Behavioral/Systems/Cognitive

Persistent Spatial Information in the Frontal Eye Field during Object-Based Short-Term Memory

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Spatial attention is known to gate entry into visual short-term memory, and some evidence suggests that spatial signals may also play a role in binding features or protecting object representations during memory maintenance. To examine the persistence of spatial signals during object short-term memory, the activity of neurons in the frontal eye field (FEF) of macaque monkeys was recorded during an object-based delayed match-to-sample task. In this task, monkeys were trained to remember an object image over a brief delay, regardless of the locations of the sample or target presentation. FEF neurons exhibited visual, delay, and target period activity, including selectivity for sample location and target location. Delay period activity represented the sample location throughout the delay, despite the irrelevance of spatial information for successful task completion. Furthermore, neurons continued to encode sample position in a variant of the task in which the matching stimulus never appeared in their response field, confirming that FEF maintains sample location independent of subsequent behavioral relevance. FEF neurons also exhibited target-position-dependent anticipatory activity immediately before target onset, suggesting that monkeys predicted target position within blocks. These results show that FEF neurons maintain spatial information during short-term memory, even when that information is irrelevant for task performance.

Introduction

It is known that spatial information—in the form of attentional cues—can enhance object and feature information during perception of visual stimuli (Posner, 1980; Carrasco et al., 2000; Vogel et al., 2005). Likewise, spatial cueing can gate the entry of objects or features into short-term memory (Sperling, 1960; Averbach and Coriell, 1961; Schmidt et al., 2002). The role of spatial information during object memory maintenance, however, is less clear. Some studies suggest that a persistent spatial signal may contribute to object memory maintenance (Treisman and Zhang, 2006; Fougnie and Marois, 2009; Wood, 2011). For example, several laboratories have now demonstrated the ability of spatial cues provided during memory maintenance, well after stimulus offset, to improve both accuracy and reaction time on short-term object memory tasks (Griffin and Nobre, 2003; Matsukura et al., 2007; Theeuwes et al., 2011). If, as these studies suggest, spatial information helps maintain object representations during short-term memory, then spatial information itself should be maintained even during a purely object-based task. Here we test this hypothesis neurophysiologically and show that maintenance of spatial information indeed occurs during object-based short-term memory and therefore may contribute to performance.

Received March 23, 2012; revised May 15, 2012; accepted June 10, 2012.

Author contributions: K.L.C., B.N., and T.M. designed research; K.L.C. and B.N. performed research; K.L.C. and B.N. analyzed data; K.L.C., B.N., and T.M. wrote the paper.

This work was supported by National Institutes of Health Grant EY014924, National Science Foundation Grant IOB-0546891, the McKnight Foundation, and a Stanford Bio-X Fellowship (K.L.C.). We thank Doug S. Aldrich for technical assistance.

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DOI:10.1523/JNEUROSCI.1450-12.2012

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The frontal eye field (FEF) has long been known to exhibit persistent delay period activity during memory-guided saccade tasks (Bruce and Goldberg, 1985). More recently, it has been shown that this sustained spatial selectivity is present in the FEF even in the absence of eye movements (Armstrong et al., 2009; Lawrence and Snyder, 2009). The FEF has also been implicated both in mediating the behavioral benefits of attention (Moore and Fallah, 2001; Monosov and Thompson, 2009; Schafer and Moore, 2011) and in modulating activity in visual cortex (Moore, 2006; Ekstrom et al., 2009; Noudoost and Moore, 2011). In addition, the FEF is reciprocally connected with posterior visual areas (Webster et al., 1994) and nearby prefrontal regions (Stanton et al., 1993) in which object- and feature-selective delay activity has been reported during short-term memory (Miyashita and Chang, 1988; Miller et al., 1996; Zaksas and Pasternak, 2006). Unlike ventrolateral prefrontal cortex, however, the FEF exhibits little or no object or feature selectivity (Bichot et al., 1996; Peng et al., 2008). These functional and anatomical properties make the FEF a candidate for maintaining spatial signals that interact with feature information during short-term memory.

To test whether spatial information is maintained during object-based short-term memory, we recorded from the FEF during an object-based delayed match-to-sample (DMS) task, in which monkeys remember object identity regardless of changes in location. Despite the irrelevance of sample location for task performance, FEF neurons encoded sample position throughout the delay period. Furthermore, neurons continued to encode sample position in a variant of the task in which the matching stimulus never appeared in their response field (RF). FEF neurons also exhibited target-position-dependent anticipatory activity immediately before target onset, suggesting that the monkeys can predict target position within blocks. The persistence of this

spatial information in the FEF during an object memory task is consistent with its possible use in the maintenance of object memory.

Materials and Methods

General and surgical procedures. Two male rhesus monkeys (*Macaca mulatta*, 11 and 12 kg) were used in these experiments. All experimental procedures were in accordance with the National Institutes of Health *Guide for the Care and Use of Laboratory Animals*, the Society for Neuroscience Guidelines and Policies, and Stanford University Animal Care and Use Committee. General surgical procedures have been described previously (Armstrong et al., 2006). Each animal was surgically implanted with a titanium head post and a scleral search coil. Surgery was conducted using aseptic techniques under general anesthesia (isoflurane), and analgesics were provided during postsurgical recovery. Structural magnetic resonance imaging was performed to locate the arcuate sulcus in each monkey for the placement of a recording chamber in a subsequent surgery. A craniotomy was performed on each animal, allowing access to the FEF on the anterior bank of the arcuate sulcus.

