Suppression of frontal eye field neuronal responses with maintained fixation

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Edited by Robert H. Wurtz, National Institutes of Health, Bethesda, MD, and approved December 12, 2017 (received for review September 18, 2017)

The decision of where to make an eye movement is thought to be driven primarily by responses to stimuli in neurons’ receptive fields (RFs) in oculomotor areas, including the frontal eye field (FEF) of prefrontal cortex. It is also thought that a saccade may be generated when the accumulation of this activity in favor of one location or another reaches a threshold. However, in the reading and scene perception fields, it is well known that the properties of the stimulus at the fovea often affect when the eyes leave that stimulus. We propose that if FEF plays a role in generating eye movements, then the identity of the stimulus at fixation should affect the FEF responses so as to reduce the probability of making a saccade when fixing an item of interest. Using a visual foraging task in which animals could make multiple eye movements within a single trial, we found that responses were strongly modulated by the identity of the stimulus at the fovea. Specifically, responses to the stimulus in the RF were suppressed when the animal maintained fixation for longer durations on a stimulus that could be associated with a reward. We suggest that this suppression, which was predicted by models of eye movement behavior, could be a mechanism by which FEF can modulate the temporal flow of saccades based on the importance of the stimulus at the fovea.

In natural viewing, each saccade is part of a stream of consecutive eye movements and, for each, our brain has to decide the goal, rapidly and accurately. Making a decision about where to go in the context of visual search is a complex process that is thought to rely on a combination of factors, such as a representation of salience (1), the task relevance of visual objects (2), and expectations or predictions based on past experience (3). Neuronal correlates of such factors have been examined in multiple areas of the brain, including the frontal eye field (FEF) of prefrontal cortex (4), the superior colliculus (5), and the lateral intraparietal area (LIP) of parietal cortex (6). In all cases, studies have focused on the properties of the stimulus within each neuron’s receptive field (RF), which is ubiquitously thought of as the main factor in the neuronal response. In natural visual foraging behavior, however, the properties of the object at the center of gaze and deciding when to leave it are of critical importance. The physical shape, complexity, or familiarity of an object (7–10) and how it is related to the task (11) significantly influence the amount of time we spend gaz ing at it. Indeed, a fundamental aspect of models of eye movements in visual search (12, 13), scene perception (14, 15), and reading (9, 16) is the inclusion of an inhibitory action that keeps the eye from moving if the object being fixated is important for the task.

We hypothesize that if activity in FEF plays a role in when and where a saccade is to be made, then it should incorporate the sort of suppression that these models include to accurately mimic human behavior. In particular, we predict that the response to a stimulus in the RF should be reduced when the animal is looking at an object that it should continue to fixate.

Results

To test the hypothesis that properties of the stimulus at the fovea affect the responses of neurons in FEF, we trained two monkeys (Macaca mulatta) to forage for a target by freely moving their eyes among 10 objects (Fig. 1A). While the monkeys were performing the foraging task, we recorded the activity from single FEF neurons using extracellular electrodes. Five potential targets (Ts; T shape) and five distractors (+ shape) were arranged on the screen in a way that when the animal was looking at one of the objects, no more than one other object could be in the RF (large circle in Fig. 1A). One T was loaded with a reward, which the animals received if they fixated it for 500 ms. Since distractors never delivered any reward, the animals tended to forage among the Ts, fixating each for about 600 ms until they found the target and received the reward (17). Fixations of distractors were rare (less than 5% of fixations) and were significantly (P = 8.70 × 10−158, paired t test; n = 231) and substantially shorter [237.6 ± 50.5 ms (mean ± SD)] than fixations of potential targets (613.7 ± 48.9 ms).

Previous studies have shown that shortly after array onset, FEF neuronal responses differentiate between a target and distractor in the RF in standard visual search tasks (18, 19). We found a similar result in our population when the array appeared: The response to a potential target in the RF (dark trace, Fig. 1B) was consistently higher than the response to a distractor in the RF (light trace, Fig. 1B). This difference began to become consistently significant ~180 ms after array onset (black bar on x axis of Fig. 1B; P < 0.01, paired t test every millisecond on the spike density function). Using trials in which the fixation point was replaced by a stimulus and another stimulus appeared in the RF, the mean response in a 150-ms window starting 150 ms after array onset was significantly greater when a T was in the RF than when a distractor was in the RF.

