Interaction between Visual- and Goal-related Neuronal Signals on the Trajectories of Saccadic Eye Movements

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Abstract

■ During natural viewing, the trajectories of saccadic eye movements often deviate dramatically from a straight-line path between objects. In human studies, saccades have been shown to deviate toward or away from salient visual distractors depending on visual- and goal-related parameters, but the neurophysiological basis for this is not well understood. Some studies suggest that deviation toward is associated with competition between simultaneously active sites within the intermediate layers of the superior colliculus (SC), a midbrain structure that integrates sensory and goal-related signals for the production of saccades. In contrast, deviation away is hypothesized to reflect a higher-level process, whereby the neural site associated with the distractor is actively suppressed via a form of endogenous, top–down inhibition. We tested this hypothesis by measuring presaccadic distractor-evoked activation of SC visuomotor neurons while monkeys performed a simple task configured specifically to induce a high degree of saccades that deviate away. In the SC, cognitive processes such as top–down expectation are represented as variation in the sustained, low-frequency presaccadic discharge. We reasoned that any inhibition at the distractor-related locus associated with saccade deviation should affect the excitability of the neuron, thereby affecting the discharge rate. We found that, although the task produced robust deviation away, there was no evidence of a relationship between saccade deviation and distractor-evoked activation outside a short perisaccadic window that began no earlier than 22 msec before saccade onset. This indicates that deviation away is not adequately explained by a form of sustained, top–down inhibition at the distractor-related locus in the SC. The results are discussed in relation to the primary sources of inhibition associated with saccadic control. ■

INTRODUCTION

Saccades are rapid eye movements whose primary purpose is to align the high-acuity fovea with interesting parts of a scene as we scan our visual world. Interestingly, the trajectories between successively fixated locations during natural viewing are rarely straight (see, e.g., the classic free-viewing studies by Yarbus, 1967). In recent years, human studies have shown that saccade trajectories can deviate toward or away from salient visual distractors depending on visual and cognitive parameters (Van der Stigchel, 2010; Mulckhuyse, Van der Stigchel, & Theeuwes, 2009; Van der Stigchel, Meeter, & Theeuwes, 2007; McSorley, Haggard, & Walker, 2006; Walker, McSorley, & Haggard, 2006; Ludwig & Gilchrist, 2003; Doyle & Walker, 2001). This has popularized a view that saccade deviation reflects a dynamic interaction between visual- and goal-related processes, but the neural basis for it remains largely unknown. Some studies suggest that deviation toward a salient distractor is associated with competition between simultaneously active sites on some saccadic map around the time a saccade is launched (McPeek, 2006; McPeek, Han, & Keller, 2003; Port & Wurtz, 2003). In contrast, deviation away from a salient

distractor has been hypothesized to reflect a higher-level process, whereby the neural site associated with a distractor is actively suppressed via a form of endogenous, top–down inhibition (Van der Stigchel et al., 2007; Walker et al., 2006; Tipper, Howard, & Houghton, 2000).

We tested this latter hypothesis using a task configured specifically to induce a high degree of saccades that deviate away from a salient distractor stimulus. Simultaneously, we recorded distractor-evoked activation of visuomotor neurons from the intermediate layers of the superior colliculus (SC), a midbrain structure that integrates sensory- and goal-related signals for the production of saccadic eye movements (for recent review, see White & Munoz, 2011). In the SC, visual signals are represented as a transient burst of action potentials beginning around 50 msec after the appearance of a visual stimulus in a neuron's response field (Boehnke & Munoz, 2008). In contrast, goal-related signals are represented as sustained low-frequency presaccadic activation, which can be modulated by cognitive processes such as top–down expectation (Basso & Wurtz, 1998; Dorris & Munoz, 1998; Dorris, Paré, & Munoz, 1997; Glimcher & Sparks, 1992) and covert attention/perception (Lovejoy & Krauzlis, 2010; Muller, Philiastides, & Newsome, 2005; Ignashchenkova, Dicke, Haarmeier, & Thier, 2004; Kustov & Robinson, 1996). We reasoned that any form of inhibition

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at the distractor-related locus should affect the excitability of neurons representing that location, thereby affecting the discharge rate. Therefore, if deviation away is because of a form of top–down inhibition at the distractor-related locus, it should be associated with significantly lower distractor-related response, in particular, the sustained low-frequency discharge well in advance of the target-directed saccade itself.

