Correction and Retraction

CORRECTION

NEUROSCIENCE

Correction for "Feature attention evokes task-specific pattern selectivity in V4 neurons," by Anna E. Ipata, Angela L. Gee, and Michael E. Goldberg, which appeared in issue 42, October 16, 2012, of *Proc Natl Acad Sci USA* (109:16778–16785; first published October 5, 2012; 10.1073/pnas.1215402109).

The authors note that Fig. 3 and its corresponding legend appeared incorrectly. The corrected figure and its corrected legend appear below. This error does not affect the conclusions of the article.

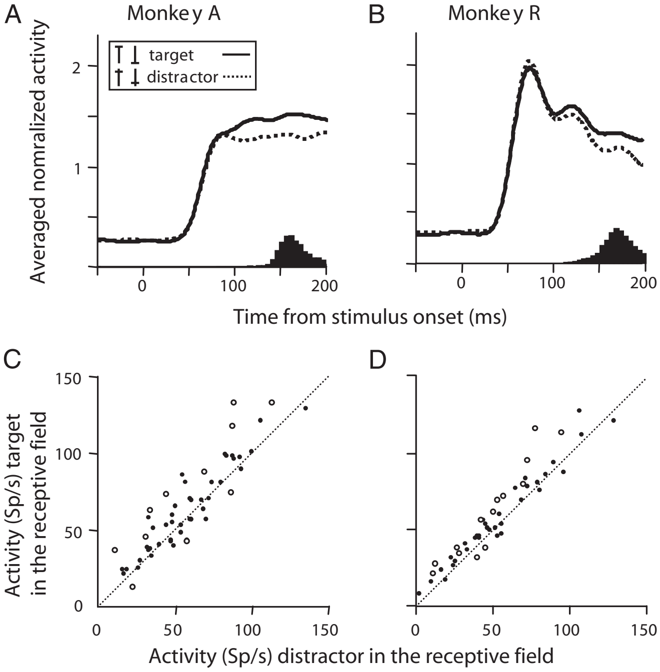

Fig. 3. V4 neurons discriminated the target during the search task when monkey made a saccade to the receptive field. (*A* and *B*) Average normalized activity (ordinate) plotted against time (abscissa) for monkeys A and R, respectively, for trials in which the first saccade was made to the receptive field. Solid black line: target in the receptive field; dotted black line: distractor in the receptive field. The histogram on the inset shows the mean saccadic latency time for each neuron during these conditions. (*C* and *D*) Mean activity of each cell on trials in which the monkey made a saccade to a target in the receptive field (ordinate) plotted against the same activity when the monkey made a saccade to a distractor in the receptive field (abscissa), for an epoch of 100–150 ms after array onset for monkey A and for 125–175 ms after array onset for monkey R. Open circles represent single neurons that showed significantly different activity to the target or distractor using a standard *t* test with $P < 0.05$.

www.pnas.org/cgi/doi/10.1073/pnas.1220828110

RETRACTION

CHEMISTRY, APPLIED BIOLOGICAL SCIENCES

Retraction for "Selective cell death mediated by small conditional RNAs," by Suvir Venkataraman, Robert M. Dirks, Christine T. Ueda, and Niles A. Pierce, which appeared in issue 39, September 28, 2010, of *Proc Natl Acad Sci USA* (107:16777–16782; first published September 7, 2010; 10.1073/pnas.1006377107).

The undersigned authors wish to note the following: "Anomalous experimental results observed by multiple members of the Pierce lab during follow-on studies raised concerns of possible research misconduct. An investigation committee of faculty at the California Institute of Technology indicated in its final report on this matter that the preponderance of the evidence and the reasons detailed in the report established that the first author falsified and misrepresented data published in this paper. An investigation at the United States Office of Research Integrity is ongoing. The undersigned authors hereby retract this paper and sincerely apologize for the inconvenience caused to other investigators."

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www.pnas.org/cgi/doi/10.1073/pnas.1221212110

Feature attention evokes task-specific pattern selectivity in V4 neurons

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This contribution is part of the special series of Inaugural Articles by members of the National Academy of Sciences elected in 2011.

Contributed by Michael E. Goldberg, September 5, 2012 (sent for review April 9, 2012)

A hallmark of visual cortical neurons is their selectivity for stimulus pattern features, such as color, orientation, or shape. In most cases this feature selectivity is hard-wired, with selectivity manifest from the beginning of the response. Here we show that when a task requires that a monkey distinguish between patterns, V4 develops a selectivity for the sought-after pattern, which it does not manifest in a task that does not require the monkey to distinguish between patterns. When a monkey looks for a target object among an array of distractors, V4 neurons become selective for the target ~50 ms after the visual latency independent of the impending saccade direction. However, when the monkey has to only make a saccade to the spatial location of the same objects without discriminating their pattern, V4 neurons do not distinguish the search target from the distractors. This selectivity for stimulus pattern develops roughly 40 ms after the same neurons' selectivity for basic pattern features like orientation or color. We suggest that this late-developing selectivity is related to the phenomenon of feature attention and may contribute to the mechanisms by which the brain finds the target in visual search.

vision

Rather than responding to all objects in their receptive fields, neurons in visual cortex are selective for specific features of those objects, such as orientation, color, pattern, retinal disparity, and/or speed and direction of motion (1). This feature selectivity is usually manifest from the first spike of the response (2) and is assumed to be due to hard wiring in the network and to a certain extent a feed-forward process (3). When an animal searches for a visual target among distractors it is not unreasonable to assume that neurons in the brain will be selective for the search target, and we have recently shown that neurons in the lateral intraparietal area of the monkey (LIP) become selective for the target in a visual search task even when the monkey makes a saccade away from the receptive field (4). Unlike selectivity in earlier visual areas, selectivity for the search target in LIP develops roughly 50 ms after the onset of the visual response to the array appearance.

