9 Visual Processing in the Macaque Frontal Eye Field

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CONTENTS

9.1 INTRODUCTION

Following Ferrier's[1] original demonstration that electrical stimulation of certain parts of frontal cortex elicits eye movements, the frontal eye field (FEF) has been regarded most commonly as part of the oculomotor system. The evidence for this is beyond dispute. Low-intensity electrical stimulation of FEF elicits saccadic eye movements.[2] Saccades are the rapid shifts of gaze that redirect the focus of vision to different locations in an image. Reversible inactivation of FEF prevents saccade production,[3,4] complementing earlier observations that ablation of FEF causes an initially severe impairment in saccade production that recovers in some but not all respects over time.[5–8] The direct influence of FEF on saccade production seems to be mediated by neurons in FEF that are activated specifically before and during saccades.[9–13] Two kinds of neurons that control gaze have been distinguished. In general, *movement* neurons contribute to gaze shifting, and *fixation* neurons contribute to gaze holding. Neurons in FEF that generate movement-related or fixation-related activity are located in layer 5 and innervate the superior colliculus[14–16] and parts of the neural

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circuit in the brainstem that generate saccades.[17] Physiological recordings indicate that these neurons, in concert with a network including the superior colliculus[18–22] produce signals necessary to produce saccadic eye movements. In fact, a recent experiment has demonstrated that inactivation of the superior colliculus disrupts or prevents microstimulation of FEF from eliciting saccades.[23] The function of FEF in gaze control has been reviewed previously.[24–27]

Experiments probing the control of saccades in monkeys provide compelling evidence for the sufficiency of the activity of movement and fixation neurons in FEF to specify whether and when saccades will be produced.[11,13] In monkeys performing a countermanding task that requires control over whether a saccade is initiated, particular neurons in the FEF are modulated in a manner sufficient to control gaze. Specifically, when a partially prepared saccade is canceled because of a stop signal, neurons with movement and fixation activity exhibit a marked deviation of the modulation that occurs early enough to cancel the saccade (Figure 9.1).

However, certain other neurons in FEF are not modulated in a manner sufficient to be said to control gaze. As shown in Figure 9.1, *visual* neurons in FEF are modulated not at all or too late when planned saccades are canceled. These neurons respond to the visual target, but nothing about their modulation can control whether or not the eyes move. Therefore, not every neuron in the FEF is linked directly to the oculomotor system.

In this chapter we review the evidence that we have obtained over the last 10 years that FEF should be regarded as part of the visual pathway. We focus on the role of the FEF in the selection of targets for covert and overt orienting. We would note that other laboratories have made important observations about the role of the FEF in selecting the target for saccadic and pursuit eye movements.[28–31] It is also crucial to note that the kinds of neural signals reviewed for FEF have been or most likely will be observed in related structures such as the superior colliculus or posterior parietal cortex. Thus, the processes that are described must be regarded as occurring concurrently in a network of interconnected structures.

9.2 VISUAL INPUTS TO THE FRONTAL EYE FIELDS

The evidence that the FEF is involved in visual processing is compelling. One source of visual signals to FEF is the central thalamus. The FEF is innervated mainly by the lateral segment of the mediodorsal nucleus as well as parts of neighboring thalamic nuclei.[32] Neurons in these nuclei can convey a diversity of signals to FEF including visual afferents.[33–35] These thalamic nuclei receive visual signals most directly from the intermediate layers of the superior colliculus.

FEF also receives abundant inputs from a multitude of visual cortical areas in both the dorsal and ventral streams[36–39] (Figure 9.2). In fact, FEF is unique in the extent of its connectivity with extrastriate visual cortex.[40] However, it should not be overlooked that FEF provides reciprocal connections to equally many extrastriate visual areas. In fact, according to a recent analysis of intracortical connectivity, FEF may be in a feedforward anatomical relation to prestriate areas like V4.[41] Thus, FEF can influence the activation of neurons in extrastriate visual cortex.

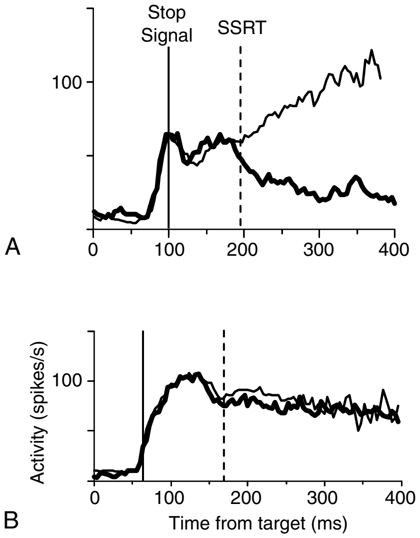

FIGURE 9.1 Relationship between FEF neural activity and canceling a partially prepared saccade. (A) Activity of a FEF neuron with movement-related activity in trials in which the movement was produced but would have been canceled if the stop signal had been presented (thin line) is compared with activity on trials when the planned saccade was canceled because the stop signal appeared (thick line). The time of the stop signal is indicated by the solid vertical line. The time needed to cancel the planned movement — stop signal reaction time (SSRT) — is indicated by the dashed vertical line. When the movement was canceled, neural activation decayed rapidly. This modulation occurred within an interval known as the stop signal reaction time, which is an estimate obtained from behavioral data of the time needed to cancel the movement. Observing the strong modulation of the discharge rate within the stop signal reaction time demonstrates that this neuron conveys a signal sufficient to control whether the eyes move. (B) Activity of a neuron in FEF with a visual response but no saccade-related modulation when saccades were initiated or canceled. The discharge rate of this neuron did not differ between trials when the saccade was produced and trials when the saccade was withheld. Therefore, neurons like this do not produce a signal sufficient to control gaze. (Modified from Reference 13.)

The connectivity of FEF with visual areas caudal to the central sulcus is topographically organized.[38] The more ventrolateral portion of FEF, which is responsible for generating shorter saccades, is interconnected with the perifoveal representation in retinotopically organized areas, from areas that represent central vision in inferotemporal cortex and from other areas having no retinotopic order. In contrast, mediodorsal FEF, which is responsible for generating longer saccades, is interconnected with the peripheral visual field representation of retinotopically organized areas, from areas that emphasize peripheral vision or are multimodal and from other areas that have no retinotopic order.