Two rhesus monkeys were trained to perform a simple distractor task configured specifically to induce a high degree of saccades that deviate away by using a spatially predictable distractor (Figure 1). Monkeys made a simple step-saccade to a peripheral target stimulus for a block of trials. Next, we introduced a salient distractor at a nearby spatially predictable location (red stimulus in Figure 1B and C)—the same location on every trial. This distractor could appear simultaneous with (Figure 1B) or in advance of (Figure 1C) the target stimulus. We reasoned that pre-
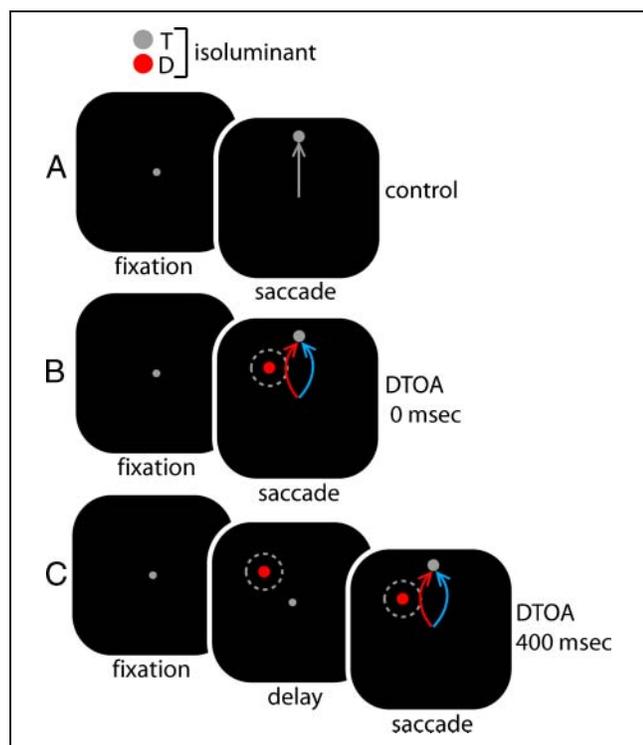

Figure 1. Spatially predictable distractor task. Monkeys were required to fixate a central stimulus for a random period (900–1100 msec), after which it disappeared with the simultaneous appearance of a peripheral target stimulus (step task; A). After a block of distractor-absent control trials, a distractor appeared at a spatially predictable location (same location on every trial; B and C). In B (DTOA$_{0 \text{ msec}}$), the distractor appeared simultaneous with target-on/fixation-off. In C (DTOA$_{400 \text{ msec}}$), the distractor appeared 400 msec before target-on/fixation-off, and the monkey had to remain fixating the central stimulus during the delay. DTOA conditions were randomly interleaved. Saccades launched closer to the distractor than the target were considered incorrect, and errors were not rewarded. Red and blue arrows represent saccade deviation toward versus away from the distractor, respectively. Dotted circle represents the response field of a neuron. T = target; D = distractor.

senting distractors in advance of the target would provide a simple means of testing our hypothesis for two reasons: (1) It provided a window in which we could measure a reliable period of sustained, low-frequency distractor-evoked discharge while monkeys prepared to launch a saccade toward the upcoming target. (2) The competitive interaction between target and distractor should be reduced, which might facilitate deviation away, because the visual transient associated with the distractor would have ended before the target appearance. We predicted that monkeys would quickly build an expectation of the distractor locus, and that the eyes would consequently deviate away from this location, consistent with human studies (Van der Stigchel, 2010; Mulckhuyse et al., 2009; Van der Stigchel et al., 2007; McSorley et al., 2006; Walker et al., 2006; Ludwig & Gilchrist, 2003; Doyle & Walker, 2001). Simultaneously, we measured distractor-evoked activation of SC visuomotor neurons leading up to the time of a saccade, because these neurons project directly to the brainstem saccade circuitry (Rodgers, Munoz, Scott, & Paré, 2006). Contrary to our hypothesis, we found no evidence of a relationship between saccade deviation and distractor-evoked activation outside a short peri-saccadic window that began no earlier than 22 msec before saccade onset. This result is inconsistent with the hypothesis that saccade deviation is because of a form of sustained, top–down inhibition at the distractor-related locus in the SC.

METHODS

Data were collected from two male Rhesus monkeys (*Macaca mulatta*, Monkey Q, 11 kg, and Monkey Y, 12 kg). The surgical procedures and extracellular recording techniques were detailed previously (Marino, Rodgers, Levy, & Munoz, 2008) and were approved by the Queen's University Animal Care Committee in accordance with the guidelines of the Canadian Council on Animal Care.

Stimuli and Equipment

Stimuli were presented on a cathode ray tube monitor at a screen resolution of 1024 × 768 pixels (75 Hz noninterlaced, 8-bit per channel intensity resolution), with a viewing angle of 54° horizontally and 44° vertically. The luminance and color properties of the stimuli were measured using the Minolta CS-100 photometer (Minolta, Japan). Stimulus presentation was controlled by a UNIX-based real-time system (REX; Hays, Richmond, & Optican, 1982). Spikes, eye position data, and event data were recorded at 40 KHz in a multichannel data acquisition system (Plexon Inc., Dallas, TX) and then down-sampled to 1 kHz for analysis.

Stimuli were circular disks (1° diameter) presented at a luminosity of 6.5 cd/m^2 against a black background (<0.01 cd/m^2). The fixation point and target were gray (CIE $x = 0.29, y = 0.28$) and were isoluminant with the red distractor item (CIE $x = 0.64, y = 0.33$). The distractor was positioned at a 45° angle relative to the target trajectory at

70% of the target eccentricity. Its position was fixed either to the left or right of the target trajectory within a given session. Positioning the distractor closer to the fovea than the target has been shown to produce greater deviation away (Van der Stigchel & Theeuwes, 2005) and was chosen specifically for this reason.