Because LIP receives a monosynaptic projection from prestriate area V4 (4), we wondered whether the visual neurons in V4 also distinguished between target and distractors in the same search task. Here, as in many other studies (2, 5, 6), we found that the population of V4 neurons, and many single neurons did indeed give enhanced responses to the search targets compared with the distractors. Like neurons in LIP, V4 neurons become selective roughly 50 ms after the beginning of the visual response to the appearance of the search array. Surprisingly, however, when we tested the visual response of the neurons when the monkeys had only to make a saccade to the targets or the distractors and not discriminate their patterns, V4 neurons were no longer selective for the target. We suggest that this selectivity is very different from the hard-wired feature selectivity such as color or orientation that has been described in V4, and arises from top-down, feature-attentional signals engendered by the demands of the search task, rather than an enhancement of the hard-wired feature selective properties of the area.

Results

Behavior. We trained two adult male rhesus monkeys to perform two different tasks: a visually guided delayed saccade task and a visual search task. In the saccade task, the monkey fixated a central point and a single object appeared on a screen in front of the monkey. Roughly 1 s later the fixation point disappeared, and the monkey made a saccade to the object (Fig. 1*A*). In the search task, each monkey initiated a trial by grasping the two bars in its chair. Then a small central point appeared in the middle of the screen, which the monkey had to fixate for 1–1.75 s. Then the fixation point disappeared, and an array of upper and lowercase "T"s appeared (Fig. 1*B*). The target was an inverted or upright capital T, and the monkey had to indicate its orientation by releasing the appropriate bar. During this time the monkey was completely free to move its eyes. The trial did not end until the monkey released a bar or a 3-s time limit was reached. The remaining distractors were upright and inverted lowercase t's. They had the same width and height as the target and differed only in the position at which the horizontal line crossed the vertical line. Both monkeys performed the visually guided saccade task correctly on at least 99% of the trials and the search task correctly on more than 95% of the trials. In the search task, they made an average of 1.7 saccades per trial. Although it was not required, both monkeys always fixated on an object, and usually fixated the target. Monkey A had an average saccade latency of 164 ms ± 20 ms (Figs. 3*A* and 4*A* histograms). Monkey R had an average saccade latency of 184 ms ± 28 ms (Figs. 3*B* and 4*B* histograms).

Dataset. We studied the activity of 112 single units in area V4 that responded to the objects used in the search task—51 in monkey R, 61 in monkey A—in both the saccade and search tasks. Of these 112 neurons, 60% were orientation selective, and all of the neurons responded to either a vertical or horizontal bar, which were components of the target and distractor shapes. For the subset of neurons that were also tested for color, 67% were color selective, and 37% were selective for both orientation and color. We adjusted the color of the search array to the

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Author contributions: A.E.I., A.L.G., and M.E.G. designed research; A.E.I. and A.L.G. performed research; A.E.I., A.L.G., and M.E.G. analyzed data; and A.E.I., A.L.G., and M.E.G. wrote the paper.

The authors declare no conflict of interest.

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This article contains supporting information online at www.pnas.org/lookup/suppl/doi:10.1073/pnas.1215402109/-/DCSupplemental.

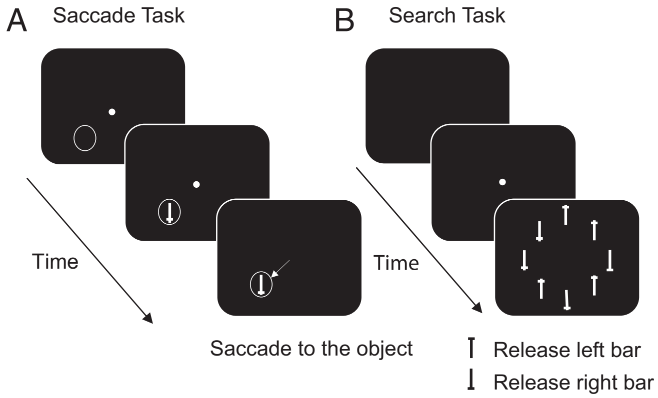

Fig. 1. Visually guided saccade task and the free-viewing search task. (*A*) Visually guided saccade task. After an initial fixation period (1–1.75 ms), an object appeared in the receptive field of the neuron. Monkeys had to maintain fixation for ∼1 s. When the fixation point disappeared, monkeys had to make a saccade to the object. (*B*) Free-viewing search task. After an initial fixation period (1–1.75 s), the search array appeared and the fixation point disappeared simultaneously. One of the stimuli, either the target (upright or inverted T) or distractor appeared in the center of the neuron's receptive field. Monkeys had 3 s to report the orientation of the target by releasing one of two bars. During the presentation of the search array there were no constraints on eye movements.

optimum color of the neurons. All objects analyzed in the search array were identical in color and luminance.

Activity of V4 Neurons During the Visually Guided Saccade Task. In the saccade task, when the monkeys had to locate the saccade target but not report anything about its pattern, 100 of 112 neurons did not discriminate between the similarly shaped capital T and the closest resembling lowercase t (Fig. 2; $P > 0.05$ by t test), nor did they distinguish between upright and inverted Ts. Six out of 112 distinguished between upright T's and inverted T's ($P < 0.05$ by t test) but not between capital T's and lowercase t's of either orientation. Three of 112 neurons were selective for uppercase T's of either orientation, and 3 of 112 were selective for lowercase t's of either orientation ($P < 0.05$, by t test). Thus, in the population only 3 of 112 neurons were selective for the target as opposed to the distractor. This lack of selectivity in the population could be seen in the average spike density diagrams (Fig. 2 *A* and *B*) and the population scatter plots (Fig. 2 *C* and *D*) for the time interval after the target appearance. In the time interval of 100–150 ms after the appearance of the array for monkey A and 125–175 ms for monkey R, there was no significant difference in the responses to the capital T or lowercase t (Wilcoxon signed-rank test, monkey A, $P = 0.90$; monkey R, $P = 0.48$). We used different time intervals to best encompass the period surrounding the time of the target discrimination during the search task for each individual monkey. The neurons also did not distinguish between target and distractor in the 50 ms preceding the saccade (Fig. S1; Wilcoxon signed-rank test, Monkey A, $P = 0.45$; Monkey R, $P = 0.76$).