FEF neural recordings. Single-neuron recordings in awake monkeys were made through a surgically implanted cylindrical titanium chamber (20 mm diameter) overlaying the arcuate sulcus. Electrodes were lowered into the cortex using a hydraulic microdrive (Narishige International). Activity was recorded extracellularly with varnish-coated tungsten microelectrodes (FHC) of 0.2–1.0 MΩ impedance (measured at 1 kHz). Extracellular waveforms were digitized and classified as single neurons using both template-matching and window-discrimination techniques either online or offline (FHC and Plexon). During each experiment, a recording site in the FEF was first localized by the ability to evoke fixed-vector, saccadic eye movements with stimulation at currents of $<50\ \mu A$ (Bruce et al., 1985). Electrical microstimulation consisted of a 100 ms train of biphasic current pulses (0.25 ms, 200 Hz) delivered with a Grass stimulator (S88) and two Grass stimulation isolation units (PSIU-6; Grass Instruments). Current amplitude was measured via the voltage drop across a 1 kΩ resistor in series with the return lead of the current source. During each experimental session, we mapped the saccade vector elicited via microstimulation at the cortical site under study with a separate behavioral paradigm (Moore and Fallah, 2001). In this paradigm, the monkey was required to fixate on a visual stimulus (0.48° diameter circle) for 500 ms, after which time a 100 ms stimulation train was delivered on half the trials. Evoked saccades had vectors with amplitudes ranging from 5 to 13° eccentricity and angles of −90 to 65° theta (left FEF, monkey H) and 135 to 220° theta (right FEF, monkey S). Landing points of microstimulation-evoked saccades were considered to be the center of the RF of the FEF site under study (FEF RF). After mapping the saccade vector, we recorded the responses of any neuron that could be isolated

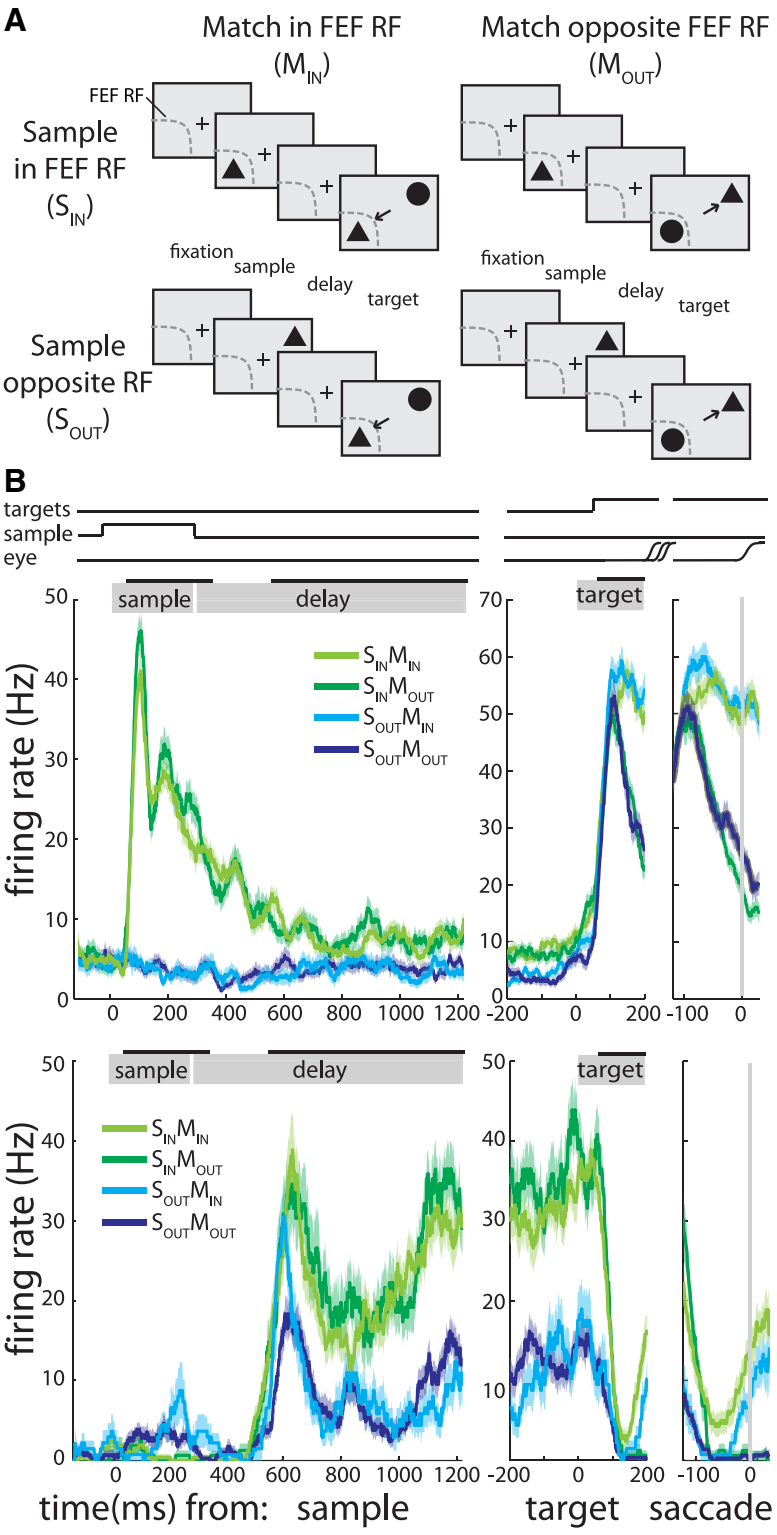

Figure 1. The activity of FEF neurons during the object-based short-term memory task. ***A***, Object DMS task: monkey fixates the small central spot. A sample image appears either inside of or opposite the FEF RF for 300 ms (sample period). The monkey maintains fixation throughout a 1 s delay (delay period) during which only the fixation spot remained on the screen. The match and nonmatch images appear at positions inside and opposite the RF, and the monkey saccades to the match to receive a reward (target period). The location of the match is randomized with respect to the sample image position. ***B***, The response of example FEF neurons (top and bottom) to samples presented in the FEF RF (greens) or opposite the FEF RF (blues), when the match appeared in (light green, cyan) or opposite (dark green, navy) the FEF RF, aligned to sample image onset (left), target array onset (middle), and onset of the saccade (right). Lines and shading represent mean ± SEM. Black lines above the task epoch bars indicate time windows used for subsequent analysis.