Significance

In natural viewing, such as reading or scene perception, fixation can be extended temporally when subjects look at a word or object that is important or requires more processing. Numerous models have suggested that this could occur by a suppressive mechanism. Here, we show that responses in the frontal eye field (FEF) are suppressed when animals maintain fixation on a stimulus that may give them a reward. This suggests that FEF may be able to modulate the temporal flow of eye movements in natural viewing using enhanced activity to generate eye movements and suppression to maintain fixation.

Author contributions: K.M. and J.W.B. designed research; K.M. and Z.B. performed research; K.M. and J.W.B. analyzed data; and K.M. and J.W.B. wrote the paper.

The authors declare no conflict of interest.

This article is a PNAS Direct Submission.

Supported by the PNAS license.

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This article contains supporting information online at www.pnas.org/lookup/suppl/doi:10.1073/pnas.1716315115/-/DCSupplemental.
the RF [18.95 ± 1.47 spikes per second (sp/s) vs. 17.26 ± 1.35 sp/s; P = 2.01 × 10⁻⁵, Wilcoxon signed-rank test; n = 195 neurons; Fig. 1C]. At the single neuron level, 40 neurons responded significantly more to a T in the RF than to a distractor in the RF (P < 0.05, t test), whereas only four had a significantly greater response to the distractor, a number that is within the false-positive rate.

A similar effect was seen when we sorted data based on what was in the RF and at the fovea. Fig. 24 shows the mean normalized response of 193 FEF neurons aligned by array onset as a function of both stimulus identity in the RF and stimulus identity at the fovea for fixations that lasted at least 300 ms (vertical dashed line). Although the difference between the response to a T in the RF and the response to a distractor in the RF is visible (compare dark and light traces in Fig. 24, particularly the dark and light blue traces), the more obvious result is the much higher activity when a distractor was at the fovea (blue traces) than when a T was at the fovea (green traces), which was similar to the baseline response (horizontal dashed line).

When we compared the responses based on what was at the fovea, 107 of 204 neurons showed significantly higher responses when a distractor was at the fovea than when a T was at the fovea (P < 0.05, t tests; blue points, Fig. 2B), whereas only 24 responded more when a target was at the fovea (green points, Fig. 2B). Across the population of 204 neurons, the mean response when a distractor was at the fovea (22.13 ± 1.76 sp/s; 150-ms window starting 150 ms after array onset) was significantly greater than when a T was at the fovea (15.30 ± 1.21 sp/s; P = 1.64 × 10⁻¹⁵, Wilcoxon signed-rank test; Fig. 2B) and the response when a T was at the fovea was not significantly different from the baseline activity seen in the 100 ms before array onset (14.25 ± 1.11 sp/s; P = 0.269). The effect of stimulus identity at the fovea was significant both when a T was in the RF (P = 8.18 × 10⁻¹⁵; Fig. 2C) and when a distractor was in the RF (P = 1.41 × 10⁻⁹; Fig. 2D). It is worth noting that both the response difference and the number of neurons showing a significant difference were substantially greater when comparing the identity of the stimulus at the fovea (Fig. 2B) than when comparing the identity of the stimulus in the RF (Fig. 1C). Thus, the effect of the identity of the stimulus at the fovea is far greater than the effect of the identity of the stimulus in the RF.

