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Feature-Based Attention in the Frontal Eye Field and Area V4 during Visual Search

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SUMMARY

When we search for a target in a crowded visual scene, we often use the distinguishing features of the target, such as color or shape, to guide our attention and eye movements. To investigate the neural mechanisms of feature-based attention, we simultaneously recorded neural responses in the frontal eye field (FEF) and area V4 while monkeys performed a visual search task. The responses of cells in both areas were modulated by feature attention, independent of spatial attention, and the magnitude of response enhancement was inversely correlated with the number of saccades needed to find the target. However, an analysis of the latency of sensory and attentional influences on responses suggested that V4 provides bottom-up sensory information about stimulus features, whereas the FEF provides a top-down attentional bias toward target features that modulates sensory processing in V4 and that could be used to guide the eyes to a searched-for target.

INTRODUCTION

When we search for an object in a crowded scene, such as a particular face in a crowd, we typically do not scan every object in the scene randomly but rather use the known features of the target object to guide our attention and gaze. In areas V4 and MT in extrastriate visual cortex, it is known that attention to visual features modulates visual responses (Bichot et al., 2005; Chelazzi et al., 2001; Hayden and Gallant, 2005; Martinez-Trujillo and Treue, 2004; Maunsell and Treue, 2006; McAdams and Maunsell, 2000; Motter, 1994), and these effects seem to occur throughout the visual field, independently of the locus of spatial attention (Bichot et al., 2005; Martinez-Trujillo and Treue, 2004). Neurons in area V4, for example, show enhanced responses to stimuli within their receptive fields (RFs) during visual search when they contain a color or shape feature that is shared with the searched-for target (Chelazzi et al., 2001), even when the animal is planning an eye movement (and, thus, directing spatial attention) to another stimulus in the search array (Bichot et al., 2005). Thus, feature-selective attentional enhancement appears to occur in parallel across the visual field representations of extrastriate visual areas and presumably helps guide the eyes to searched-for targets.

Although extrastriate neuronal responses are modulated by feature attention, to our knowledge, the source of the top-down feedback that biases responses in favor of the attended feature is unknown. During spatial attention, there is evidence that the response enhancement with attention observed in extrastriate visual areas results from top-down feedback from areas such as the frontal eye field (FEF) and lateral intraparietal area (LIP) (Desimone and Duncan, 1995; Gregoriou et al., 2009; Kastner and Ungerleider, 2000; Serences and Boynton, 2007). Electrical stimulation of the FEF causes enhancement of V4 responses and activation of the cortex measured by fMRI, similar to what is found during spatial attention (Ekstrom et al., 2008; Moore and Armstrong, 2003), and neurons in the FEF and V4 synchronize their activity with each other in the gamma frequency range during spatial attention (Gregoriou et al., 2009). However, to our knowledge, whether these areas play the similar role during feature-based attention is still unknown.

Like neurons in area V4, neurons in the FEF and LIP also show enhanced responses to targets (or distracters that share features with the targets) compared to dissimilar distracters in their RFs, even when these stimuli are not selected for the next saccade during visual search (Bichot and Schall, 1999; Ipata et al., 2009). This suggests that the responses of FEF and LIP neurons to stimuli in their RFs are influenced by the target features in parallel across the visual field, independently of spatial attention. However, the target stimuli used in these studies were fixed, at least within the same session, raising the possibility that the parallel effects of target features on responses arose from learning effects rather than flexible feature attention mechanisms. Learning effects on target responses have been found in prior studies in the FEF (Bichot et al., 1996). Indeed, one recent study of FEF neurons with a target that changed from trial to trial during visual search found that cells exhibited a serial shift of spatial attention effects from one stimulus to another in the search array, rather than parallel, feature attention effects (Buschman and Miller, 2009). Most importantly, to our knowledge, it is not known how the latency of feature attention effects on FEF and LIP responses compare to those in V4. The relative timing bears on the question of whether feature attention influences in the FEF are the cause or consequence of feature attention mechanisms in V4.

For example, consider a model in which V4 is a source of a feature-based saliency map in the FEF. In this case, V4 could receive top-down information about the target features from other sources, then locally compute the similarity between the

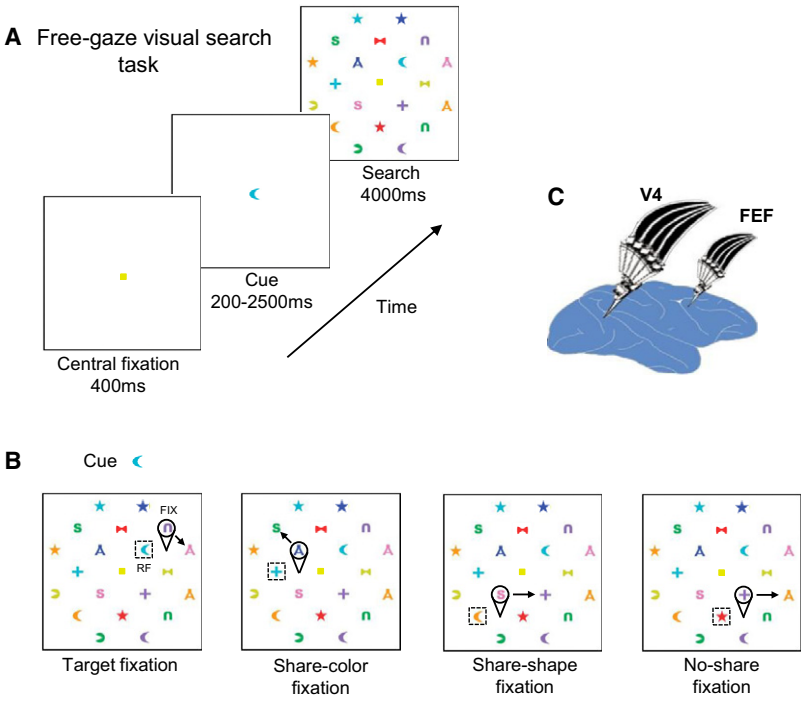

Figure 1. Task and Recording Sites

(A) Illustration of the behavioral task.

(B) Four types of fixation epochs during search. Location of gaze is indicated by the inverted cone. Dashed rectangle indicates the neuron's RF, and the arrow indicates the upcoming saccade.

(C) Illustration of simultaneous recording sites in the FEF and V4.

target and the stimulus in the RF, and finally send this information to the FEF to help build the salience map there. If this were the case, the latency of feature attention effects in V4 should be earlier than those in the FEF. Alternatively, consider a model in which the FEF is the source of feature-based saliency in V4. In this case, the similarity between the searched-for target and the stimuli in the search array could first be computed in the FEF (or areas that project to the FEF, such as other prefrontal areas or the LIP) and then this feature-based saliency signal could be fed back from the FEF to V4 at the topographic locations of all the stimuli in the array, to enhance V4 responses to all stimuli that share the attended target features. In this case, the latency of feature attention effects in V4 should be later than in the FEF.

To help understand the relative roles of V4 and FEF in feature attention during visual search, we recorded multiunit activity in both areas simultaneously while monkeys performed a free-gaze visual search task with 64 different target stimuli that changed from trial to trial. In particular, the target stimulus on one trial could be a distracter on the next trial. We compared responses to stimuli in the RF with and without attended features, when animals were directing their gaze to a stimulus outside the RF, i.e., when spatial attention was directed elsewhere. Furthermore, we tested whether the effects of feature attention on responses were correlated with the animal's behavior in the task. Our data showed that the response to stimuli with attended features was significantly enhanced in both areas. This response enhancement occurred significantly earlier in the FEF than in V4, which is consistent with the hypothesis that the FEF serves as a source of top-down signals during feature-based attention. The strength of the feature enhancement in the FEF and V4 predicted the number of saccades to find the target stimulus, suggesting that this signal is actually used in behavior.

RESULTS

Both monkeys (*Macaca mulatta*) performed very well in the free-gaze visual search task with 20 stimuli (Figure 1A), with 95% correct by monkey L and 98% correct by monkey G. Figures S1A and S1B (available online) show the distributions of saccade latencies of the two monkeys during search, which had a median of 155 ms in monkey G and 175 ms in monkey L.

On average, monkey L took 3.0 saccades to find the target, and monkey G took 3.6 saccades to find the target. The fact that there were 20 stimuli in the array but it took less than 4 saccades to find the target supported the idea that the monkeys used the target features to guide their search. The same conclusion was also supported by the distribution of saccades to the different types of stimuli. In the search array with 20 stimuli, the average percentages of total stimuli comprised by the target, by distracters that shared the target color (share-color), by distracters that shared the target shape (share-shape), and by distracters that shared no target features (no-share) were 5% (1 of 20), 10% (2 of 20), 10% (2 of 20), and 75% (15 of 20), respectively. If monkeys made saccades to stimuli without using the target features to guide their search, the percentage of saccades to each type of stimulus should match the stimulus frequency. Instead, the percentage of saccades to these four types of stimuli were 34.3%, 14.1%, 12.3%, and 39.3%, respectively, for monkey G, and 34.7%, 20.1%, 8.7%, and 36.4%, respectively, for monkey L. Thus, the animals made eye movements to the targets and distracters that shared target features more often than to no-share distracters expected by their frequency in the array, supporting the idea that the monkeys used the target features to guide their search.

We recorded 134 sites with visual responses in the FEF and 136 sites with visual responses in V4 in the two monkeys (Figure 1C). The results were qualitatively similar in both monkeys and were therefore combined. RFs were mapped in a memory-guided saccade task (see Experimental Procedures). On average, the RFs of FEF sites covered 4.5 ± 0.16 stimuli in the search array. Figure S1E shows responses of a FEF site during this task. To isolate the feature-based attention effect, we sorted fixations during the search period according to the category of stimuli in the RF: "target," "share-color," "share-shape," and "no-share" distracter (Figure 1B). In the target fixations, the

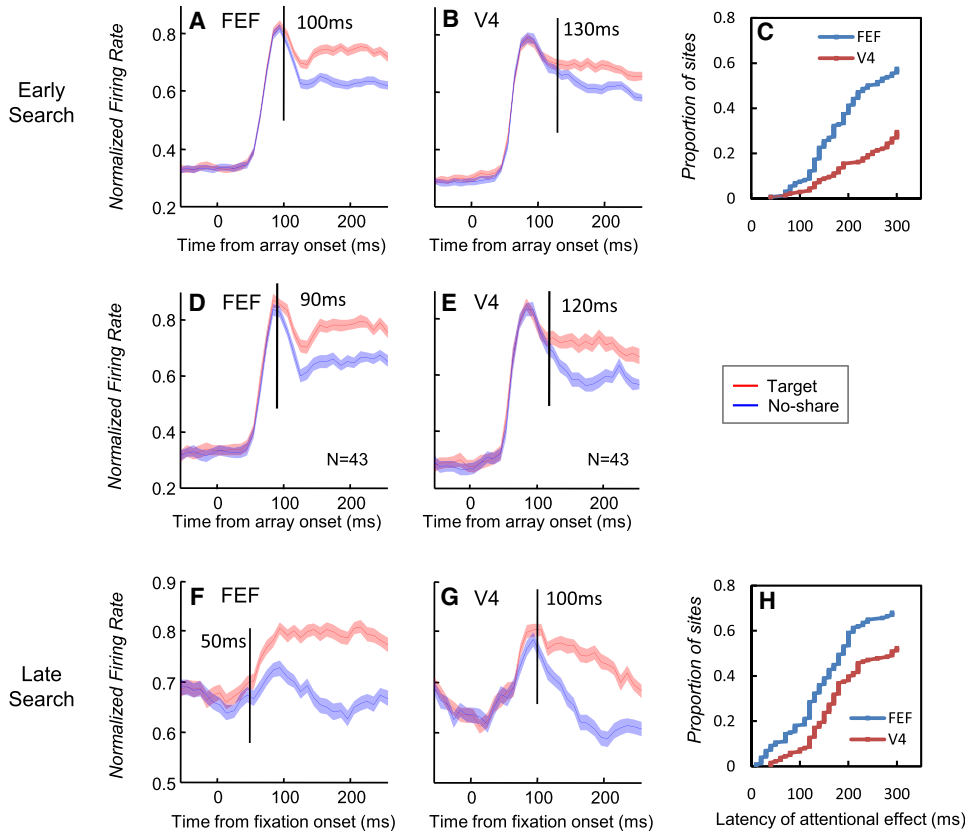

Figure 2. Feature-Based Attention in the FEF and V4

Normalized firing rates averaged across the population during the target and no-share fixations. All firing rates were normalized to the maximum rates of the target responses. The SEM (±) of the population averages are marked by the shading above and below the averages. Vertical black lines in the middle of plots mark the times when the target and no-share responses reached a significant difference at the population level, which we defined to be the latency of the feature-based attention effect.