The concept of hierarchy as an organizing principle has been applied to the extensive network of connectivity among visual cortical areas,[42] but it has been shown that the precise organization based on connectivity is indeterminate.[43] The

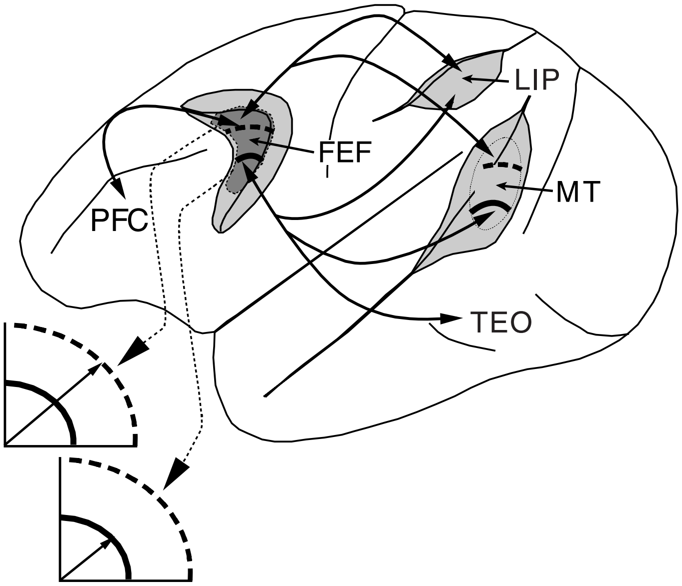

FIGURE 9.2 Cortical connectivity of the FEF. The FEF contributes to the preparation and initiation of saccades through projections to the superior colliculus and brain stem saccade generator. There is a rough map of saccade amplitude in FEF; shorter saccades are generated ventrally, and longer saccades, medially. FEF is reciprocally connected with a multitude of extrastriate visual areas in both the dorsal and ventral streams. The projections are topographically organized; the foveal representation of retinotopic areas projects to the ventrolateral part of FEF (which produces shorter saccades), and the peripheral representation projects to the dorsomedial part of FEF (which produces longer saccades). These diverse visual inputs convey an elaborate representation of the image that contributes to specifying which saccade to produce. The FEF is also interconnected with areas in prefrontal cortex. These connections convey the influence of context, which can supplement or override the outcome of visual processing.

indeterminacy may be resolved to some extent, however, with converging evidence. A recent study measured the visual response latency of neurons in several parts of the visual pathway[44] (Figure 9.3). The results show clearly that activation is earliest in the magnocellular followed by the parvocellular layers of the dorsal lateral geniculate nucleus (LGNd). In the cortex, visual responses are earliest in V1, particularly in layer 4 of V1.[45–47] The next wave of activation occurs effectively concurrently in several areas including MT and FEF as well as V3 and MST (not shown). This activation is rather early. For example, at the time when 50% of FEF neurons have responded — ~70 ms — 25% of V1 neurons have yet to respond to the visual stimulus. Thus, areas associated with the dorsal stream of processing are activated by visual stimuli early and concurrently. In contrast, neurons in areas V2 and V4 are activated later and sequentially in these data.

The hierarchical schemes of visual area organization commonly include multiple levels. For example, FEF is commonly regarded as situated rather high in the hierarchy of visual areas (level 8 in Reference 42). The appearance of the hierarchy invites the conception that visual processing occurs in a sequential manner,

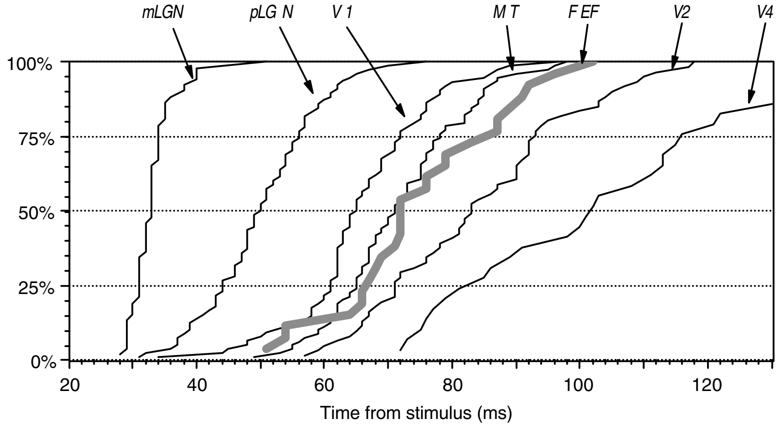

FIGURE 9.3 Times of first response to an optimal visual stimulus are plotted for the indicated stages of the visual pathway. The earliest visual responses are observed in the magnocellular layers (mLGN) and the parvocellular layers of the dorsal lateral geniculate nucleus (pLGN) followed by activation in V1. Area MT and the FEF respond over approximately the same time period followed in order by V2 and V4. (Modified from Reference 44.)

percolating up the network. However, the visual response latency data are not entirely consistent with this. These data were incorporated into a new analysis of the relationship of the visual areas, and the hierarchy collapses if based on a rule of the shortest path to accommodate this independent, converging evidence.[48]

Because of the extensive convergence of afferents from the thalamus and multiple extrastriate visual areas, the FEF receives signals representing the color, form, direction of motion, and stereoscopic depth of objects in the image. Unlike neurons in occipital and temporal visual areas, neurons in FEF typically do not exhibit feature selectivity.[49] However, under particular conditions reviewed below, neurons in FEF can exhibit a form of selectivity based on color, form, and motion. At least some neurons in FEF are responsive to acoustic stimuli.[10,50] In addition, a recent study has shown that neurons in FEF are sensitive to disparity.[51] This may be related to new evidence that FEF or neighboring cortex contributes to vergence eye movements.[52]

Responses of neurons to single stimuli are informative, but they cannot reveal all that is involved in visual processing because rarely is an organism presented with a single stimulus. The rest of this chapter reviews the evidence that FEF contributes to selecting a target for a saccade among distracting stimuli. It is shown that the extensive anatomical convergence contributes to a system that can select targets for gaze shifts regardless of the visual properties of the stimuli.