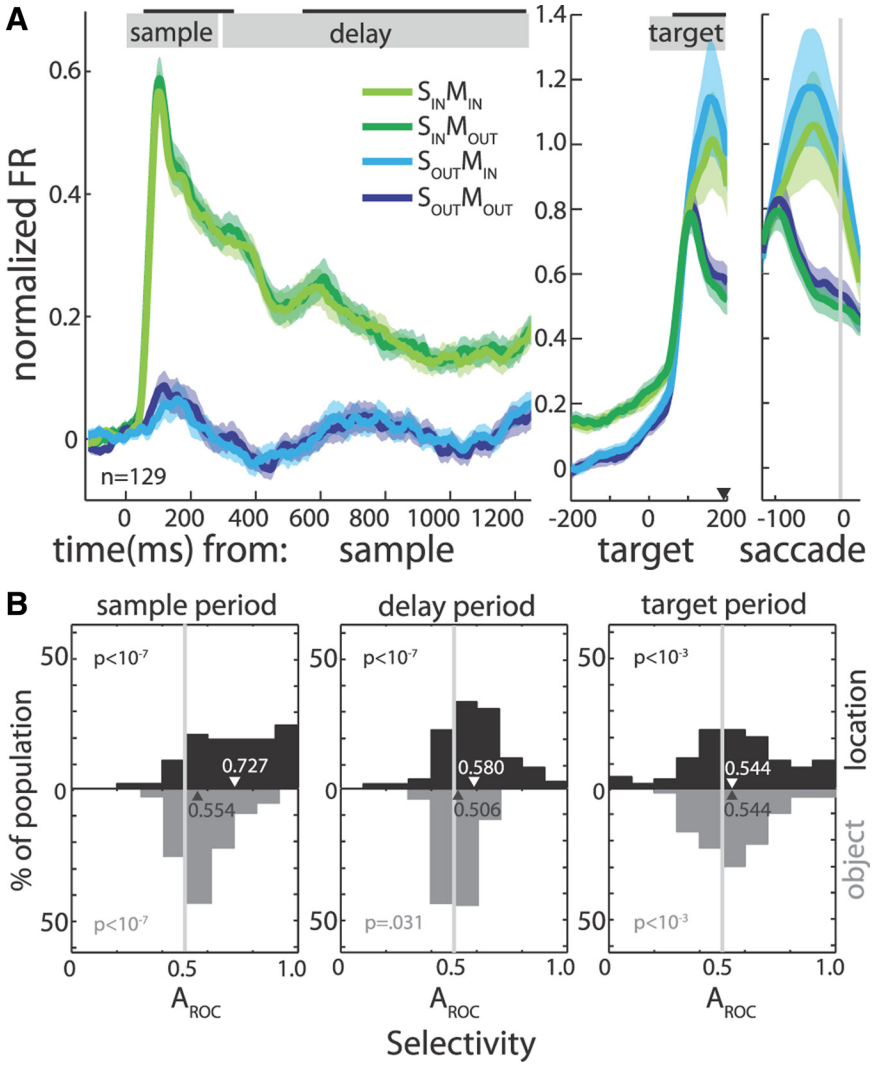

Figure 2. FEF population selectivity for sample location and object identity. ***A***, The mean normalized response of FEF neurons ($n = 129$) to samples presented inside (greens) or opposite (blues) the FEF RF, when the matching target appeared inside (light green, cyan) or opposite (dark green, navy) the FEF RF, aligned to sample image onset (left), target array onset (middle), and onset of the saccade (right). Black lines above the task epoch bars indicate the time windows used for the ROC analysis. Arrowhead on target-aligned plot indicates mean saccadic latency. ***B***, Population histograms for the A_{ROC} reflecting discriminability of neural responses to different image locations (black) and identities (gray) during various task epochs. Arrowheads mark medians of each distribution.

by advancing the electrode within 0–250 μm of the stimulation site (average distance from stimulation site was <150 μm) while monkeys performed the DMS task. FEF neurons with visual activity generally responded to stimuli positioned at the location to which saccades could be evoked with microstimulation (Bruce and Goldberg, 1985). In some experiments, we also measured the visual responses of studied FEF neurons in a memory-guided saccade task to assess the extent of the visual RF. These measurements confirmed that the responses to visual stimuli were stronger at the estimated RF compared with other locations displaced 90° theta. These observations are consistent with previous measurements of the extent of visual RFs in the FEF (Schall et al., 1995; R. Schafer and T. Moore, unpublished observations).

Visual stimuli and behavior. Throughout the experimental session, monkeys were seated in a primate chair, and eye position was monitored with a scleral search coil with a spatial resolution of <0.1° (Armstrong et al., 2006) and was digitized at 100–200 Hz. Monkeys were trained to fixate within a 1.5–3° diameter error window surrounding a central spot (0.4° diameter). The DMS task is depicted in Figure 1*A*. At 250–750 ms after fixation, a colored photo image (5° diameter) was presented for 300 ms (sample period). A delay period of 1014 ms followed the sample offset (delay period), after which two images—one match, one nonmatch—appeared (target period), and the monkey was rewarded for making saccades directly to the match. Monkeys were required to maintain fixation throughout the sample presentation and delay; breaks in fixation before the trial was completed immediately terminated the trial, and these trials were not included in the data analysis. Three images were used in each experimental session, and all three images appeared with equal frequency as the sample/match and the nonmatch. The location of the match was randomized with respect to sample location.

