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Activity of Neurons in Cortical Area MT During a Memory for Motion Task

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Bisley, James W., Daniel Zaksas, Jason A. Droll, and Tatiana Pasternak. Activity of neurons in cortical area MT during a memory for motion task. *J Neurophysiol* 91: 286–300, 2004. First published October 1, 2003; 10.1152/jn.00870.2003. We recorded the activity of middle temporal (MT) neurons in 2 monkeys while they compared the directions of motion in 2 sequentially presented random-dot stimuli, sample and test, and reported them as the same or different by pressing one of 2 buttons. We found that MT neurons were active not only in response to the sample and test stimuli but also during the 1,500-ms delay separating them. Most neurons showed a characteristic pattern of activity consisting of a small burst of firing early in the delay, followed by a period of suppression and a subsequent increase in firing rate immediately preceding the presentation of the test stimulus. In a third of the neurons, the activity early in the delay not only reflected the direction of the sample stimulus, but was also related to the range of local directions it contained. During the middle of the delay the majority of neurons were suppressed, consistent with a gating mechanism that could be used to ignore task-irrelevant stimuli. Late in the delay, most neurons showed an increase in response, probably in anticipation of the upcoming test. Throughout most of the delay there was a directional signal in the population of MT neurons, manifested by higher firing rates following the sample moving in the antipreferred direction. Whereas some of these effects may be related to sensory adaptation, others are more likely to represent a more active task-related process. These results support the hypothesis that MT neurons actively participate in the successful execution of all aspects of the task requiring processing and remembering visual motion.

INTRODUCTION

The integration of sensory processing and working memory is fundamental to behavior, yet little is known about the underlying neural mechanisms. In the hierarchy of visual processing, the early cortical areas are involved in sifting and identifying various attributes of visual stimuli, whereas higher levels, such as prefrontal cortex, have been implicated in active storage of such information (Asaad et al. 2000; Fuster and Alexander 1971; Miller and Desimone 1994). However, the exact roles of intermediate visual cortical areas remain unclear, despite mounting evidence that visual processing and working memory are mediated by a distributed network of neurons (for review see Fuster 1995b; Goldman-Rakic 1995; Miller and Cohen 2001).

The middle temporal (MT) area is a midlevel region in primate cortex thought to be a major site of visual motion processing in the primate brain (for recent review see Pasternak et al. 2003). Its neurons have been shown to play a role in a number of behavioral tasks involving motion discrimination (Bisley et al. 2001; Britten et al. 1992, 1996; Ditterich et al. 2003; Nichols and Newsome 2002; Salzman et al. 1992) and their loss results in deficits in motion perception (for recent review see Merigan and Pasternak 2002). Recently, a series of studies used psychophysical (Pasternak and Zaksas 2003; Zaksas et al. 2001), microstimulation (Bisley et al. 2001), and lesion (Bisley and Pasternak 2000) approaches to examine the role of MT in the performance of working memory tasks involving visual motion. These studies provided evidence that MT neurons may be involved not only in processing of visual motion but also in its temporary storage.

The present study examined the activity of MT neurons during a match-to-sample task. We were particularly interested in neuronal activity during the memory period and whether this activity reflects the properties of the remembered stimulus. We recorded from MT neurons while monkeys compared the directions of motion of 2 stimuli, sample and test, separated by a brief delay. We found that the activity of many MT neurons did not return to baseline during the delay. Rather, they showed a characteristic pattern consisting of a small burst of activity early in the delay, followed by a period of suppression and subsequent increase in firing rate. The activity throughout most of the delay, but especially in the early delay, was directionally biased in a way that could not be entirely explained by adaptation. Together with previous studies, these data suggest that MT neurons both process the information about visual motion and may be involved in the circuitry supporting temporary storage of this information.

METHODS

Subjects

Recordings were performed in 2 adult macaque monkeys (*Macaca nemestrina*) weighing about 8 and 9 kg. On weekdays, water was restricted for a period of 22 h before testing and the daily water ration, in the form of a fruit drink, was provided during the behavioral testing. On weekends, the monkeys were not tested behaviorally and received 100 ml/kg water per day. Food was continually available in the home cage and monkeys received supplements of fresh fruit and vitamins daily. Body weights were recorded at least 3 times/wk to ensure good health and normal growth. The monkeys were implanted with scleral search coils and head-restraint devices to monitor their eye position, and had recording cylinders placed above the superior temporal sulcus (STS). Before the present study, these monkeys were tested on a variety of visual discrimination tasks involving random-dot stimuli. The results of these measurements have been published elsewhere (Bisley et al. 2001; Pasternak and Zaksas 2003; Zaksas et al. 2001). Experiments were carried out in accordance with the guidelines published in the National Institutes of Health Guide for the Care and Use of Laboratory Animals (National Institutes of Health publi-

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cation no. 86-23, revised 1987) and were approved by the University of Rochester Committee for Animal Research.

Stimuli

Visual stimuli were presented on a video display (76-Hz frame rate) located 42 cm in front of the monkey. The random-dot stimuli were identical to those used in previous studies (Bisley and Pasternak 2000; Rudolph and Pasternak 1999) and consisted of dots placed randomly within a circular aperture, the size of which was matched to the receptive field size of the recorded neuron. Each dot was displaced by a constant step size (Δx) and temporal interval ($\Delta t = 13$ ms). The lifetime of an individual dot was equal to the duration of the stimulus presentation (500 ms) and in each frame the dots moved independently in any direction chosen at random from a uniform distribution. This distribution could range from 0° (all the dots moving in parallel) to 360° (only random motion; see Fig. 1*A*). This value is termed the *direction range* of the stimulus. The dots, viewed at a distance of 42 cm, were 0.03° in diameter, and their luminance was set about 3.5 log units above human detection threshold. Optimal dot density and speed were determined for a given neuron and those values were used during behavioral testing. The dot densities ranged from 2 to 5 dots/deg^2 and the velocities varied from 3°/s ($\Delta x = 0.03$) to 35°/s ($\Delta x = 0.45$).

Behavioral paradigm

We used a version of a working memory task, first introduced by Konorski (1959), in which the monkeys compared the directions of 2 moving stimuli separated by a delay and reported them as the same or different. The monkeys initiated each trial by fixating a small spot for 1,000 ms within a 1.5° window. Two random-dot stimuli, the *sample* and *test*, then appeared sequentially, separated by a 1.5- or 3-s delay (Fig. 1*B*). Both the sample and test stimuli were presented within the receptive field for 500 ms. After the termination of the test, the monkeys had 3 s to respond by pressing one of 2 buttons—signaling either that the net direction of motion was the same or opposite in the 2 stimuli. On each trial, the direction range of the sample was selected at random from 4 values (usually 0, 150, 300, and 360°), keeping performance at approximately 80% correct. The test stimulus always consisted of coherently moving dots (0° range) that moved in either the same or the opposite direction. Because most of the analysis was performed on trials containing a coherently moving sample stimulus (0° range) the number of such trials was maximized by presenting them twice as often as the other 3 range values. On trials with the 360°-range sample (i.e., that with no net direction of motion) the animals were rewarded at random.

Surgical procedures

After the monkeys had learned the basic behavioral task, they received scleral search coils and head-restraint devices for monitoring eye position (Remmel 1984). For all surgical procedures, which were performed under aseptic conditions, the animals were initially anesthetized with ketamine hydrochloride (15 mg/kg intramuscularly) and maintained with 3% isoflurane. Craniotomies were made over parietal cortex and a commercial recording chamber (Crist Instruments, Hagerstown, MD) was implanted. The chamber was 20 mm in diameter and was attached to the skull by a ring of bone cement anchored by 6 to 8 titanium screws evenly distributed around the craniotomy. The chamber was placed above the STS, allowing a dorsal approach to MT. The precise location and shape of the STS for each monkey was determined from T2-weighted magnetic resonance images (MRIs) obtained in 2- and 1.5-T GE magnets with a small surface coil. This procedure was described in detail previously (Bisley and Pasternak 2000; Rudolph and Pasternak 1999). Briefly, the monkeys were anesthetized with sodium pentobarbital (25 mg/kg intravenously), and placed in a specially constructed MRI-compatible stereotaxic frame.

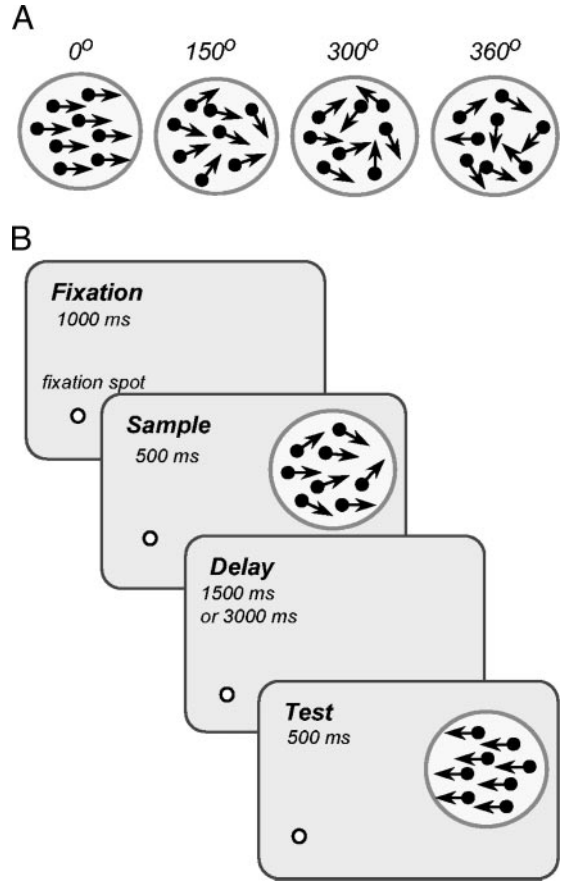

FIG. 1. *A*: direction range stimuli. During each session the sample stimulus consisted of random dots with one of the 4 direction ranges chosen at random from trial to trial. Direction range threshold was measured during each session. *B*: behavioral task. On each trial, the monkeys compared the direction of motion of 2 sequentially presented stimuli, the sample and test, separated by a delay. To initiate a trial, the animal had to fixate a small spot for 1,000 ms, after which the first visual stimulus (the sample) was presented for 500 ms, followed by a delay (usually 1,500 ms) at the end of which the second stimulus (the test) was presented for 500 ms. At the end of the trial the monkeys indicated whether the 2 stimuli moved in the same or different directions by pressing one of 2 response buttons. The sample stimulus was composed of dots moving within a predetermined range of directions (shown in *A*) producing a net direction of motion in one of 2 opposite directions or 4 orthogonal directions. One of the directions always matched the preferred direction of the middle temporal (MT) neuron. Dots in the test stimulus moved coherently in the direction that was either the same as or opposite to the direction of motion in the sample. Monkeys were required to maintain fixation throughout the duration of the trial.