9.3 SELECTION OF A TARGET AMONG UNIFORM DISTRACTORS

The visual search paradigm has been used extensively to investigate visual selection and attention.[53] The results of many experiments distinguish two general modes of

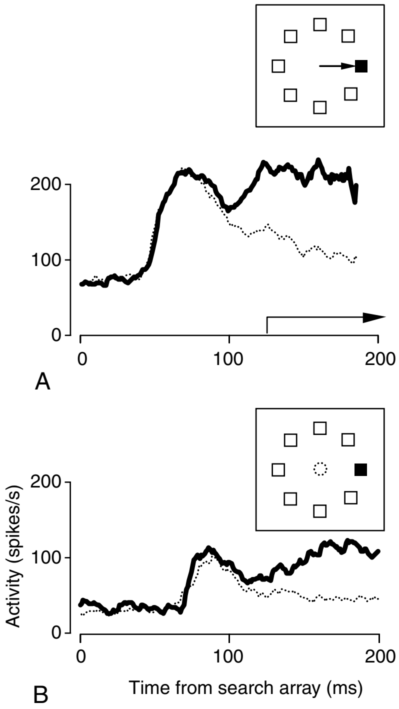

FIGURE 9.4 Activity of a FEF visual neuron following presentation of a popout search array when the monkey produced (A) or withheld (B) a saccade to the singleton. Each plot shows the average activation when the singleton stimulus appeared in the receptive field (solid line) and when only distractors appeared in the receptive field (dotted line). When a saccade was produced to foveate the target, the initial response to the search array did not discriminate whether the target or distractors were in the receptive field. However, after ~100 ms the activation evolved such that the neural representation of the distractors was suppressed, and the activation representing the location of the target was sustained or elevated. When no saccade was produced (B), the overall level of activation was attenuated, but the same selection process was observed. Thus, the neural selection process was not contingent on production of the saccade. (Modified from References 68 and 72.)

visual search. One mode is the efficient search for, say, a black spot among several gray spots (Figure 9.4). The second mode is the less efficient, more effortful search for, say, a randomly oriented T among randomly oriented Ls.

To investigate how the brain selects targets for visually guided saccades, we have recorded the activity of neurons in the FEF of monkeys trained to shift gaze to the oddball target in either of two complementary popout visual search arrays.[54,55] Most visually responsive cells in FEF responded initially indiscriminately to the target or the distractor of the search array in their receptive field (Figure 9.4A). The absence of a feature-selective response in FEF during visual search is consistent with the original observation that neurons in FEF are not feature selective.[49] However, before gaze shifted, a selection process transpired by which most visually responsive cells in FEF ultimately signaled the location of the oddball target stimulus.

A visual target selection process has been observed in FEF during natural scanning eye movements as well.[56] Similar results have also been obtained under somewhat different conditions in the superior colliculus[57–60] and posterior parietal cortex.[61,62] The selection of the target expressed by visuomotor structures such as FEF must be based on the selection process observed in extrastriate visual cortex areas selective for color or form.[63–67]

The evolution of activity over time from nonselective to selective for the location of the target does not distinguish whether this selection process corresponds to explicit visual selection or instead to saccade preparation. A series of experiments has been conducted to evaluate these alternative hypotheses. In one study, FEF activity was recorded while monkeys maintained fixation during presentation of a search array with a single conspicuous oddball.[68] Although no saccade was made to the oddball, FEF neurons still discriminated the oddball from distractors at the same time and to the same degree as when a gaze shift was produced (Figure 9.4B). Thus, the visual selection observed in FEF does not require saccade execution. This study also concluded that saccade preparation was not happening because the saccade made after the trial was rarely directed to the location where the oddball had been.

Another experiment created a condition in which monkeys frequently shifted gaze to a location different from that occupied by a target.[69] A search-step task combines a standard visual search task with the classic double-step saccade task.[70,71] On most trials (referred to as no-step trials) monkeys were rewarded for making a saccade to a color oddball target among distractors. On the remaining trials (step-trials) the target and one distractor unexpectedly swapped positions after presentation of the array. When the target stepped from its original position to a new position, monkeys were rewarded for directing gaze to the new target location (compensated trials). However, monkeys often failed to compensate for the target step and made a saccade to the original target location (noncompensated trials). This behavior was not rewarded. Noncompensated saccade trials provided data to test the dissociation of visual target selection from saccade preparation. Even when gaze shifted away from the popout oddball of a search array, visual neurons in FEF represented the current location of the target (Figure 9.5). Given the evidence that attention is allocated automatically to the conspicuous oddball in a search array, these findings are consistent with the hypothesis that the activation of visually responsive neurons in FEF corresponds to or guides the covert orienting of visual attention.[72]

9.4 RELIABILITY OF TARGET SELECTION BY FEF NEURONS

The conclusions just reviewed were drawn from a comparison of the average activity of neurons contrasted between trials with the target or the distractors in the response field. However, this kind of analysis does not reveal how reliably neurons signal the different stimulus conditions given the variability in discharges of cortical neurons under identical conditions.

A recent study measured the reliability of individual neurons in signaling the target location in correct trials using a neuron–antineuron approach within a winner-take-all architecture.[73] Specifically, the number of trials or neurons that needed to