Activity of V4 Neurons During the Search Task. In the saccade task the monkey merely had to make a saccade to the stimulus. In the search task the monkey not only had to locate the target but also had to make a decision about its orientation. Under this condition, the same neurons that did not distinguish the capital T from the lowercase t during the visually guided saccade task were now pattern selective for the capital T, the target in the search task (Fig. 3). This ability to discriminate the target from distractors was present both in the population spike density diagrams (Figs. 3 *A* and *B*) and at the single-neuron level (Figs. 3 *C* and *D*). When the monkey made a saccade to the receptive field in the search task, there was a significant difference in activity evoked by the target compared with the distractor in the receptive field in the time interval of 100–150 ms after the appearance of the array for monkey A and 125–175 ms for monkey R (Wilcoxon signed-rank test, monkey A, $P = 0.0005$; monkey R, $P = 0.0006$). Eight of 55 individual neurons in monkey A and 12 of 49 in monkey R had a significantly higher response to the target rather than the distractor ($P < 0.05$, by t test). In both cases, the discrimination was well before the initiation of the saccade. During the 50 ms preceding the time of the saccade, the difference in activity between target and distractor was even more pronounced (Wilcoxon signed-rank test, monkey A, $P < 0.0001$; monkey R, $P < 0.0001$). Eleven of 55 individual neurons in monkey A and 15 of 49 in monkey R had significantly different responses to the target and distractor during this presaccadic time epoch ($P < 0.05$, by standard t test; Fig. S1). In addition, the six neurons that were pattern selective for the upright vs. inverted t (but not for the target or distractor) in the saccade task showed significantly higher activity to the target than the distractor during the search task (Wilcoxon signed-rank test, $P = 0.0313$).

V4 neurons were selective for the target rather than the distractor in the receptive field in the search task, even when the monkey made a saccade away from the receptive field (Fig. 4). This distinction was true both for the population spike density histogram (Figs. 4 *A* and *B*) and the population of individual

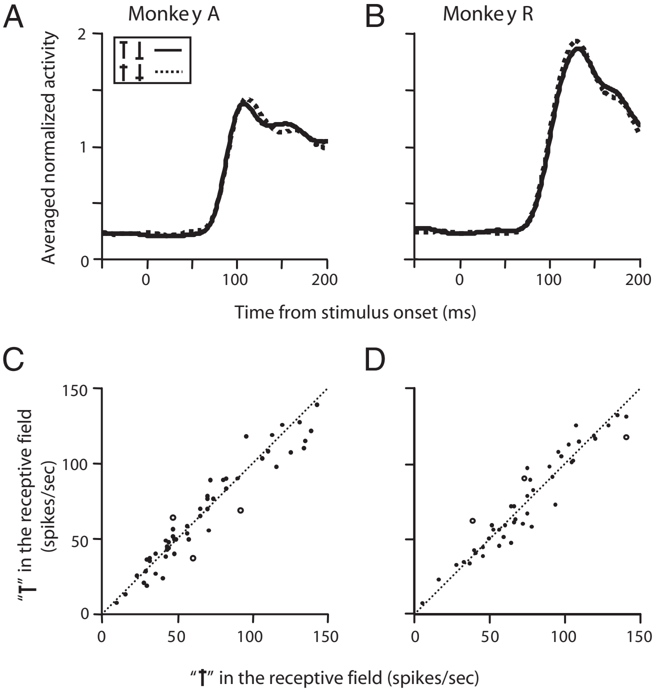

Fig. 2. V4 neurons did not discriminate the target from the distractor during the visually guided saccade task. (*A* and *B*) Average normalized activity (ordinate) plotted against time (abscissa) for monkeys A and R, respectively. Solid black line shows activity from trials in which the target, an upright or inverted capital T, appeared in the receptive field. Dotted black line shows activity from trials in which a distractor stimulus, an upright or inverted lowercase t, appeared in the receptive field (see legend, *Inset*). (*C* and *D*) Mean activity of each cell when the upright or inverted capital T stimuli appeared in the receptive field (ordinate) plotted against the mean activity when the upright or inverted lowercase t stimuli appeared in the receptive field (abscissa) for an epoch of 100–150 ms after array onset for monkey A and for 125–175 ms after array onset for monkey R. Open circles represent single neurons that showed significantly different activity between the target and distractor stimuli using a standard t test with $P < 0.05$.

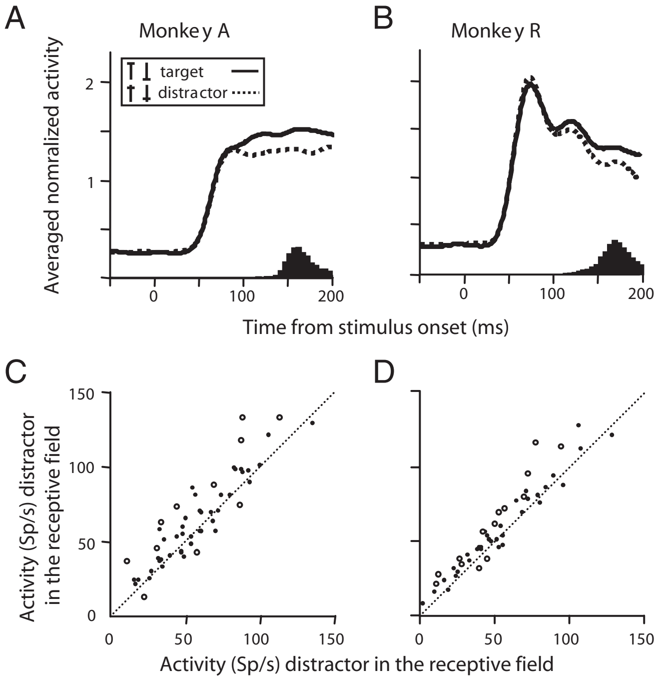

Fig. 3. V4 neurons discriminated the target during the search task when monkey made a saccade *to* the receptive field. (*A* and *B*) Average normalized activity plotted against time for monkeys A and R, respectively, in which the first saccade was made to the receptive field. (*C* and *D*) Mean activity of each cell on trials in which the monkey made a saccade to a target in the receptive field plotted against the same activity when the monkey made a saccade to a distractor in the receptive field. Conventions as in Fig. 2.