Procedure

Monkeys were seated in a primate chair (Crist Instruments Co., Inc., Hagerstown, MD) in a dark room, head-restrained and facing the video monitor. Once an SC neuron was isolated, the center of its response field was determined using a rapid visual stimulation procedure detailed in a previous study (White, Boehnke, Marino, Itti, & Munoz, 2009). Monkeys then performed the spatially predicable distractor task, while the distractor stimulus was centered in the response field of the neuron (Figure 1). The monkey fixated the central stimulus for a random period from 900 to 1100 msec. The fixation stimulus then disappeared simultaneously with the appearance of the peripheral target, which acted as the go-signal. Because saccades are often characterized by an idiosyncratic curvature, we first ran a block of 20 or more distractor-absent trials to derive a reliable control trajectory (see Analyses). Next, the distractor was presented on every trial at a fixed location, with a randomly interleaved onset asynchrony of 0 or -400 msec relative to the target (distractor–target onset asynchrony, DTOA). We chose only two onset asynchronies to maximize the trial count per condition, which was critical for obtaining reliable within-neuron correlations between distractor-evoked activation and behavior (saccade deviation). A reward was issued only for correctly directed first saccades, whose endpoint fell within an invisible computer controlled window around the target ($2° \times 2°$ or less). Each trial was followed by a momentary (800 msec) increment in background luminance to prevent dark adaptation. We sampled at least 30 correct trials per condition across each session.

Analyses

A saccade was defined by a velocity criterion $\geq 35°$/sec, and only first saccades were analyzed. Saccadic RT (SRT) was the time from target appearance to saccade onset. Saccade direction errors were defined as saccades whose endpoint fell closer to a distractor than the target.

A saccade deviation metric was derived using a method similar to Quaia, Paré, Wurtz, and Optican (2000). First, we translated the origin of each saccade to the central fixation point. Second, all trajectories within a given session were converted from Cartesian to polar coordinates, resulting in vectors of polar angles and radii. Third, for each trajectory, we derived the polar angle at equally spaced steps in the radius (0.1° steps). This required interpolating between points where no sample existed and was crucial for averaging and normalizing trajectories in space instead of time. Fourth, we computed an average distractor-

absent control trajectory by averaging the polar angles of the group of trajectories at each radius step. Finally, each distractor-present trajectory was normalized against the distractor-absent control trajectory by computing the difference in the polar angle between the two at each radius step. An angular deviation metric for each normalized distractor-present trajectory was then derived by averaging the respective vector of polar angles. The sign of these values was set such that positive values represent deviation toward, and negative values represent deviation away.

Single units were verified using off-line spike sorting software (Plexon, Inc.). Spike density functions were created by convolving individual spikes with a Gaussian kernel ($\sigma = 5$ msec). Forty-three SC neurons were identified and characterized using a delayed saccade task before the actual experiment. Briefly, monkeys fixated a central fixation stimulus followed by the appearance of a bright peripheral target (6.5 cd/m^2 against a black background) in the response field of the neuron. The monkey was required to maintain fixation for an additional delay period of 500–800 msec after which the fixation was removed, signifying to the monkey to launch a saccade to the peripheral target. A neuron was defined as having a visual component if the activity just following target appearance (40–120 msec) was significantly ($p < .05$) greater than a baseline (-80 msec to target onset). A neuron was defined as having a motor component if the average firing rate around the time of the saccade directed into the response field (-25 to $+25$ msec) was significantly ($p < .05$) greater than a baseline (-150 to -50 msec presaccade). A neuron was defined as having a significant visual delay component if the average firing rate around a delay period (200–400 msec posttarget) was significantly ($p < .05$) greater than a baseline (-80 msec to target onset). Only visuomotor neurons with a significant delay component were included because our hypothesis required analyses of perisaccadic and presaccadic low-frequency activation generated by the distractor stimulus over a delay period leading up to target appearance. A total of 34 of 43 (79%) neurons fit these criteria ($n = 20$ and $n = 14$ from Monkey Q and Monkey Y, respectively). In addition, most of these neurons (21 of 34, 62%) showed a significant increase in the mean discharge rate leading up to saccade onset during the delay task ($p < .05$, repeated measures ANOVA on activation from -400 to -100 msec, relative to saccade onset in 100-msec bins). This suggests that most of these neurons were the buildup type described previously (Munoz & Wurtz, 1995).

RESULTS

Behavior

Saccade Trajectories

Figure 2 shows examples of the distractor-present trajectories (DTOA$_{0 \text{ msec}}$ condition), normalized against the distractor-absent condition for two monkeys (see Methods). Red represents deviation toward the distractor, and blue

Figure 2. Example trajectories for two monkeys ($DTOA_{0\ msec}$ condition). Trajectories were normalized against a mean distractor-absent control trajectory illustrated by the vertical black line (see Methods). Red and blue traces illustrate trajectories that deviated mostly toward versus away from the distractor, respectively (percentages presented alongside). D = distractor.

represents deviation away from the distractor (distractor location was fixed within each block). When the distractor appeared to the right of the target direction, most saccades deviated leftward, away from the distractor (92% and 57% for Monkey Q and Monkey Y, respectively). In a subsequent block of trials, when the distractor appeared to the left of the target direction, most saccades then deviated rightward, again away from the distractor (64% and 71% for Monkey Q and Monkey Y, respectively). The proportion of saccades that deviated toward versus away varied from session to session, but on average 32% of saccades fell to the side of the control trajectory toward the distractor and 68% fell to the side of the control trajectory away from the distractor (the proportion of deviation away ranged from 20% to 96% across all sessions).