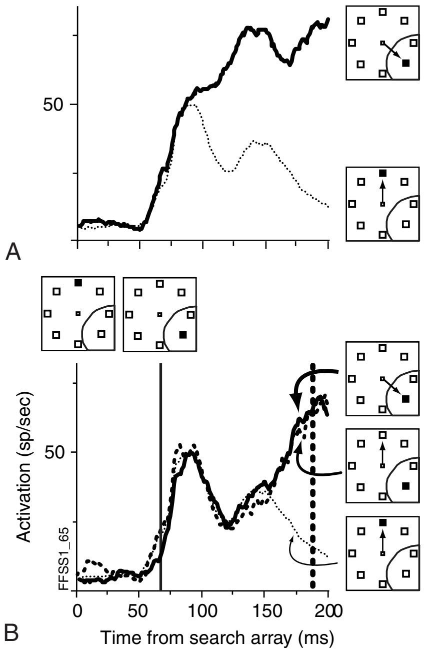

FIGURE 9.5 Response of FEF neuron during search-step task. (A) Activation when the target (black line) or distractors (dotted line) fell in the receptive field (indicated by the boundary in the stimulus arrays). Following the initial 100 ms of activation that did not discriminate target from distractor, the activity was modulated strongly before the saccade to the target. The response to the distractor was suppressed, and the response to the target grew. (B) Averaged activity in compensated (solid black) and noncompensated (thick dotted black) target-step trials when the distractor in the receptive field unexpectedly became the target compared with activity on no-step trials when distractors remained in the receptive field (thin dotted line). In both compensated and noncompensated trials the neuron responded equally strongly to the unexpected appearance of the target in the receptive field. The fact that the activity before the noncompensated saccades was indistinguishable for the search-step trials with opposing saccade directions means that the activity of this neuron could not be involved directly in saccade production. (Modified from Reference 69.)

be combined to match performance was determined through a random sampling procedure. Before the activity representing the target and various distractors became different, the target could not be found in the activity across pools of any size. As the selection process began, the activity of large pools of neurons could locate the target with near perfect reliability (Figure 9.6). As the selection process ran to completion, the activity of pools of around ten neurons represented the location of the target among distractors with high reliability. At the asymptote, on average, the activity from a pool of seven neurons was sufficient to support nearly perfect performance in the easiest search, and pools of about 14 trials generated signals sufficient for nearly perfect localization of the target in the most difficult search. However, monkeys did not achieve nearly perfect performance. In fact, the actual

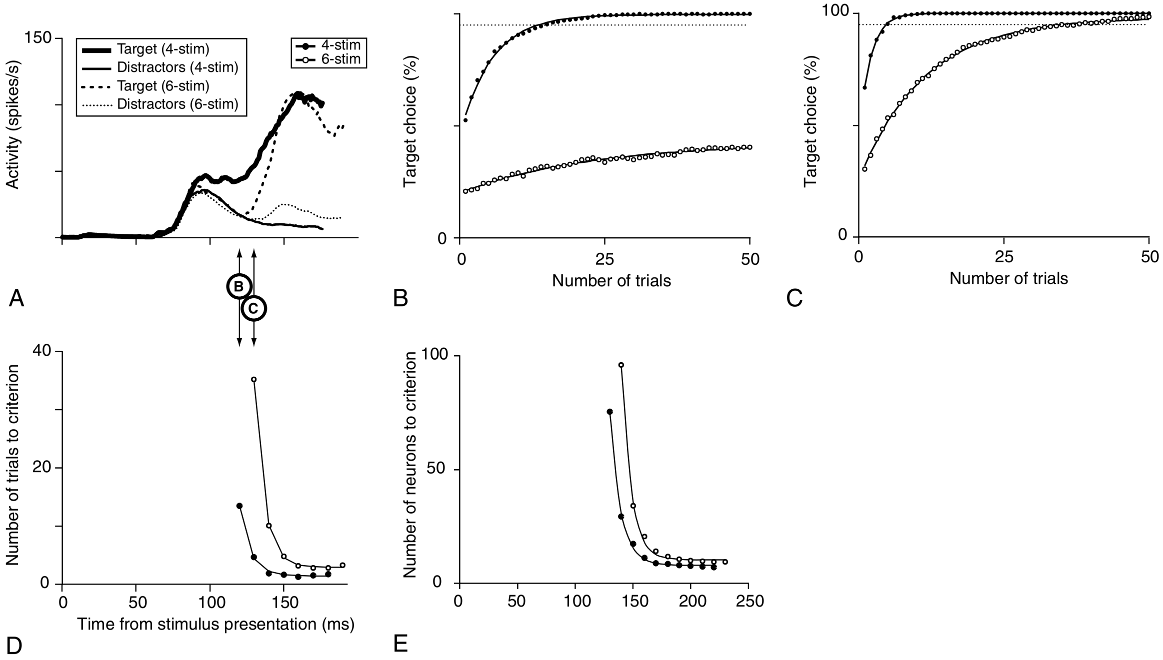

FIGURE 9.6 Reliability of FEF target selection. (A) Average activation of a FEF neuron during search for a target (thick) among distractors (thin) in four-element (solid) and six-element (dotted) arrays. Spike density functions were aligned on stimulus presentation at time 0 and are plotted up to the mean saccade latency during each search condition. Only spikes that occurred before saccade initiation were used in the calculations. (B, C) Probability of target choice as a function of number of trials drawn randomly from the set of trials contributing to panel A at the two time points shown between A and D. Filled circles represent simulations for search with four stimuli, and open circles represent simulations for search with six stimuli. The number of trials needed to reach a fixed criterion of 95% (indicated by dotted line) was calculated. (D) The number of trials required to reach the criterion level is plotted as a function of time from stimulus presentation for search with four (solid) and six (open) element arrays. The best-fit exponential curves are shown overlaid on the data points. (E) The number of neurons randomly sampled from the entire data set required to reach the criterion level is plotted as a function of time from stimulus presentation for search with four (solid) and six (open) element arrays. In the asymptote fewer than ten trials or neurons suffice to locate the target with 95% accuracy. (Modified from Reference 73.)

behavioral accuracy across the range of feature and conjunction search tasks employed was approximated when only six trials or neurons were combined.

The pool sizes obtained in this study were consistent with findings of several studies of neural coding in various visual and other cortical areas reporting pool sizes ranging from 5 to 40 neurons.[74–78] In contrast, the pool sizes determined in this study of FEF were one or two orders of magnitude smaller than those determined by Shadlen and co-workers[79] in their analysis of the relationship between neural and behavioral responses to visual motion. Several factors may contribute to this difference. In addition to basic differences in task requirements and area of the cortex, perhaps the most important difference is that the analysis of area MT activity included neurons with optimal directions of motion different from the one being discriminated, whereas all of the FEF neurons contributing to the sample provided clear information about the location of the target and distractors. Concern about distinguishing between signals in pools of 10 or 100 neurons pales in significance when viewed from the perspective of the total number of neurons comprising the causal chain between stimulus and response. The apparent potency or relevance of so few among so many neurons reveals a profound principle of brain function. The importance of small signals in guiding visually guided behavior is emphasized in the next topic reviewed.