neurons (Figs. 4 *C* and *D*; monkey A, $P < 0.0001$; monkey R, $P = 0.0008$ by Wilcoxon signed-rank test). Fourteen of 58 neurons in monkey A and 14 of 45 in monkey R individually showed a significant difference in response to target vs. distractor ($P < 0.05$, by standard t test). These discrimination times occurred at ∼105 ms for monkey A and 145 ms for monkey R. During the 50 ms around the time of the saccade, the difference in activity between target and distractor was even more pronounced (Wilcoxon signed-rank test, monkey A, $P < 0.0001$; monkey R, $P < 0.0001$), with 16 of 58 individual neurons in monkey A and 14 of 45 in monkey R showing a significant difference in activity to the target and distractor ($P < 0.05$, by standard t test). In addition, the three cells that showed selectivity for the distractor stimuli in the saccade task lost their selectivity for the same distractor stimuli in the search task ($P > 0.05$, by standard t test). Because in the saccade task the neurons often responded submaximally to objects in the array locations adjacent to the center of the receptive field, we only included saccades to locations in the saccade-away analysis that evoked no visual or presaccadic response in the saccade task. Because the saccade task had 12 trials per object, for certain stimuli it often had fewer trials than the search task. To determine whether the selectivity found in the search task resulted merely from a larger sample, we checked whether limiting the analysis in the search task to the first 12 trials lessened the significance of our results. It had no effect. Similarly we found no difference if we limited the analysis only to responses to upright targets and distractors or downward targets and distractors.

Although the monkeys had to maintain fixation in a relatively large (6° × 6° or 4° × 4°) window, they actually maintained a fixation window in a smaller portion of space (Table S1). Their actual fixations were well within the fixation limits used for other V4 studies (7, 8). Despite the narrow fixation zones, for 31 of 112 cells there was a significant difference ($P < 0.05$ by t test) in the mean fixation positions. Nonetheless these slight differences in fixation had no effect on whether the cells developed task-related selectivity (Fig. S2).

Comparing Activity in the Search and Saccade Tasks. Selectivity can emerge under one circumstance and not under a second if the firing rate in the first condition is greater than that of the second. However, the responses in the saccade task were greater than those in the search task. In the search task the stimulus in the receptive field was flanked by distractors, but in the saccade task the stimulus in the receptive field was alone in the visual field. V4 has powerful nonclassic suppressive surrounds (9). In keeping with this, the peak of the initial visual response was less in the search task than in the saccade task, even on those trials in which the monkey made a saccade to the receptive field (Fig. 5; $P = 0.0197$, monkey A; $P = 0.0026$, monkey R; Wilcoxon signed-rank test). For monkey A the mean response measured in the interval 0–25 ms after the mean visual latency was 75 spikes per second in the saccade task and 60 spikes per second in the search task. For monkey R the mean response measured during the interval of 25–50 ms after the mean visual latency was 87 spikes per second for the saccade task and 66 spikes per second for the search task. We used different windows in each monkey to encompass the peak of the initial visual response. The magnitude of the initial visual response was independent of the object in the receptive field (saccade task; monkey A, $P = 0.80$; monkey R, $P = 0.86$; standard t test). Thus, the task-related selectivity of V4 neurons occurred despite the lower firing rate in the search task.

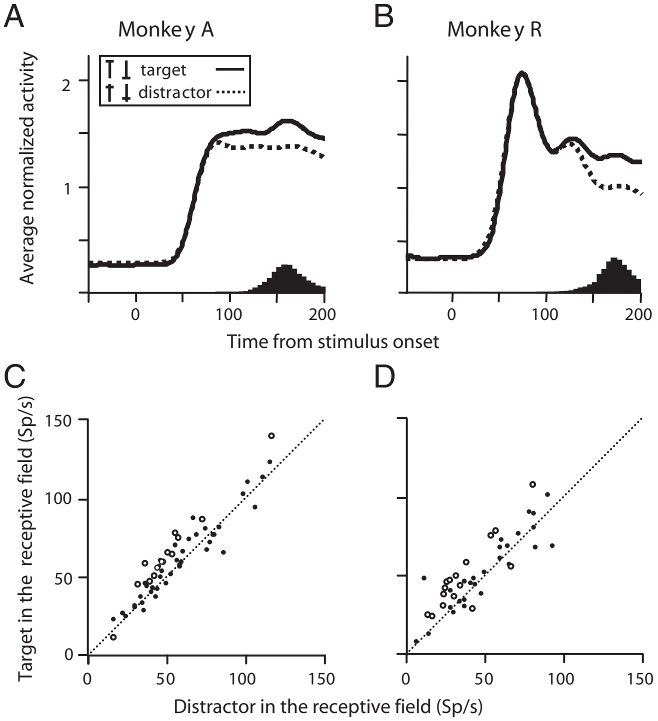

Fig. 4. V4 neurons discriminated the target during the search task when monkey made a saccade *away* from the receptive field. (*A* and *B*) Average normalized activity plotted against time for monkeys A and R, respectively, in which the monkeys made the first saccade away from the receptive field. (*C* and *D*) Mean activity of each cell on trials in which the monkey made a saccade away from a target in the receptive field plotted against the same activity when the monkey made a saccade away from a distractor in the receptive field. Conventions as in Fig. 2.

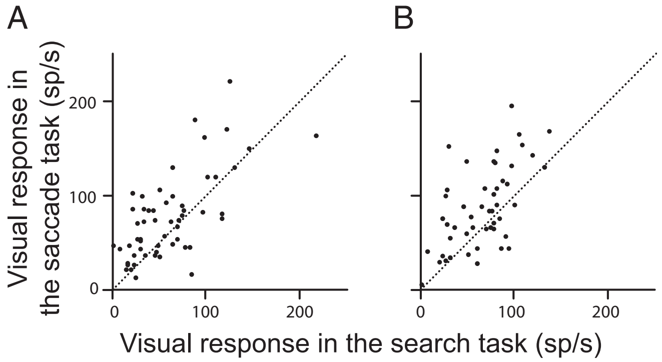

Fig. 5. Visual response in the saccade task is greater than visual response in the search task. (*A*) Mean activity during the peak of the initial visual response of each cell during the 25-ms interval after the mean visual latency plotted for the search task (on the abscissa) against the visually guided saccade task (on the ordinate) for monkey A. (*B*) Same conventions as in *A*, but activity during the 25- to 50-ms interval after the mean visual latency for monkey R.