Coronal and horizontal scans were performed with the following parameters: TE/TR: 5,000/90 or 3,000/85; 1.5-mm-thick slices 0.2 mm apart; 256 × 256 array, field of view: 10 or 15 cm.

Electrophysiological recordings

MAPPING AND CHARACTERIZATION OF RECEPTIVE FIELDS. Single-unit activity was recorded through tungsten microelectrodes (1.5–5.0 MΩ; FHC). The electrode was inserted through a guide tube positioned in a grid (Crist et al. 1988). Once a neuron was identified and well isolated, the position and size of its receptive field was mapped first by hand with a patch of random dots while the monkey passively viewed a fixation stimulus (a small cross) for variable periods of time ranging from 2 to 8 s. The optimal speed, dot density, and preferred direction were then determined with coherently moving random dots by selecting the parameters that produced maximal firing rates. A

direction-selectivity profile was then generated by moving the random-dot stimulus at an optimal speed and with optimal dot density at least 5 times in each of the 4 cardinal and 4 oblique directions. Responses to each of these 8 directions were used to compute a vector average and the resulting direction was taken as the preferred direction of the cell. In about one third of the behavioral testing sessions, the sample stimulus could move in the preferred, the antipreferred (directly opposite to the preferred), or either of the 2 orthogonal directions. In the remaining sessions, possible sample directions were limited to the preferred and the antipreferred directions. Here, we examine only the data collected from the preferred and antipreferred directions. For each cell 8–30 trials were collected for each mean direction and for each direction range.

BASELINE ACTIVITY. Baseline activity was measured on each trial during the last 500–800 ms of the period of fixation preceding the presentation of the sample stimulus. It was averaged and used to evaluate neuronal activity (see example neurons in Fig. 2).

Data analysis

Action potentials during the trial were discriminated using a BAK Dual Window Discriminator and pulses were time stamped and stored together with information about the current stimulus using custom-made software. Only well-isolated single units with an absolute refractory period were used for analysis that was performed using MATLAB (Mathworks).

For all statistical tests the firing rates recorded during the trial were compared with the baseline rates recorded throughout the session. Activity recorded during each testing session was visualized by convolving the raw data into spike density functions (SDFs) with a sigma of 15 ms (Richmond et al. 1987). These SDFs were used for visual inspection only and were not used in the subsequent analysis of firing rates. The rate of activity at different stages of the task was analyzed by computing the mean number of action potentials over a given epoch in repeated presentations. For stimuli with a net direction of motion, only correct trials were used in analysis unless otherwise stated. For 360°-direction range stimuli, all trials were included in analysis.

RESPONSES DURING SAMPLE AND TEST STIMULI. Responses to the visual stimuli were computed by averaging the activity during a 400-ms epoch of stimulus presentation that excluded the initial period of visual latency. The latency was calculated for each neuron, as follows. A threshold level was determined by computing the mean + 2SDs of the baseline activity and then sliding a 50-ms window in 1-ms steps along the spike train starting at stimulus onset. The response latency was defined as the midpoint of the 50-ms epoch in which the mean firing rate reached the threshold. For each neuron, a conventional direction selectivity (DS) index was computed on the basis of the response to the random-dot stimuli coherently moving in the preferred and antipreferred directions

$$DS = 1 - \frac{R_A - \text{Baseline}}{R_P - \text{Baseline}}$$

where R_A is the activity following the antipreferred direction and R_P is the activity following the preferred direction.

ROC ANALYSIS. To determine whether activity during the delay contains information about the direction of the preceding sample, we used a receiver operating characteristic (ROC) based analysis (Britten et al. 1992). This analysis computes the probability that an ideal observer could report the direction of motion in the sample based solely on the activity during the delay. We will refer to this as the

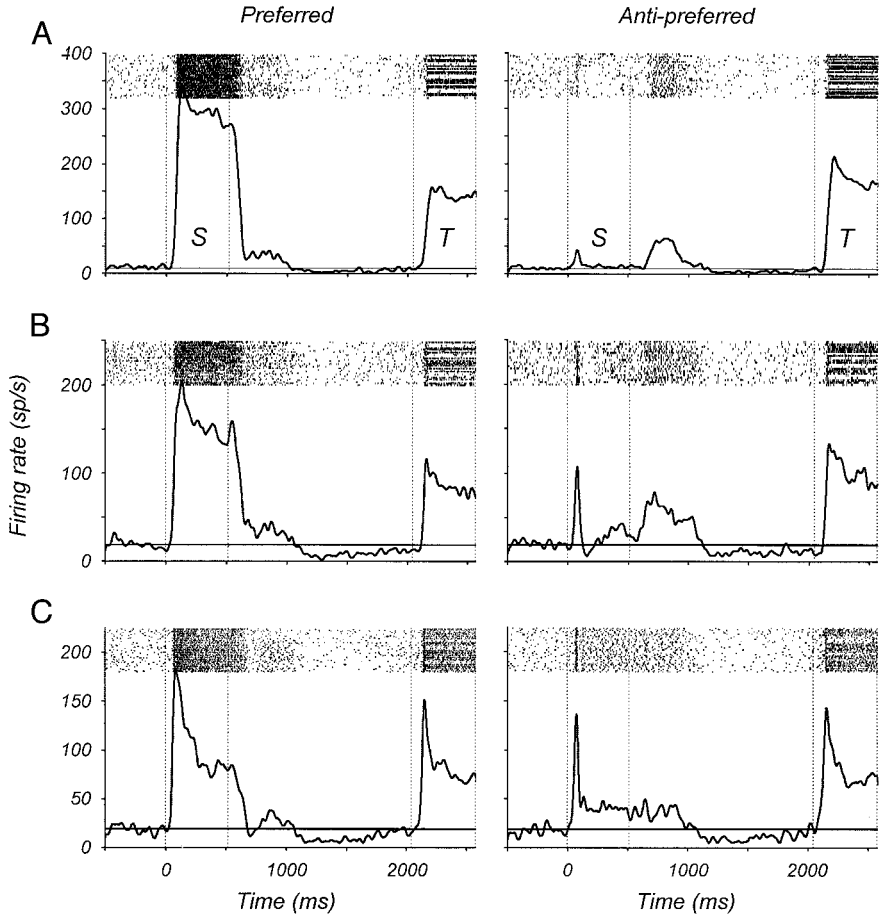

FIG. 2. Example data from 3 recording sessions. Average activity recorded during the session is shown as a spike density function. Sample (*S*) and test (*T*) times are bounded by the vertical dotted lines. Trials in which the sample moved in the preferred (*left column*) and antipreferred (*right column*) directions are shown separately. Baseline activity was recorded during the period of fixation preceding each sample presentation. Average baseline activity is indicated by a horizontal black line and its thickness represents ±SE. Rasters for each condition are shown at the top of each graph. Only the data for the coherently moving sample (direction range, 0°) are shown. Because the test stimulus could move in the preferred or antipreferred direction, activity during the test is an average of responses to the 2 directions.

direction discrimination probability (DDP). We performed this analysis on consecutive 100-ms epochs. For each epoch an ROC curve was created by setting 12 threshold levels of activity covering the range of firing rates that followed the 2 directions of motion. For each threshold level the probability that the sample stimulus had moved in the preferred or antipreferred direction was calculated. To this end, we asked what proportion of the trials for each direction showed activity greater than the threshold. These data were plotted creating an ROC curve, with the area under the curve representing the DDP. A DDP of 0.5 indicates no difference in the distribution of responses in that epoch following the 2 directions. A value of 1 indicates that the activity following the preferred sample was always higher than the highest activity following the antipreferred sample, and a value of 0 indicates that the activity following the preferred sample was always lower than the lowest activity following the antipreferred sample.

To test the significance of each DDP value we ran a permutation test. This was done by randomly distributing all the trials from a single epoch for a single neuron into 2 groups, independent of the actual sample direction. These groups were nominally called the *preferred group* and *antipreferred group* and contained the same number of trials as the experimentally obtained groups. The DDP was calculated from the redistributed data, and the procedure was repeated 2,000 times, creating a distribution of DDPs. We then determined where in the distribution the actual DDP lay (the *P* value). Values in the top or bottom 2.5% were defined as significant (i.e., $P < 0.05$, 2-tailed test).

ANALYSIS OF ACTIVITY DURING THE DELAY. Analysis of delay activity was performed by dividing the delay into 4 epochs: 200–400, 600–800, 1,000–1,200, and 1,300–1,500 ms and calculating the mean number of action potentials that occurred during each of the epochs.