9.5 SELECTION OF INVISIBLE TARGETS

The search for neural correlates of visual awareness has received considerable interest. Bistable stimuli have been used to dissociate the presentation of a stimulus from perception of that stimulus in neurophysiological,[80,81] neuroimaging,[82–84] and event-related potential studies.[85–87] Implicit in such studies of awareness is the subject's voluntary response to an environmental event that allows an inference about the subject's perceptual state. We investigated the neurophysiological link between sensation and action by training macaque monkeys to shift gaze to a visual target that was rendered intermittently perceptible by backward masking (Figure 9.7).[88,89] The experiment was designed to discourage guessing by requiring monkeys to report either the perceived presence or absence of a target.

When monkeys fixated a central spot, a dim target appeared at one of eight possible target locations followed by a bright white mask stimulus at all possible locations. On a high fraction of trials no target was presented. The interval between the appearance of the target and the appearance of the mask was varied according to monkeys' performance. Monkeys were rewarded for correctly reporting with a shift of gaze whether or not the target was present. Monkeys indicated "yes" (target present) by shifting gaze to the target location. Monkeys indicated "no" (target not present) by maintaining fixation on the central spot. Single trials were scored according to the conventions of signal detection theory as either hits (correctly responding "yes"), misses (incorrectly responding "no"), correct rejections (correctly responding "no"), or false alarms (incorrectly responding "yes").

It has been suggested that visual responses in frontal cortex occur specifically for stimuli engaged by action and awareness.[90] Hence, we were surprised to find that visual neurons in FEF responded to undetected masked stimuli,[88,89] This

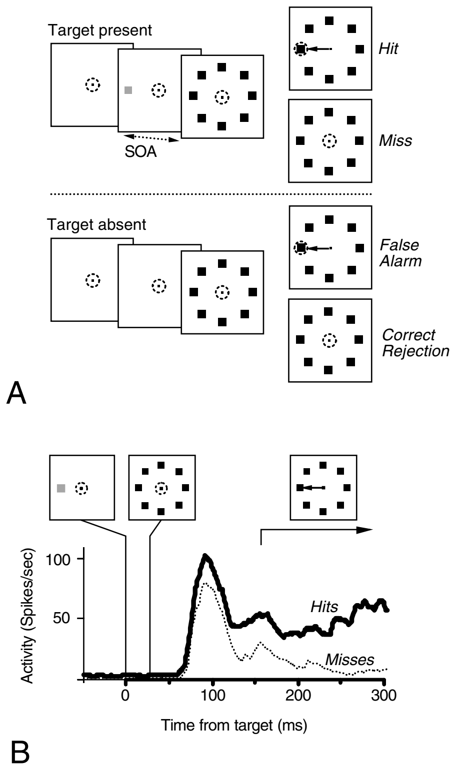

FIGURE 9.7 Response of FEF to a masked target. (A) Visual backward masking task. The target appeared followed after an adjustable stimulus onset asynchrony (SOA) by a mask in target-present trials. A saccade directly to the location where the target had been was scored a *Hit*. Continued fixation was scored a *Miss*. Only the mask appeared on target-absent trials. A saccade to any location was scored a *False Alarm*. Continued fixation was scored a *Correct Rejection*. Monkeys were rewarded for hits and correct rejections. (B) Activity of a FEF visual neuron. The panel compare the activity during target-present trials leading to hits (thick) and misses (thin). Trials are aligned on the time of target presentation in the left panels and on time of mask presentation in the right panels. The differences between alternative trials are shown in the bottom panels. (Modified from Reference 89.)

unexpected result challenges the view that neuronal responses to undetected stimuli that are masked by light do not get out of the retina[91] and indicates that a psychophysical response criterion must be reached for target detection. In fact, we observed that monkeys shifted gaze to the masked stimulus when the initial visual response was only slightly stronger than otherwise (Figure 9.7). It is most plausible that the response of FEF neurons to the target independent of the overt report is conveyed by the afferents from areas MT and MST in which neurons are sensitive to dim, low-contrast stimuli.[92,93] The observation that a difference in activity amounting to just one or two spikes per neuron predicts the ultimate overt response is consistent with observations in area MT.[94] In fact, a small difference in the activation of MT neurons can predict subsequent reports even if no stimulus is present. Likewise, we found that the same small difference in the initial response of neurons in FEF was present even in false-alarm trials.

When saccades were produced, we found that the saccade was preceded by prolonged selective activation of many FEF neurons. The selective pattern of activation of visual neurons preceding the saccade to a detected masked stimulus resembled the selective activation preceding the saccade to a visual search target. However, the prolonged elevated activation was observed in false-alarm trials as well. What is the function of this prolonged elevated activity? Perhaps the late, enhanced activation of visual neurons when the target was detected is related to preparation of the eye movement? In a weak sense this must be the case because the late activation of the visual neurons occurs specifically before the saccade is made. However, several lines of evidence suggest that the relationship between the late visual activation and saccade production is more distal. First, as described above, visual neurons do not play a direct role in controlling gaze; when a planned saccade is canceled, visual neurons are modulated not at all or too late to participate in the act of control.[13] Second, many (but not all) neurons participating in visual selection during search are located in the supragranular layers of FEF.[72] Neurons in the superficial layers do not innervate subcortical oculomotor structures. Third, the remoteness of the visual cells in FEF relative to the motor system is confirmed by the fact that to elicit saccades with microstimulation, higher currents are needed at the sites of visual neurons (>50 μA).[2]

Another interpretation of the late visual activation in FEF is guided by the fact that FEF provides a strong feedback projection to extrastriate visual cortex.[38] A number of studies have suggested that prolonged activation of certain neurons in extrastriate visual cortical areas is a correlate of visual awareness.[80,81] Accordingly, under the conditions of the masking task, it is possible that the selective postmask activation in FEF is correlated not only with “yes” responses, but also with a perceptual experience of the target. The prolonged postmask activity when the monkeys responded “yes” satisfies the condition that activity is of necessary magnitude and duration to be related to awareness.[95,96]

Of course, we would not suggest that FEF is uniquely responsible for visual awareness. Nevertheless, evidence from several studies indicates that prefrontal cortex plays some role in awareness. First, functional imaging studies have shown that areas of prefrontal cortex, possibly including FEF, exhibit activation associated with binocular rivalry[83] even when subjects make no overt motor report.[84] Second, in another functional imaging study, activation of prefrontal cortex including FEF was observed specifically when a blindsight patient reported being aware of presented stimuli.[97] Thus, even if FEF is not directly responsible for generating visual awareness, a plausible hypothesis suggests that activation similar to the selective modulation observed in FEF visual neurons occurs in whichever brain regions are related to the production of visual awareness.