To assay the selectivity of the responses evoked in the search and saccade responses we calculated a contrast index for saccade and search trials. Because the results were similar in the two monkeys we pooled the contrast indices to increase the power of the analysis. The population for saccade trials had a unimodal (but not normal by Lilliefors test) distribution, with median contrast index of 0.0027, not different from zero (Fig. 6, *Upper*; $P = 0.87$ by Wilcoxon signed rank). The population for search trials had a unimodal distribution (again not normal), with a median of 0.0279, significantly different from zero (Fig. 6, *Lower*; $P < 0.003$ by Wilcoxon signed-rank test). The two populations were significantly different ($P < 0.0001$ by Wilcoxon signed-rank test), showing selectivity in the search task but not the saccade task.

Although the population of neurons had significantly different responses to target and distractor in the search task but not in the saccade task, this alone does not prove that their neural processing is, in fact, different (10). To prove this selectivity, we had to establish that the responses to the target differed between the search and saccade tasks. Because the responses in the saccade task for both target and distractor were greater than those in search task, we computed the difference between the responses to the target and distractor in the saccade task (mean 11.2 ± 0.34 SEM) and the search task (16.8 ± 0. 35, SEM). The two populations were normally distributed by Lilliefors test and significantly different ($P < 0.002$ by t test). Across the population of neurons, the response difference of target and distractor was significantly different between the saccade and search tasks.

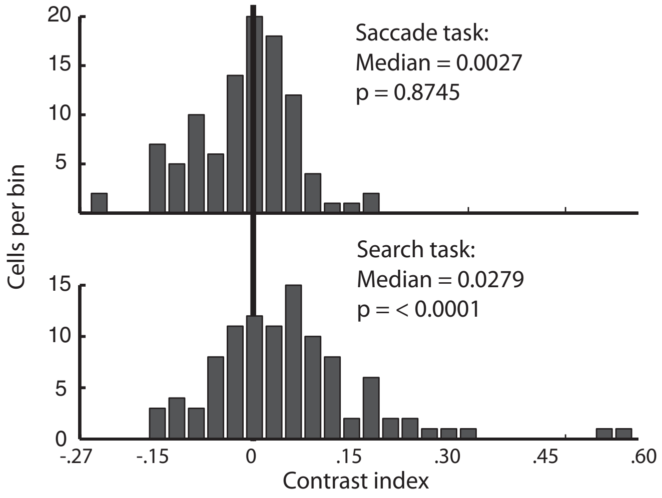

Fig. 6. Distributions of contrast indices for search and saccade tasks. We calculated the contrast index as (target response − distractor response)/(target response + distractor response). *Upper*: Distribution of contrast indices for saccade task. Ordinate cells/bin. Abscissa contrast index of center of bin. *Lower*: Distribution of contrast indices for search task. Conventions same as in *Upper*.

We used relatively generous fixation windows (±6° on some cells and ±4° on others), and although the monkeys tended to stay much closer to the fixation point than to the borders of the window the monkeys' fixation differed slightly but significantly between the saccade and search for some cells. For monkey A 22 of 62 cells had a significant difference in the fixation point between the saccade and search tasks, and for monkey R 9 of 50 cells had a significant difference in fixation (Table S1). However, this difference had no effect on task-related selectivity. Both the population of cells for which there was no difference in fixation and the population of cells for which there was a difference in fixation between the saccade and search tasks were selective for the target in the search task but not in the saccade task (Fig. S2).

The higher activity for the target was not merely related to the next saccade. We were careful to eliminate from analysis all trials in which the target remained in the neuron's receptive field after the first saccade, so the response could not be a simple presaccadic enhancement. One monkey made a reasonable number of trials with more than two saccades. Even when the monkey made the second saccade to another distractor, the response evoked by the target in the receptive field before the first saccade was still greater than the activity evoked by a distractor in the receptive field for the population ($P < 0.001$, Wilcoxon signed-rank test), so the target selectivity could not have simply been an enhanced signal for the next saccade.

Latency Difference Between Task-Specific Selectivity and Hard-Wired Feature Selectivity. Classic orientation and color selectivity are manifest from the first or second spike; a neuron may respond briskly to its preferred stimulus and not at all to a nonpreferred stimulus. The search task-specific selectivity that we have demonstrated here is very different from traditional hard-wired feedforward feature selectivity because rather than arising from around the first spike it develops much later. We recorded full orientation tuning curves for 15 neurons. The time at which the visual responses of the neurons to the best and second-best stimuli could be distinguished averaged 10 ms after the visual latency. The time at which the same neurons became selective for the target was much later (Fig. 7). There was no correlation between the emergence of orientation selectivity and the emergence of task-specific selectivity. Six neurons were selective for the target or distractor in the saccade task. This selectivity emerged 10 ms after the stimulus appearance, suggesting that the selectivity for the target or distractor of these neurons was similar to that of orientation selectivity and quite different from the late-developing task-specific selectivity manifest by the rest of the neurons.

Discussion

In this study we demonstrated that V4 neurons develop new selectivity for visual objects when they have to distinguish between the targets and the distractor in a search task. The great bulk of the neurons were not innately selective for the search target. When the monkey did not have to distinguish between the target and the distractor in a simple overlap saccade task, only a few neurons exhibited any selectivity. However, when the search task required the monkey to attend to and identify the orientation of a capital T target among different lowercase t distractors, the same neurons become selective for the capital T.