RESULTS

We recorded the activity of 197 neurons from 2 monkeys. The majority of these neurons (90%) were strongly direction selective with DS values ranging between 0.47 and 1.23. For the entire population, the mean DS was 0.78 (±0.02, SE) and the median was 0.87. These values and their distribution are very similar to those previously reported for MT (Britten et al. 1992; Maunsell and Van Essen 1983). The receptive field sizes increased with eccentricity from about 2° near the fovea to 10° at 23° eccentricity. Linear regression through all the data gave a slope of 0.44 with an intercept of 1.76 ($R^2 = 0.54$). These properties are consistent with those reported previously in MT cells (e.g., Albright and Desimone 1987; Desimone and Ungerleider 1986).

Figure 2 shows activity from 3 example neurons. Trials in which the preferred (*left plots*) or antipreferred (*right plots*) directions were presented during the sample are shown separately. In these examples all trials for each sample direction are shown, and for that reason the activity seen during the test period of the task reflects responses to both the preferred and antipreferred directions.

As is true of most MT neurons, responses were strong to a coherent stimulus moving in the preferred direction (sample responses in *left plots*), and low or suppressed when the antipreferred stimulus was presented (sample responses in *right plots*). The activity of these neurons recorded during the delay is representative of many neurons in our population. They show a short period of increased activity in the first third of the delay. Often this response was composed of a discrete burst of activity (Fig. 2*A*, *right plot*; Fig. 2*C*, *left plot*). After this early activity, many neurons showed a period of suppression during the middle of the delay and a slight increment in response toward the end. A striking feature of the activity recorded during the delay is the difference in the strength of the early delay activity following the preferred and antipreferred directions; often being greater following the antipreferred than the preferred direction.

Responses during stimulus presentation

SAMPLE: DIRECTION RANGE. Figure 3 illustrates responses of MT neurons to stimuli containing a range of local directions. The average stimulus response functions for the 162 neurons tested with the 4 standard direction ranges (0, 150, 300, and 360° range) are shown for stimuli moving in the preferred (solid circles) and antipreferred (open circles) directions. As the direction range in the sample increased, responses to the sample stimulus moving in the preferred direction decreased and responses to the sample moving in the antipreferred direction increased. Note that the neurons retained strong directional selectivity over a broad range of local directions, which decreased only when the direction range approached the level of a typical psychophysical threshold (i.e., over 320°; Bisley and Pasternak 2000).

COMPARISON OF RESPONSES TO SAMPLE AND TEST STIMULI. Our behavioral task consisted of 2 types of trials: sample and test stimuli moved either in the same or in opposite directions. During the "same" trials that contained a coherently (0° range) moving sample, the test stimulus was identical to the sample but the behavioral requirements during the presentation of sample and test were different. During the sample, the animal's task was to encode and identify the direction of stimulus motion. On the other hand, during the test the task was more complex: the monkey had to process the current visual stimulus, compare it to the remembered sample, make a decision, and plan a response. To determine whether the differences in the behavioral requirements during the presentation of the sample and test were reflected in the response of MT neurons we compared neural responses during the 2 phases of the task. We found no significant differences in activity for either direction ($P > 0.05$, paired *t*-test). Furthermore the responses to the sample and the test were nearly identical both when they moved in the preferred direction (linear regression of test response as a function of sample response gave a slope of 0.99 and an intercept shift of 0.47; $R^2 = 0.97$) and when

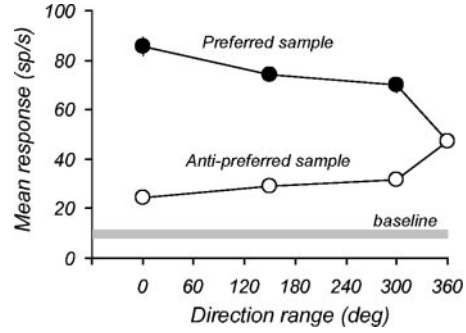

FIG. 3. Effect of direction range on responses of MT neurons. Mean responses recorded during the presentation of the sample are plotted against the direction range of the sample (see stimuli in Fig. 1*A*). For the 360°-range sample, data were randomly assigned to one or the other direction. Error bars (SE) are generally smaller than the size of the symbols. Thickness of the baseline (gray) line includes the means ± SE.

they moved in the antipreferred direction (slope: 0.93, intercept: 1.30, $R^2 = 0.97$).

We also assessed whether the response to the test was affected by the direction of the preceding stimulus. This was done by comparing responses to the test stimulus from trials in which the test direction either matched or did not match the direction of the sample. We found that following the preferred sample, responses to the test moving in the preferred direction were slightly, but significantly, smaller than after the antipreferred sample (means: 96.3 and 98.1 spikes/s; $P < 0.05$, paired *t*-test). This was also the case for the antipreferred test; it was slightly lower following preferred direction than following the antipreferred direction (means: 27.9 and 28.7 spikes/s; $P < 0.05$, paired *t*-test). The response to the antipreferred test following the preferred sample was also significantly lower than the response to the antipreferred sample ($P < 0.05$, paired *t*-test), suggesting that this effect is likely to represent a decrease in the neuronal response, rather than an increase related to the match between the directions of the test and sample stimuli. This effect is consistent with a weak adaptation effect (Van Wezel and Britten 2002).

Activity of MT neurons during the delay

PATTERN OF DELAY ACTIVITY. The examples in Fig. 2 illustrate the behavior of many MT neurons. They show that after the offset of the response to the sample activity did not return to baseline and remain there until the presentation of the test. Rather, it displayed a characteristic pattern with an early period of activation, followed by suppression and then by a subtle increase in firing shortly before the onset of the test stimulus. To examine the incidence of these features, we divided the delay into 4 equal epochs: 200–400, 600–800, 1,000–1,200, and 1,300–1,500 ms. The first 200 ms of the delay were excluded from the analysis, based on the observation that responses of MT neurons to visual stimuli often persist for about 100–150 ms after the stimulus (Britten and Heuer 1999). The epoch of 200–400 ms was chosen because it includes most of the activity bursts seen early in the delay. The second and third epochs were chosen primarily to investigate the suppression during the middle of the delay. The last epoch, the period immediately preceding the onset of the test stimulus, was chosen to examine the apparent increase in firing rate in a large proportion of neurons.

Figure 4 compares the firing rates of individual neurons to the baseline activity recorded during the fixation period, in the 500–800 ms preceding the sample. Activity following the preferred (*left plots*) and antipreferred (*right plots*) samples is plotted separately for each of the 4 epochs. The plots show that the activity of many neurons deviate from baseline with points scattered both above and below the unity line. During the early epoch (200–400 ms) the majority of cells showed excitation with firing rates above the baseline, whereas in the middle of the delay (600–800 and 1,000–1,200 ms) the activity of many neurons was suppressed, dropping below baseline. Toward the end of the delay, the population returned to a slightly more excited state. Each of these patterns was significant at the population level ($P < 0.005$, paired *t*-test).

Figure 5 shows that this pattern holds when we plot the incidence of neurons with significant excitation and suppression encountered during each of the 4 epochs. Activity was considered as excitation or suppression if it was significantly higher or lower than the baseline measured during the same block of trials ($P < 0.0125$, Bonferroni corrected 2-tailed *t*-test). The *top plot* shows that significant excitatory activity was most prevalent during the early delay. Its incidence decreased drastically during the 2 middle epochs of the delay and increased again at the end of the delay. In contrast, the incidence of suppression was maximal in the middle of the delay and relatively low at the start and the end of the delay. Thus whereas early and late in the delay the majority of active neurons showed excitation, suppression dominated the middle portions of the delay.

Because the activity of many neurons deviated from baseline during the delay we were interested in knowing to what extent

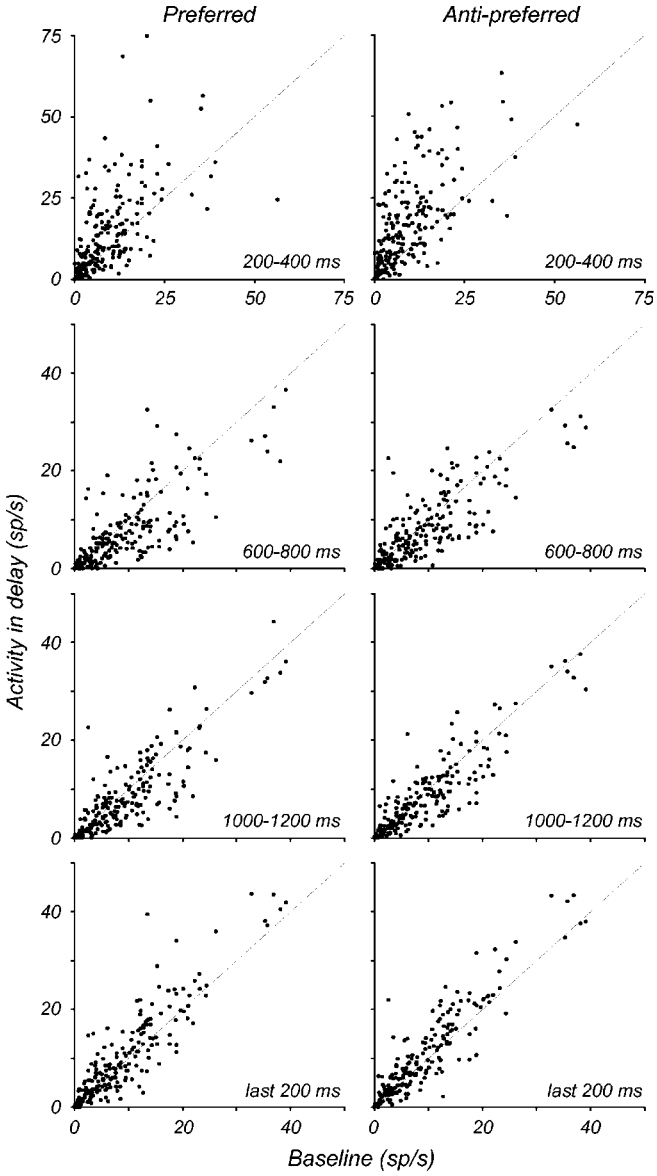

FIG. 4. Comparison of activity recorded during the delay to baseline activity. Activity was recorded from 197 MT neurons during 4 consecutive periods of the 1,500-ms delay following the sample moving in the preferred (*left plots*) and antipreferred (*right plots*) directions. Baseline activity was recorded 500–800 ms before the appearance of the sample. Activity is shown for the 4 epochs in the delay: early (200–400 ms), middle (600–800 and 1,000–1,200 ms), and late (1,300–1,500 ms).