(A and F) Responses in the FEF during the early search and late search, respectively.

(B and G) Responses in V4.

(C) Cumulative distribution of FEF and V4 attentional effect latencies, computed from individual recording sites during the early search, represented as proportions of the total recording sites.

(D) Responses during target and no-share fixations in early search in the FEF after matching the magnitude of attention effects between the two areas.

(E) Responses during target and no-share fixations in early search in V4 after matching the magnitude of attention effects between the two areas.

(H) Cumulative distribution of FEF and V4 attentional effect latencies during the late search.

target was in the RF. In the share-color and share-shape fixations, a distracter was in the RF, and it shared the target color or shape, respectively, and in the no-share fixations the distracter in the RF shared no target features. To isolate the effects of feature attention from those of spatial attention, we only included fixations in which the following saccade was made away from the RF for this analysis, e.g., a share-color fixation was one where a share-color distracter was in the RF, but the saccade was made to a stimulus outside of the RF. We also matched the stimuli in the RF across comparison conditions, so there was no difference in the stimuli themselves across attention conditions (see Experimental Procedures). Finally, because the pattern of response and the latency of the attentional effects differed for the fixation period prior to the first saccade after array onset compared to all subsequent fixations, we separately analyzed the results on the fixation prior to the first saccade (early search) and all other fixations after the first saccade (late search). The early search results, before the first saccade, also served as a control for the possibility that the attention results in the late search fixations were influenced by differences in scan paths to the different attended stimuli in the RF.

Responses Modulated by Feature Attention in the FEF and V4

The responses of cells in both the FEF and V4 were modulated by feature attention, even when the animal was planning an eye movement to a stimulus outside the RF. Figures 2A and 2B show normalized firing rates averaged across the entire populations of FEF and V4 sites during target and no-share fixations in early search, i.e., prior to the first saccade after the array onset. The response to the targets in the RF was significantly larger in comparison to the same stimuli on trials when they

were the no-share stimuli in the RF, in both the FEF and V4, although the stimuli in the RF were matched across these two conditions. Thus, both areas show feature attention effects on their responses.

Although both areas showed feature attention effects, they began earlier in the FEF than in V4. The effect of feature attention began with a latency of 100 ms after search array onset in the FEF (Wilcoxon signed rank test, $p < 0.05$), versus a 130 ms latency after search array onset in V4 (Wilcoxon signed rank test, $p < 0.05$), and this latency difference was significant (two-sided permutation test, $p < 0.05$). Very similar results were obtained using a mutual information measure. We also measured the latencies of the effects of attention at each individual recording site. The cumulative distribution of latencies for the sites is shown separately for the FEF and V4 in Figure 2C, and the distribution is clearly shifted to earlier times in the FEF (Wilcoxon rank-sum test, $p < 0.05$). There was one site in each area with an early attention latency of 40 ms, but the FEF site is obscured by the V4 distribution line in the figure. The cumulative distributions do not reach 100% in either area because many cells in each area did not have a significant effect of attention at any latency in this analysis (Wilcoxon signed rank test, $p < 0.05$). The median latency was 240 ms in the FEF, and it was not measurable in V4 because less than 50% of the V4 sites showed a significant effect of feature attention.

To rule out the possibility that the shorter latency of attention effects in the FEF was due to the larger magnitude of attention effects in that area, we recomputed the latencies using a subset of sites with similar magnitudes of attention effects in each area. We only considered sites in each area with a 10%–30% increase in response to the target versus the no-share stimulus, in the period of 120–220 ms after the onset of the search array. We matched the sites in the FEF to the same number of sites in V4 with similar effect sizes (43 sites in both areas). As shown in Figures 2D and 2E, the overall magnitude of attentional effects was now similar in the two populations, but the latency of attentional effects on the population response was 90 ms in the FEF versus 120 ms in V4. Again, the population latency was significantly earlier in the FEF (two-sided permutation test, $p < 0.05$). We also compared the latencies of the attentional effect at each site individually in these two subsets of sites, and the median latency of 180 ms in the FEF was significantly earlier than the 280 ms median latency in V4 (Wilcoxon rank-sum test, $p < 0.05$).

We computed the distributions of attention effects in the FEF separately for sites with saccade-related activity (visual-motor sites, $n = 73$) and without this activity (visual-only sites, $n = 61$), and there was no significant difference in the distributions of latencies for the two types of sites (Wilcoxon rank-sum test, $p > 0.05$). We also considered whether V4 sites might have shorter latencies if they were either feature selective or if the target stimulus was the preferred stimulus for the cells. However, there was no significant difference in latencies between the feature-selective sites ($n = 98$) and nonselective sites ($n = 38$) (Wilcoxon rank-sum test, $p > 0.05$). Likewise, the latency of attentional effects using only targets with the preferred feature of the cells was 150 ms at the population level during early search, which was still later than in the FEF. We also tested whether V4 cells showed any effect of the attended feature (cue) on their activity before the presentation of the search array, but there was no significant difference in response depending on whether the cue had a preferred or nonpreferred feature for the V4 feature-selective sites (Wilcoxon signed rank test, $p > 0.05$). In total, the results strongly support the idea that the FEF shows earlier feature attention effects than V4.

As shown in Figures 2F and 2G, the feature attention effect in the FEF was also earlier than in V4 during late search, i.e., after the first saccade. However, the latencies of attention effects at the population level in both areas were reduced by about 50 ms compared to the latencies in early search. This suggested that the comparison of the searched-for target features to the stimuli throughout the array might start at array onset and continue through multiple fixations, although we cannot rule out the possibility that the transient response to the array onset also contributed to the longer latencies during early search. At the population level, the latency of feature attention effects was 50 ms in the FEF, which was significantly earlier than the latency of 100 ms in V4 (two-sided permutation test, $p < 0.05$). Likewise, the cumulative distribution of attentional latencies (Figure 2H) had a median of 190 ms in the FEF versus 290 ms in V4, which was a significant difference (Wilcoxon rank-sum test, $p < 0.05$). As in early search, the distributions of attentional latencies were not significantly different for the visual-motor sites and visual-only sites in the FEF, or for the feature-selective sites versus nonselective sites in V4 (Wilcoxon rank-sum test, $p > 0.05$).

To test the possibility that the feature attention effects were due to systematic differences in the distances between the saccade endpoints and the RFs in the target versus no-share conditions in either early or late search, we computed these distances in both conditions for all recording sites (Early search: Figure S1C; Late search: Figure S1D). We found no significant difference between the distributions of distances between saccade endpoints to the FEF RFs for target and no-share conditions at the population level in either early or late search (Wilcoxon signed rank test, $p > 0.05$). We also computed these differences for each recording site separately and found only a few recordings that had significant feature attention effects during early ($n = 2$) or late search ($n = 2$) and also had significantly shorter distances between the saccade endpoint and the RF in the target than in the no-share condition. When we removed these recordings from the population distributions, it had no effect on the relative latency of attention effects in the FEF and V4.

In sum, the shorter latency of feature attention effects in the FEF than in V4 during both early and late search suggests that direct or indirect inputs from the FEF to V4, rather than the reverse, are responsible for the feature attentional enhancement.

Response enhancement occurred not only for the target versus no-share stimulus in the RF, but also for the share-color and share-shape stimuli versus the no-share stimuli. In the share-color and share-shape conditions, the color or shape of the distracter stimulus in the RF matched the target color or shape, respectively, but the other feature differed from the target. Figure 3 shows averaged population responses in the FEF and V4 during these two conditions and the matched

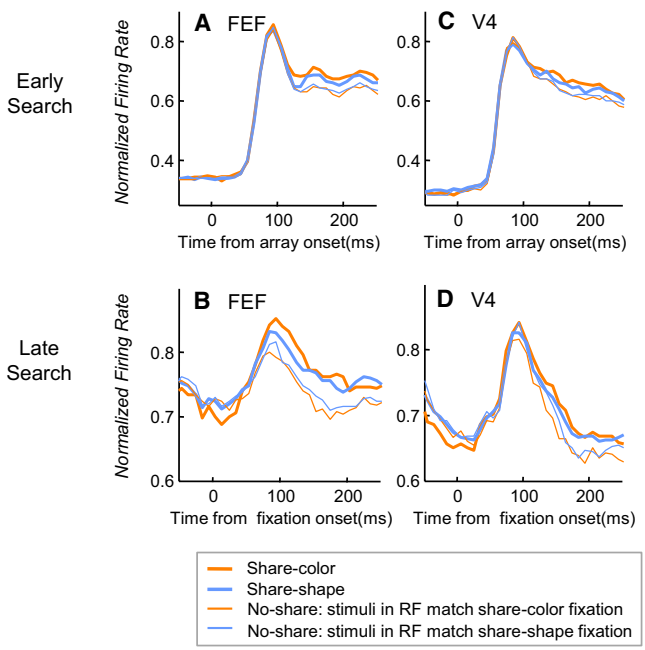

Figure 3. Feature-Based Attention during Share-Color and Share-Shape Fixations

Normalized firing rates averaged across the population during the share-color, share-shape, and matched no-share fixations are shown. All firing rates were normalized to the maximum rates of the share-color responses.

(A and B) Responses in the FEF during early search and late search, respectively.

(C and D) Responses in V4.

no-share conditions, in all cases when the animal was preparing a saccade outside the RF. The enhancement during share-color and share-shape fixations was smaller than during the target fixations, but the feature enhancement for shared color and shape features was significant in both areas (Wilcoxon signed rank test, $p < 0.05$), consistent with prior studies (Bichot et al., 2005; Bichot and Schall, 1999). This enhancement of responses to distracters that shared features with the target is possibly the basis for the frequent finding that visual search difficulty increases with target-distracter similarity (Duncan and Humphreys, 1989).