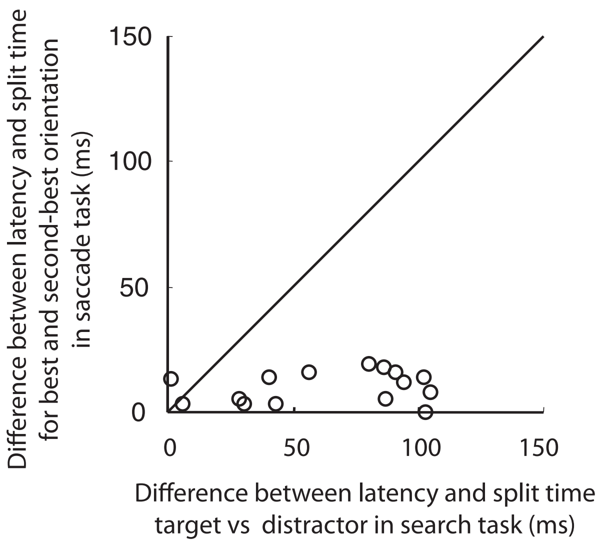

Fig. 7. Comparison of the times at which selectivity develops for orientation selectivity (a first-spike selectivity) and task-specific selectivity in V4 neurons. Each dot is a single cell. We calculated split time as the time at which a significant difference emerges between the responses to the target and distractor in search task, and the best and second-best responses to an oriented bar (45° difference in orientation) in the saccade task. Ordinate: Difference between split time and latency in the response to the best and second-best oriented bars in the saccade task. Abscissa: Difference between split time and latency in the responses to target and distractor in the search task. Solid line x = y. There is no correlation between the orientation split time and the task-selectivity split time ($R^2 = 0.01$).

This selectivity for the search target developed much later than hard-wired feature selectivity such as orientation and color. We will discuss these results in the possible causes of the difference in selectivity between the search and saccade task, the context of the attentional modulation of neural responses in V4 and other areas, the distinction between task-related and first-spike feature selectivity, the nature of top-down control in V4, and the role of task-specific stimulus specificity in the generation of visual behavior.

Causes of the Difference in V4 Responses in the Search and Saccade Tasks. In our data V4 neurons give enhanced responses to the target from similar distractors in a search task but do not when the monkeys merely make a saccade to a target or a distractor presented by itself as a saccade goal. There are several reasons why this might occur. The first is the effect of surround suppression. V4 neurons have powerful nonclassic surrounds (11–13), and it could be that the task-related selectivity arose from the surround suppression by adjacent objects in the array. Inhibition would also be expected to act later than feed-forward excitation (14). However, if surround suppression were entirely responsible for the effect we saw, one would expect an increase in selectivity for the distractor in some cells, and a broadening rather than an upward shift of the population in Fig. 3 relative to Fig. 2.

A second possibility is that the effect is a feature-attention enhancement of a preexisting selectivity of V4 neurons. We found no evidence for preexisting selectivity for the target in V4. The contrast index in the saccade task had a unimodal distribution, with a median close to 1 (−0.0027) and not different from 1 with a high probability ($P = 0.87$ by Wilcoxon). The median difference in response in the saccade and search tasks to the distractor was 0, and the difference population also had a unimodal distribution. Furthermore, if there were a hard-wired selectivity for the target one would expect that the presaccadic burst of the neurons in the saccade task would have enhanced the response to the preferred stimulus (15). There was no difference in the responses to target and distractor in the 50 ms preceding the saccade in the saccade task, although there was in the search task.

A third possibility is that fixation differences between the two tasks caused the difference in responses. There was a slight difference in the mean fixation between the search task and the saccade task, but eye position did not affect the difference between the responses in the search and saccade tasks.

Feature attention, however, did differ between the tasks; the monkey did not have to pay attention to stimulus features in the saccade task and did in the search task. The feature attention enhanced the response of V4 neurons to the target but not to the distractor. This enhanced response resulted in the population of V4 neurons becoming selective for the target. The late onset of this feature selectivity is consistent with its arising from feature attention (16).

Attentional Modulation of Neural Responses in V4. Visual attention has been shown to raise the response gain of neurons in many visual areas, including cortical areas V1 (17, 18), V4 (8, 18), the LIP (19), and the superior colliculus (20). In V4, spatial attention increased sensitivity to the middle range of contrasts but did not change contrast thresholds or asymptotes (21). Under other circumstances, spatial attention also increased response gain (22). Spatial attention also changed the topography of receptive fields of V4 neurons. The V4 receptive field profile to a task-irrelevant stimulus shifted toward the locus of attention (23) and to the goal of an impending saccade (24). Li et al. (25) found that context changed the effect of flankers on the response of V1 neurons, but the question of whether context changed the feature selectivity of the excitatory center did not arise. Feature attention increases the gain of V4 responses (26–28), even for stimuli with attended features that are not at the current locus of spatial attention (2, 29).

In all of the studies quoted above, attention modified the amplitude of a preexisting selectivity of V4 neurons. However, attention did not change the specific pattern selectivity of the neurons. In most cases this was not stated explicitly, but McAdams and Maunsell (8, 30) specifically looked for an effect of spatial attention on orientation tuning, either in a sharpening of the tuning curve or a shift of cases rendered nonselective neurons broadly selective for orientation. They found that cells that could be fit with a Gaussian tuning curve did not change their selectivity. Cells that could not be fit with a Gaussian in the unattended condition had a Gaussian tuning curve in the attended condition, but the average of the unfittable cell responses showed a tuning that was not different from the attended case. In contrast, Spitzer et al. (31) showed that increasing task difficulty in an orientation or color match-to-sample task, by inference increasing the attention necessary to solve the task, decreased the bandwidth of the color and orientation tuning curves of V4 neurons, and in a few cases rendered neurons unselective for orientation broadly tuned for orientation. They studied the response to the sample, not the match, so were unable to state whether the neurons had different responses to nonmatch stimuli. The seeming conflict between these two studies may be due to differences in their data analysis. McAdams and Maunsell measured bandwidth as the SD of fitted Gaussians. Spitzer et al. measured bandwidth as the full width 1/e below the peak. There would have been no difference between these two methods if the tuning curves went down to zero spikes per second, or if the vertical scaling by attention were exactly proportional to rate of firing. However, neither is true for V4. We suspect that if McAdams and Maunsell had measured orientation tuning as the full width 1/e below the peak, they would have said that attention sharpened tuning as well. Conversely, if

Spitzer et al. had fit Gaussians, they would have seen no overall sharpening. Nonetheless, these studies did not clearly demonstrate a change in the peak feature selectivity of V4 neuron. More crucially, they did not examine the difference between spatial attention without a feature component and feature attention. A recent study by David et al. (6) demonstrated that feature attention shifted V4 spectral receptive fields toward the spectral features of a searched-for object. However, it is unclear whether this shift directly resulted in an actual change in selectivity for the searched-for object.