Figure 3 shows a quantitative analysis of saccade trajectories across the 34 sessions. Panels A–C show the mean proportion of saccades that deviated away, mean angular deviation, and mean proportion of saccade direction errors, respectively, as a function of trial quartile. Because the distractor was spatially predictable within a given session (although its location changed from day to day), we pre-

dicted a change in performance over the course of a session as the monkey acquired a representation of the distractor locus. We ran a two-way (trial quartile by DTOA) repeated measures ANOVA for each dependent variable represented in Figure 3. First, there was no significant difference in the proportion of deviation away (Figure 3A) as a function of trial quartile ($F(3, 198) = 0.87, p = .45$), or DTOA ($F(1, 198) = 0.21, p = .65$), and no trial quartile by DTOA interaction ($F(3, 198) = 1.8, p = .14$). However, the overall proportion of saccades that deviated away from the distractor was significantly greater than 0.5 ($t(33) = 27.9, p < .00001$). Although this varied somewhat from session to session, we can conclude that across all the sessions, saccades deviated away more often than toward the salient distractor. This was most likely because of the predictable nature of the stimuli (Walker et al., 2006), coupled with the degree of overtraining typical of monkey studies, indicating that our task was effective for the purpose of this study. Second, there was a significant increase in mean angular deviation away (Figure 3B) as a function of trial quartile ($F(3, 198) = 3.73, p = .012$), but no effect of DTOA ($F(1, 198) = .058, p = .45$), and no trial quartile by DTOA

Figure 3. Mean proportion deviation away (A), mean angular deviation (B), and mean proportion direction errors (C) as a function of trial quartiles ($n = 34$ sessions). In A, <0.5 indicates deviation toward, and >0.5 indicates deviation away. In B, positive values indicate deviation toward, and negative values indicate deviation away. Error bars represent ±1 SEM.

interaction ($F(3, 198) = 1.2$, $p = .29$). The difference between the results in Figure 3A and 3B (proportion of deviation away vs. mean angular deviation) was because of the fact that the latter was a more subtle measure of the magnitude of the deviation, whereas the former simply categorized the trajectories into one of two bins (toward vs. away). For this reason, mean angular deviation was chosen as the more valid measure for subsequent analyses. Lastly, there was a significant decrease in the proportion of saccade direction errors (Figure 3C) as a function of trial quartile ($F(3, 198) = 20.92$, $p < .00001$). Also, there were significantly more saccade direction errors in the $DTOA_{0\ msec}$ condition relative to the $DTOA_{400\ msec}$ condition ($F(1, 198) = 8.15$, $p = .0058$). The trial quartile by DTOA interaction on saccade direction errors was not significant ($F(3, 198) = 2$, $p = .11$).

Two things are worth noting from these results: First, it was somewhat surprising that the degree of deviation away was not substantially lower in the $DTOA_{0\ msec}$ condition, given that the competitive interaction was certainly greater, as evidenced by the greater proportion of saccade direction errors. Second, these results were based on 34 independent sessions that spanned the course of several months. Therefore, this affect in performance over time suggests a form of short-term learning that occurred over the duration of a session, particularly in terms of the proportion of errors. This suggests that top–down expectations played a role in modulating saccadic behavior. More importantly, the task produced a high degree of deviation away in the monkey, which is comparable to the human literature (Van der Stigchel, 2010; Van der Stigchel et al., 2007; McSorley et al., 2006; Walker et al., 2006; Ludwig & Gilchrist, 2003), and was ideal for testing our hypothesis.

SRT

If deviation away is determined by a form of top–down inhibition at the distractor locus, one might argue that an attenuated distractor-related signal would facilitate target selection and induce faster SRTs. However, in humans, deviation toward versus away has been associated with faster versus slower SRTs, respectively (McSorley et al., 2006). Our results do not support either view. Figure 4 shows mean SRT across the key conditions. First, we ran a two-way repeated measures ANOVA on SRT, with saccade deviation (toward vs. away) and DTOA as independent variables (red and blue bars). There was no significant effect of saccade deviation on SRT ($F(1, 66) = 2.7$, $p = .1$), and the trend was in fact opposite to the prediction based on McSorley and colleagues. In addition, there was no effect of DTOA ($F(1, 66) = 0.08$, $p = .77$), and no saccade deviation by DTOA interaction ($F(1, 66) = 0.22$, $p = .64$). However, overall SRTs were elevated for correct distractor-present trials relative to distractor-absent trials ($t(33) = 7.9$, $p < .00001$), which is in agreement with the competitive interaction associated with remote dis-
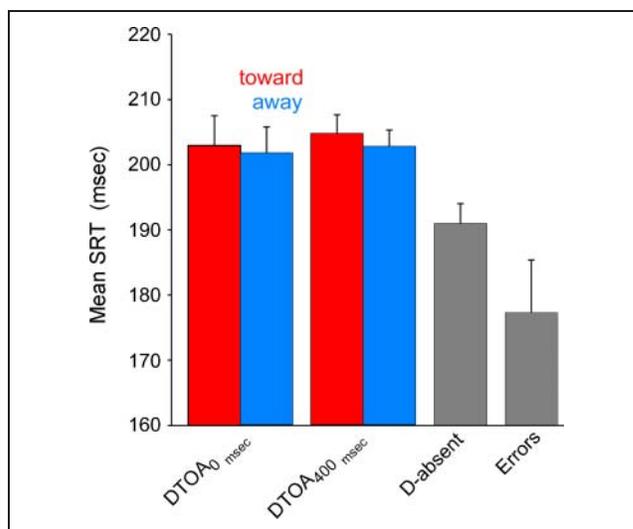

Figure 4. Mean SRT across conditions. D-absent represents the distractor-absent control condition. Errors refer to saccade direction errors when the eyes were directed toward the distractor in the response field of the neuron. Error bars represent ±1 *SEM*.

tractors (Born & Kerzel, in press; Bompas & Sumner, 2009; White, Gegenfurtner, & Kerzel, 2005; Walker, Deubel, Schneider, & Findlay, 1997). In contrast, SRTs were faster for saccade direction errors relative to correct distractor-present trials ($t(33) = 3.2$, $p < .01$). These results indicate that saccade deviation is not exclusively coupled with differences in SRT, which is consistent with a human study that showed a similar pattern when the target was predictable (Walker et al., 2006).