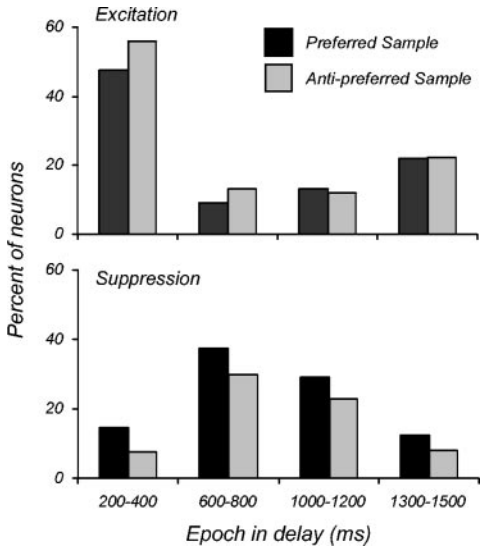

FIG. 5. Incidence of significant excitation and suppression during the delay. Proportions of neurons showing excitation (*top plot*) and suppression (*bottom plot*) during the 4 epochs in the delay: early (200–400 ms), middle (600–800 and 1,000–1,200 ms), and late (1,300–1,500 ms). Activity following the preferred (black columns) and antipreferred (gray columns) direction is shown separately. Significant excitation or suppression was defined when the mean firing rate during a given epoch was significantly higher or lower than the baseline ($P < 0.0125$, Bonferroni corrected 2-tailed *t*-test).

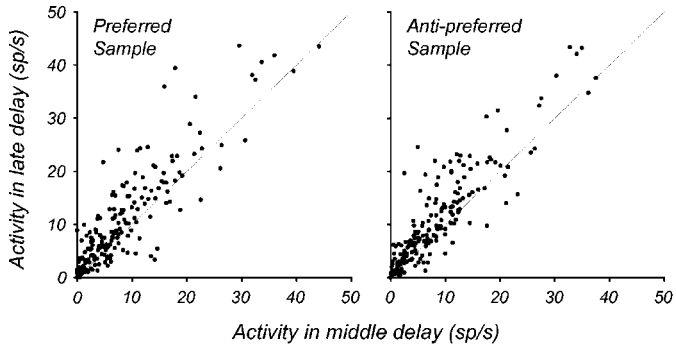

FIG. 6. Activity during the late delay. Firing rates of individual neurons recorded during the second middle epoch (1,000–1,200 ms) are compared with firing rates recorded during the last 200 ms of the delay (1,300–1,500 ms). Data are shown for the preferred (*left plot*) and antipreferred (*right plot*) sample directions. Note that firing rates of the majority of neurons are above the diagonal line, indicating higher firing rates during the last 200 ms of the delay. Activity of the whole population of neurons ($n = 197$) was significantly higher at the end of the delay for both directions ($P \ll 0.001$, paired *t*-test).

excitation or suppression occurred in more than one delay epoch. In other words, if significant activity is found in one epoch is it also likely to occur during other epochs? We found that in 49.7% of the neurons excitation or suppression was present during at least 3 of the epochs for at least one sample direction. Furthermore, in 86.4% of the neurons showing at least one epoch with significant activity (153/177), this activity occurred during the early delay. These values are greater than predicted by chance (45 and 79%; calculated assuming that the occurrence of activity in each epoch was independent) and suggest a relationship between activity appearing in the early epoch and later in the delay. In fact, 86.9% (133/153) of neurons with significant early activation also showed activity later in the delay, whereas only 54.5% (24/44) of neurons with no early activity showed significant deviations from baseline later in the delay. This difference is highly significant ($P \ll 0.001$, χ^2 test) and suggests that the excitation and suppression occurring in different epochs of the delay are not completely independent.

We found that toward the end of the delay many neurons showed an increase in activity (see examples in Fig. 2). The data in Fig. 5 show that this increase was relatively common in the population of our neurons and there was an increase in the incidence of excitation toward the end of the delay. We quantified this increase by comparing the firing rates of all neurons from the third epoch (1,000–1,200 ms) to the rates measured during the final epoch for each direction (Fig. 6). Most neurons showed an increase in activity from the middle to the end of the delay and, for the population as a whole, this effect was highly significant ($P \ll 0.001$, paired *t*-test for each plot).

LENGTH OF THE DELAY. In the majority of our experiments the delay lasted 1.5 s and, as a consequence, its length and the time of appearance of the test stimulus were highly predictable. We examined whether the increase in activity at the end of the delay reflected this predictability by doubling the length of the delay. This manipulation also allowed us to determine whether the temporal dynamics of other features of the activity, observed during the shorter delay, depend on the length of the delay. In these experiments the activity of 23 neurons was examined in separate blocks of trials, beginning with a block of trials with a 1.5-s delay followed by a block of trials with a 3-s delay. The behavior of an example neuron recorded during the 1.5- and 3-s delays is shown in Fig. 7. During the standard 1.5-s delay trials (*top plot*), early activity ended about 800 ms after the start of the delay, followed by brief suppression in activity and a subsequent increase shortly before the appearance of the test. During the 3-s delay condition (*bottom plot*) early activity was similar in size and temporal characteristics, also ending about 800 ms into the delay. However, this was followed by more prolonged suppression and a subsequent

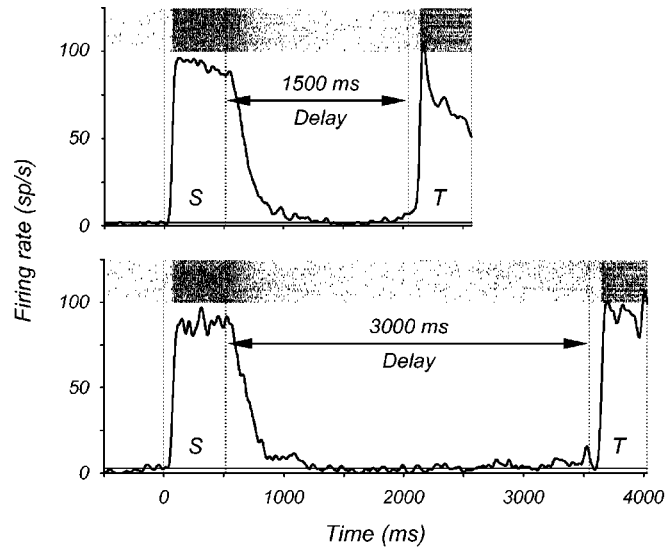

FIG. 7. Spike density functions showing activity of an example neuron during a session containing trials with 1.5-s (*top*) and 3-s (*bottom*) delays. Only trials with the sample moving coherently (0° range) in the preferred direction are shown. Test stimulus moved either in the preferred or antipreferred direction. During this experiment the monkey was first presented with a block of 250 trials with 1.5-s delay, followed by a block of 250 trials of the 3-s delay condition. Other details as in Fig. 2.

increase, beginning about 1 s before the end of the delay, at about the time when the 1.5-s delay trial normally ends. This pattern of activity was observed in most of the 23 neurons we studied. A comparison of the early activity measured during the 1.5- and 3-s delay revealed no significant differences in timing or response amplitude across the population ($P > 0.05$, paired *t*-test), suggesting that the early activity is more likely to be related to the preceding stimulus.

Activity in the later part of the 3-s delay was analyzed by calculating the mean responses from 6 epochs (600–800, 1,000–1,200, 1,300–1,500, 1,900–2,100, 2,400–2,600, and 2,800–3,000 ms) and comparing them to 3 corresponding epochs in the 1.5-s delay (600–800, 1,000–1,200, and 1,300–1,500 ms). These data are plotted separately for the 2 sample directions in Fig. 8. The significant increase in activity late in the delay ($P < 0.01$, paired *t*-test comparing first and last epochs for each direction) was more rapid for the 1.5-s than for the 3-s delay. The activity at the end of the shorter delay was significantly higher than the activity at the same time (1,300–1,500 ms) in the longer delay ($P < 0.05$, paired *t*-test), but by the end of the 3-s delay, it had reached a similar level ($P > 0.05$, paired *t*-test). The increase in the firing rate at the end of delays of such disparate lengths as well as the similarity in their final firing rates suggests that this increase is likely to be related to the expected appearance of the second stimulus. The anticipatory nature of this activity is further supported by the observation that during the 3-s delay its increase begins at about the time when the more commonly experienced 1.5-s delay trial ended.