9.6 CHRONOMETRY OF TARGET SELECTION

Explaining the duration and variability of response times is a central problem in psychology.[98–100] A general hypothesis guiding cognitive psychology holds that behavioral response times are occupied by more or less distinct stages of processing.[101,102] If it were possible to identify physiological markers for the end of one stage and the beginning of another, then the alternative hypotheses about the existence of stages and the time course of activation could be distinguished. A series of studies has investigated how the time of visual target selection relates to the total time taken to initiate the saccade. During search for a single, conspicuous target in a search array the large majority of visually responsive neurons in FEF discriminated the target from distractors at a constant interval after search array presentation[72,103] (Figure 9.8). This finding indicates that at least under the conditions of efficient,

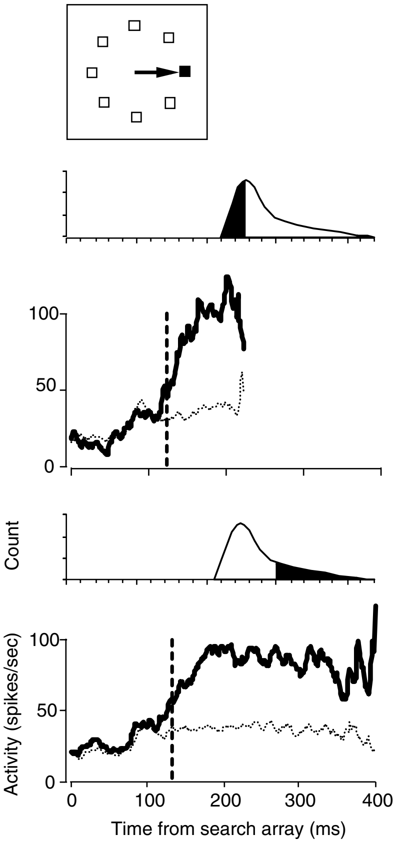

FIGURE 9.8 Relation of time of neural target selection to time of saccade initiation during efficient search for a green target among red distractors. The activity of a FEF neuron representing the target (thick) or distractors (thin) is shown during trials with saccades of the shortest (top) or longest (bottom) latencies. The upper plots in each panel indicate the distribution of saccade latencies with the range selected for the analysis of activity shaded. The time at which the activity distinguished whether a target or distractor was in the receptive field is marked by the dashed vertical line. The neuron discriminated the target from distractors following a relatively constant interval after presentation of the search array. (Modified from Reference 103.)

popout search, a relatively constant period of time is needed to locate potential targets, and the additional variability in saccade latency is introduced by the time needed to prepare and execute the eye movement. When the discrimination of the target is more difficult because the target more closely resembles distractors and search is less efficient,[104] the time taken by FEF neurons to locate the target increases.[103] This increase in time taken to locate targets among more similar distractors is accompanied by an increase in the variability of the selection time across trials. Consequently, the variability in the visual selection time accounts for a larger fraction of the variability in saccade latency. This occurs because the production of an accurate saccade cannot proceed until the target is located (Figure 9.9).

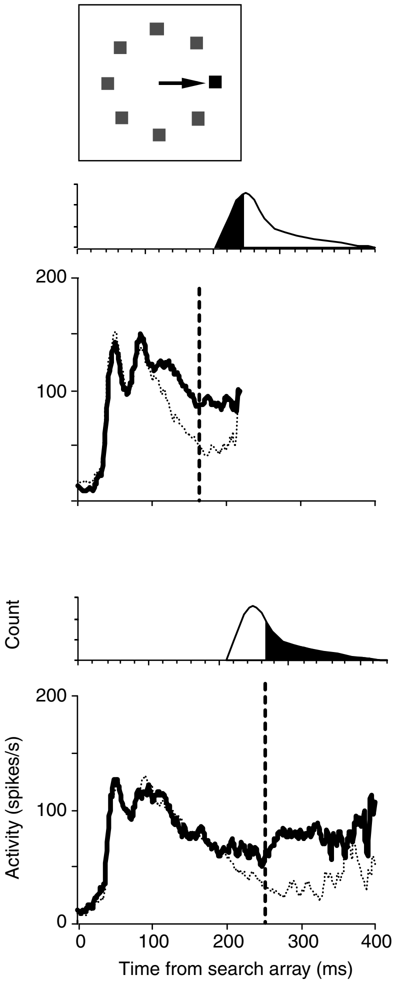

FIGURE 9.9 Activity of an FEF neuron during trials searching for a target that was difficult to distinguish from the distractors. The neural selection of the target is delayed in proportion to the increase of reaction time. Conventions as in Figure 9.8. (Modified from Reference 103.)

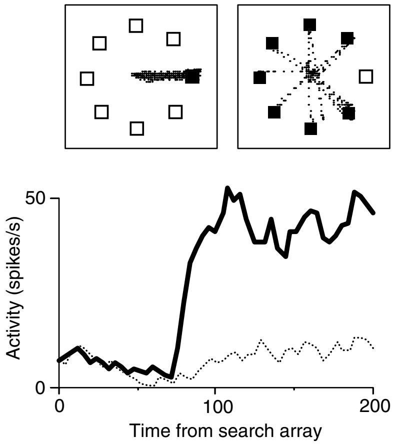

FIGURE 9.10 Effect of cognitive strategy on target selection in FEF. Top panels illustrate performance of a monkey that had been trained on just one visual search array. When presented an array in which the target and distractor colors were switched, instead of looking at the conspicuous singleton (left panel), this monkey looked at a distractor that was the same color as the target in the complementary array (right panel). The time course of activation of a single FEF neuron during the visual search task when the target was in the receptive field (thick) and when distractors were in the receptive field (thin) is shown in the lower panel. Unlike what was observed in monkeys trained on both complements of the search array, in these particularly trained monkeys half of the neurons in FEF exhibited a selective response from the earliest spikes that could be measured. (Modified from Reference 106.)

