could test four preferred pictures in each session.

The limitation on the number of preferred pictures also constrained the number of neurons we could target for our study during a single experimental session. In some sessions, the four stimuli we chose drove four different neurons that would count toward the total number of neurons in the change-blindness experiment. In most cases, in the screening session only two or three neurons would have strong responses and would respond significantly to a few pictures. Accordingly, in these cases, a smaller number of neurons would contribute to the total count. All in all, we recorded 534 units in 17 change-detection sessions in nine patients. Of these 534 cells, 208 were located in the amygdala, 138 in the hippocampus, 140 in the entorhinal cortex, and 48 in the parahippocampal gyrus. For the change-detection sessions, although we had recorded 110 visually responsive neurons in the corresponding screening sessions, because of the time limitations mentioned above, only 43 visually responsive neurons were targeted (i.e., had been preselected on the basis of the screening session, and preferred and nonpreferred stimuli had been determined for these cells). Only these 43 targeted cells were included in our analysis. On each trial of the experiment, only one of the stimuli was selected from one cell's set of preferred pictures. The other stimuli in each display period were chosen from the group of nonpreferred pictures (common to all targeted cells). As described in the main text and shown in Figure 1B, four different trial types ("disappear," "appear," "both," and "none") could be determined with respect to a unit's preferred stimulus. For every preferred stimulus, there were 20 "disappear," 20 "appear," and 14 "both" trials over the recording session. Overall for all preferred stimuli, there were at least 50 "none" trials.

Data Analysis

Visual Responsiveness

For each cell, preferred and nonpreferred stimuli were determined on the basis of the results of the screening experiment. In the screening session, we determined which stimuli were preferred for each cell by requiring that the response was larger than the mean plus five standard deviations of the baseline [S5]. In the change-detection experiment, we simply verified that the preferred stimulus was still visually responsive by computing a paired t test. The t test compared the distribution of firing activity during the −1000 to −300 ms baseline interval and the 300 to 1000 ms interval during which the stimulus was present on the screen, over all trials (0 ms represents the time of stimulus onset) [S5]. A cell was considered to have remained visually responsive if the p value of the t test was < 0.05. As mentioned in the main text, 29 out of 43 units remained visually responsive during the change-detection experiments. We did not have more than two simultaneously recorded

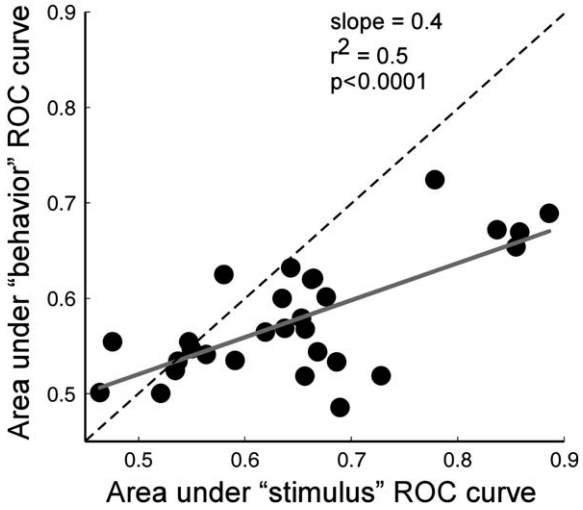

Figure S4. Comparison of the Two ROC Analyses

Comparison of the ability to predict change and the ability to predict behavioral choice on a trial-by-trial basis, for each cell, calculated over all trials. On average, each cell is better able to predict changes in the stimuli rather than the behavioral choice of the subject on a trial-by-trial basis.

units that were visually responsive to the same image in any one session.

Population Responses

Population responses were computed by using the normalized spike-density function (sdf) [S6]. For each neuron, the sdf was obtained by convolving the spike train on each trial with a 200 ms fixed width Gaussian and then averaging over all trials. The spike trains were binned in 5 ms bins before convolution. For each unit, the sdf was normalized by dividing by its peak activity. The normalized sdf was then averaged over the population of cells. Although the maximum of this normalized sdf was equal to 1 for each neuron, over the population of cells the maximum value was less than 1 because the activity in different cells peaked at different times. The average responses were computed separately for correct and incorrect trials in all trial types.

Supplemental References

S1. Kreiman, G. (2002). On the neuronal activity in the human brain during visual recognition, imagery and binocular rivalry. PhD thesis, California Institute of Technology, Pasadena, California.

S2. Kreiman, G., Fried, I., and Koch, C. (2002). Single-neuron correlates of subjective vision in the human medial temporal lobe. Proc. Natl. Acad. Sci. USA *99*, 8378–8383.

S3. DiCarlo, J.J., and Maunsell, J.H. (2000). Form representation in monkey inferotemporal cortex is virtually unaltered by free viewing. Nat. Neurosci. *3*, 814–821.

S4. Rolls, E.T., Aggelopoulos, N.C., and Zheng, F. (2003). The receptive fields of inferior temporal cortex neurons in natural scenes. J. Neurosci. *23*, 339–348.

S5. Quiroga, R.Q., Reddy, L., Kreiman, G., Koch, C., and Fried, I. (2005). Invariant visual representation by single neurons in the human brain. Nature *435*, 1102–1107.

S6. Richmond, B.J., Optican, L.M., and Spitzer, H. (1990). Temporal encoding of two-dimensional patterns by single units in primate primary visual cortex. I. Stimulus-response relations. J. Neurophysiol. *64*, 351–369.