The strong modulation of the neuronal response by the identity of the object at the fovea was also observed during ongoing visual search. Fig. 34 shows the mean normalized response to the population of all 231 neurons during ongoing search from fixations of at least 150 ms (vertical dashed line) and
in which there was a stimulus at the fovea and a stimulus in the RF. For this and the following analyses, we have pooled the responses to Ts and distractors in the RF, but the results are qualitatively similar if we restrict the analyses to only one of the two stimulus categories, as illustrated in Fig. 2 B–D. The response when a distractor was at the fovea (blue trace, Fig. 3A) was substantially and significantly ($P = 2.34 \times 10^{-13}$, Wilcoxon signed-rank test; $n = 231$ neurons; Fig. 3B) higher than when a T was at the fovea (green trace, Fig. 3A). Interestingly, this difference started ~140 ms before the fixation onset (black bar on x axis of Fig. 3A; $P < 0.01$, paired $t$ test at each millisecond) and was significant in 100 of 231 neurons ($P < 0.05$, $t$ tests) and in the population as a whole ($P = 8.17 \times 10^{-7}$, Wilcoxon signed-rank test; Fig. 3C) in the 100-ms window before the fixation onset. This is a greater proportion of neurons than the proportion showing traditional RF remapping in FEF (20), and it suggests that knowledge about the identity of the stimulus that is about to be fixated affects a large proportion of the neurons in FEF and may be independent of previously documented RF remapping.

The modulation of the neuronal response by the stimulus at the fovea was seen in all classes of neurons as categorized in the memory-guided saccade (class definitions are provided in SI Methods). Fig. S2 plots the data from Fig. 3B for the 157 neurons that had sufficient memory-guided saccade mapping data to characterize the neurons as visual (Fig. S2A), visuomovement (Fig. S2B), or movement (Fig. S2C) neurons. For each class of neuron, we found that the response to a stimulus in the RF was significantly greater when a distractor was at the fovea than when a T was at the fovea (all $P < 6 \times 10^{-2}$, Wilcoxon signed-rank tests). In addition, the percentage of neurons that responded significantly more when a distractor was at the fovea than when a target was at the fovea was not statistically different across each population [17 of 37 neurons (45.9%), 54 of 91 neurons (59.3%), and 14 of 29 neurons (48.3%) for visual, visuomovement, and movement, respectively; all $P > 0.170$, $\chi^2$ tests].

To quantify the magnitude of the effect of each factor on the response of all 231 neurons, we ran an ANOVA model on the neuronal responses from a 150-ms window starting at fixation onset using the identity of the object at the fovea and the identity of the object in the RF as fixed variables and neuron identity as a random variable. Neuron identity is an identifier associated with each neuron. We included this as a random variable to take into
account the overall responsiveness of the neuron; in this way, the ANOVA can deal with nonnormalized responses across neurons with different response gains and variations. The only significant fixed factor was the identity of the object at the fovea ($P = 0.00054$). The magnitude of this factor was about 30-fold stronger than the factor representing the identity of the object in the RF ($3.413$ compared with $0.113$) and there was no significant linear interaction between the fixed factors ($P = 0.97$). Note that the effect of the stimulus identity in the RF is considerably weaker in ongoing visual search compared with array onset. This is due to some heterogeneity in the responses to the stimulus in the RF in ongoing search. At the single-neuron level, 110 (51%) neurons showed a significant effect of object identity at the fovea, compared with only 38 (18%) of neurons with RF effect. Only a few neurons [25 (12%)] showed any interaction between the fixed variables (average absolute value of the ANOVA coefficients for all neurons = 1.339).