9.7 SELECTION OF A TARGET REQUIRING KNOWLEDGE

Several lines of evidence demonstrate that gaze can be guided as much by knowledge as by the visual features of stimuli. First, cognitive strategies can override both covert[105] and overt[106] selection of a single oddball in a search array. Second, experts are more likely than novices to ignore conspicuous but irrelevant parts of a visual image from their field of expertise.[107–109] Finally, the pattern of visual fixation can be influenced by verbal instruction.[110]

To study the effects of training experience on gaze behavior and associated neural activity in FEF, monkeys were trained exclusively with search arrays that contained a single item of a constant color among distractor items of another constant color (for example, always a red target among green distractors or always a green target among red distractors).[106] Control monkeys were trained to shift gaze to the oddball of both configurations of the search array (that is, alternating between red among green and green among red). The control monkeys shifted gaze to the oddball stimulus, regardless of the feature that defined it. In contrast, experimental monkeys persistently directed gaze to stimuli with the color of the target even when the configuration of the array was switched for a few trials. In other words, when the experimental monkeys were presented with the search array complementary to that with which they had been trained, they shifted gaze to one of the distractors (that was the color of the overlearned target) and not to the target (even though it was the oddball). As described above, FEF neurons in control monkeys did not exhibit feature selectivity, but their activity evolved to signal the location of the oddball stimulus. In monkeys trained exclusively with a search array with constant target and distractor colors, however, about half of FEF neurons exhibited selectivity for the color of the stimuli in the initial response (Figure 9.10). That is, if the overlearned target fell in the receptive field, the neurons responded strongly, but if the overlearned distractors fell in the receptive field, the neurons responded significantly more weakly or not at all. Subsequently, the appearance of selectivity for stimulus features that consistently guide eye movements has been reported for neurons in the parietal cortex[111,112] and superior colliculus.[113] It appears that the visuomotor system can commit itself to particular interpretations of the image to guide saccadic eye movements. The mechanisms underlying this form of plasticity deserve investigation.

In addition to these long-term changes, target selection during visual search is influenced by shorter-term implicit memory representations arising through repetition of location or stimulus features affecting covert[114,115] and overt[116,117] orienting. Evidence for this is provided by particular changes in performance following sequential changes in stimulus features and target location. Until recently, the neuronal mechanisms underlying such sequential effects had not been examined. Single neurons were recorded in the FEF of monkeys performing a popout search during which stimulus features and target position changed unpredictably across trials.[118] In keeping with previous studies, repetition of stimulus features improved performance (Figure 9.11). This feature-based facilitation of return was manifested in the target discrimination process in FEF. Neurons discriminated the target from distractors earlier and better following repetition of stimulus features, corresponding to improvements in saccade latency and accuracy, respectively. The change of neuronal target selection occurred through both target enhancement and distractor suppression. This result shows adjustments of the target selection process in FEF corresponding to and therefore possibly contributing to the changes in performance across trials due to sequential regularities in display properties.

Knowledge gained through experience is necessary when objects of interest cannot be located based solely on their visual features. Such cases are exemplified by a search for a conjunction of features such as color and shape in which an explicit memory representation is needed to identify the target.[119] A recent study investigated how the brain combines knowledge with visual processing to locate targets for eye movements by training monkeys to perform a visual search for a target defined by a unique combination of color and shape (e.g., red cross). The color–shape combinations that defined the target were varied pseudo-randomly between sessions. Two separate, contextual influences were exerted on gaze behavior and the neural selection process: visual similarity to the target and the history of target properties.[1160,120] The evidence for the influence of visual similarity was that monkeys made occasional errant saccades during this conjunction search, which tended to direct gaze to distractors that resembled the current target. Similar observations have been made with human observers during covert[121] and overt orienting.[122,123] When monkeys correctly shifted gaze to the target, FEF neurons not only discriminated the target from distractors but also discriminated among the nonselected distractors resulting