Relationship between Feature Attentional Enhancement and Number of Saccades Made to Find the Target

As a test of whether the enhanced responses to targets versus no-share stimuli might actually influence the selection of saccade targets, we measured the correlation between the magnitude of the response to the target in the FEF in the period extending from 50 ms before to 50 ms after the first saccade onset, and the number of saccades it took the animal to find the target. As shown in the example of Figure 4A, there was a clear relationship between the magnitude of response and the number of saccades to find the target on a trial by trial basis. Figure 4B shows the distribution of slopes between firing rates and the number of saccades for all FEF sites. The median slope was −5.28 spikes/s/saccade. Thus, smaller responses led to greater numbers of saccades to find the target. This result is consistent with the idea that the response enhancement to the target stimulus in the FEF helps guide the eyes to the target location. It was not possible to do the same analysis in V4 because the response to the target on a given trial was too highly dependent on the stimulus preferences of the individual cells.

We investigated this relationship between response enhancement and saccades in another way: by calculating the response to the target in the RF in those fixation epochs when the target stimulus would be selected for a saccade two saccades later, compared to fixation epochs when the target stimulus would be selected for a saccade more than two saccades later (Figures 5A–5C). If greater response enhancement to the target leads to fewer saccades to find the target, then the response to the target in the RF should have been greater when it subsequently took two saccades to find target (Type I target, Figure 5) than when it took more than two saccades (Type II target, Figure 5). We only considered fixations when the two subsequent saccades were all away from the RF to avoid the influence of saccades into the RF. The predicted result was indeed found, as shown in Figures 5D–5F for early search and Figures 5G–5I for late

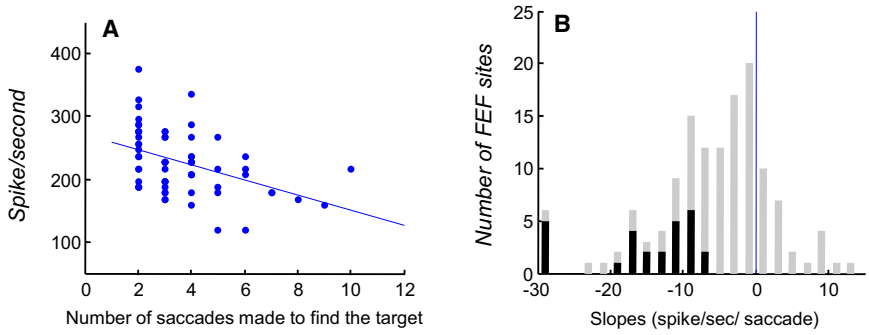

Figure 4. The Response to the Target Was Inversely Correlated with the Number of Saccades that the Monkeys Took to Find the Target

(A) An example from one recording site. Firing rates were averaged during the period of −50–50 ms around the onset of the first saccade. Each point in the plot represents the averaged firing rate and number of saccades made to find the target on a trial.

(B) The distribution of slopes between firing rates and the number of saccades for all FEF sites. The black bars show the numbers of sites with significant correlation (multiple linear regression, $p < 0.05$). The gray bars show the total number of sites. The number of sites with slopes smaller than −30 spike/s/saccade is plotted in the left end of the plot.

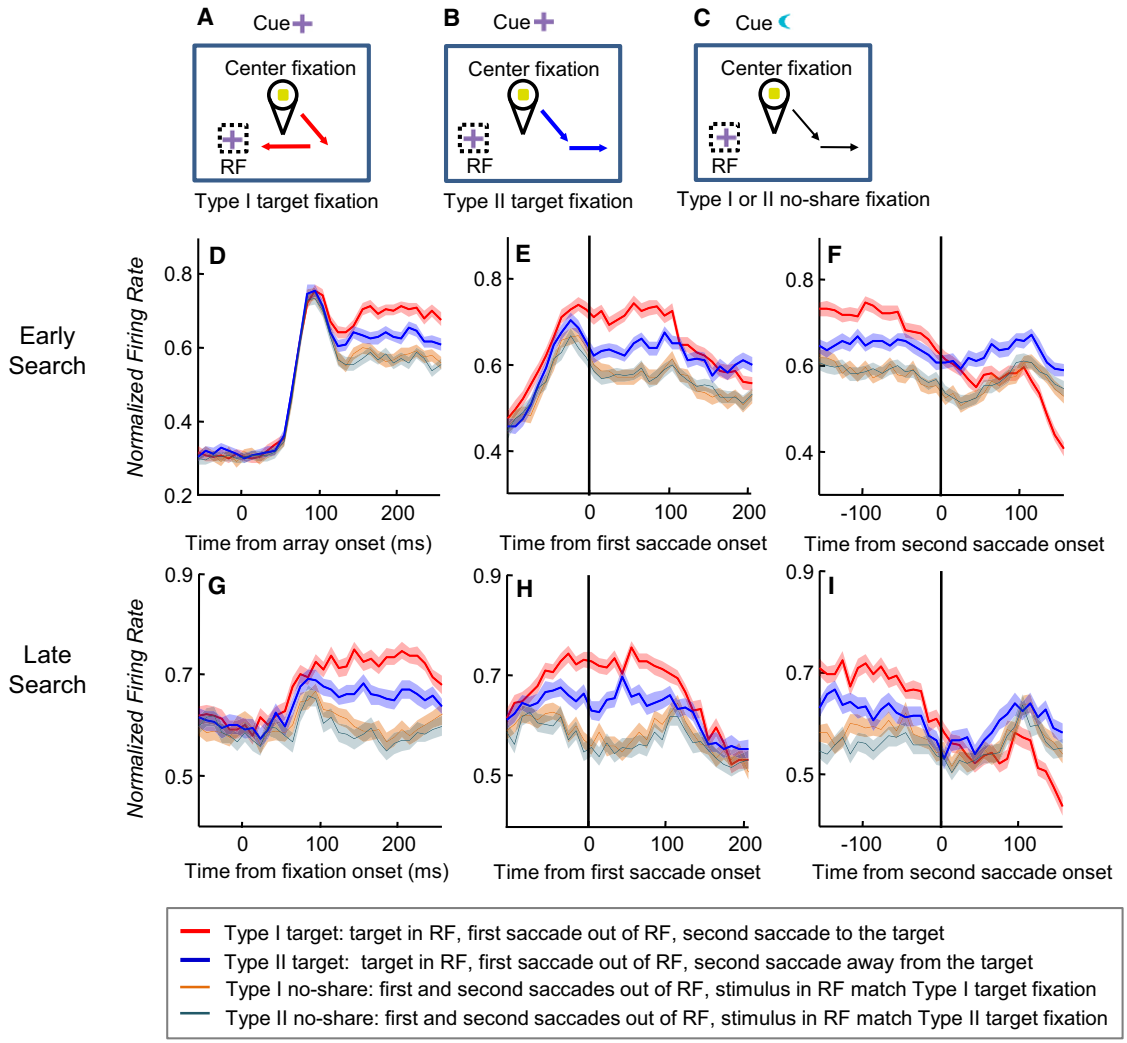

Figure 5. Feature-Based Attention in the FEF and Its Relationship to Saccades

(A–C) Illustration of experimental conditions during early search. The searched-for targets (or cues) are shown above each picture.

(A) The "Type I target" fixation, in which the target was in the RF before the first saccade away from the RF, and the second saccade ended at the target. The two arrows indicate the two saccades. The RF and fixation position are indicated by the dashed rectangle and inverted cone, respectively.

(B) The "Type II target" fixation, in which the target was in the RF before the first saccade away from the RF, and the second saccade was also away from the target.

(C) The "Type I no-share" and "Type II no-share" fixations, in which the stimulus in the RF was a distracter sharing no features with the target, and both first and second saccades were away from the RF. The stimuli in the RF during Type I no-share and Type II no-share fixations were matched to the stimuli in the RF during Type I target and Type II target fixations, respectively. The four types of fixations during late search were similar to the corresponding fixations during early search, with the exception that the positions of fixations during late search were on stimuli in the search array rather than on the center spot.

(D–F) Normalized firing rates averaged across the population during the Type I target, Type II target, Type I no-share, and Type II no-share fixations in early search. All firing rates were normalized to the maximum rates of the Type I target responses. The SEM (±) of the normalized population averages are marked by the shading above and below the population averages. (D) Responses aligned to search array onset.

(E and F) Responses aligned on the first saccade and second saccade onsets, respectively. The feature-based attentional effects were significantly larger during Type I target conditions than the effects during Type II target conditions. In addition, the feature-based attention effects lasted longer than the Type I target or Type II target fixations and persisted well after the first saccade, at which time stimuli in the RF did not contain the attended features.

(G–I) Responses during late search. All conventions are the same as in (D)–(F).

search. Response enhancements were significantly larger to the target when it was found after two saccades than when it was found after more than two saccades (Wilcoxon signed rank test, $p < 0.05$). This enhanced response to the target continued for approximately 100 ms after the initiation of the first saccade but ended before the second saccade began (see Figures 5E–5I), during which period only distracters sharing neither the color nor the shape with the target appeared in the cell's RF. For comparison, Figure 5 also shows the responses to the no-share stimuli that were matched in properties to the target stimuli

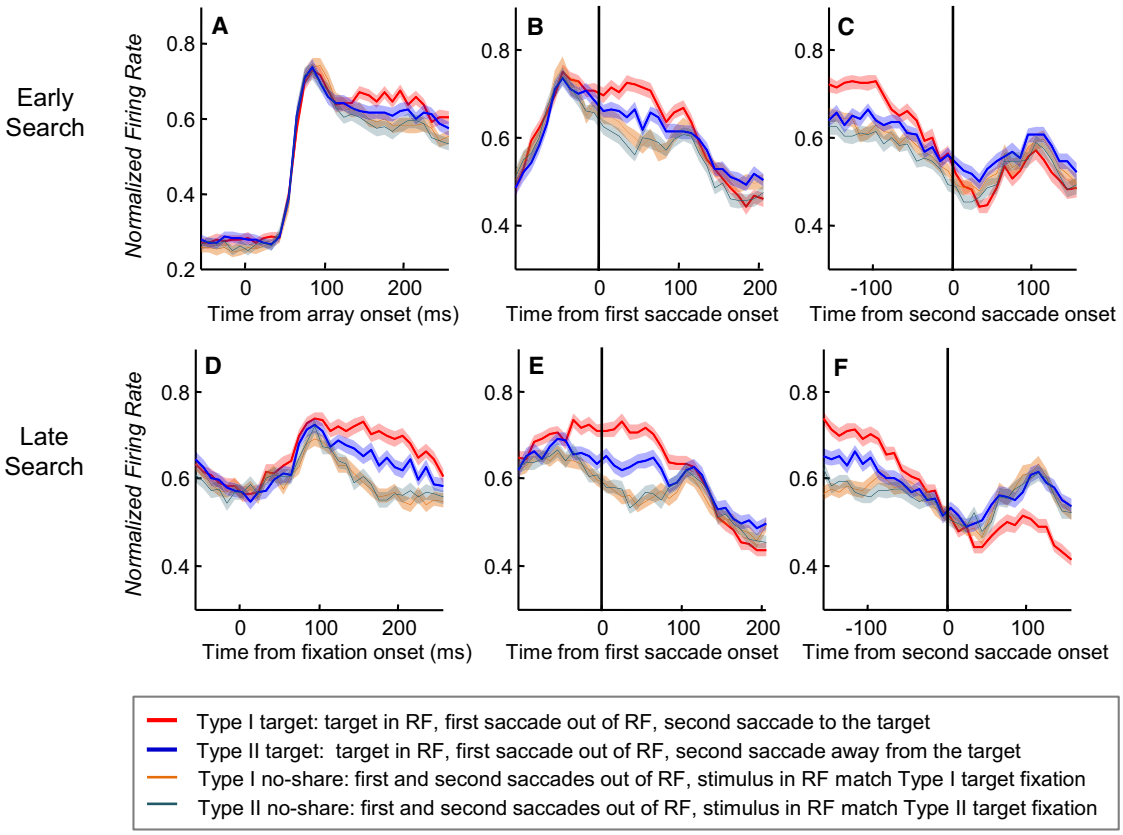

Figure 6. Feature-Based Attention in V4 and Its Relationship to Saccades
Conventions are as in Figures 5D–5I.

in the above comparisons. For these no-share stimuli, the responses were smaller than to the target stimuli in all conditions (Wilcoxon signed rank test, $p < 0.05$). The effects of feature attention were larger when the animal took only two saccades to find the target, but they remained significant even when the animal took more than two saccades (Wilcoxon signed rank test, $p < 0.05$). This specificity of the enhanced responses to the target versus no-share stimuli is consistent with a feature attention effect and is inconsistent with increases in general arousal, etc., on trials with fewer saccades to find the target.