The target array could appear in one of two configurations, with the match and nonmatch appearing in either the two potential sample locations ("aligned" targets) or positions rotated 90° with respect to the sample positions ("orthogonal" targets). In the orthogonal block, once the sample disappeared from the screen, its location was irrelevant for the remainder of the trial: neither match nor nonmatch ever appeared at the sample location, and saccades to that location were not rewarded. To allow maximum familiarity with the block structure, only two blocks were run in each experimental session: target positions were held constant for a block of 200–400 trials and then switched for a second block of similar duration. The order of the aligned and orthogonal blocks was randomized for monkey H, whereas the orthogonal block was always first for monkey S. All sample location, sample/match identity and nonmatch target identity conditions were pseudorandomly interleaved and were controlled by the CORTEX system for data acquisition and behavioral control. During each experiment, the two sample positions were selected so that one stimulus was positioned inside the RF of the FEF site, based on the endpoints of saccades evoked with microstimulation (5–13° eccentricity). Both monkeys were initially trained exclusively on the orthogonal target version of the task and only learned the aligned target version after reaching criterion (70%) performance with the orthogonal targets. All visual stimuli were displayed on a liquid crystal display monitor (52 cm vertical × 87 cm horizontal) positioned 57 cm in front of the monkey, with a refresh rate of 60 Hz. It should be emphasized that stimulus images were not selected in such a way as to either optimize or conclusively prove the existence of object selectivity in the FEF. Any neuron might show greater object selectivity to other pairs of images or less selectivity if controlling for color, shape, or luminance. Shape selectivity in the FEF has been more rigorously demonstrated by Peng et al. (2008), and our observations are consistent with their findings.

Data analysis. All data analysis was performed in MATLAB (MathWorks). Only completed trials were included in the analysis. A criterion level of $p < 0.05$ was used in all statistical analysis; p values not specified were below 10^{-7}. All p values were based on the Wilcoxon's signed-rank test (for paired comparisons) or the Mann–Whitney U test (for unpaired comparisons), unless otherwise specified; all reported average values are the median of the distribution unless otherwise specified. Task responsiveness was determined based on significant effects ($p < 0.05$) in a time × condition two-way ANOVA on the firing rate (FR) of each recorded neuron. Normalized FR histograms were calculated according to the formula $FR(t) = [Rate(t) - Baseline]/(MaxRate - Baseline)$, where Baseline is the average rate during the 200 ms of the fixation period before sample onset, and MaxRate is the maximum across all time points and conditions.

Object and spatial selectivity were quantified using receiver operating characteristic (ROC) analysis (Green and Swets, 1966). ROC analysis was performed on the distributions of neuronal FRs measured during the execution of the DMS task. The areas under ROC curves (A_{ROC}) were used as an index of stimulus discrimination and were calculated as in previous studies (Britten et al., 1992; Armstrong and Moore, 2007). Specifically, we computed the average FR in a moving 100 ms window, during various epochs within the trial. We then computed the probability that the FR in each stimulus condition exceeded a criterion. The criterion was incremented from 0 to the maximum FR, and the probability of exceeding each criterion was computed. Thus, a single point on the ROC curve is produced for each increment in the criterion, and the entire ROC curve is generated from all of the criteria. The area under the ROC curve is a normalized measure of the separation between the two FR distributions obtained with the preferred and nonpreferred RF stimuli and provides a measure of how well the neuronal response discriminates the two stimuli. We also quantified sample position selectivity during the delay period using a location selectivity index (SI), computed as $SI = (FR_{IN} - FR_{OUT})/(FR_{IN} + FR_{OUT})$, where FR_{IN} and FR_{OUT} correspond to the FR of the neuron on trials in which the sample was presented inside and outside of the RF of the FEF site under study, respectively.

Results

We report the activity of 147 neuronal recordings (78 single and 69 multiunit) during the aligned target block of the DMS task. A subset of 113 of these neurons was further studied during the orthogonal target block. Eighteen recordings showed suppression with visual stimulation within the neuronal RF and were excluded from the analysis.

Activity of FEF neurons during the DMS task

The response of a representative example neuron during the object DMS task (Fig. 1*A*) is shown in Figure 1*B*, for samples presented either inside of (Sample In) or opposite (Sample Out) its RF, with the match appearing either inside of (Match In) or opposite (Match Out) the RF. This example neuron illustrates several properties observed in the population response: a visual response to a sample in the RF, sustained delay activity representing the previous sample location, and match location selective activity after target array onset. The visual response to a sample image appearing in the RF was significant whether comparing FRs from 50 to 350 ms after the sample onset to rates during fixation or to the same time period on Sample Out trials (both $p < 10^{-7}$). This sample location selectivity persisted throughout the delay period, with Sample In activity remaining elevated for the period from 250 ms after sample offset until 100 ms before target onset (Sample In FR vs baseline or vs Sample Out, both $p < 10^{-7}$). After target onset, activity reflected the location of the matching target (Match In vs Match Out, $p < 10^{-7}$). Some neurons with no visual response to the sample also exhibited spatially selective delay activity. An example of such a neuron is shown in the bottom panel of Figure 1*B*. The response