Neurons

We sought to test directly the hypothesis that deviation away is because of a form of sustained inhibition at the distractor-related locus (Van der Stigchel et al., 2007; Walker et al., 2006; Tipper et al., 2000). If this hypothesis is correct, we predict a direct relationship between saccade deviation and presaccadic distractor-related activation, specifically the low-frequency discharge in advance of saccade onset, which is known to be modulated by cognitive processes such as top–down expectation (Basso & Wurtz, 1998; Dorris & Munoz, 1998; Dorris et al., 1997; Glimcher & Sparks, 1992).

We analyzed extracellular activity from 34 SC visuomotor neurons ($n = 20$ and $n = 14$ from Monkey Q and Monkey Y, respectively; see Methods) while monkeys performed the spatially predictable distractor task, with the distractor in the response field of the neuron (Figure 1). Figure 5 shows rasters and spike density functions for an example neuron aligned on saccade onset, for the $DTOA_{0\ msec}$ and $DTOA_{400\ msec}$ conditions. In the $DTOA_{0\ msec}$ condition (Figure 5A), there was an initial burst of action potentials associated with the appearance of the distractor in the neuron's response field (gray square symbols represent

Figure 5. Single SC visuomotor neuron. A and B show rasters (top) and spike density functions (bottom) aligned on saccade onset for the $DTOA_{0 \text{ msec}}$ and $DTOA_{400 \text{ msec}}$ conditions, respectively (distractor in the response field). Filled squares illustrate distractor onset for each trial, and trials were sorted by SRT. Each tick mark represents a spike. Red represents correctly directed saccades that deviated toward the distractor; blue represents correctly directed saccades that deviated away from the distractor; dotted represents saccade errors directed toward the distractor into the response field of the neuron. Gray-shaded regions represent the presaccadic epochs in which we performed within-neuron correlations with saccade deviation (Epoch ***a***, −400 to −100 msec; Epoch ***b***, −30 msec to saccade onset).
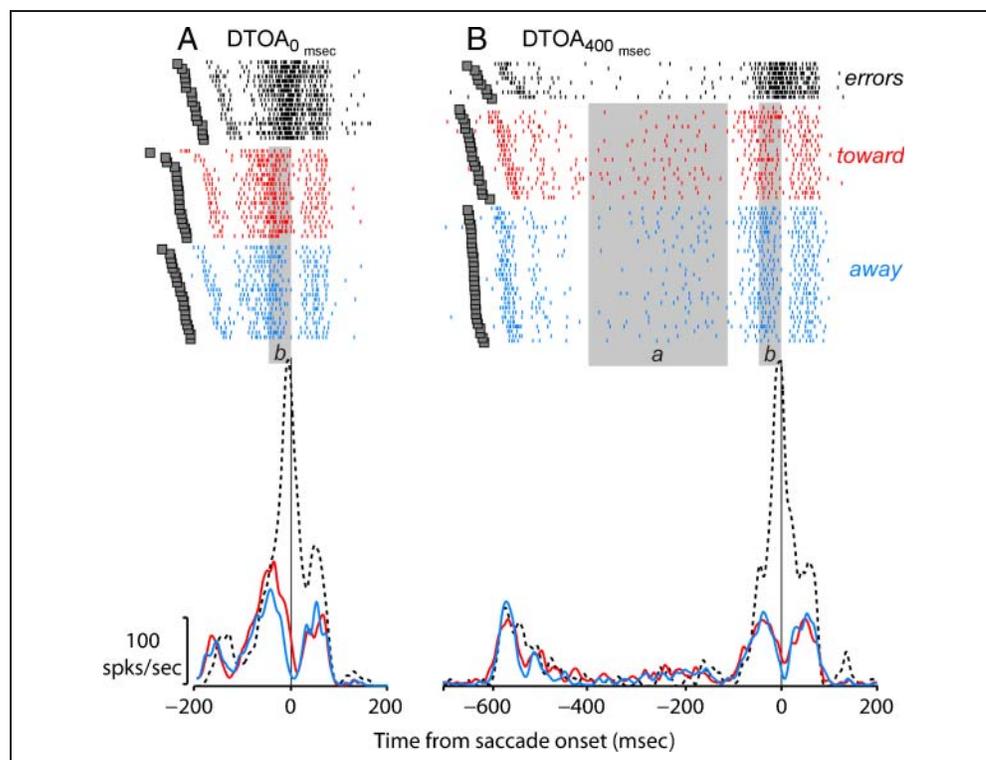
distractor onset for each trial, sorted by SRT). For error trials (black dotted curve), this activation then accelerated quickly toward a saccade burst that exceeded 500 spks/sec as the eyes were launched toward the distractor. In contrast, for correctly directed saccades that deviated toward (red solid curve), distractor-related activation momentarily increased but was rapidly quenched at around 30 msec before saccade onset. This suppression was notably greater for correctly directed saccades that deviated away (blue solid curve). This is consistent with a study by McPeek and colleagues who noted a similar result during a visual search task (McPeek et al., 2003). In the $DTOA_{400 \text{ msec}}$ condition (Figure 5B), the pattern was similar, except that the distractor-evoked response began ~400 msec earlier, and continued to discharge at a low-frequency during the delay period leading up to target appearance. What is important here is that there was no obvious difference in the low frequency delay activity for saccades that deviated toward (red curve) versus away (blue curve). We quantify this pattern in more detail below.