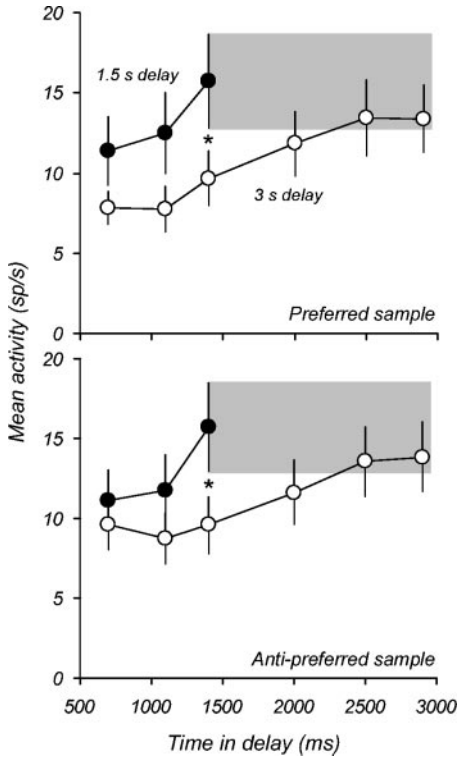

FIG. 8. Effect of delay length on activity during the late delay. Data were recorded from 23 neurons during 2 blocks of 200–250 trials, presented in sequence: 1.5-s delay block of trials always preceded the 3-s delay trials. The plot for the 1.5-s delay condition (solid symbols) shows mean activity during three 200-ms epochs (600–800, 1,000–1,200, and 1,300–1,500 ms). Plot for the 3-s delay condition (open symbols) shows mean activity during six 200-ms epochs (600–800, 1,000–1,200, 1,300–1,500, 1,900–2,100, 2,400–2,600, and 2,800–3,000). Data are plotted separately for preferred (*top plot*) and antipreferred (*bottom plot*) sample conditions. Error bars: ±SE. Shading shows the level of activity during the last epoch of the 1.5-s delay condition to facilitate the comparison with the late activity during the 3-s delay.

To assess whether this activity was related to the upcoming stimulus or the reward, we recorded from 24 neurons during a "no-task" condition run in blocks of 200–250 trials. These trials were similar to the task trials, except that the fixation point was replaced by a cross (the same stimulus used for the mapping protocol) and the delay was terminated by a reward, rather than by the test stimulus. We found that after both the preferred and antipreferred stimuli, there was no increase in activity toward the end of the delay ($P > 0.35$, paired *t*-test). In fact the responses were almost the same in the 1,000- to 1,200- and 1,300- to 1,500-ms epochs (regression analysis gave slopes of 0.94 and 1.10; intercepts of 0.5 and −0.7; and R^2 values of 0.89 and 0.94 for the preferred and antipreferred data, respectively). Thus the increase in activity toward the end of the delay appears to be related to the appearance of the test stimulus (and/or to the preparation for the response) and not related to the prior stimulus, the length of delay, or anticipation of reward.

Representation of stimulus features in the delay activity

Thus far, we have shown that many neurons in MT increase or decrease their firing during the delay. In the remaining sections of the study, we will show that information about the preceding sample stimulus is contained in a subset of MT neurons that display the activity described above.

DIRECTIONALITY OF DELAY ACTIVITY. We examined whether activity during the delay reflects the direction of the preceding sample by comparing firing rates of individual neurons following the preferred and antipreferred direction. This comparison was performed on activity recorded during each of the 4 epochs representing early, middle, and late delay (Fig. 9). Only activity following the coherently moving sample was used in this analysis (0°-direction range). Early in the delay (200–400 ms), 24% of the neurons showed significantly higher firing rates following the antipreferred stimulus than the preferred stimulus ($P < 0.0125$, Bonferroni corrected *t*-test; circles), whereas only 4% showed the opposite effect (triangles). The rest of the neurons showed no significant directional bias in their activity (crosses). An analysis of the population activity revealed a significant shift toward higher firing rates following the antipreferred direction ($P \ll 0.001$, paired *t*-test). The directional bias of activity during the delay was also present during the second epoch (600–800 ms) despite the fact that this period of the delay was dominated by suppression (see Fig. 5). Although the number of neurons showing significant differences in firing rates decreased to 4%, the population continued showing a significant shift toward higher firing rates following the antipreferred direction ($P < 0.01$). In the later epochs (1,000–1,200 ms and the last 200 ms) the proportion of cells with significantly different activity following the 2 directions dropped to <3% and the population no longer appeared to show significant directional bias ($P > 0.2$).

This analysis revealed a number of neurons with significantly more activity following the antipreferred direction than following the preferred direction, particularly during the early

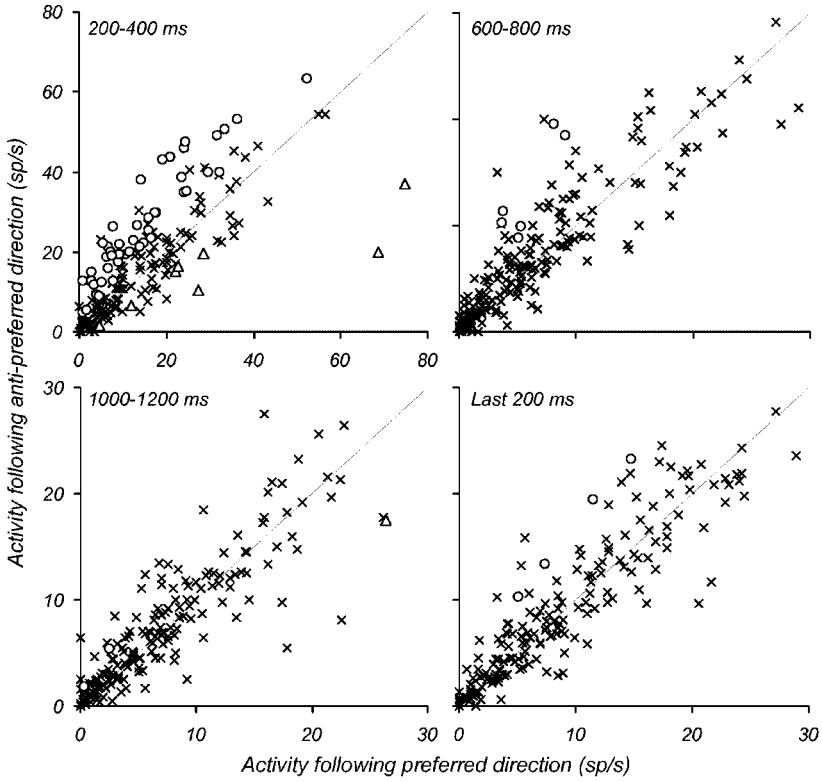

FIG. 9. Directionality of activity during the delay. Comparison of firing rates of individual neurons ($n = 197$) following the sample moving in the preferred and the antipreferred direction recorded during the 4 epochs. Circles represent neurons in which activity was significantly higher ($P < 0.0125$, Bonferroni corrected *t*-test) following the antipreferred direction, the triangles represent neurons in which the activity was significantly higher following the preferred direction, and crosses represent neurons in which the response was not different following the 2 directions. *200- to 400-ms epoch*: population response was significantly shifted toward higher activity following the antipreferred direction ($P \ll 0.001$, paired *t*-test). *600- to 800-ms epoch*: population activity was significantly higher following the antipreferred direction ($P < 0.01$). *1,000- to 1,200-ms epoch*: population activity was not significantly different following the 2 directions ($P > 0.2$). *1,300- to 1,500-ms epoch*: population activity was not significantly different following the 2 directions ($P > 0.3$).

and middle epochs of the delay. To determine whether there was directional information in the entire population of 197 neurons throughout the delay, we divided it into 100-ms bins and performed an ROC analysis for each epoch for each neuron (see METHODS for details). The values produced by this analysis, termed DDPs, represent the probability that the direction of the sample stimulus could be determined on the basis of the activity of a given neuron in a single epoch. The mean values of DDP for the entire population of recorded neurons are shown in Fig. 10*A*. At 200 ms into the delay these values were significantly below the value of 0.5 and remained there for most of the delay, indicating that the firing rates following the antipreferred direction were generally higher than the firing rates following the preferred direction. Only toward the end of the delay did the directional bias of the population shift up toward 0.5. This pattern of results is consistent with the data shown in scatter plots in Fig. 9. We used a permutation test to evaluate the statistical significance of each value of DDP (see METHODS for details). The data in Fig. 10*B* show the proportion of neurons with significant DDPs during each epoch. In the first epoch (200 ms after stimulus offset) over 50% of all neurons had DDPs that significantly deviated from the value of 0.5. This proportion decreased to 10–25% during the subsequent period of 400–1,100 ms and dropped to about 5% during the last 2 epochs. Thus despite a relatively small proportion of individual cells showing significant directional bias during the middle delay (see Fig. 9), activity of the population was still directionally biased toward higher firing rates following the antipreferred sample.

NONDIRECTIONAL ACTIVITY DURING THE DELAY. Although almost all of the neurons with directionally biased delay activity (71/72, 98.6%) showed significant deviations from baseline (excitation or suppression, as defined in Fig. 5), many of the neurons with significant deviations from baseline showed no directional bias during the delay (crosses in Fig. 9). The proportion of neurons with significant activity (either excitation or suppression) but no directional bias is shown in Fig. 11. In the early epoch of the delay (200–400 ms) a little over half of the neurons showed significant deviations from baseline with no directional bias. This proportion grew to about 95% in the remaining epochs. From the data in Fig. 5, we know that during the middle of the delay, the activity of these neurons was dominated by suppression and toward the end of the delay excitation became more prevalent. This suggests that much of the suppression and late excitation may be driven by nondirectional inputs.