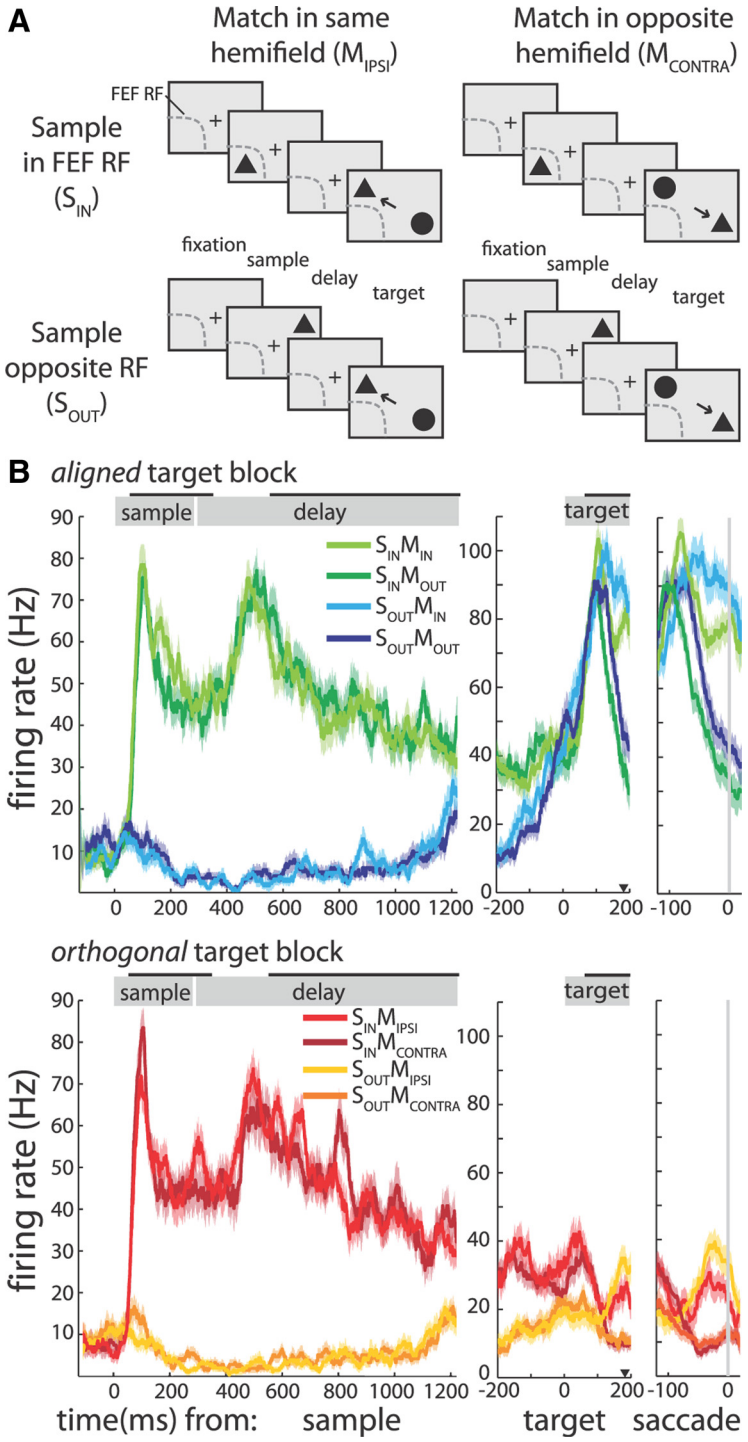

Figure 3. The activity of an example FEF neuron during the aligned and orthogonal blocks. ***A***, Object DMS task, orthogonal target positions: the match and nonmatch images appear at locations rotated 90° from the FEF RF. ***B***, Top, The response of an example neuron to samples in (greens) and out (blues) of the FEF RF during the aligned target block (bright red, yellow: Match In; orange, brick red: Match Out). Bottom, The response of the same neuron during the orthogonal target block (reds, S_{IN}; yellow, orange: S_{OUT}) for targets in the same hemifield as the FEF RF (M_{IPSI}: bright red, yellow) or the opposite hemifield (M_{CONTRA}: brick red, orange). Black lines above the task epoch bars indicate time windows used for statistical analysis. Arrowheads in target-aligned plots mark mean saccadic response.