V4 Search-Target Selectivity Is Different from Classic First-Spike Feature Selectivity. It is well known that many V4 neurons are selective for color and/or orientation even when the stimulus in the receptive field is irrelevant to the current behavior (9, 12, 32). Feature attention enhances preexisting feature selectivity when the monkey is searching for a target with a feature for which the neuron is selective (2). It could be that the feature selectivity we have demonstrated in the search task is, in fact, merely such a feature-attention enhancement of a preexisting hard-wired pattern selectivity. This is unlikely for a number of reasons. (*i*) The statistical method that we used for determining that there was no difference of response to target or distractor was very robust: we calculated a contrast index between the response to the target and the distractor, such that a value of zero would be consistent with no response. The median contrast index in the saccade task was 0.0027 (by Mann-Whitney *U* test), which failed to reject the hypothesis that the responses to the target and distractor were different, with a probability of 0.87. The median contrast index in the search task was median = 0.0279, which is significantly different from zero ($P < 0.006$, Mann-Whitney *U* test), showing that in the search tasks the responses to saccade and distractor were very different. (*ii*) Feature-attention enhancement of hard-wired feed-forward selectivity, such as orientation or color selectivity, occurs at or near the first spike. This early selectivity can be seen in previous studies of visual search in V4 in which the monkeys searched for a feature discriminated by V4 neurons [e.g., figure 2 in Bichot et al. (2)]. Zhou and Desimone (5) showed that V4 neurons can become selective for search targets at later times, but this study did not compare this feature-attentional enhancement with a task requiring spatial attention alone. The selectivity we have described occurs an average of 50 ms after the first spike. We found this difference in the latency of selectivity when we compared the development of selectivity for orientation (comparing the responses to the best and second-best orientation in the saccade task) with the development of selectivity for the target in the search task. Furthermore, the few cells that were selective for the target in the saccade task developed this selectivity within 10 ms of the target appearance, suggesting that hard-wired selectivity and not task-related selectivity was at play in these neurons. A few neurons were selective for upright or inverted t's, but not for target or distractor of the selected orientation. This selectivity also was early, but the neurons subsequently developed selectivity for the target. (*iii*) If the search task had been associated with an increased responsiveness to both target and distractor, the increase in neuronal excitability in the search task might have brought out a hard-wired selectivity. However, the appearance of the array evoked a weaker response than the appearance of a single saccade target, perhaps because of the nonclassic surround suppression in V4 (12), so the task-related pattern selectivity could not merely have been brought out of the noise by increased mean activity.

Nature of Top-Down Control in V4. Because V4 task-related selectivity develops 50 ms after the visual response begins it most likely occurs as a result of top-down rather than purely bottom-up signals. The top-down signal could arise from some or all of a number of areas: dorsal stream areas important in attention like FEF (33), prefrontal cortex (34), and LIP (35); and ventral stream areas like inferior temporal cortex area TE (36), all of which project to V4 (37, 38). Both spatial and feature attention can act as top-down enhancers in V4, but only feature attention can evoke task-related selectivity. If the monkey does not have to find the target, then V4 does not distinguish it from the distractor.

Role of V4 in Visual Search. V4 has two different sets of projections. On the one hand, it is the conduit by which the feature analysis performed in striate and prestriate cortex reaches inferior temporal cortex. On the other hand, it has a powerful projection to LIP, which develops a priority map usable by the visual system to pin attention to a certain object, and the oculomotor system to select the goal of an impending saccade (39). Neurons are typically thought to be responsive and hard-wired for certain features (i.e., orientation, color, shape). When monkeys search for a particular object feature, feature-based attention causes neurons selective for that feature to be activated in parallel across the entire visual field. In our search task V4 has a small number of neurons hard-wired for the discrimination between t and T, but this small population might be too insignificant to affect behavior. Instead, the present data suggest that as the search process becomes more refined, top-down signals cause many previously unselective V4 neurons to be selective for the target (40). As the search process proceeds, the entire population of V4 neurons representing the search target develops significantly greater activity than the population representing the distractors. Sending this signal to LIP will result in the emergence of a small but significant peak on the priority map at the spatial location of the target, making it more likely that the monkey will find the target. We suggest that the process by which selectivity develops in V4 for the target in neurons that are not hard-wired for this selectivity facilitates the process of visual search.

Methods

We used two male rhesus monkeys (*Macaca mulatta*) weighing 7–14 kg in this experiment. The Animal Care and Use Committees at Columbia University and the New York State Psychiatric Institute approved all protocols as complying with the guidelines established in the Public Health Service Guide for the Care and Use of Laboratory Animals.

We used standard methods (41) to implant subconjunctival scleral search coils (42), head-restraining devices, and recording chambers implanted during aseptic surgery under ketamine and isoflurane anesthesia. We positioned chambers over ventral area V4 at 25 mm lateral and 8 mm posterior from the midpoint, guided by T1 magnetic resonance images.

Behavior. We designed two different tasks. The first was a visually guided delayed saccade task (Fig. 1*A*). Monkeys sat in a dimly illuminated room with their head fixed and viewed a tangent screen that stood ~75 cm away. Each trial started when a red fixation point appeared at the center of the screen. If the monkey maintained fixation in a 6° × 6° or 4° × 4° window for a randomly chosen time period from 1 to 1.75 s, an object appeared in the receptive field of the neuron. Roughly 1 s later the fixation point disappeared, and the monkey had to make a saccade to the object. If the monkey broke fixation before the fixation point being turned off, the trial ended without reward or punishment for the monkey. The object was either one of the objects used in the second task (a capital T, inverted capital T, upright or inverted lowercase t) or a line of four various orientations (vertical, horizontal, 45° oblique, 135° oblique). At 10° eccentricity, the stimuli were 1.0° wide and 2.9° tall, and their size was adjusted for cortical magnification as the eccentricity of receptive field center changed. We defined neurons as being orientation or shape selective if an n-way ANOVA was significant for the responses to the different orientations or shapes during the time window of 80–180 ms after the onset of the stimulus. The identity of the object was not important. The monkeys had only to locate the stimulus correctly and make a saccade to it to complete the task correctly. Although we did not measure attention explicitly (35), we assumed that the monkeys were attending to the object in the receptive field because other studies have shown that attention is pinned to the goal of a delayed saccade throughout the delay period (35, 43).