To test whether the large effect of object identity at the fovea may represent a change in response gain, we looked at two pairs of conditions in which we compared the response to an object in the RF (Fig. 3D) or the activity when nothing was in the RF (Fig. 3E) as a function of the identity of the object at the fovea. If the increase in activity is due to a consistent gain increase, then the activity should be correlated with a slope that is significantly different from 1 and with slopes that are the same whether a stimulus was in the RF or not. We found that whether a stimulus was in the RF or not, the activity when a distractor was at the fovea was a little more than 1.2-fold greater than when a T was at the fovea, with best-fit slopes of $1.23 \pm 0.079$ ($P = 8.1 \times 10^{-8}$, $R^2 = 0.81$) with an object in the RF (Fig. 3D) and $1.26 \pm 0.081$ ($P = 4.9 \times 10^{-9}$, $R^2 = 0.84$) with nothing in the RF (Fig. 3E). Intercepts of the fits were close to the origin ($3.57 \pm 2.26$ sp/s with an object in the RF and $1.17 \pm 1.88$ sp/s with nothing in the RF), showing that the difference in activity could easily be due to a gain change. To confirm that this was not due entirely to the overall responsiveness of individual neurons, we plotted the ratio of the activity with a distractor at the fovea divided by the activity with a T at the fovea for conditions in which an object was in the RF or nothing was in the RF (Fig. 3F). The ratios in the two conditions were correlated ($P = 0.0081$), but, more importantly, the majority of the cells [145 of 219 (66.2%)] lie in a cluster in the top right quadrant (Fig. 3F), meaning they have a positive gain in both conditions. If we only look at neurons that showed a significant effect of object identity at the fovea from the ANOVA analysis described in the previous paragraph, then 75.2% (82 of 109) lie in the top right quadrant (Fig. 3F) and the correlation is much stronger ($P = 2.35 \times 10^{-4}$, $R^2 = 0.189$), with a slope of $1.03 \pm 0.41$ and an intercept of $0.73 \pm 0.81$. Thus, the data are consistent with the hypothesis that the identity of the stimulus at the fovea changes the gain of the neuronal response and that this gain change is relatively consistent across neurons and sessions and is independent of the overall responsiveness of each neuron.

We propose that the reduced response seen when a T is at the fovea is due to a mechanism that suppresses responses throughout the peripheral representation in FEF, thereby minimizing the chance that a saccade will be generated when fixation should be maintained. We have previously shown that animals rarely fixate previously examined Ts (less than 5% of fixations), which will not give them a reward (17). Because fixation durations of previously fixated Ts are bimodal (Fig. 4A), we can test our hypothesis by examining the responses during the two types of fixation. If the reduced response seen when the animal fixates a T is due to a suppressive input aimed at keeping the animal from moving on, then we should see suppression when the animal fixates a previously fixated T for a long duration (>350 ms; vertical dashed line in Fig. 4A), even though it should know that it will not get a reward from the stimulus. Likewise, we should see a strong response, similar to that when the distractor is at the fovea, if the animal only fixates the previously fixated T for a short duration (<350 ms). Alternatively, if the response modulation is purely due to the identity of the stimulus at the fovea, then we would predict that fixation duration should not affect the response when a previously seen T is being fixated.

Fig. 4B shows the response of the neurons to a previously fixated T at the fovea for long- and short-fixation durations, as well as the mean response to a distractor and unseen T at the fovea (lines without error bars). All data are from trials with fixations that lasted for more than 150 ms (vertical dashed line in Fig. 4B). In fixations in which the animals fixated the previously fixated T for more than 350 ms, the response was suppressed to a level that was not significantly different from the response when an unseen T was at the fovea ($P = 0.406$, Wilcoxon signed-rank test; $n = 207$; 100-ms window starting 50 ms after fixation onset; Fig. 4C). For short-duration fixations, the response was significantly higher than for longer durations ($P = 8.32 \times 10^{-19}$) and was statistically indistinguishable from the response when a distractor was at the fovea ($P = 0.165$, Wilcoxon signed-rank test; Fig. 4D). This is consistent with our hypothesis that responses in FEF are suppressed when the animal maintains fixation for longer durations.

All of the analyses presented so far utilized the responses aligned by the start of fixation when the animals made a saccade away from the RF of the neuron. Consistent with previous...
studies, when the animals made a saccade to the RF, the response of the population ramped up to the highest levels we measured (Fig. 5A). Notably, starting ~180 ms before the saccade was made, this movement-related activity was not affected by the identity of the stimulus at the focus (thick black line on x axis, Fig. 5A; P < 0.01, paired t-tests every millisecond). Looking at the activity in the 100-ms window leading up to the saccade, there was no significant difference in response as a function of what was currently at the focus (P = 0.978, Wilcoxon signed-rank test; n = 138; Fig. 5B), and this was true even in the subset of neurons that showed a significant effect of object identity at the focus in the ANOVA analysis described above (P = 0.801; n = 71). In addition, the saccade metrics were similar in both cases (details are provided in SI Results). Thus, in the time leading up to the saccade, the identity of the stimulus at the focus no longer affects the movement-related activity or the movement itself, and the identity of the stimulus that will end up at the focus starts to have an effect on responses in other locations away from the saccade goal (as shown in Fig. 3A).