As show in Figure 6, a similar pattern of results was found in V4. In late search, the responses were significantly enhanced on trials when the target was found in two saccades versus more than two saccades (Figure 6D; Wilcoxon signed rank test, $p < 0.05$). In early search, the enhancement for targets found after two saccades did not reach significance during the standard analysis window (Figure 6A; Wilcoxon signed rank test, $p > 0.05$). However, the difference became significant if we moved the analysis window 10 ms later (Wilcoxon signed rank test, $p < 0.05$). Consistent with the results in the FEF, these feature-based attentional enhancements also persisted well beyond the target fixations—they continued into the period between the first and second saccade and disappeared about 50–60 ms before the second saccade (Figures 6B, 6C, 6E, and 6F).

Multiple Saccade Planning

So far, the results indicate that feature-based attention may influence saccades during visual search. Specifically, stronger response enhancement to the target is associated with fewer subsequent saccades for monkeys to find the target. An alternative possibility is that the target response enhancement was due only to planning saccades beyond the next saccade, i.e., perhaps responses were enhanced when any stimulus in the RF would become selected for a saccade, two saccades later versus more than two saccades. If so, similar enhancement should be observed for nontargets that would be selected in two saccades versus more than two saccades. To test this possibility, we compared the responses to the no-share stimuli in the RF when they would be selected for a saccade two saccades later, to the response to the same stimuli in the RF when they would not be selected within two saccades.

Responses in the FEF to the no-share stimuli are shown in Figure 7. There was a very small but significant response enhancement to the distracters that would be reached after two saccades versus more than two saccades (No-share1 versus No-share2 fixation in Figure 7; also see Figure S3; Wilcoxon signed rank test, $p < 0.05$), supporting the idea that saccade planning does influence FEF responses two saccades in advance (Phillips and Segraves, 2010). However, these

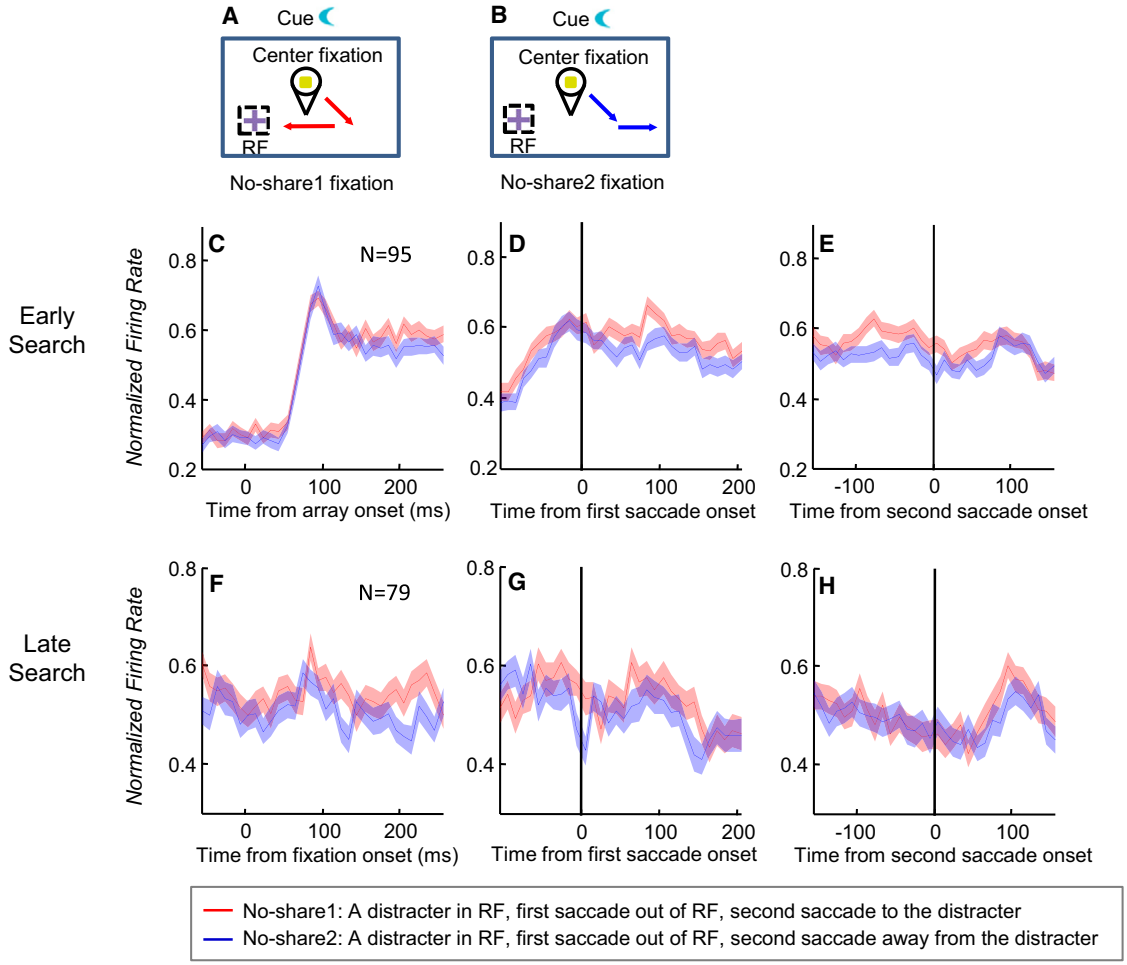

Figure 7. Multiple Saccade Planning in the FEF

(A and B) Illustration of experimental conditions during early search. The searched-for targets are shown above each picture.

(A) The "no-share1" fixation, in which a distracter did not share any feature with the target in the RF before the first saccade away from the RF, and the second saccade ended at the distracter. The two arrows indicate the two saccades. The RF and fixation position are indicated by the dashed rectangle and inverted cone, respectively.

(B) The "no-share2" fixation, in which a distracter shared no features with the target in the RF before the first saccade away from the RF, and the second saccade was still directed away from the distracter. These two types of fixations during late search were similar to the corresponding fixations during early search, with the exception that the positions of fixations during late search were on stimuli in the search array rather than on the center spot.

(C) Normalized firing rates averaged across the population during the no-share1 and no-share2 fixations in early search. All firing rates were normalized to the maximum rates of the no-share1 responses. The SEM (±) of the normalized population averages are marked by the shading above and below the population averages.

(D and E) Responses aligned on the first saccade and second saccade onsets, respectively.

(F–H) Responses during late search. All conventions are the same as in (C)–(E). The differences between the no-share1 and no-share2 responses were very small during these periods.

saccade-related response enhancements were still significantly smaller than the feature-based target enhancement described above (Figure S4; Wilcoxon rank-sum test, $p < 0.05$). Therefore, saccade planning beyond the next saccade could not by itself explain the relationship between the magnitude of target response enhancement and the number of saccades needed to find the target. In V4, there was no significant effect of saccade planning in advance during early search (Figures S2 and S3; Wilcoxon signed rank test, $p > 0.05$), but there was a very small difference during late search (Figures S2 and S3; Wilcoxon signed rank test, $p < 0.05$), which was also significantly smaller than the feature-based attentional enhancement (Figure S4; Wilcoxon rank-sum test, $p < 0.05$).

Spatial Attention

Finally, we tested the effects of overt spatial attention (or saccade target selection) to the stimulus in the RF on responses in the FEF and V4. We measured responses to stimuli in the RF on fixations when the animal was planning the saccade into the RF, compared to when the animal was planning the next

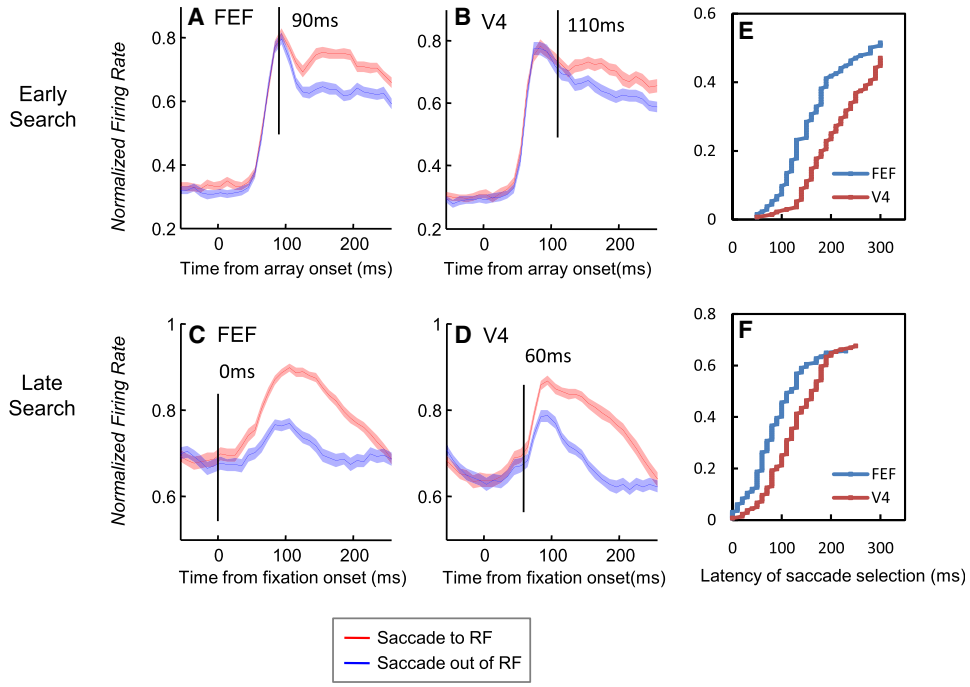

Figure 8. Overt Spatial Attention in the FEF and V4

(A–D) Normalized firing rates averaged across the population during the "saccade to RF" and "saccade out of RF" fixations. All firing rates were normalized to the maximum rates of the "saccade to RF" responses. The SEM (±) of the population averages is marked by shading above and below the averages. Vertical black lines in the middle of the plots mark the times when the two responses reached a significant difference at the population level, which we defined to be the latency of the spatial attention effect.