REPRESENTATION OF DIRECTION RANGE IN THE DELAY. The data in Figs. 9 and 10 show that the strongest directionality in MT during the delay is present in the early portion of the delay (200–400 ms). To determine whether this activity encodes information about other aspects of the stimulus, we determined whether it was affected by changes in the direction range of the sample (see Fig. 1*A*). The population of 162 neurons for which we had relevant data were divided into 3 groups on the basis of their behavior during early delay: neurons showing no directional bias ($n = 100$, $P > 0.05$, paired *t*-test), neurons with significantly higher activity following the preferred direction ($n = 12$, $P < 0.05$), and neurons with higher activity following the antipreferred direction ($n = 50$, $P < 0.05$). Figure 12 shows the sample responses (Fig. 12*A*) and the early delay activity (Fig. 12*B*) as a function of the direction range of the sample stimulus. The neurons with nondirectional early activity showed typical direction-selective responses to the sample that decreased with an increase in direction range (compare Fig. 12*A*, *left plot* to Fig. 3). The early delay activity of these

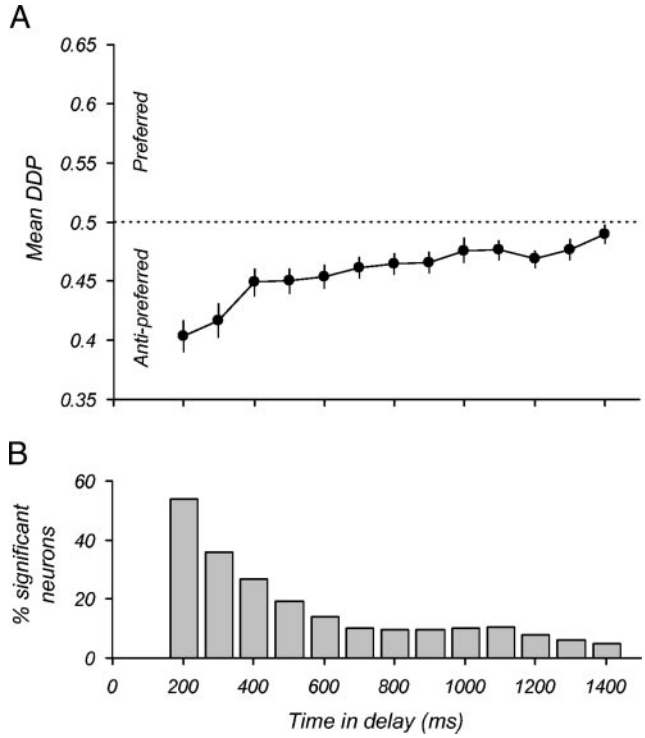

FIG. 10. *A*: receiver operating characteristic (ROC) analysis of delay activity. ROC analysis was performed on data from consecutive 100-ms epochs from 194 neurons. Direction discrimination probability (DDP) represents the overlap of the distributions of activity from the 2 directions: a value of 0.5 shows that there was no difference in the activity following the preferred and antipreferred stimuli; a value <0.5 shows that there was greater activity following the antipreferred direction than following the preferred direction; and a value >0.5 shows that there was more often greater activity following the preferred direction. Error bars: ±SE. *B*: incidence of neurons with significant DDPs for each 100-ms epoch ($P < 0.05$, permutation test).

neurons was not affected by the direction range of the sample (Fig. 12*B*, *left plot*). On the other hand, neurons with directional bias during the early delay showed the same pattern in the sample stimulus response functions (Fig. 12*A*, *middle and right plots*) but very different patterns in the early delay (Fig. 12*B*, *middle and right plots*). The small proportion of neurons that fired more following the preferred stimulus (Fig. 12*B*, *middle plot*) showed a strong dependency on the direction range of the preferred sample (solid circles). Their activity decreased as the direction range in the preferred sample increased—a result that almost mirrors the response during the sample stimulus moving in the preferred direction. On the other hand, when the sample moved in the antipreferred direction these neurons were not affected by the increase in direction range (open circles). Conversely, the neurons that fired more following the antipreferred sample were affected by the direction range, but only when the sample had moved in the antipreferred direction (open circles, Fig. 12*B*, *right plot*). An important feature of these data is that the activity during the delay did not appear to be directly related to the firing rates in the sample response. This is exemplified by the change in delay activity with direction range following the antipreferred sample. When the range increased from 300 to 360°, the sample response rose by 25 spikes/s and this increase was accompanied by a decrease of 5 spikes/s in delay activity. When the range increased from 0 to 120°, a similar decrease in delay activity was seen, yet there was only a small increase in the sample response (7 spikes/s).

The data in Fig. 12 also reveal that neurons showing a directional bias during the early delay, particularly following the antipreferred direction, also show substantially higher firing rates to the preferred sample than neurons showing no directional bias during early delay ($P \ll 0.001$, 2-tailed *t*-test). This difference in maximal firing rates may be indicative of the 2 groups of neurons belonging to different populations.

ANALYSIS OF ERROR TRIALS. To determine whether the directional bias of delay activity shown in Fig. 10 was behaviorally relevant, we performed an ROC analysis for trials leading to errors. Because most of the errors occurred on trials in which the sample contained a direction range of 300°, the analysis was limited to this stimulus condition. Sixty-seven neurons had a sufficient number of error and correct trials (minimum of 2 per category per direction) for this analysis and the DDP values were computed every 100 ms beginning 500 ms before the start of the delay. The results of this analysis are shown in Fig. 13. Despite some variability in the data, most likely attributable to the relatively small number of trials, there were differences between the indices computed for the 2 types of trials. During the sample, the DDP values were dominated by the preferred direction and the values for the correct trials (solid circles) were consistently higher than those for the error trials ($P < 0.04$; 2-tailed paired *t*-test), suggesting that during error trials sample responses were slightly less directional. The opposite pattern was seen during the delay. The DDP values from both correct and error trials dropped below 0.5, indicating higher firing rates following the antipreferred direction. However, the values for correct trials were still consistently higher than those for the errors ($P < 0.01$; 2-tailed paired *t*-test), suggesting that on error trials the activity following the antipreferred direction was greater (or that the activity following the preferred direction was weaker). Furthermore, a comparison of the values measured for the correct trials with 300°-range sample with those for 0°-range sample revealed a striking similarity (gray line), suggesting that the values from the incorrect trials may have been abnormally low. Thus the greater directionality on error trials may be indicative of neuronal activity dominated by

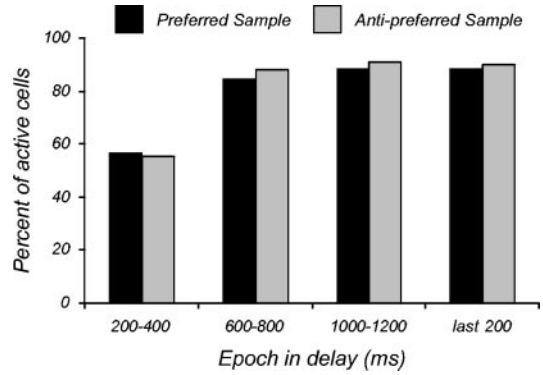

FIG. 11. Incidence of nondirectional activity in neurons with significant modulation in activity. Neurons with significant modulation in activity were those with mean firing rates that were significantly higher or lower than the baseline (i.e., those represented in Fig. 5). Neurons with no directional bias were those with no differences in mean firing rates following the 2 sample directions (shown by crosses in Fig. 9).

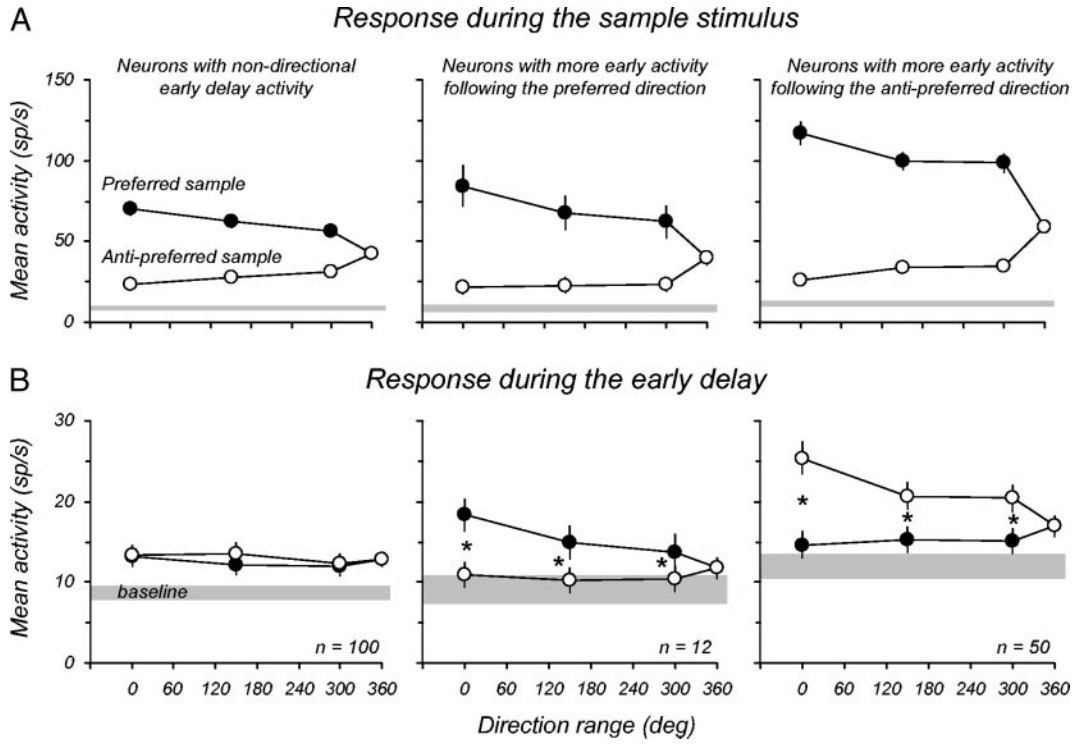

FIG. 12. Effect of sample direction range on early delay activity. *A*: sample response. Three groups of neurons were identified on the basis of early delay directionality: neurons with no directional bias during early delay (*left plot*, $n = 100$); neurons with higher firing rates following the preferred direction (*middle plot*, $n = 12$); and neurons with higher firing rates following antipreferred direction (*right plot*, $n = 50$). Activity during the preferred (solid symbols) and antipreferred (open symbols) directions is shown separately. Responses to direction ranges smaller than 360° were significantly different following the 2 directions ($P \ll 0.01$, paired *t*-test). *B*: early delay activity. Activity recorded during the early delay epoch (200–400 ms) plotted as a function of direction range. Data are plotted from the same 3 groups of neurons as in *A*. *$P < 0.05$, paired *t*-test.

the factors not related to remembering sample direction (e.g., sensory adaptation).