Discussion
Here, we showed that the response to a stimulus in the RF was greatly affected by the properties of the stimulus at the focus: When the animal maintained fixation on a stimulus that could be related to a reward for at least 350 ms, the response was strongly suppressed. This surprisingly strong effect appeared to be implemented by a gain control mechanism. This resulted in a robust response to a stimulus in the RF, but only when the animal was fixing a stimulus it would quickly move away from. These results fit with the idea of FEF as an oculomotor area that not only identifies where the next saccade should go but can also affect the flow of saccadic behavior.

Within the eye movement literature, the mechanisms thought to be important in driving the temporal flow of saccades are quite different depending upon the field of research. Within the field of reaction time analyses, particularly in decision making and visual search, and within the neurophysiology community, studies have primarily focused on models in which evidence is accumulated before an eye movement is triggered (21–23), including recent work in FEF (24, 25). However, these studies almost all involve eye movements that are punished or rewarded based on whether the eyes go to the correct stimulus. Given that this does not generally occur in natural behavior, it is unclear whether such mechanisms are involved in generating eye movements in unrestrained conditions; indeed, when animals were allowed to move their eyes freely, we previously found that a saccade was generated ~50 ms after a peak of activity emerged in LIP (26) rather than when the activity reached a threshold response (27).

On the other hand, within the reading (9, 16) and scene perception (14, 28) communities, it has long been thought that at least part of the intersaccadic interval is due to a suppressive mechanism that keeps the eyes from moving away from items of interest. Models of these eye movements usually include a mechanism in addition to the suppressive mechanism to affect fixation duration, which can include an adaptive timer (13) or an accumulator mechanism (15). Our data bridge the divide between these two communities of oculomotor research by clearly showing that activity in FEF can be suppressed in a way consistent with these models and indicate that this mechanism, which is necessary to describe fixation durations in natural behavior, is present in the brain. In doing so, we validate these models at the neural level, while showing the neurophysiological field that understanding when a saccade will occur depends on more than accumulators alone. Indeed, whether the suppression mechanism in natural viewing works in concert with accumulator mechanisms, as suggested by Tatler et al. (15), or whether there is an alternative mechanism that allows saccades to go to locations of high priority after a timer expires (13) or a peak emerges (26) is yet to be determined.

Although it is not possible to pinpoint the exact origins of this modulatory signal in such a free parameter task, the phenomenological value of this observation is not changed. Considering that most of the neurons showed no interaction between the modulation of the RF and focus, this gain-based mechanism can easily represent both inside and outside RF parameters, such as salience (29) or task relevance (30), although it is unlikely that reward modulation itself causes this effect, since reward modulation in FEF has been reported to be spatially selective and nonsignificant outside the RF (31, 32). The fact that both signals are evident in the response suggests that the activity represents the integration of eye movement priority signals, such as shown in LIP (17, 33), with ongoing cognitive control to fine-tune the flow of eye movements.

It may be noted that the difference in response between a T and distractor in the RF (Fig. 1B) occurs later and is not quite as strong as shown in some previous studies (18, 34, 35). This is due to our choice of comparing the responses on trials in which a saccade was not made to the T in the RF. A similarly small difference can be seen when comparing across conditions in FEF (4) and has been shown in LIP when comparing the responses of targets and distractors when a saccade is made outside of the RF (26) compared with when it is made toward the RF (26).