(A and C) Responses in the FEF during the early search and late search, respectively.

(B and D) Responses in V4.

(E) Cumulative distribution of FEF and V4 attention latencies for individual recording sites during the early search period, represented as proportions of the total recording sites.

(F) Cumulative distribution of FEF and V4 attention latencies during late search.

saccade outside of the RF. Responses in the FEF and V4 during these fixations are shown aligned to fixation onset in Figure 8 and aligned to saccade initiation in Figure S5. In early search, responses in the FEF and V4 at the population level were both significantly enhanced (Wilcoxon signed rank test, $p < 0.05$) when the animal planned a saccade into the RF, with a latency of 90 ms after search array onset in the FEF and 110 ms in V4. This 20 ms latency difference did not reach statistical significance (two-sided permutation test, $p > 0.05$). However, the median for the distributions of attentional latencies of all recorded sites calculated individually (Figure 8E) was significantly earlier in the FEF (280 ms) than in V4, where less than 50% of the cells showed significant spatial attention effects (Wilcoxon signed rank test, $p < 0.05$). In late search, responses in the FEF and V4 were also significantly enhanced (Wilcoxon signed rank test, $p < 0.05$) when the animal was planning a saccade into the RF, with a latency of 0 ms in the FEF and 60 ms in V4 at the population level, which was a significant difference (two-sided permutation test, $p < 0.05$). The 0 ms latency in the FEF strongly suggests that the saccade target was chosen in the FEF during the previous fixation period. The distribution of attentional latencies computed for each recording site (Figure 8F) also showed a shorter median latency in the FEF (median, 120 ms) than in V4 (median, 160 ms; Wilcoxon rank-sum test, $p < 0.05$). Together, the earlier effects of spatial attention in the FEF compared to V4 are consistent with results from previous studies (Armstrong et al., 2006; Gregoriou et al., 2009) suggesting that the FEF might be a source of top-down signals to V4 during spatial attention.

Analysis of Visual Features

Although the latencies of attentional effects are earlier in the FEF than in V4 for both feature and spatial attention, the attention effects in the FEF must depend on feature information analyzed in areas such as V4, and this information must presumably be available early enough to guide attention. We therefore calculated the latency of color and shape information in V4, for all sites showing significant color and shape selectivity, respectively. The proportions of V4 sites showing significant color or shape selectivity were 58% and 54% (one-way ANOVA, $p < 0.05$), respectively, in the memory-guided saccade task, and they remained selective in the search task (Figures S6 and S7). Interestingly, the response differences between the preferred versus nonpreferred colors and shapes in V4 persisted for almost 100 ms after the initiation of the next saccade in the search task, which moved the stimuli out of the RF. By comparison, 22% of FEF

sites showed significant shape selectivity in the memory-guided saccade task (one-way ANOVA, $p < 0.05$), consistent with previous studies (Peng et al., 2008). However, this selectivity was not present during the search task because the averaged population responses to the preferred and nonpreferred shapes were the same in this task. None of the FEF sites showed color tuning in either task.

As shown in Figure S7, during early search, the latency of color selectivity and shape selectivity in V4 at the population level was 60 ms and 70 ms, respectively, which is earlier than the attentional latencies for feature and spatial attention effects in the FEF during early search, which were 100 ms and 90 ms, respectively. Thus, color and shape information in V4 is apparently available early enough to influence attention to features and locations, at least in the time period immediately after the onset of the array. During late search, the latencies for color and shape selectivity in V4 were 60 and 40 ms, respectively, which were not earlier than the feature and spatial attention effect latencies in the FEF, which were only 50 ms and 0 ms, respectively. Overall, the short latency of feature attention effects in the FEF during late search suggests that the comparison of the target and array stimulus features begins on earlier fixations, possibly immediately after array onset, and spans subsequent saccades during search.

DISCUSSION

We found that attention to target features enhanced responses to stimuli that shared the target features in both the FEF and V4, even while monkeys were preparing saccades to stimuli outside the RF. The attended features must have switched quickly and flexibly from trial to trial, because the target stimulus changed randomly from trial to trial, and thus, an attended feature on one trial could be irrelevant on the next. In the FEF, the magnitude of the response to target was inversely correlated with the number of saccades to find the target in the array. In both areas, response enhancements to the target were larger when it would subsequently be found following two saccades than following more than two saccades. We also found effects of saccade planning on responses that spanned at least two saccades, although these effects on the FEF and V4 responses were smaller than the feature enhancement effects. One might interpret these saccade planning effects on response to be spatial attention effects if the animal was able to split spatial attention across multiple locations. In total, these results suggest that the feature enhancement in the FEF and V4 is actually used to select stimuli, or find the target, during search.

Although the FEF is often associated with spatial attention, we found, surprisingly, that the latency of the feature attention effects was actually shorter in the FEF than the latency of feature attention effects in V4, suggesting that the FEF could be a source of top-down attention biases to V4 during feature attention. In contrast to the late effects of attention, bottom-up shape and color feature information was present in V4 at latencies shorter than any attentional effects. Thus, V4 could be the source of basic feature information needed to create an attentional bias toward stimuli sharing target features. The absolute values of the latencies for attention and feature information found in the present study are undoubtedly stimulus and task dependent, and vary somewhat from latencies found in other studies, e.g., Bichot et al. (2001) and Hayden and Gallant (2005). However, the critical comparisons are the latencies across areas when measured in the same task and in the same recording sessions, as were measured here. The latency differences between the FEF and V4 were present both in the summed population histograms as well as the distribution of latencies for all sites measured individually. Nonetheless, it is always possible that we may have missed specific cell types in either area that had latencies shorter than the rest of the population, and this issue can only be conclusively settled by additional studies in both areas.

The magnitude of the latency difference varied across conditions and does not clearly argue for a direct versus polysynaptic functional pathway from the FEF to V4. We also cannot rule out the possibility that other extrastriate visual areas, or even thalamic sources such as the pulvinar (Desimone et al., 1990; McAlonan et al., 2008), might have shorter latencies for feature attention effects than either the FEF or V4 and could therefore provide V4 with the necessary feature attention signals independently of the FEF. V1 and V2 seem unlikely as sources because we have recently found that spatial attention latencies in V1 and V2 are actually later than in V4 (Buffalo et al., 2010), and neither area seems to have direct connections with the FEF (Schall et al., 1995). The inferior temporal (IT) cortex might feed back target feature information to V4, but the latency of object identity information in the IT cortex is longer than the latency of attentional effects in the FEF (Monosov et al., 2010). The LIP is another potential candidate, but attentional latencies in the LIP are later than in the FEF during visual search (Buschman and Miller, 2007). Although this analysis of latencies casts doubt on cortical feedback sources other than the FEF, establishing ''causality'' in the signals from the FEF to V4 would require additional types of experimental approaches (Armstrong et al., 2006; Gregoriou et al., 2009).

Several previous studies have showed that feature-based attention selectively enhances the responses to stimuli sharing the attended features throughout the visual field in areas V4 and MT (Bichot et al., 2005; Chelazzi et al., 2001; Hayden and Gallant, 2005; Martinez-Trujillo and Treue, 2004; Mazer and Gallant, 2003; McAdams and Maunsell, 2000; Motter, 1994). In V4, FEF, and LIP, attention to features modulates responses even when the animals are planning a saccade, and therefore directing attention, to a stimulus outside the neuron's RF (Bichot et al., 2005; Bichot and Schall, 1999; Ipata et al., 2009). Furthermore, in the present study we found evidence in both V4 and FEF that this feature-based enhancement is actually used to guide the eyes to the target. A top-down feature signal that biases activity in parallel throughout the visual field representation of extrastriate visual areas is consistent with biased competition and feature-similarity-gain models of attention (Ardid et al., 2007; Desimone and Duncan, 1995; Hamker, 2005; Reynolds and Chelazzi, 2004; Treue, 2001), all of which incorporate feature attention components.

In fMRI studies, the FEF is often activated together with other areas in prefrontal cortex when subjects perform tasks requiring feature attention (Egner et al., 2008; Giesbrecht et al., 2003). The

feature attention effects in the FEF enhance the notion that the FEF functions as a "saliency map" (Goldberg et al., 2006; Itti and Koch, 2001; Thompson and Bichot, 2005; Wolfe, 1994), in which the magnitude of activity at each point in the map is a function of bottom-up sensory strength (e.g., stimuli of high contrast) and top-down task relevance (e.g., stimuli at the focus of attention or that share target features).

The effect of feature attention on the FEF and V4 responses occurs quickly after the onset of the search array: 100 ms and 130 ms, respectively. However, these feature attention effects on responses occur with a latency even earlier in the FEF and V4 during fixations following the first saccade: at 50 ms and 100 ms, respectively. These very rapid attention effects on responses strongly suggest that the comparison of each stimulus in the array to the target proceeds over more than one saccade. That is, every time the animal moves its eyes, it seems likely that the comparison of stimulus features to target features has some "memory" from the previous fixation. If so, this must require a mechanism to update or "remap" the location of every stimulus after every saccade, and evidence for such a remapping mechanism has been reported previously in the FEF and LIP (Colby and Goldberg, 1999; Melcher and Colby, 2008).

How Is the Salience Map Generated?

The saliency map for behaviorally relevant features in the FEF could be generated in a variety of ways. One possibility suggested by biased competition models (Desimone and Duncan, 1995; Hamker, 2005) is that information about the relevant target features is sent to V4 from parts of prefrontal cortex that mediate working memory for features, and this feedback signal would then bias V4 activity in favor of stimuli that match the searched-for target. For example, if the target were red, then prefrontal areas with connections with V4, such as area 45 (Ungerleider et al., 2008), might feed back this target information to all of the red-preferring cells in V4, which would then show enhanced responses if a red stimulus fell within their RFs. This enhanced representation of stimuli resembling the target could then be used to help construct salience maps in the FEF and LIP. However, this hypothesis conflicts with our finding that the latency of feature attention effects in the FEF is earlier than in V4, by 30–50 ms. The FEF seems to "know" the similarity of every stimulus in the array to the searched-for target, earlier than does V4.

An alternative possibility is that the computation of the similarity of every item in the array to the searched-for target takes place first in prefrontal cortex rather than V4. Both area 8 and area 45 in prefrontal cortex receive inputs from V4 (Schall et al., 1995; Stanton et al., 1995; Ungerleider et al., 2008), and V4 contains color and shape information at relatively short latencies after stimulus onset. Cell in area 45, for example, may carry out a test of similarity of every item in the array with the searched-for target and convey this task-based salience information to nearby cells with spatial RFs in the FEF. Lesion and imaging studies suggest that this role of prefrontal cortex may be particularly important in attentional tasks in which the target changes frequently from trial to trial (Buckley et al., 2009; Nakahara et al., 2002; Rossi et al., 2007). Once the salience map is constructed in the FEF, the salience of every item could then be fed back to all sites in V4, in parallel. The saliency map in the FEF could be viewed in analogy to a "contour map," in which the height of each point is proportional to the target-RF stimulus similarity at that location. If the FEF saliency signal at each point in the map were fed back topographically, in parallel, to the entire visual field map in V4, it would bias V4 responses to all stimuli that were similar to the target throughout the visual field.