DISCUSSION

We have shown that MT neurons are active not only during the presentation of a visual motion stimulus but also during the delay, when no stimulus was present in the receptive field. Many MT neurons showed suppression during the middle phase of delay, and most neurons increased their firing rates toward the end of the delay, probably in anticipation of the upcoming test. Early in the delay, a third of MT neurons had activity that reflected the properties of the preceding sample, and throughout most of the delay the population of MT neurons showed a directional bias. Below we discuss the behavior of MT neurons during individual phases of the task, some of the possible sources of the directional signal observed during the delay and to what extent it is likely to play a role in the successful performance of the task.

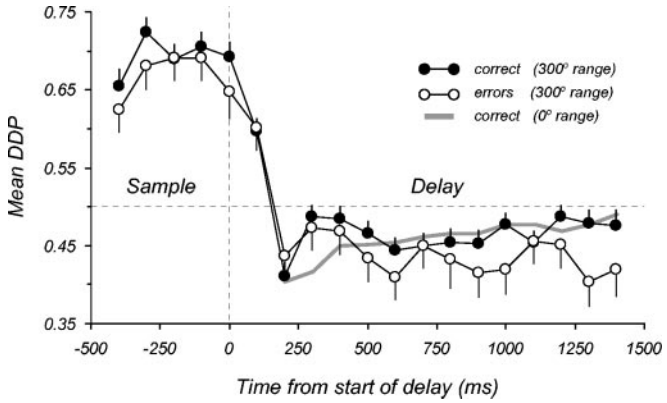

FIG. 13. ROC analysis of delay activity during error and correct trials. DDPs were computed for correct (solid symbols) and error (open symbols) trials in which the sample contained 300° range. Data were collected from 100-ms bins starting 500 ms before the beginning of the delay until the end of the delay. $n = 67$. Error bars: SE. Data from Fig. 10 were plotted in gray, showing the DDPs for correct trials in which the sample contained 0° range. For other details see Fig. 10.

Responses to the direction range of random-dot stimuli

The responses of MT neurons to random-dot stimuli have been studied extensively (e.g., Britten et al. 1993; Newsome et al. 1989); however, the stimuli in those studies were composed of random motion with a certain percentage of the dots moving in the same direction. Our stimuli are quite different; they consist of local vectors representing a limited range of directions that must be integrated into a percept of global motion. These stimuli, introduced by Williams and Sekuler (1984), have been used extensively in psychophysical studies examining the properties of motion integration mechanisms in humans and animals (Pasternak et al. 1990; Rudolph and Pasternak 1999; Watamaniuk and Sekuler 1992; Watamaniuk et al. 1989; Williams et al. 1991). Although involvement of MT neurons in processing of such stimuli has been suggested by lesion studies (Bisley and Pasternak 2000; Pasternak and Merigan 1994;

Rudolph and Pasternak 1999), the response of MT neurons to these stimuli has not been previously studied.

The present results confirm the conclusions from the lesion studies that MT neurons play a role in integration of local motion signals. We found that MT neurons responded well to these stimuli and retained their direction selectivity over a broad range of local directions up to the levels when the range of local directions approached the level of a psychophysical threshold for the monkeys (see Fig. 3). This behavior is consistent with previous reports that MT neurons perform an averaging algorithm when presented with complex motion consisting of more than one local directional signal (Britten and Heuer 1999; Ferrera and Lisberger 1997; Recanzone et al. 1997).

Responses to sample and test stimuli

Although modulation of responses by the matching stimuli during the performance of match-to-sample tasks has been observed in neurons in inferotemporal and prefrontal cortex (Miller et al. 1993), we did not find this type of activity in MT. However, we did see subtle effects of the preferred sample on the responses to the test stimuli occurring 1.5 s later. Specifically, responses to the preferred and antipreferred test were slightly weaker following the preferred sample than following the antipreferred sample. This observation is consistent with previous studies of stimulus adaptation in MT (Kohn and Movshon 2003; Petersen et al. 1985; Van Wezel and Britten 2002), although the magnitude of the effect is less in the present study. There are 3 possible reasons for the weaker effect. First, the sample stimulus was presented for only 500 ms, a much shorter adapting time than that used in the other studies. Second, the 1.5-s delay was substantially longer that the interstimulus time employed in the studies of adaptation in MT. Finally, it is possible that during a behavioral task like ours adaptation-induced changes in firing rates are less detectable because other task-related activity also affects neuronal firing rates. This final point is addressed in more detail below.

Activity during the delay

Area MT is known to play a key role in processing of complex motion and only recently has evidence emerged that its neurons may also make a contribution to remembering motion stimuli. This evidence was provided by studies of monkeys with MT lesions (Bisley and Pasternak 2000) and by applying microstimulation to MT (Bisley et al. 2001) during the performance of a task identical to that used in this study. Additional evidence has been provided by psychophysical experiments (Pasternak and Zaksas 2003; Zaksas et al. 2001).

The present data provide new insights into the nature of the participation of MT neurons suggested by these studies. Although we did not observe the type of sustained delay activity commonly found in cortical areas implicated in working memory (Funahashi et al. 1989; Fuster 1973; Miyashita and Chang 1988; Quintana and Fuster 1999; Rainer et al. 1998), we found that the activity of many neurons early in the delay contain information about the preceding stimulus, and that throughout most of the delay, a directional signal is present.

CAN SENSORY ADAPTATION ACCOUNT FOR DELAY ACTIVITY? Before discussing the relationship between the activity during the delay and storage of visual motion information, we must consider the possibility that the directionality present in the population may be caused by poststimulus sensory adaptation. Of the 5 studies that have examined motion adaptation in MT neurons (Kohn and Movshon 2003; Lisberger and Movshon 1999; Petersen et al. 1985; Priebe et al. 2002; Van Wezel and Britten 2002), none has specifically examined the activity during the interval that immediately followed the adapting stimulus. The only available information about the activity during the interstimulus interval comes from Britten (personal communication), who recently examined the activity of 68 of the neurons described in the study by Van Wezel and Britten (2002) during the 500 ms separating the 3-s adapting stimulus and the test (Britten, unpublished results). Although many of the features of the activity during the delay were similar to those we observed, there were some notable differences. The main similarity was the presence of excitation following the antipreferred direction in the early delay (200–400 ms) in both sets of data. A direct comparison of this activity revealed a small difference ($P < 0.05$, ANOVA), with our data showing slightly higher firing rates during early delay (mean firing rates after subtracting baseline activity: 7.3 vs. 4.5 spikes/s). The difference between the 2 data sets was more pronounced in the early delay following the preferred stimulus. Although most of the neurons in Britten's adaptation study were either suppressed or at baseline (mean firing rate: −0.17 spikes/s), activity of the majority of our neurons was enhanced (see Fig. 4, *top left*; mean firing rate: 4.7 spikes/s). This difference was highly significant ($P < 0.0001$) and implies that active engagement in the task may generate a bias in activity toward the preferred direction, which may balance the activity attributed to adaptation. This interpretation would explain the stronger directional bias we see on error trials (see Fig. 13)—when the monkey was performing poorly, adaptation may have had more impact than on trials in which the animal performed the task correctly. We should note that we cannot rule out the possibility that the differences in activity following the preferred direction are attributed to the different stimulus durations used in the 2 studies (3-s adapting stimulus compared with a 500-ms sample stimulus). However, it seems unlikely that a shorter stimulus would result in excitation while a longer stimulus would result in suppression. We also cannot rule out the possibility that a delayed burst after the presentation of a stimulus is characteristic of some MT neurons, and that this burst may be suppressed after a long adapting stimulus. If this was the case, then the activity we have observed is not necessarily task-dependent, although as we argue below, this does not preclude its being used to perform the task optimally.

EARLY DELAY ACTIVITY. The most interesting activity seen in MT during the delay was found in the first 500 ms when a majority of neurons had responses significantly higher than baseline following both directions. We were careful to discount any response that could be directly attributed to the sample by ignoring the activity in the first 200 ms of the delay. Although in many neurons early delay activity was directionally biased, in a large number of cells this activity showed no directionality, suggesting the presence of a nondirectional input into MT. It is tempting to speculate that the source of this activity may be an area involved in working memory. However, it is also possible that the nondirectional signal originates from within MT and is a neural correlate of the normalization process

suggested by models of MT (Koechlin et al. 1999; Simoncelli and Heeger 1998).

One third of the neurons in MT showed significant directionality early in the delay. A small number of them had higher firing rates following the preferred direction and this activity was affected only by the increase of the direction range of the preferred sample. Broadening of the direction range of the antipreferred sample had no affect on their firing rate. The remaining neurons, representing 29% of the entire population recorded, showed the opposite effect: their activity was greater following the antipreferred sample and was strongly affected by the direction range in that stimulus but was unaffected by the direction range of the preferred sample. These data show that activity early in the delay contains information about both the direction and the range of motion in the sample stimulus, although it appears to be segregated by sample direction—one population encoding changes in the preferred and the other encoding changes in the antipreferred direction. The existence of separate subpopulations of neurons showing opposing types of activity during the delay may be an important feature of the network underlying memory and may offer insights as to how the stimulus features are stored.