Our results can also be seen as a multiplexing scheme that integrates multiple factors into a neural code that controls eye movement patterns. In this scheme, the priority of the motor movement is defined by the final readout, but the parameters of the decision are also decodable. Although the task we presented here was relatively simple, with two categories of objects and one level of reward, we hypothesize that the results may be extended to more complex situations. Therefore, a contingency of multiple layers of stimulus identity and reward value related to eye movements could be multiplexed with a gain change mechanism as suggested in other brain areas (37). This kind of coding scheme would not only make the cortical representations more efficient and condensed but could also be beneficial in solving the dynamic relationship between the current task state in general and a focal object as the goal of the eye movement during strategic planning. In addition, having different levels of gain can be used as the source of diverse top-down modulations on other cortical areas independent of eye movement execution.
Methods
Details can be found in the SI Methods. All experiments were approved by the Chancellor’s Animal Research Committee at University of California, Los Angeles as complying with the guidelines established in the Public Health Service Guide for the Care and Use of Laboratory Animals (38). Electrophysiological recordings were made from two rhesus monkeys, which were trained on a standard memory-guided saccade task and the visual foraging search task (Fig. 1A). Single-unit activity was analyzed during fixations in which there was a single object inside the RF and the animal was foveating an object.

ACKNOWLEDGMENTS. We thank members of the UCLA Division of Laboratory Animal Medicine for their superb animal care. This work was supported by the National Eye Institute (Grant R01 EY019273).

**Supporting Information**

**Mirkour et al. 10.1073/pnas.1716315115**

**SI Results**

**Effect of Foveated Object on Metrics of the Next Saccade.** To determine whether the accuracy or peak velocity of a saccade was related to the object being foveated before the saccade, we examined a subset of saccades with similar lengths from each session. Within a session, saccades of many lengths were made (Fig. S4A). As in most sessions, there were two modes of saccade lengths, which were a result of the arrangement of the array. To analyze saccade metrics, we took two groups of saccades within the session (gray columns, Fig. S4A): those that were within 1° length of the peak of the highest mode (mode 1) and those that were within 1° length of the peak of the second highest mode (mode 2). To avoid analyzing the same data twice when the peaks were close together or a single peak was present, the second peak had to be at least 2° in length longer or shorter than the first peak. No saccades shorter than 1.25° were analyzed (vertical dashed line, Fig. S4A). A session was only included if there were at least five saccades in each mode in each condition. This resulted in the use of 70 sessions. On average, mode 1 included 28.9 ± 0.66% (mean ± SEM) of all saccades and mode 2 included 18.3 ± 0.60% of all saccades. In the example shown, mode 1 and mode 2 included 33.4% and 22.9% of saccades, respectively, within the session.

We analyzed two metrics for each saccade: peak velocity and accuracy. While peak velocity is a standard metric easy to identify, determining accuracy in ongoing search is less well defined. In this case, we calculated an error distance, which we defined as the distance between the saccade landing point and the center of the closest stimulus. Fig. S4B shows the error distance as a function of the saccade length for all saccades in the same session shown in Fig. S4A, separated based on whether the saccade started from a target (blue points) or from a distractor (black points). Fig. S4C shows the error distances for modes 1 and 2 plotted close to their mean length. For both modes, there was no difference in error distance based on whether a T was at the fovea or a distractor was at the fovea (P = 0.794, mode 1; P = 0.890, mode 2; Wilcoxon rank-sum tests). For mode 1, only five of 70 sessions showed a significant difference in error distance (P < 0.01, Wilcoxon rank-sum test). For two sessions, the error was greater after leaving a target, and for the remaining three sessions, the error was greater after leaving a distractor. Only four sessions showed a significant difference in peak velocity, with three having a greater peak velocity after leaving a distractor. For mode 2, only four sessions showed a significant difference in error distance, with all having greater errors after leaving a distractor, and four sessions showed a significant difference in peak velocity, with three having a greater peak velocity after leaving a target. Thus, at the single-session level, there was no evidence that saccade metrics were affected by the stimulus the animal was foveating before the saccade. Consistent with this, we found no clear effect of the identity of the stimulus at the fovea before the saccade on error distance or peak velocity across the population. For this analysis, we calculated the median peak velocity and error distance for each mode and condition for each session. We then plotted the median error distances (Fig. S4D and E) and peak velocity for each session for both modes and tested whether they were different using Wilcoxon signed-rank tests. Neither metric showed a significant difference in the mode 1 data (P = 0.665, error distance; P = 0.390, peak velocity), and while both metrics showed trends in the mode 2 data (P = 0.063, error distance; P = 0.033, peak velocity), neither passed a simple Bonferroni correction (P < 0.0125). Thus, overall, we found no clear and consistent effect of the identity of the stimulus at the fovea on either saccadic metric.