It now actually seems simpler to feed back signals from a FEF saliency map in a point-to-point fashion to the topographic map in V4 than to feed back a target-feature signal that targets just those cells in V4 that represent the appropriate feature value. The idea that feedback from the FEF actually causes the modulation of V4 responses during spatial attention is supported by electrical stimulation (Moore and Armstrong, 2003) and coherence studies (Gregoriou et al., 2009). The present results suggest that something similar occurs for feature attention.

If this idea is correct, it still leaves open the question of how and where the comparison between every stimulus in the array and the searched-for target is computed. Although we found some modest shape selectivity in the FEF during the memory-guided saccade task, consistent with prior reports (Peng et al., 2008), many FEF cells only show stimulus selectivity when animals are trained on a particular target-feature relationship (Bichot et al., 1996). It is therefore not clear if the stimulus-target similarity computations could be computed in the FEF. Imaging studies suggest that the critical sites may be in other parts of prefrontal or parietal cortex (Egner et al., 2008; Giesbrecht et al., 2003), which could create the saliency map in the FEF.

Although the present results support the idea that the selection of the target is based on the computation of target-array stimulus similarity, in parallel across the visual field, a recent study in the FEF reported evidence in prefrontal cortex for a covert, "serial" selection of stimuli during search, with a selection time per item of about 40 ms (Buschman and Miller, 2009). The animals appeared to use spatial attention to covertly "scrutinize" every item in the array before making a decision. Importantly, in that study, there were only four stimuli in the search array, positioned in a fixed ring around the fovea, and the stimulus locations were held constant for many months of training. Unlike in the current study, the monkey was not permitted free gaze, and it was counted as an error if the monkey made an eye movement to a distracter before it made an eye movement to the target. Consequently, the latency of the monkey's saccade to the target was twice as long as in the current study: approximately 300 ms. These stimulus and response limitations appear to promote a serial selection strategy by monkeys; it was probably in the monkey's interest to covertly scrutinize each of the four array items before making a saccade to the target. In the present study, we used more naturalistic conditions, with many distracters and free gaze. The monkeys' saccadic reaction times to any stimulus in the array had a median latency of only 150 ms, which was presumably too short to allow for a serial scan of the 20-element search array using spatial attention. Thus, we would argue that under naturalistic conditions with many distracters, parallel feature attention is a more common strategy. However, taking the two studies together, the results serve as a caution that a variety of strategies may be used to optimize performance with a given set of stimuli and task demands.

EXPERIMENTAL PROCEDURES

Subjects

Two male rhesus monkeys (*Macaca mulatta*) weighing 11–15 kg were used. Monkeys were implanted under aseptic conditions with a post to fix the head and two recording chambers, one over the FEF and one over area V4. Localization of the areas was based on MRI scans obtained before surgery. All procedures and animal care were in accordance with the NIH guidelines.

Stimuli

The stimuli were combinations of one of eight colors and one of eight shapes, subtended approximately 1.1°, and were matched for number of pixels. The colors were matched for luminance (~32 cd/m^2) and were red (CIE, x = 0.621, y = 0.341), orange (x = 0.522, y = 0.410), yellow-green (x = 0.418, y = 0.486), green (x = 0.256, y = 0.526), cyan (x = 0.204, y = 0.301), blue (x = 0.165, y = 0.089), purple (x = 0.236, y = 0.116), and magenta (x = 0.378, y = 0.199). Stimuli were presented on a 14.5 cd/m^2 gray background. In total, there were 64 different stimuli, 20 of which were randomly chosen for the search array on a given trial. The target/cue for a given trial was always 1 of the 20 stimuli (i.e., 1 of 64 possible stimuli), chosen randomly on each trial.

Behavioral Tasks

Monkeys were trained to perform a free-gaze conjunction visual search task. After center fixation for 400 ms, the monkeys were presented with a central cue that was identical to the search target. The cue stayed on for 200–2500 ms randomly, after which time a search array with 20 stimuli was presented, and the center cue was replaced by the center fixation spot. Monkeys were required to hold fixation at the center of the screen before the search array onset. After the onset, monkeys had 4 s to find the target that was the same as the central cue. No constraints were placed on their search behavior in order to allow them to conduct the search naturally. Monkeys were required to fixate the target stimulus for 700 ms continuously to receive a juice reward. The position of the target on the screen was changed randomly from trial to trial.

A memory-guided saccade task was used to determine a cell's RF and stimulus selectivity. Briefly, the trial started with the monkey fixating a central spot. A peripheral stimulus flashed for 100 ms in one of the stimulus positions used in the search array. After a random period between 500 and 1500 ms, the central spot was extinguished, and the monkey was rewarded for making a saccade to the memorized position of the peripheral stimulus. Before the offset of the fixation spot, monkeys were required to maintain center fixation. Eleven locations, including nine in the contralateral visual field and two on the vertical middle line, were used, which comprised 11 of the 20 locations used in the search array. Firing rates were compared between the prestimulus period, 200–0 ms before stimulus flash onset, and the poststimulus period, 50–250 ms after the flash onset, using the Wilcoxon rank-sum test, and stimulus locations with significant increased responses ($p < 0.05$) were defined to be in the RF. Sites with RFs extending into both hemisfields were rarely found and were excluded from further analyses after a preliminary RF mapping.

Recording

Multiunit spikes and local field potentials (LFPs) were recorded from the FEF and V4 simultaneously using a Multichannel Acquisition Processor system by Plexon. On a given day, up to four tungsten microelectrodes (FHC) were advanced through the dura in each area. Electrodes within an area were spaced 650 or 900 μm apart. Neural signals were filtered between 250 Hz and 8 kHz and amplified and digitized at 40 kHz to obtain spike data. The location of recordings in both the FEF and V4 was verified with MRI. In both monkeys, we electrically (<50 μA) stimulated in the FEF and elicited eye movements. Eye movements were recorded by an infrared eye tracking system (Eye Link II, SR Research) at a sampling rate of 500 Hz.

Data Analysis

Recording sites that showed a significant visual response (Wilcoxon rank-sum test, $p < 0.05$) were included for analysis. The intervals used for this statistical comparison were as described before. Firing rates were calculated with 10 ms nonoverlapping bins.

To isolate the effects of feature-based attention, we divided fixations during the search period into four groups ("target," "share-color," "share-shape," and "no-share"), in which stimulus in the cell's RF shared both color and shape, only color, only shape, or nothing with the searched-for target, respectively. In the first three groups, one or two features in the cell's RF were attended. In no-share fixations, no features of the distracter were shared with the target. To avoid the influence of saccades, only fixations followed by a saccade away from the RF were included for this analysis. The search period was divided into two periods: "early search" and "later search." The early search was the period just after the onset of the search array and before the monkeys made the first saccade. The later search was the period after the first search saccade. Neural activities in the two periods were calculated separately.

When we compared responses between two conditions, we matched the stimuli in the RF of the recorded sites across the two compared conditions. If the RF contained only 1 of the 20 stimuli in the search array, we selected fixation periods in which the stimulus in the RF was the same in the two comparison conditions. If the RF contained more than one stimulus, we first selected fixation periods in which the RF contained only one stimulus that shared at least one stimulus feature with the target in the attended conditions (target, share-color, or share-shape) and all other stimuli in the RF shared no features with the target. We then selected no-share fixations with the same stimulus as the stimulus with target feature on the attended trials in the same location in the RF. Only matched trials were included for analysis.

To assess the latency of the attentional effect, firing rates in attended and unattended conditions were normalized to the maximum rate in the attended condition, and significant differences between the two conditions were determined in each 10 ms bin for each site across trials using a Wilcoxon signed rank test ($p < 0.05$). The latency of the effect for each site was defined to be the first bin out of two successive bins that were significantly different in the two compared conditions. The latencies at the population level were determined by averaged responses across sites instead of responses across trials. The latency of a given attention effect was defined to be the first of three consecutive bins that were all significantly different (Wilcoxon signed rank test, $p < 0.05$) in the two compared conditions. The distributions of latencies for individual sites were compared using a Wilcoxon rank-sum test. To test whether the difference in the latency estimates at the population level in the two areas was statistically significant, we conducted a two-sided permutation test (see Supplemental Experimental Procedures).

SUPPLEMENTAL INFORMATION

Supplemental Information includes seven figures and Supplemental Experimental Procedures and can be found with this article online at doi:10.1016/j.neuron.2011.04.032.

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Supplemental Information

Feature-Based Attention in the Frontal Eye Field and Area V4 during Visual Search

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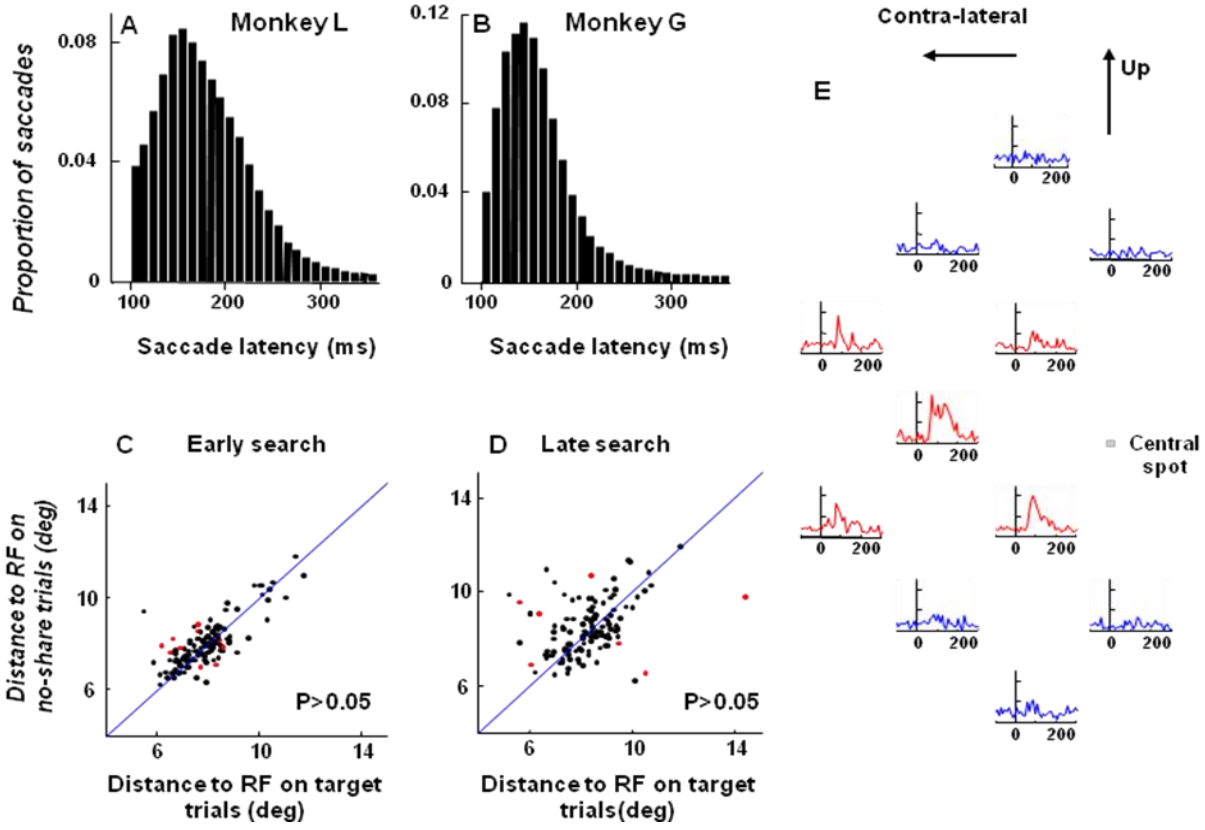

Figure S1. Saccade Latencies and Receptive Field Properties (Related to Figure 1)
(A-B) Distributions of saccade latencies for the two monkeys during search.
(C) Distributions of distances of saccade endpoints relative to FEF RF on target and no-share trials during early search. Red dots represented sites with significant differences between target and no-share conditions. X: distance to RF on target trials; Y: distance to RF on no-share trials.
(D) Distance distributions during late search.
(E) Example of responses of a FEF site during RF mapping in a memory-guided saccade task. Responses were aligned on stimulus flash onset. Red histograms indicate responses when a stimulus was flashed in the RF, and the blue histograms indicate responses for a stimulus outside the RF. The locations of the histograms in the visual field indicate the locations of the stimuli flashed relative to the central spot (the gray square).