It should be noted that there was sometimes a small amount of perisaccadic activity associated with the distractor location on distractor-absent trials. Although this activation was invariably lower than on distractor present trials, it suggests that there was some overlap between movement fields associated with the target- and distractor-related sites.

To test the hypothesis described earlier, we performed within-neuron correlations between the trial-by-trial saccade deviation and distractor-evoked activation within two epochs, −400 to −100 msec relative to saccade onset

(Epoch ***a***) and −30 to saccade onset (Epoch ***b***). Epoch ***a*** was chosen because it captured a sufficient period of low-frequency discharge excluding perisaccadic activity and the transient visual response evoked by the distractor. Epoch ***b*** was chosen because previous research had shown a relationship between distractor-evoked SC activation during this period and deviation toward a distractor in a visual search task (McPeek et al., 2003). Because the predicted relationship between saccade deviation and distractor-evoked activity is in the same direction (i.e., greater deviation away = less deviation toward, both of which should be associated with lower distractor-evoked activation), we chose to perform the correlations on the combined trials that deviated toward and away to increase statistical power.

Figure 6 shows within-neuron correlations between saccade deviation and the presaccadic distractor-related activation at each epoch. Panels A, C, and E show the results of a single neuron (each point represents a trial), and Panels B, D, and F show the distributions of correlation coefficients (*r* values) across the total sample of 34 SC neurons. For the example neuron in the $DTOA_{0 \text{ msec}}$ condition (Figure 6A), there was a highly significant positive correlation between saccade deviation and presaccadic distractor-related activation during Epoch ***b*** ($r = .64, p < .00001$). That is, deviation away was associated with lower activation, whereas deviation toward was associated with greater activation during this epoch. This result was observed in 19 of 34 (56%) neurons (Figure 6B, black bars). Also, the overall distribution of *r* values for these correlations was shifted significantly in the positive direction ($t(33) = 6.14, p < .00001$). These

results were similar for Epoch *b* in the DTOA$_{400 \text{ msec}}$ condition (Figure 6C and D), but it was not as robust. Only 8 of 34 (24%) neurons showed a significant positive correlation between saccade deviation and presaccadic distractor-related activation during Epoch *b* in the DTOA$_{400 \text{ msec}}$ condition. The critical test of our hypothesis is illustrated in Figure 6E and F. For the single unit, there was no correlation between saccade deviation and presaccadic distractor-related activation during Epoch *a* ($r = .04$, $p = .73$). Furthermore, only 2 of 34 (5%) neurons showed a significant positive correlation during Epoch *a*, and the overall distribution of *r* values was not significantly different from zero ($t(33) < 1$, $p = .9$). In short, there was

no relationship between saccade deviation and the low-frequency distractor-related discharge. On the basis of these results, deviation away cannot be adequately explained by a form of sustained inhibition at the distractor-related locus in the SC.

Because there was often a smaller proportion of trials that deviated toward rather than away (Figures 3 and 4), one might argue that sessions with fewer trials that deviated toward may result in a truncated range of trajectory deviation, which might reduce the chance of finding a significant correlation. However, for most sessions, there was a clear spread of saccades in both directions. Also, we did not find a significant correlation between the proportion