**SI Methods**

**Subjects.** All experiments were approved by the Chancellor’s Animal Research Committee at the University of California, Los Angeles as complying with the guidelines established in the Public Health Service Guide for the Care and Use of Laboratory Animals (1). Using standard techniques (2, 3), two rhesus monkeys (8–12 kg) were implanted with head posts, scleral coils, and recording cylinders during sterile surgery under general anesthesia (3); animals were initially anesthetized with ketamine and xylazine and maintained with isoflurane. Surgery was conducted using aseptic techniques and analgesics, and antibiotics were provided during postoperative recovery.

**Behavioral Tasks.** Both animals were trained on a standard memory-guided saccade (MGS) and the foraging visual search task (3). To begin a trial of the MGS, the animals had to fixate a central spot for 300–500 ms, after which a peripheral target was flashed for 200 ms. After the target was extinguished, the animal had to remember the location of the target for 600 ms, after which the fixation point was extinguished and the animal had 450 ms to make a saccade to the remembered location of the target. If the animal landed and remained within 2° of the target location, the target reappeared, after which the trial ended and the animal was rewarded with a small drop of juice.

To begin a trial of the foraging task (Fig. 1A), the monkeys had to fixate on a spot placed to one side of the screen. After a delay of 450–700 ms, an array of five potential Ts and five distractors (+) was presented, with one over the fixation spot. One of the Ts had a juice reward associated with it, such that if the monkey looked at it for 500 ms within 8 s after the start of the trial, it would get the reward. As in previous free-viewing visual search studies in LIP (3, 4), the stimuli were arranged in such a fashion that when the monkey looked at one stimulus, the RF of an FEF neuron was likely to encompass one other stimulus (large oval in Fig. 1A).

**Electrophysiological Recording.** We recorded extracellular single-unit activity from FEF using tungsten microelectrodes from the anterior bank of the arcuate sulcus guided by coordinates from MRI images. We confirmed that we were in FEF by the ability to evoke saccades with microstimulation using current intensities of up to 50 μA. Microstimulation was done while animals performed a blink task (5), with a 70-ms train of biphasic pulses (negative first, 0.2-ms width/pulse phase) delivered at a frequency of 330 Hz. Recorded neurons were included in the study if they showed increased activity to one of the stages of visual, delayed, or motor MGS and they were significantly higher than the response during fixation on the fixation point. Consequently, fixation neurons (6) were excluded from this study. The size and position of the RF of each neuron were mapped using an automated MGS task covering nine and then 25 locations (details are provided in ref. 7). Neurons were also excluded from the study if their RFs were so large that they would encompass two stimuli in the array. RF centers ranged from 2.8 to 15° eccentricity, and RF sizes ranged from a 1.25 to 6.5° radius in the horizontal direction and a 1.25 to 4° radius in the vertical direction. After mapping, the foraging task was run and neuronal data were recorded.
**Data Analysis.** Neuronal data were recorded from 231 FEF neurons (78 from monkey E and 135 from monkey M). We roughly discriminated action potentials online and then accurately sorted spikes offline using SortClient software (Plexon, Inc.). The experiments were run using the REX system (8), and data were recorded using the Plexon system (Plexon, Inc.). Data were analyzed using custom code written in MATLAB (MathWorks, Inc.).