The second task was a free-viewing visual search task (44) (Fig. 1*B*). Each trial started when the monkey grabbed one of two bars with each hand. Then a small white central fixation point appeared in the center of a black background. If the monkey maintained his fixation inside a window (between 6° × 6° or 4° × 4°, depending upon the cell) for a randomly chosen time period from 1 to 1.75 s, the fixation point disappeared and an array of six or eight stimuli appeared, depending on the eccentricity of the receptive field of the isolated neuron. The array consisted of a target and five or seven distractors, which were positioned symmetrically around an imaginary circle, centered on the former fixation spot, such that one object was always in the center of the neuron's receptive field. We altered the color of all of the analyzed stimuli to match the color selectivity of neurons, and used neurons whose orientation selectivity included a horizontal or vertical bar. On each trial the relative position of all of the stimuli changed pseudorandomly. The target was a capital T that could be upright or inverted. The orientation of the target on each trial was unpredictable. All of the distractors had the same dimensions, color, and luminance as the target but differed only in the position where the horizontal component crossed the vertical component. Monkeys earned their reward by reporting the orientation of the target by releasing one of the two bars (the left bar when the target was the upright capital T and the right bar when the target was the inverted capital T). Monkeys were free to move their gaze and did not need to fixate the target to receive the reward. They were given 3 s to respond correctly. After that, the trial aborted. We presented the visually guided saccade task and the search task in blocks. The order of presentation of the task did not affect the results.

Recording. We recorded single units from area V4 with glass insulated tungsten electrodes (Alpha Omega Engineering). We introduced the electrodes through a guide tube positioned in a 1-mm-spaced grid. To amplify, filter and discriminate action potentials, we used a software amplitude window discriminator (MEX, designed by John McClurkin at the Laboratory of Sensorimotor Research at the National Eye Institute).

Once we isolated a neuron, we mapped the receptive field informally by a joystick-controlled stimulus, and having done so set up a search array so that one object was in the stimulus location that gave the best response from the neuron. Receptive fields ranged from 3° to 20° in eccentricity, in the lower visual field. We studied a total of 112 neurons in V4 (61 from monkey A; 51 from monkey R) that were responsive to the objects used in the search task. We recorded from these neurons while the monkeys performed the visually guided saccade task and the search task. We used the saccade task for mapping the receptive field location and characterizing the responses of the neuron to orientation, shape, and color. Because the stimulus was at the goal of the saccade, we could ensure that the monkey was paying attention to the stimulus and therefore lessen any possible attention-related fluctuations in response. We categorized a neuron as orientation or color selective if it responded significantly differently (two-tailed *t* test, $P < 0.05$) to a particular color (i.e., red, green, blue, yellow) or orientation (0°, 45°, 90°, 135°) during the 80–180 ms after the onset of the stimulus. Every neuron we studied responded significantly (two-tailed *t* test, $P < 0.05$) 80–180 ms after the onset of the stimulus to at least one set of target and distractor-shaped objects used in the search task. We determined the response of the neuron to the saccade targets and distractors for all of the object positions in the array.

After mapping the receptive field and characterizing the neuron, we recorded from the same neuron while the monkey performed the free-viewing visual search task. In this study, we analyzed the activity of the neurons during the interval between the onset of the array and the onset of the first saccade.

Data Analysis. We wrote all data analysis programs in MATLAB (MathWorks). To examine the pattern of activity, we calculated spike-density functions by convolving the spike train, sampled at 1 kHz, with a Gaussian of σ 10 ms. We defined the neuronal response for an interval of interest as the mean of the spike density over the interval.

To reduce the effect of outliers we used the square-root normalization method described by Prince et al. (45). On average, there were $\sim$12 trials per condition per cell in the saccade task. For the search task, there was an average of 92 and 63 trials per cell when a saccade was made to the target and distractor, respectively, in the receptive field. There was an average of 49 and 602 trials per cell when a saccade was made away from a target and distractor, respectively, in the receptive field. When we analyzed trials in which the monkey made a saccade away from the receptive field, we only included trials in which saccade goal was not in the receptive field.

To calculate the split time, the time at which the activity from two types of trials started to separate, we used a sliding window test. For each millisecond, we calculated the activity in a 50-ms bin centered at that time for each class of response. We then compared the activity in each pair of bins using a two-tailed *t* test. We defined the time of separation as the first bin of 20 out of 25 consecutive bins that all had P values <0.05.

We calculated response latencies using the Poisson fit threshold method described in detail previously (46). Briefly, we derived a Poisson distribution from the baseline activity 100 ms before array onset analyzed in 2-ms bins. We then set the threshold as the 99th percentile of the Poisson fit. Finally, we defined the latency as the first of three consecutive 2-ms bins each of which contained more spikes than the threshold.

ACKNOWLEDGMENTS. We thank James Bisley for invaluable discussions and help, Joy Hirsch for MR imaging, Girma Asfaw and Yana Pavlova for veterinary assistance, Glen Duncan for computer hardware and software, John Caban for machining, and Latoya Palmer for facilitating everything. This research was supported in part by grants from the Zegar, Keck, and Dana Foundations, the National Science Foundation (to A.L.G.), and the National Eye Institute (Grants R24EY015634, R21EY017938, R01EY017039, R01 EY014978, and 5P30EY019007 to M.E.G.; National Research Service Award 5F31 NS058059-02 to A.L.G.; and Training Grant T32 EY13933-01 A.E.I.).

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