Figure 6. Correlation between presaccadic distractor-related activation and saccade deviation for the epochs defined in Figure 5. A, C, and E show single unit examples (each point is a trial). B, D, and F show histograms of corresponding correlation coefficients (*r* values) for *n* = 34 SC visuomotor neurons. Black-shaded bars denote neurons with significant correlations ($p < .05$). Also embedded are *t* statistics for test that the mean of the distribution is >0.
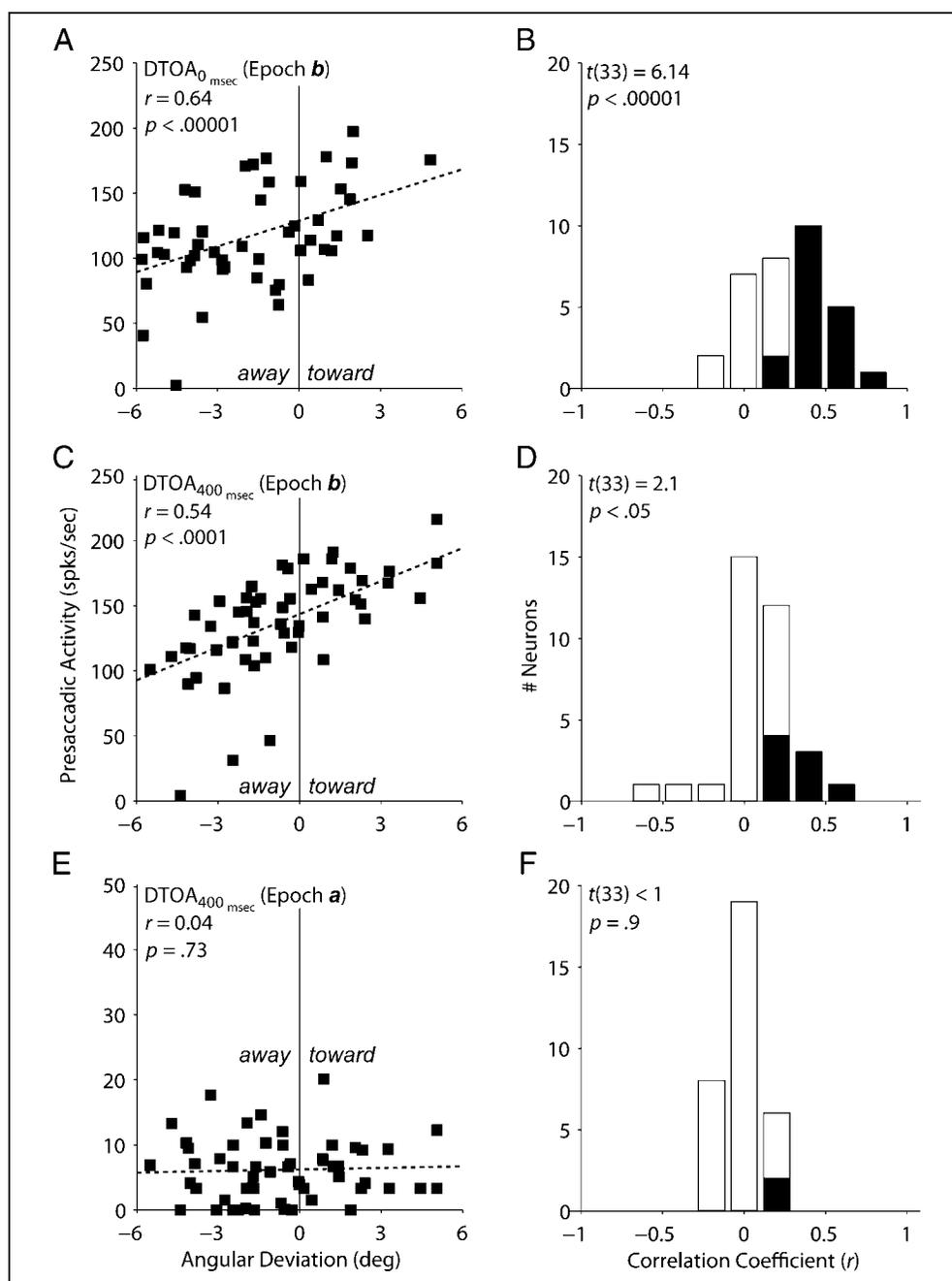
Figure 7. Mean angular deviation (A) and mean distractor-evoked activation (B, C) aligned on saccade onset for saccades that deviated toward (red) versus away (blue) from the distractor ($n = 34$ sessions/neurons). Black dotted lines represent saccadic errors directed toward the distractor into the response field of the neuron (y axis is truncated at 120 spks/sec for clarity). Horizontal black markers along the x axes of B and C show periods where average discharge rate was significantly lower for saccades that deviated away versus toward the distractor ($p < .01$, moving 5-msec window in 1-msec steps from -200 to $+50$ msec in A and -600 to $+50$ msec in B). Gray shading between the curves highlights the main perisaccadic difference. Error bars in A represent ± 1 *SEM*.

of trials that deviated toward and the overall variance in angular deviation ($r = -.07$, $p = .66$). Moreover, neither the spread of trajectory deviation nor the proportion of trials that deviated toward were greater for sessions where significant correlations between saccade deviation and distractor-evoked activation were observed ($p > .15$ across all comparisons). This indicates that the poor correlations in the DTOA$_{400 \text{ msec}}$ condition cannot be adequately accounted for by variation in spread of the trajectories.

Our conclusion is corroborated by the results shown in Figure 7. For each session/neuron, we divided the correct trials into those that deviated toward (red) versus away (blue) from the distractor. Figure 7A shows the mean angular deviation across the 34 sessions sorted in this manner,

and Figure 7B and C shows the respective spike density functions averaged across the 34 neurons. By sorting the trials in this way, mean angular deviation (Figure 7A) associated with the trials that deviated toward versus away was considerably separated, and both were significantly different from zero at both DTOAs ($t(33) > 10$, $p < 1.0454e{-}011$, for all comparisons against zero). We then quantified the difference in distractor-evoked activation for saccades that deviated toward versus away from the distractor (Figure 7B and C) by performing a running t test between the two in a moving 5-msec window at 1-msec steps (from -200 to $+50$ msec and -600 to $+50$ msec for the DTOA$_{0 \text{ msec}}$ and DTOA$_{400 \text{ msec}}$ conditions, respectively). The horizontal black markers along the x axis of

Figure 8. Mean distractor-evoked activation for the DTOA$_{400 \text{ msec}}$ condition (A), in which the trials were separated by the median split in activation level during Epoch *a* (illustrated by shaded region). The thick line represents the mean of the upper half of the split in activation, and the thin line represents the mean of the lower half of the split in activation. B shows mean angular deviation associated with the two levels of presaccadic activation described in A. Error bars in B represent ± 1 *SEM*.