When sufficient trials were available from the MGS mapping protocol, we used the definitions from Bruce and Goldberg (9) to categorize neurons as visual, visuomovement, and movement neurons. We compared the visual response (50–150 ms after target onset) and the movement response (in the 50 ms before saccade onset) with a baseline response (100 ms before target onset) from that trial. We used paired t tests at the \( P < 0.01 \) level to indicate significance. Neurons were categorized as visual neurons if only the visual response was significantly higher than the baseline response. Neurons were categorized as visuomovement neurons if both the visual and movement responses were significantly higher than the baseline response. Neurons were categorized as movement neurons if only the movement response was significantly higher than the baseline response.

To analyze the data in the visual foraging task, we first separated trials into fixations in which there was a single object inside the RF. Data were aligned by the beginning of fixation or by the onset of the saccade, using an eye-velocity detection algorithm to detect the saccades. Data are presented as spike density functions (10) using a sigma of 10 ms. Before averaging across neurons, the spike density functions for each neuron were normalized by dividing the activity by a normalizing factor. The factor was calculated for each neuron from all fixations that occurred after the first saccade, which lasted at least 300 ms and had a T at the fovea and a distractor in the RF. The window for the calculation was 150 ms long, starting 150 ms after fixation onset. When plotting the spike density functions, we plot the mean and SEM, where \( N \) is the number of neurons.

Different epochs were used to examine spike rates for population and single neuron statistical tests. During the appearance of the visual array, an epoch of 100 ms starting 100 ms after stimulus onset was used. For these analyses, fixations were only included if the animal maintained fixation for at least 300 ms. After the first saccade and during the search, an epoch of 100 ms starting 50 ms after the start of fixation was used, and for these analyses, fixations were only included if the animal maintained fixation for at least 150 ms. Population tests were performed on average epochs using paired nonparametric Wilcoxon signed-rank tests. Student \( t \) tests were used for comparing neural responses in different conditions at the single-cell level.


Fig. S1. Mean responses of 221 neurons during ongoing search from fixations of at least 150 ms (vertical dashed line) when a distractor (D; blue) or a potential T (green) was at the fovea (fov) and the following saccade would go away from the RF. Error bars indicate SEM across the neurons.
Fig. S2. Mean responses of single FEF neurons to a distractor (D) at the fovea (fov) compared with a T at the fov during a 100-ms window starting 50 ms after fixation onset plotted separately based on neuron class. These figures plot the same data as in Fig. 3B, except they have been sorted based on the neuronal classification using the MGS: visual neurons (A), visuomovement neurons (B), and movement neurons (C). P values are from Wilcoxon signed-rank tests. sqrt(sp/s), square root of spike rate.

Fig. S3. Mean activity of single FEF neurons to a distractor (D) at the fovea (fov) compared with a T at the fov during a 100-ms window starting 50 ms after fixation onset, in which an object (obj) was in the RF (A) or in which nothing was in the RF (B). These panels show the same data as in Fig. 3D and E, but are plotted as the square root of spike rate [sqrt(sp/s)] for better visualization. In these panels, the line of best fit does not directly relate the mean activity when a distractor (D) is at the fov to the mean activity when a T is at the fov.

Fig. S4. Illustration of how we tested whether saccade accuracy was affected by the identity of the stimulus at the fovea. (A) Distribution of saccade lengths from all saccades within a single session. The gray bars show the modes of saccade lengths that were used in the detailed analyses. Saccades shorter than 1.25° (vertical dashed line) were not analyzed as these represented saccades within the stimulus. deg, degrees. (B) Error distance for each saccade is plotted against the length of that saccade for all saccades within the same session shown in A for fixations with a T in the fovea (blue points) and with a distractor (D) in the fovea (black points). (C) Error distance from all saccades with lengths of 4.25–6.25° and with lengths of 10.5–12.5° are plotted as a function of the identity of the stimulus at the fovea (fov). The P value above each pair is from a Wilcoxon rank-sum test. (D and E) Median error distance for each session in which there were at least five saccades in each mode and condition are compared according to the identity of the stimulus at the fovea (fov or Fov). D, distractor. The results from mode 1 (D) and mode 2 (E) are shown. The P values are from Wilcoxon signed-rank tests.