There are 2 independent lines of evidence that suggest that the delay activity we see in MT may be involved in the memory process. First, animals with MT lesions showed a loss in stored directional information that cannot be explained by the deficit in encoding alone (Bisley and Pasternak 2000). Second, the presentation of a noisy mask early in the delay is maximally effective at disrupting the memory of a previously seen directional stimulus (Pasternak and Zaksas 2003). Together these data suggest that activity in MT following the remembered sample, whether it is attributed to sensory adaptation or represents a more active process, may contribute to the network underlying memory for motion.

We observed that neurons with higher early activity following the antipreferred sample also tended to have significantly higher maximal firing rates than neurons with early activation that was not directionally biased. It should be pointed out these neurons were selected on the basis of their activity during the delay and the nature of the directional bias. The finding that these neurons also share another characteristic—high maximal firing rates to the preferred stimuli—suggests that they are likely to represent a separate class of MT neurons.

SUPPRESSION DURING THE MIDDLE OF THE DELAY. About half of the neurons showed significant suppression during the middle of the delay following either the preferred or antipreferred stimulus, and in many cases this suppression was greater following the preferred direction. It should be pointed out that a decrease in activity following the preferred adapting stimulus was observed during the test by Van Wezel and Britten (2002) as well as during the 500-ms interstimulus interval (Britten, personal communication). Thus some of the suppression following the preferred direction could in part be related to poststimulus adaptation processes. On the other hand, it is less likely that the prolonged suppression following the antipreferred sample is also attributable to the adaptation, given that no suppression was observed by Britten, who would be more likely to find such effects given the much longer adapting stimulus than the 500-ms sample we used. Thus it is more likely that the suppression we observed during middle delay is largely task-related.

Sustained suppression during the delay is not unique to MT and was previously observed in other cortical areas, including somatosensory regions of parietal cortex (Koch and Fuster 1989; Zhou and Fuster 1996) and extrastriate area V3a (Nakamura and Colby 2000). Although the role of this suppression is not clear, it may limit the amount of irrelevant sensory information reaching cortical areas involved in active retention of the preceding sample, and could therefore serve to decrease the background noise and to enhance neural responses to the anticipated test stimulus (Koch and Fuster 1989). A similar gating mechanism downstream of MT has been proposed in a task in which monkeys had to delay a motor response to a motion stimulus (Seidemann et al. 1998). Although the area in which the gating occurs may differ in the 2 tasks, the suppression we see during the delay may represent a neuronal correlate of this type of mechanism.

REACTIVATION LATE IN THE DELAY. In most of the testing sessions the delay duration was 1,500 ms. Thus the end of the delay and the appearance of the test were highly predictable. This predictability was reflected in many neurons in the form of increased activity during the last several hundred milliseconds of the delay. When the delay was increased to 3,000 ms, the same increase in activity was seen by the end of the delay, but the increase was more gradual and began at about the time when the more commonly encountered 1,500-ms delay trials would have ended. If the test stimulus was replaced by a reward for a block of trials, the increase in activity was no longer found. These observations strongly point to the anticipatory nature of this activity, and most likely represent "top-down" signals originating elsewhere in the brain.

A number of studies have reported an increase in activity in visual neurons before the appearance of behaviorally relevant stimuli. This effect has been observed in several extrastriate cortical areas (Colby et al. 1996; Luck et al. 1997; Nakamura and Colby 2000; Recanzone and Wurtz 2000) and has been attributed to directing spatial attention to the receptive field. Thus it is possible that this reactivation may be the result of a shift of spatial attention to the location of the upcoming test. Indeed, a number of studies have demonstrated that MT neurons are affected by the attentional demands of the task (Cook and Maunsell 2002; Martinez-Trujillo and Treue 2002; Seidemann and Newsome 1999; Treue and Martinez Trujillo 1999; Treue and Maunsell 1999). However, it is also possible that other cognitive influences, such as anticipation, may also contribute to this effect. Indeed such activity has been observed in prefrontal cortex during behavioral tasks resembling the task used here (Boch and Goldberg 1989; Niki and Watanabe 1979; Quintana and Fuster 1999; Rainer and Miller 2002; Rainer et al. 1999; Romo et al. 1999).

Toward the end of the delay, the directional bias of the population became quite weak. This apparent absence of directionality may be related to the presence of the anticipatory signal during this period. It is possible that the mechanism that produces this anticipatory activity is independent of the mechanism involved in adaptation and the signals it generates may be strong enough to make any residual directional bias difficult to detect. However, we cannot rule out the possibility that the decline in directionality seen in Fig. 10 at least in part repre-

sents the time course of the effects of adaptation, and the very weak adaptive effect we saw on the test stimuli is because the adaptation effect is so weak by the end of the delay.

Comparison with other studies

Only 2 previous studies have examined the behavior of MT neurons during the performance of tasks involving working memory. Seidemann et al. (1998) trained monkeys in a task requiring them to withhold a saccade indicating the direction of the preceding motion stimulus. Thus the monkey was required to remember the location to which the saccade would eventually be made, rather than the direction of stimulus motion. They noted, referring to unpublished observations, that recordings from MT neurons during the poststimulus delay revealed no significant activity.

Ferrera et al. (1994) recorded from MT using a task in which the monkeys were required to remember the direction of visual motion. In that study, a random-dot motion stimulus served as a cue and, after a variable delay of 200–540 ms, was followed by a sequence of stimuli one of which matched the direction of the cue. The monkeys responded by releasing a bar to the matching stimulus. The analysis was limited to a maximal period of about 200 ms, beginning 350 ms after the offset of the cue. About a third of MT neurons had substantially elevated activity, although some showed suppression during this period. Because there was little correlation between this activity and the identity of the cue, it was concluded that the delay activity was unlikely to carry information about the preceding stimulus. Apart from task differences, 2 other factors should be considered when comparing these findings to our results: differences in the delay length and in the delay epochs that were analyzed. The period between 350 and 540 ms in Ferrera et al. (1994) represents a time when most of the early delay activation we observed would already have occurred and the difference in early activation for the preferred and the antipreferred directions would have been missed. On the other hand, the significant excitation and suppression observed by these authors during the delay may correspond to some of the activity we observed during that same period. Thus there are substantial similarities between our results and those reported by Ferrera et al. (1994) and the differences are likely to be attributable largely to the different delay lengths and the phase of the delay chosen for analysis.

Match-to-sample tasks, similar to the task used here, have also been used in studies of neurons in prefrontal (Fuster and Alexander 1971; Miller et al. 1996; Rainer and Miller 2002), parietal (Sereno and Maunsell 1998), and inferotemporal (Fuster and Jervey 1981) cortices. Many neurons in these areas display sustained elevation of activity during the delay that appears to carry the information about the preceding stimulus. This type of persistent activity is commonly thought to play an important role of bridging the interval between the sensory stimulus and the behavioral response based on that stimulus (Fuster 1995b). Most of these studies emphasize the sustained nature of the delay activity and less attention has been paid to its temporal dynamics. However, recently, Rainer and Miller (2002) performed such an analysis and identified 3 activity periods, some aspects of which resembled the delay activity we observed. During the stimulus, prefrontal neurons showed a transient response followed by a burst of activity reminiscent of the activity we found early in the delay in MT. This "intermediate" period was followed by a period of "reactivation" during which activity continued to increase until the second stimulus was presented. It is noteworthy that middle delay suppression, common in area MT and in other sensory cortical areas, did not appear to be present in prefrontal neurons.

The dynamics of delay activity in prefrontal neurons in response to vibrotactile stimuli is also similar to some features of the delay activity observed in this study in MT. Romo et al. (1999) reported that many neurons fired in proportion to the frequency of the remembered stimulus, a result analogous to the relationship between firing during early delay and direction range. These authors also noted the presence of early delay activity in secondary somatosensory cortex (Salinas et al. 1998).

Are MT neurons involved in temporary storage of motion information?

The notion that the same systems involved in sensory processing also participate in retaining sensory information is generally accepted and incorporated into most models of working memory (e.g., Fuster 1997; Goldman-Rakic 1995). It is based on experiments showing that during the memory period firing rates of neurons in areas processing sensory signals reflect the identity of the remembered stimulus (Fuster and Jervey 1982; Miyashita and Chang 1988; Salinas et al. 1998; Zhou and Fuster 1996). This notion is also supported by recent lesion and microstimulation studies (Bisley and Pasternak 2000; Bisley et al. 2001), as well as by functional imaging in humans (Courtney et al. 1997; Haxby et al. 2000).

Prefrontal cortex is the region most closely associated with working memory (Fuster 1995a; Goldman-Rakic 1995; Miller et al. 1996). It receives direct projections from MT (Barbas 1988; Schall et al. 1995) and sends direct projections back (Cusick et al. 1995). These connections provide the basis for the functional interaction between the 2 regions. Indeed, neurons in dorsolateral prefrontal cortex respond to moving random-dot stimuli and their firing rates appear to reflect stimulus strength and the direction of motion (Kim and Shadlen 1999). Although the activity of prefrontal neurons during memory tasks requiring remembering visual motion has not been examined, the similarity between the behaviors of prefrontal and MT neurons during the delay suggests that both areas may participate in the same circuitry underlying the retention of motion information.

Our findings support the notion that MT may be involved in the circuitry underlying storage of motion information. There is a resurgence of activity, some of which is strongly related to the preceding stimulus, early in the delay, and a weak directional signal that continues throughout the delay. Some aspects of this activity are likely to be related to sensory adaptation to the preceding stimulus, particularly following the antipreferred sample. However, other aspects of this activity cannot be explained by passive adaptation alone. It remains to be seen whether the dynamics of this delay activity is specific to MT neurons or is present in directionally selective neurons in other cortical areas and in what way it reflects the workings of the network underlying the ability to remember visual motion.

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