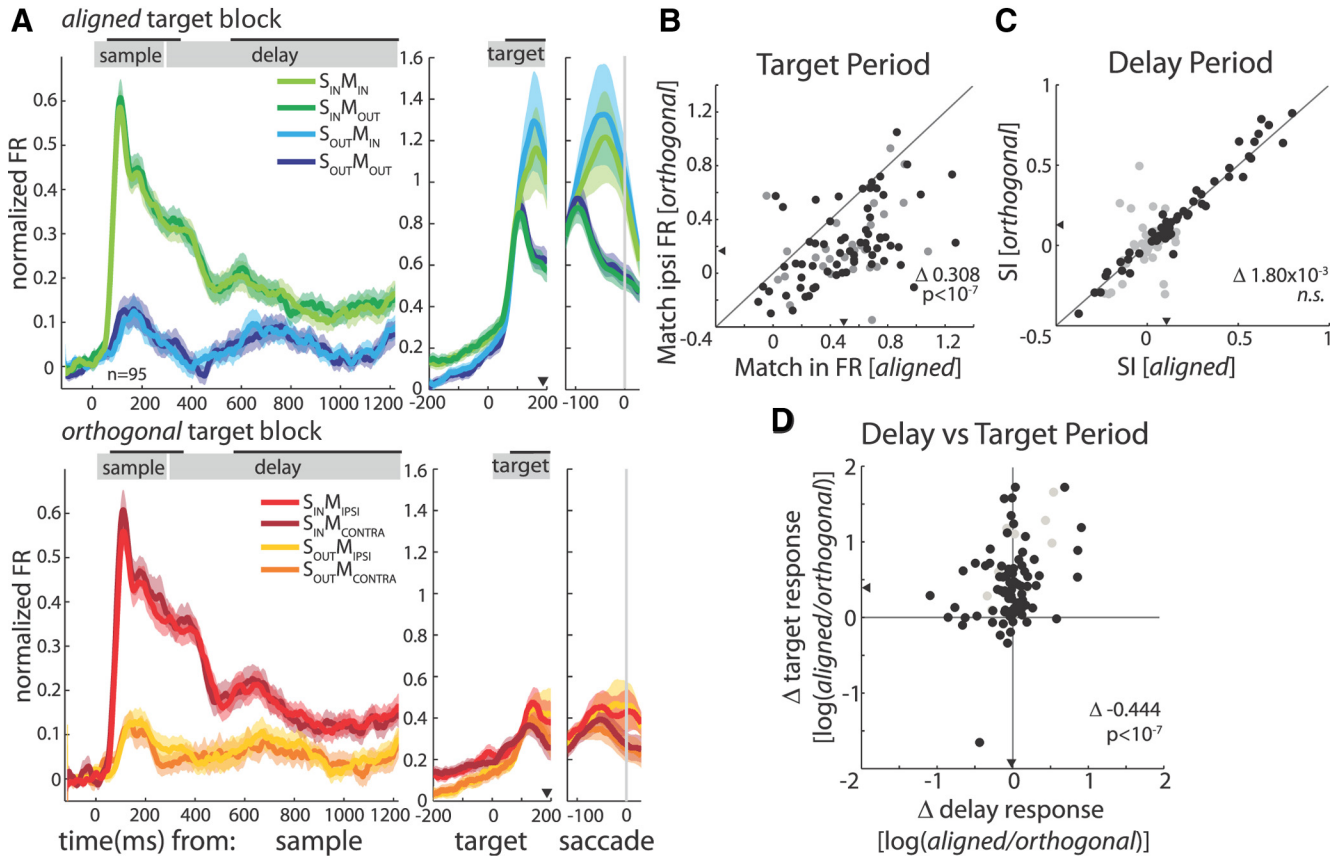

Figure 4. Delay period selectivity was unaltered by change in target positions. ***A***, The response of FEF neurons ($n = 95$) during the aligned block (top) and the orthogonal block (bottom). Conventions are as in Figure 3. ***B***, Target period responses were reduced in the orthogonal compared with the aligned block. ***C***, Sample location SIs during the delay period did not differ for aligned versus orthogonal blocks, for neurons with (black) or without (gray) significant delay period selectivity. ***D***, Change in activity between aligned and orthogonal blocks was greater for the target period than the delay period. Arrowheads mark medians of marginal distributions; Δ values indicate median of (***x–y***) for each point.

of this neuron did not change from baseline when the sample appeared in the RF (Sample In visual response vs baseline, $p = 0.730$). However, after sample offset, the response of the neuron increased and remained elevated in a manner dependent on previous sample location (Sample In delay response vs baseline, $p < 10^{-7}$; Sample In vs Sample Out, $p < 10^{-7}$).

The normalized response of a population of 129 FEF neuronal recordings is shown in Figure 2*A*. As expected, FEF neurons showed selectivity for the location of the sample during its presentation. More importantly, the sample location selectivity persisted throughout the delay period. The distributions of population A_{ROC} areas during different task epochs, reflecting the ability of neurons to discriminate between different sample locations and sample objects, are shown in Figure 2*B–D*. Both object and location information were greatest during the sample period [($ROC_{sample} - ROC_{delay}$); location = 0.153, $p < 10^{-7}$; object = 0.049, $p = 0.0220$], but significant selectivity for these properties persisted during the delay period (location $ROC_{delay} = 0.580$, $p < 10^{-7}$; object $ROC_{delay} = 0.506$, $p = 0.031$). Although there was object selectivity during the delay period, both the magnitude of that selectivity and the proportion of neurons with significant selectivity were less than those for location selectivity during the same period (99 location-selective neurons vs 29 object-selective neurons, Fisher's exact test $p < 10^{-7}$; object ROC_{delay} vs location ROC_{delay}, $p < 10^{-7}$). Delay period location selectivity was not significantly different for cells with and without a visual response ($p = 0.736$). After target array onset, FEF activity reflected both the matching target location (location $ROC_{target} = 0.544$, $p = 7.46 \times 10^{-4}$) and target identity (object $ROC_{target} = 0.544$, $p = 1.35 \times 10^{-4}$).

Delay period activity during the orthogonal target block

The relative positions of sample and target stimuli during the orthogonal block, in which the target positions were rotated 90° with respect to the FEF RF, are shown in Figure 3*A*. The activity of an example neuron during the aligned and orthogonal blocks is shown in Figure 3*B*. As expected given the change in target position, activity during the target period was greatly reduced in the orthogonal block ($p < 10^{-7}$). The critical question was whether the delay period activity would be affected by the change in target position: it was not. The delay period activity of this example neuron did not significantly change between blocks ($p = 0.699$). The population response during aligned and orthogonal target blocks is shown in Figure 4*A* ($n = 95$). As expected, responses to the targets were significantly reduced in the orthogonal block, both for Match In/ipsilateral trials (Fig. 4*B*; aligned block = 0.553, orthogonal block = 0.171, $p < 10^{-7}$) and for Match Out/contralateral trials (aligned block = 0.462, orthogonal block = 0.235, $p < 10^{-7}$). However, delay period selectivity across the population, measured with a location SI, was not significantly different between the aligned and orthogonal target blocks (Fig. 4*C*), either for the population as a whole ($p = 0.812$) or considering only neurons with significant delay selectivity ($n = 64$, $p = 0.961$). Restricting the delay period analysis to neurons with a significant change in target period activity between blocks also did not yield a difference in delay period selectivity ($n = 80$;

Sample In, $p = 0.465$; SI, $p = 0.775$). We considered that, if delay period activity reflects anticipation of the target array, then the change in Sample In activity during the delay period should correlate with the change in target period response for each recording. However, a comparison between blocks revealed that the fractional change in Sample In FR was significantly greater during the target period than during the delay period [Fig. 4*D*; log(aligned/orthogonal), target period = 0.390, delay period = -5.10×10^{-3}, target vs delay, $p < 10^{-7}$]. The fractional change in activity between aligned and orthogonal blocks was still significantly larger during the target period than during the delay period when limiting the analysis to neurons with significant delay period selectivity [log(aligned/orthogonal), delay period = −0.0119, target period = 0.370; target vs delay, $p < 10^{-7}$]. Thus, delay period activity reflected sample location independent of the upcoming target array position.