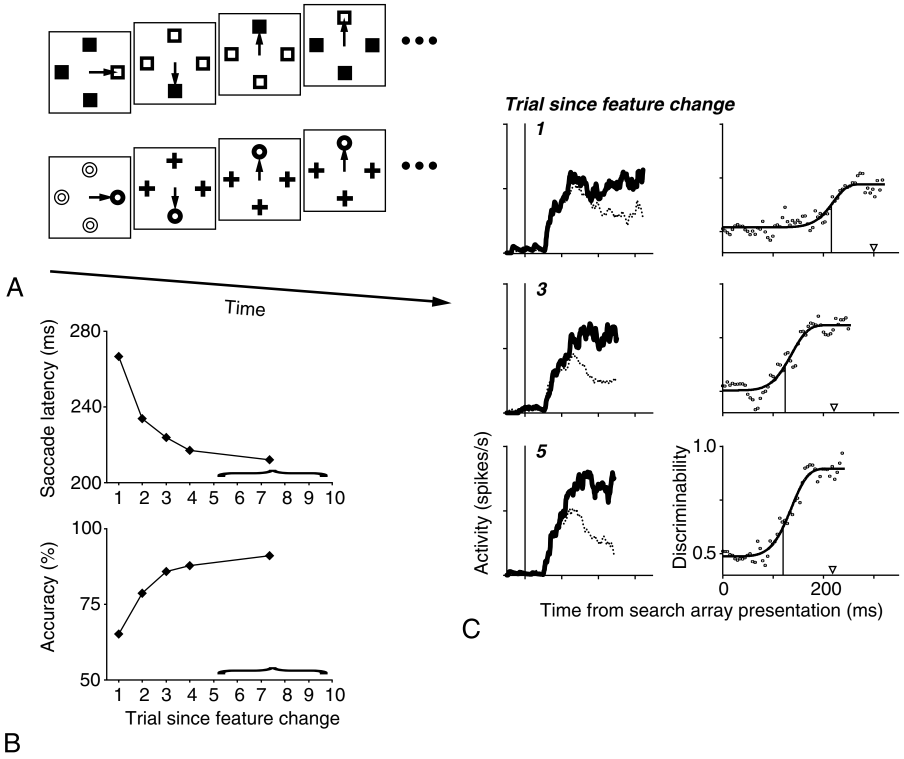

FIGURE 9.11 Priming in search and FEF. (A) Popout search task. The monkeys' task was to shift gaze to the single target defined by color (top) or shape (bottom). The arrow indicates the saccade to the target. Top panel illustrates a change from a search for green among red to a search for red among green. Bottom panel illustrates a change from a search for a red circle among green circles to a search for a red circle among red crosses. Stimuli are not drawn to scale. (B) Variation of average saccade latency (top) and accuracy (bottom) as a function of the number of trials following the change of features in the search array. Immediately following a change, performance is slower and more error prone. After trials, performance improves to asymptote. (C) Effect of feature change during popout search on the activity of one FEF neuron. Left panels illustrate average activity when the target (thick) or distractors (thin) appeared in the receptive field. Right panels illustrate the time course and magnitude of target selection through a measurement of discriminability (0.5 indicates no difference of activity; 1.0 indicates perfect discrimination of target from distractor) derived from the activity when the target or distractors appeared in the receptive field. In each plot of discriminability the vertical line marks the time of target discrimination. The open arrowhead above the abscissa marks the median saccade latency. The three rows show activity for increasing numbers of trials after the feature change with the top panels illustrating activity during the first trial after the change, and the bottom row showing the activity during the fifth trial after the change. The speed and quality of target selection improves with increasing number of trials from the feature change. (Modified from Reference 118.)

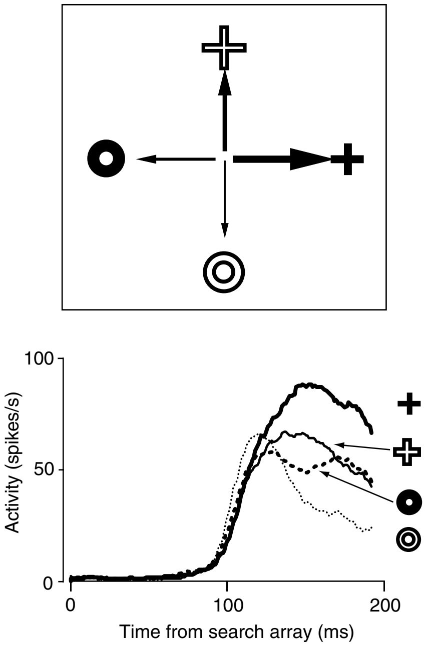

FIGURE 9.12 Visual selection of a remembered target during conjunction search. The assignment of the patterns of neural activation and the incidence of saccades to the alternative stimuli are indicated in the diagram of the search array. The width of the arrows in the search array represents the incidence of saccades to the different stimuli. Most saccades were made to the target (black cross). Occasional errant saccades were directed to distractors that were the same shape or color as the target (black circle, white cross) more often than to the distractor that shared neither feature with the target (white circle). In addition, errant saccades exhibited an additional tendency to shift gaze to the distractor that had been the target in the previous experimental session (white cross). The evolution of activity of an FEF neuron is shown during conjunction search when the target stimulus (thick solid), same-color distractors (intermediate dashed), same-shape distractors (intermediate solid), and the opposite distractors (thin dotted) fell in the receptive field. The initial response did not distinguish the target from the various kinds of distractors, but shortly thereafter the activation for the target became greater, while the activation for the distractors was reduced. The degree of suppression of the distractor activation varied according to whether the distractors resembled the target or had been the target in the previous session. (Modified from Reference 120.)

in more activation for distractors that shared a target feature than for distractors that shared none (Figure 9.12). Thus, the pattern of neural discrimination among nonselected distractors corresponded to the pattern of errors that reveals the allocation of attention. Evidently, a template of the target held in memory influenced performance and activity.

During conjunction search, the history of stimulus presentation across sessions also affected the selection process.[116] If an error was made, monkeys showed a significant tendency (in addition to the visual similarity tendency just described) to shift gaze to the distractors that had been the target in the previous session. Recordings from FEF neurons during trials with correct saccades to the conjunction target revealed a corresponding discrimination among distractors with more activation for distractors that had been the target during the previous session. This effect was evident across sessions that were more than a day apart and persisted throughout experimental sessions. The longer duration of this influence distinguishes it from the short-term priming during popout search that lasts for about ten trials or 30 s in humans,[114,115] as well as monkeys.[116,117]

In the aforementioned studies, the target was present in the search array on every trial. This means that one possible explanation of the modulation involves a direct comparison of the distractor features with the target. To determine more directly whether a memory representation spanning across trials can influence the selection of FEF neurons, an experiment with singleton search was carried out in which no target and only distractors were presented on a fraction of trials and monkeys were rewarded for maintaining fixation on the central spot.[124] Even in trials with no target present, the activation of FEF neurons in response to distractors was proportional to the visual similarity of the distractors to the target. This observation suggests that a template of the target held in memory can influence the target selection process in FEF. Although the precise relationship between memory and search is not entirely clear,[125–127] the necessity of some kind of target template seems clear.[128–130]

The source of these various expressions of contextual modulation observed in FEF is not known. Current thought would hold that the target template is represented in areas 12 and 46 of prefrontal cortex,[131] which are connected with FEF.[36,132] Recent findings have prompted the suggestion that dorsolateral prefrontal cortex encodes rules for guiding behavior.[133–134] Such contingent activation seems a necessary basis for the modulation observed in FEF. The activity of neurons in dorsolateral prefrontal areas rostral to FEF has been described during visual search or selection tasks,[135–139] but the selection was more all or none because the responses began typically after the selection process was completed. Thus, under the general conditions of search used in this work, nontarget stimuli did not activate cells in prefrontal areas 12 and 46. Much more research is needed to understand how arbitrary rules influence saccade target selection.

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