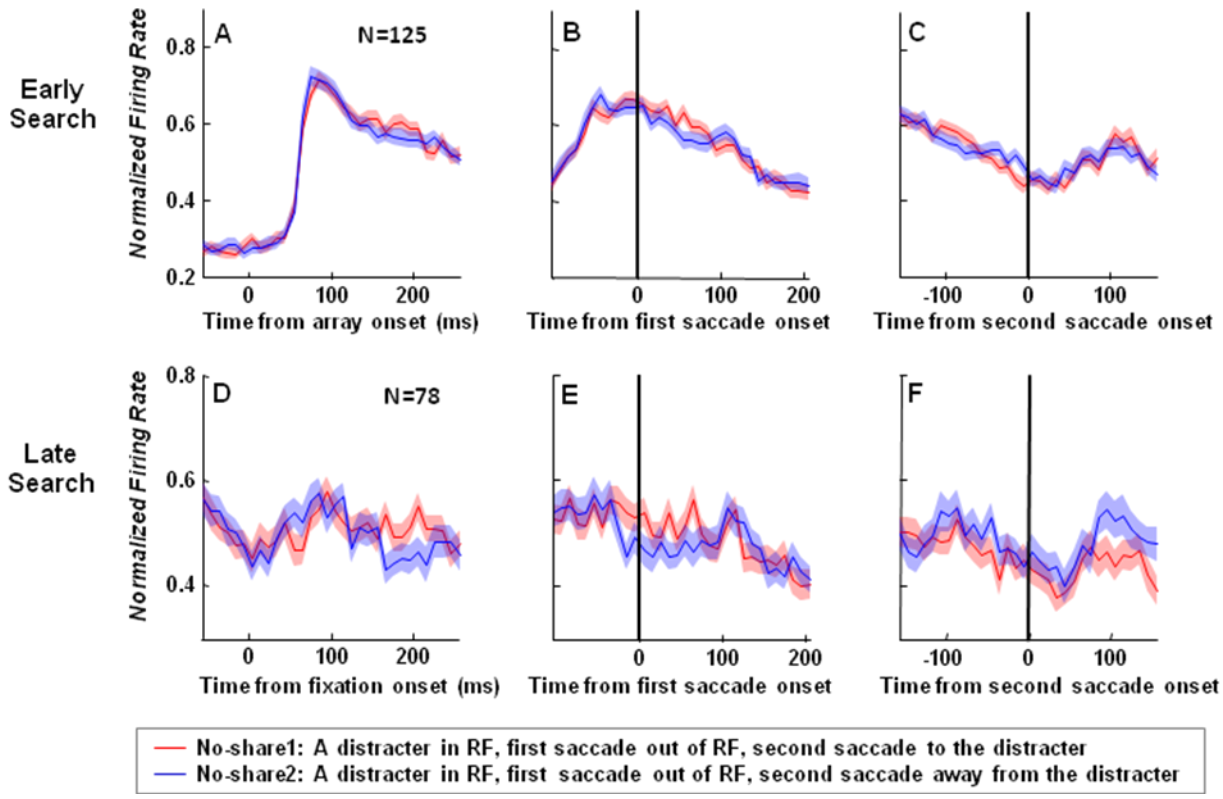

Figure S2. Multiple Saccade Planning in V4 (Related to Figure 7)
Conventions as in Figure 7 C–H.

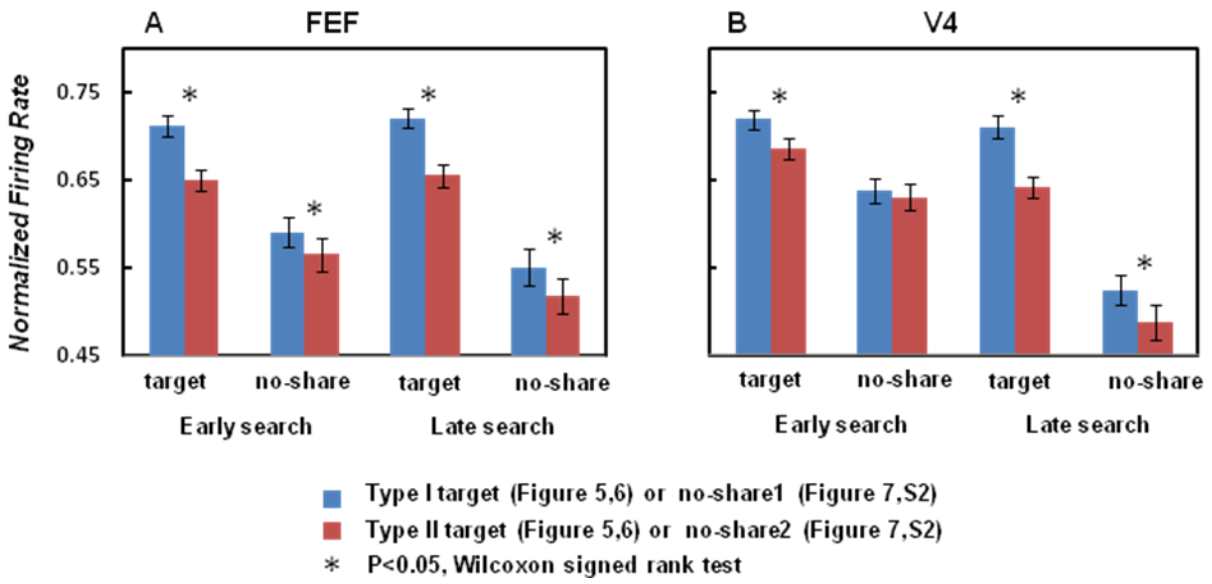

Figure S3. Feature Attention and Motor Planning Effects in FEF and V4 (Related to Figures 5, 6, 7, and S2)

(A) Comparisons in FEF. The average firing rates were calculated during the period of -50 to 50 ms around the onset of the first subsequent saccade. The target responses are as shown in Figure 5, and the no-share responses are as shown in Figure 7.

(B) Comparisons in V4. The target responses are as shown in Figure 6, and the no-share responses are as shown in Figure S2.

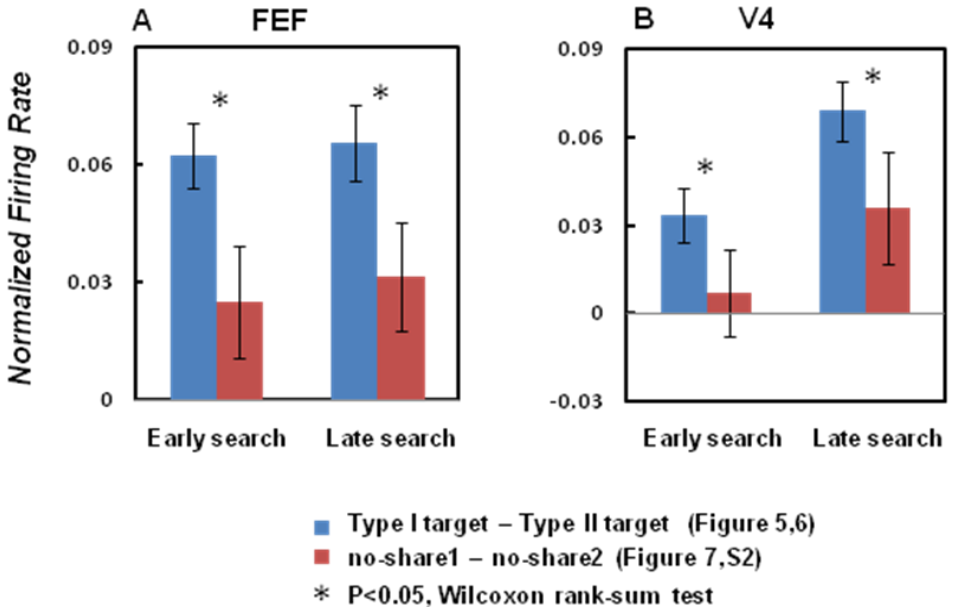

Figure S4. Comparison of Feature Attention and Motor Planning Effects (Related to Figures 5, 6, 7, and S2)

(A) Comparisons in FEF. The firing rate differences between Type I target and Type II target responses (as shown in Figure 5) were compared with differences between no-share1 and no-share2 responses (as shown in Figure 7).

(B) Comparisons in V4. The firing rate differences between Type I target and Type II target responses (as shown in Figure 6) were compared with differences between no-share1 and no-share2 responses (as shown in Figure S2). The average firing rates were calculated during the period of -50 to 50 ms around the onset of the first subsequent saccade.

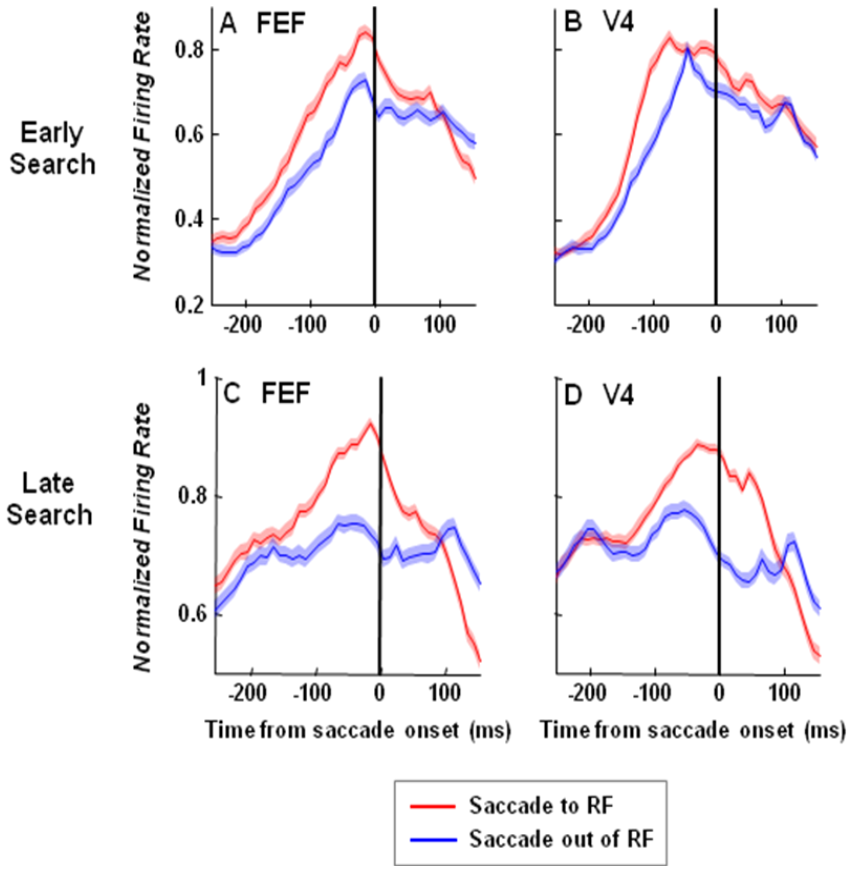

Figure S5. Overt Spatial-Based Attention in FEF and V4 with Data Aligned on Saccade Onset (Related to Figure 8)
Conventions as in Figure 8.