Pre-target activity

Delay period selectivity was statistically identical between aligned and orthogonal blocks. However, within a brief window before target onset, FEF activity reflected the location of the upcoming target array. This "pre-target" period began 100 ms before target onset and continued until the onset of the earliest visual response (50 ms after target onset). As shown in Figure 5*A*, during the pre-target period there was increased activity in the aligned block compared with the orthogonal block. This target position-dependent difference in activity was observed regardless of previous sample location (aligned vs orthogonal block; Sample In, $p = 1.61 \times 10^{-5}$; Sample Out, $p = 0.0013$; average across sample positions shown in Fig. 5*B*). We examined the magnitude of this pre-target activity over the time course of the aligned and orthogonal blocks to see whether it was affected by familiarity with the target locations. An ANOVA comparing pre-target activity across trials within a block showed a significant effect of neuron and aligned versus orthogonal block ($p < 10^{-7}$) but not of trial ($p = 0.885$). Furthermore, a significant effect of target position on pre-target period FRs was detected within the first 10 trials of each block ($p = 0.0407$), suggesting that monkeys quickly transitioned between the target position expectations of the two blocks. Delay period selectivity was likewise present in these early trials within a block and statistically indistinguishable from that seen in the remainder of the block (delay SI for first 20 trials vs remainder; orthogonal block, $p = 0.911$; aligned block, $p = 0.588$).

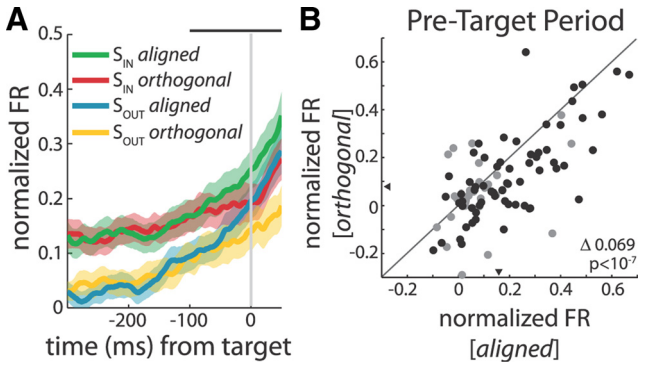

Figure 5. Pre-target activity anticipates target positions. ***A***, Pre-target activity of FEF neurons during the aligned (green, blue) and orthogonal (red, yellow) blocks, when the sample appeared inside (green, red) or opposite (blue, yellow) the FEF RF. Black bar shows analysis window used in ***B***. ***B***, Pre-target activity (−100 to +50 ms relative target array onset) was greater for the aligned block than the orthogonal block. Two outliers were excluded from the plot. Arrowheads mark median marginal distribution values for the population with significant delay selectivity ($n = 67$, black; nonsignificant delay activity in gray).

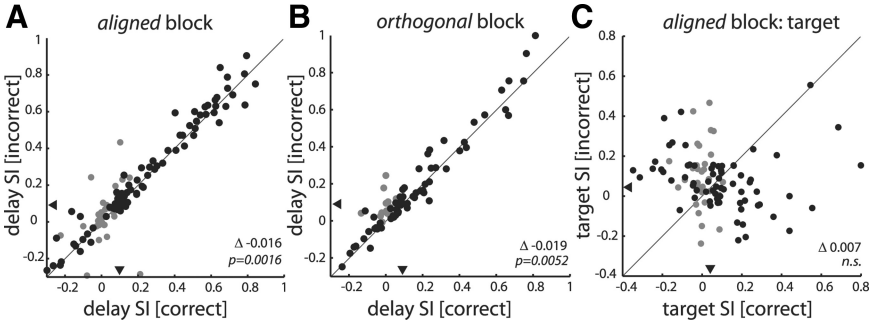

Figure 6. Delay (***A***, ***B***) and target (***C***) activity on correct vs incorrect trials. ***A***, Delay SIs were larger on incorrect trials for the aligned block ($n = 109$). ***B***, Delay SIs were larger on incorrect trials for the orthogonal block ($n = 83$). Neurons with significant delay selectivity in black. ***C***, Target SI was unaltered for incorrect trials ($n = 103$), for neurons with (black) or without (gray) significant target selectivity. Arrowheads mark marginal medians; two outliers omitted from the plot in ***C***. Δ values indicate median of (correct SI − incorrect SI) for each point.

Delay and target period selectivity on error trials

The delay period selectivity observed in both the aligned and orthogonal target blocks varied with performance. Overall, there was higher delay period selectivity on error trials than on correct trials (Fig. 6*A*,*B*). Using recordings with at least five incorrect trials of each type, delay SIs were found to be significantly larger on error trials for both the aligned block (Fig. 6*A*; $n = 109$, $p = 1.57 \times 10^{-3}$; $n = 76$ with paired orthogonal recordings, $p = 2.91 \times 10^{-3}$) and the orthogonal block (Fig. 6*B*; $n = 83$, $p = 5.23 \times 10^{-3}$). The magnitude of the difference in SIs between correct and error trials did not significantly differ for the aligned versus orthogonal block for either the population as a whole ($n = 76$ neurons with sufficient incorrect trials in both blocks; change in SI, correct − incorrect; aligned block = −0.0173, orthogonal block = −0.0188; $p = 0.864$) or neurons with significant delay selectivity ($n = 51$, $p = 0.708$). No such reduction in SI was observed during the visual responses (orthogonal block, $p = 0.482$; aligned block, $p = 0.125$). In the aligned block, target period activity often reflected target location (as shown in Fig. 2*B*). We examined the target location selectivity of the FEF for correct versus error trials, in which target selectivity on error trials indicates higher activity when the matching target appears in the RF (as opposed to indicating the direction of the saccade). We found that target selectivity across the population was the same for error trials (Fig. 6*C*; $n = 103$ neurons recorded during experiments with sufficient incorrect trials to perform analysis, $p = 0.265$; $n = 85$ neurons with significant target location selectivity, $p = 0.731$). Pre-target anticipatory activity was likewise unaltered on error trials [(aligned − orthogonal) for correct trials vs incorrect trials; Sample In, $p = 0.804$; Sample Out, $p = 0.959$]. Despite the irrelevance of sample location to task performance, sample location information was maintained throughout the delay period, and the magnitude of that spatially selective delay activity was correlated with performance in both the aligned and orthogonal versions of the task.

Discussion

FEF neurons encoded sample position throughout the delay period of an object-based short-term memory task, despite the irrelevance of sample location for task performance. Furthermore, neurons continued to encode sample position in a variant of the

task in which the matching stimulus never appeared in their RF, confirming that FEF maintains sample location independent of subsequent behavioral relevance. FEF neurons also exhibited target-position-dependent activity before target onset, suggesting that the monkeys anticipated target position within blocks. The persistence of this spatial information in the FEF during an object memory task is consistent with an involvement of spatial information in the maintenance of object memory.

Persistent representation of sample location during the delay period

The sample-location selectivity exhibited by FEF neurons during the aligned block is inconsistent with a pure "saccade probability" or "upcoming sensory discrimination" account of FEF activity (Basso and Wurtz, 1998; Zhou and Thompson, 2009). Because the probability of a potential target appearing in the RF (100%) and the probability of making a subsequent eye movement to that location (50%) were identical for Sample In and Sample Out trials, this persistent spatial activity represents at minimum an interaction between previous history and upcoming expectations. Furthermore, the fact that this selectivity was unaltered during the orthogonal block, when the location represented by the maintained activity was never a potential target location, confirms that the delay selectivity was independent of the relevance of that location to subsequent behavioral responses.

Anticipatory activity before target onset

The presence of a target-position-dependent difference in activity during the pre-target period of the aligned versus orthogonal blocks suggests that monkeys anticipated the target positions in the two blocks. This result also confirms that the absence of differential activity between blocks during the delay period did not result from a lack of statistical power. The anticipatory pre-target activity may reflect the allocation of attention to an upcoming sensory discrimination, or motor preparation toward the location of a future saccadic target, or both. An increase in activity later in the delay, in anticipation of target onset, has been observed previously in middle temporal area MT during a motion memory task (Bisley et al., 2004), in which it likewise occurs across the population regardless of the prior contribution of the neuron to the representation of the sample stimulus. The early emergence of anticipatory activity during the pre-target period, significant within the first 10 trials of each block, suggests that monkeys were quickly able to anticipate the different target positions within blocks. However, this change in anticipated target position does not affect the spatially selective delay activity.

Correlation between delay activity and performance

Although neurons in some areas of PFC have been reported to represent only behaviorally relevant stimulus properties (Rainer et al., 1998; Everling et al., 2006), we found that location information, in the form of spatially selective delay period activity, was maintained despite its irrelevance for correctly selecting the Match in the target array. The maintenance of spatial information during an object-based task, a task in which correspondence between sample and match location need not be remembered for correct performance, raises the question of whether that information actually contributes to performance. Regardless of whether the maintenance of spatial information occurs "by default" or reflects a strategy by the monkey, one can ask whether that maintenance relates to performance. We found that, despite the irrelevance of sample location to task performance, the magnitude of spatially selective delay activity was nonetheless correlated with performance in both the aligned and orthogonal versions of the task. Spatial selectivity was elevated for error trials compared with correct trials. This result might indicate that any maintenance of sample location information is detrimental to task performance, or it may be indicative of a more complex relationship between the maintenance of spatial and object signals during short-term memory. For example, there may be an optimal level of spatial information maintenance during object memory such that, at suboptimal levels, spatial and object maintenance are positively correlated and, at supraoptimal levels, they are negatively correlated. At the very least, the fact that the maintenance of spatial information correlates at all with memory performance seems to indicate that such maintenance is not independent of object memory.

Implications for object memory maintenance

The ability of spatial retro-cues to protect remembered objects from degradation during memory maintenance suggests that a spatial signal can modulate object representations within short-term memory (Griffin and Nobre, 2003; Matsukura et al., 2007; Makovski et al., 2008; Theeuwes et al., 2011), and some behavioral evidence suggests that short-term sensory memory is stored in a spatially specific manner (Zaksas et al., 2001). In this case, rather than location and object information being stored completely independently, maintenance of a spatial "tag"—whether voluntary or automatic—may contribute to maintaining an associated object representation within memory. A second way in which spatial signals may influence object representations in memory is proposed by the "feature binding theory" of object vision. The feature binding theory posits a special role for spatial attention in creating associations among different features of an object during visual perception, "binding" separate features, such as color, shape, size, etc., into a unified object representation (Treisman and Gelade, 1980; Treisman and Schmidt, 1982). It has also been suggested that spatial attention is required to maintain these bindings during short-term memory (Wheeler and Treisman, 2002; Treisman and Zhang, 2006). A role for spatial attention in maintaining feature bindings in short-term memory is supported by the finding that attentive tracking during memory maintenance selectively interferes with memory for feature bindings (Fougnie and Marois, 2009). The "retro-cuing" effect suggests that a spatial signal during object memory could contribute to performance, whereas the feature binding theory predicts that such a spatial signal is necessary to maintain object bindings. Given that the FEF has been widely implicated in the control of spatial attention (Moore, 2006), one might speculate that the persistent signaling of spatial information by FEF neurons during object-based short-term memory suggests a role for spatial attention in maintaining object memory. Nonetheless, future experiments will need to test the causal role of the observed persistent spatial signal in object memory and the relationship of that signal to attention.

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