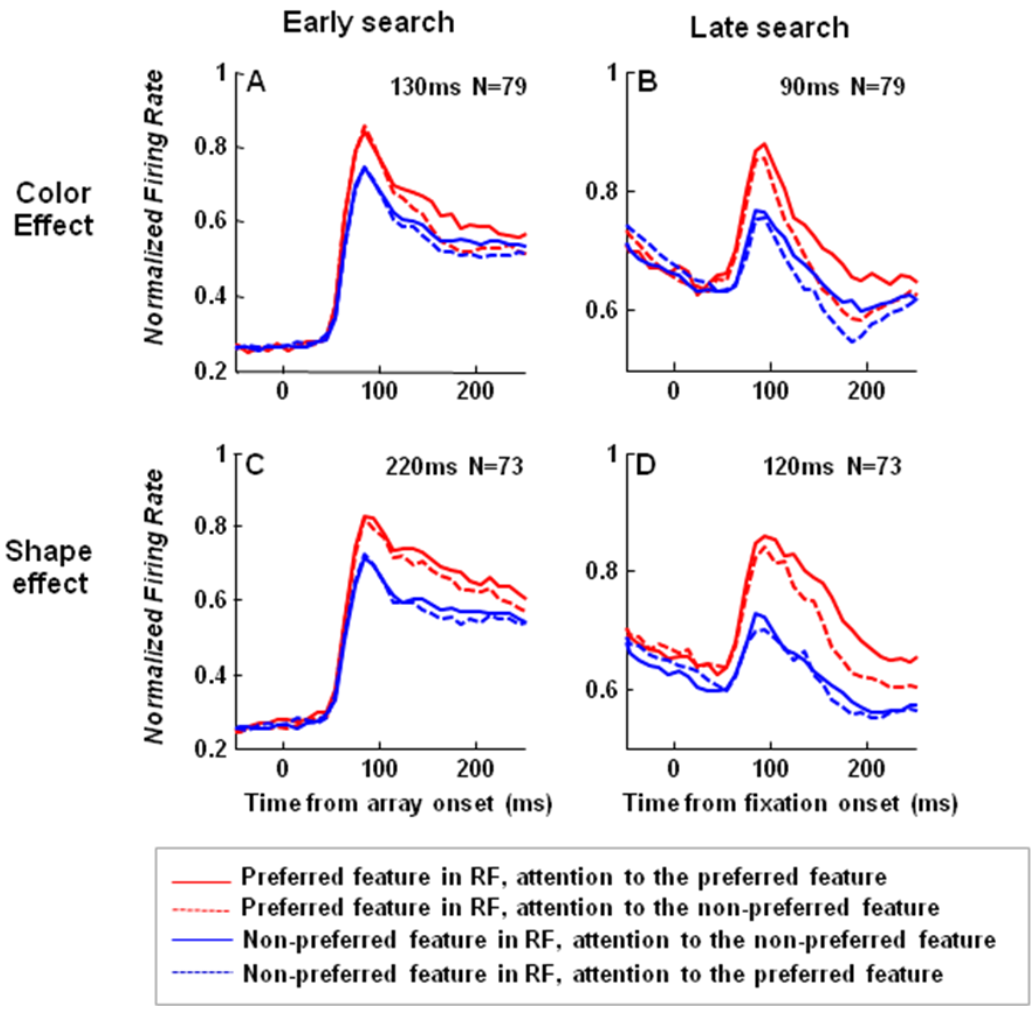

Figure S6. Feature-Based Attention Effect in V4 (Related to Figure 2)
Normalized firing rates over populations of V4 sites with color or shape selectivity. Red lines show responses when the stimulus with the preferred feature (color or shape) for the recorded sites was in the RF and the next saccade was away from the RF. Blue lines show responses when the stimulus with the non-preferred feature was in the RF and the next saccade was away from the RF. Solid lines show responses when the stimulus feature in the RF was attended, and dotted lines show responses when the stimulus feature in the RF was not attended. The time shown at the top of each plot is the latency of the feature-based attentional effect when the preferred feature appeared in the RF.
(A) Color effects during early search.
(B) Color effects during late search.
(C) Shape effects during early search.
(D) Shape effects during late search.

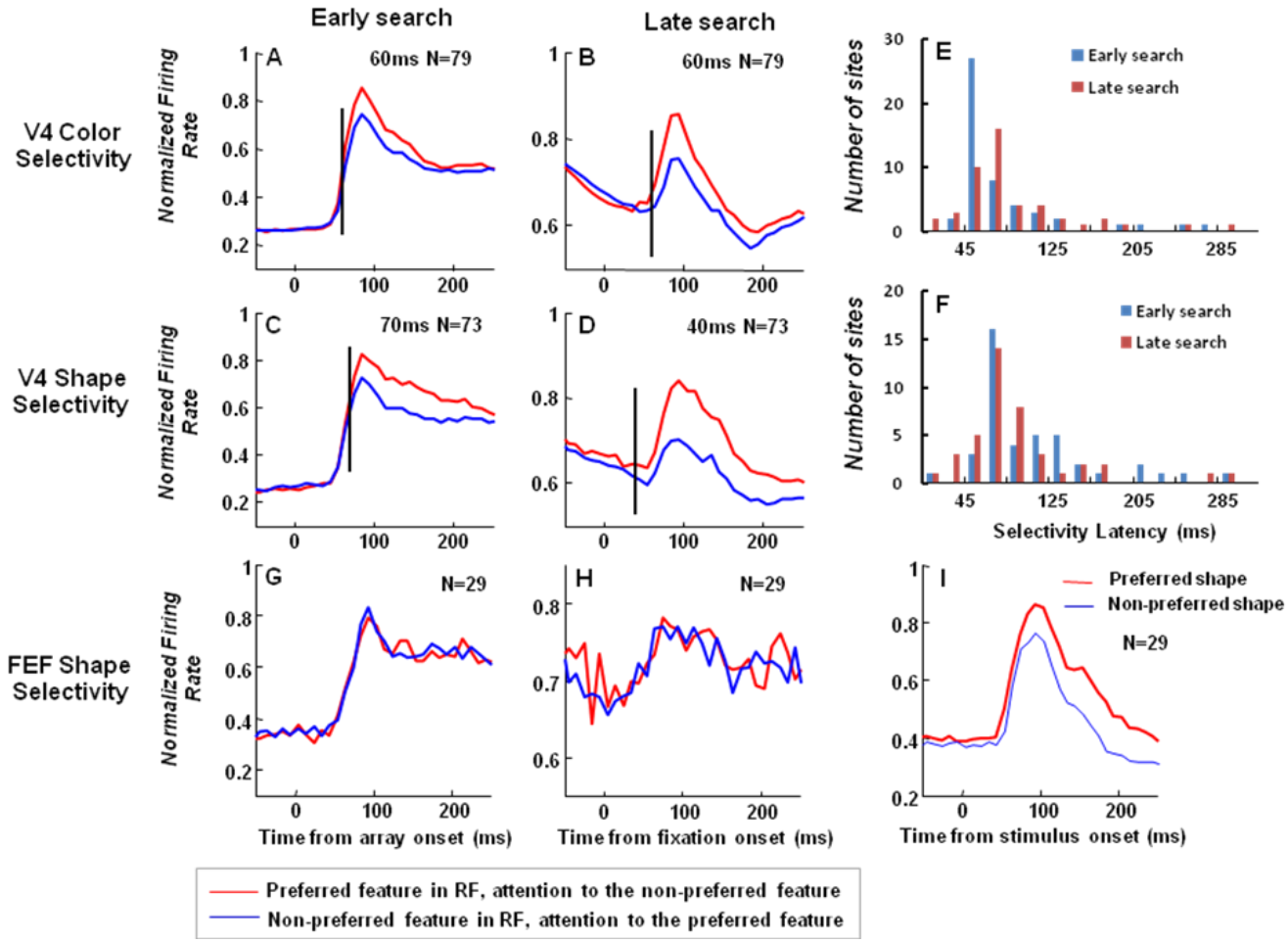

Figure S7. Color and Shape Selectivity of V4 and FEF Sites during Visual Search (Related to Figures 2 and 8)

(A-D) Normalized firing rates over populations of V4 sites with color or shape selectivity. Red lines show responses when the stimulus with the preferred color or shape for the recorded sites was in the RF and the next saccade was away from the RF. Blue lines show responses when the stimulus with the non-preferred color or shape was in RF and the next saccade was away from the RF. The stimulus features in the RF were all not attended.

(A) Color selectivity during early search.

(B) Color selectivity during late search.

(C) Shape selectivity during early search.

(D) Shape selectivity during late search.

(E) Distribution of latencies of color selectivity for all V4 color selective sites that reached a significant difference (Wilcoxon rank-sum test, $p<0.05$). Early search: N=50; late search: N=47.

(F) Distribution of latencies of shape selectivity for all V4 shape selective sites that reached a significant difference (Wilcoxon rank-sum test, $p<0.05$). Early search: N=42; late search: N=41.

(G) No shape selectivity of FEF sites during early search.

(H) No shape selectivity of FEF sites during late search.

(I) Shape selectivity of FEF sites during the memory-guided saccade task.

Supplemental Experimental Procedures

Two-Sided Permutation Test

To test whether the difference in the latency estimates at the population level in the two areas was statistically significant, we conducted a permutation test with re-sampling. The null hypothesis was that the latency at the population level was not different in the two areas. We randomly selected a number of signals equal to our FEF population from a pool of signals consisting of all (FEF and V4) recorded signals. The selected signals from the pool were arbitrarily labeled as FEF signals whereas the remaining signals (equal in size to our V4 population) were arbitrarily labeled as V4 signals. The latency at the population level was determined for each group (lat_pseudoFEF and lat_pseudoV4). We calculated the difference between the two latencies Δlat_pseudo (FEF-V4) = lat_pseudoFEF- lat_pseudoV4. We used Δlat_pseudo(FEF-V4) as the statistic to test the null hypothesis. We repeated the resampling process 10,000 times. The generated distribution of 10,000 values of the statistic (Δlat_pseudo (FEF-V4)) estimates the sampling distribution under the condition that the null hypothesis is correct. We subsequently located the value of the difference we actually observed (Δlat_real (FEF-V4)) on the permutation distribution in order to determine the probability that we would observe a value at least as large as the observed value if the null hypothesis were correct. That is, we asked what percentage of data points in the permutation distribution was equal to or greater than the observed value. To employ a two-sided test, we considered the absolute latency difference.