Figure 7B and C show periods where average discharge rate was significantly lower ($p < .01$) for saccades that deviated away versus toward the distractor. The main differences occurred during a short perisaccadic period that began no earlier than 22 msec before saccade onset for the $DTOA_{0\ msec}$ condition (Figure 7B) and 10 msec before saccade onset for the $DTOA_{400\ msec}$ condition (Figure 7C). This is consistent with McPeek et al. (2003), who highlighted a similar result for saccades that deviated toward a distractor during a visual search task. Crucially, there was no reliable difference in the low-frequency discharge rate at any point before the short perisaccadic period highlighted in Figure 7C.

Finally, using a reverse approach, we biased the conditions in favor of our hypothesis by dividing the trials for each of the 34 neurons according to the median spilt in the magnitude of distractor-evoked activation during Epoch **a** ($DTOA_{400\ msec}$ condition). Figure 8A shows the difference in the resulting spike density functions averaged across the 34 neurons. We then compared the magnitude of deviation away (Figure 8B) associated with each distractor-related activation profile (Figure 8A). The difference was not significant ($t(33) = 0.23, p = .82$), and the trend was in fact in the opposite direction of our hypothesis. In summary, there was no relationship between saccade deviation and the sustained presaccadic distractor-related discharge.

DISCUSSION

In this study, we used a simple task configured specifically to induce a high degree of saccades that deviate away from a spatially predictable visual distractor. We showed the first evidence of robust deviation away in the monkey that is comparable to findings from several human studies (Van der Stigchel, 2010; Mulckhuyse et al., 2009; Van der Stigchel et al., 2007; McSorley et al., 2006; Walker et al., 2006; Ludwig & Gilchrist, 2003; Doyle & Walker, 2001). The dominant explanation for this result has been based on a hypothesis that deviation away is because of a form of top–down inhibition of the neurons representing the distractor. On the basis of this premise, we reasoned that any inhibition at the distractor-related locus in the SC should affect the excitability of the neuron, which would be reflected in the discharge rate (i.e., greater inhibition, lower discharge rate). Furthermore, if deviation away is because of a form of top–down inhibition, it should be associated with a significant decrease in the sustained low frequency distractor-related SC discharge well in advance of the saccade, because modulation of this signal has long been associated with cognitive processes such as top–down expectation (Basso & Wurtz, 1998; Dorris & Munoz, 1998; Dorris et al., 1997; Glimcher & Sparks, 1992) and covert attention/perception (Lovejoy & Krauzlis, 2010; Muller et al., 2005; Ignashchenkova et al., 2004; Kustov & Robinson, 1996). Contrary to our predictions, we did not find evidence to support this hypothesis.

It should be noted that we do not claim that there was no inhibition associated with the distractor-related locus. The $DTOA_{400\ msec}$ condition provided a useful window in which monkeys could potentially bias neuronal resources away from the distractor in favor of the upcoming target, and for task success, it would have been in their best interest to do so. Also, recall that SRTs were prolonged when the distractor was present versus absent independent of saccade deviation (Figure 4). This suggests that there may have been a form of global suppression that delayed saccades without interrupting the trajectories. What we can conclude is that any spatially specific sustained top–down inhibition at the distractor-related locus, as inferred from spiking activity, was not associated with saccade deviation in any direction for our task.

In addition, whereas distractor-related activation during Epoch **a** was a poor predictor of saccade deviation, the correlation during Epoch **b** was quite robust (Figure 6). One may be tempted to argue that this is evidence of top–down inhibition, but there are several reasons why this is not adequate. Arguably, modulation of a voluntary top–down signal ought to be more gradual than the rapid quenching of activation observed around Epoch **b**. The perisaccadic difference that we observed occurred on average no earlier than 22 msec before saccade onset. This is around the time of the motor burst (Munoz & Wurtz, 1995a; Sparks, 1978), which typically peaks around saccade onset for visuomotor SC neurons. So the idea that deviation away was because of a reliable voluntary top–down inhibitory signal timed precisely within this period seems rather unlikely, but we cannot entirely rule out this possibility from the current study. In addition, despite the window provided by the $DTOA_{400\ msec}$ condition, the correlation between saccade deviation and distractor-related activation during Epoch **b** was in fact worse here than in the $DTOA_{0\ msec}$ condition (see Figure 6), where competition from the distractor was greatest. These observations are ultimately inconsistent with a hypothesis based on a form of sustained distractor-related top–down inhibition.

Presumably, top–down signals that influence oculomotor behavior arise from brain areas associated with executive function (e.g., frontal cortex). However, direct frontal cortical projections to the SC are invariably excitatory (see White & Munoz, 2011, for recent review of the SC). Also, given that the SC is a crucial node where top–down and bottom–up signals converge, and SC visuomotor neurons project directly to the brainstem saccade generator (Rodgers et al., 2006), any modulation of a top–down signal that influences saccadic behavior ought to be observed here. Although our results do not support the role of a sustained distractor-related inhibitory mechanism on saccade deviation, some discussion of the sources of inhibition in the SC could provide important constraints for future studies that formulate new hypotheses of top–down control on saccade trajectories.

The first, and most likely, candidate for a top–down inhibitory mechanism is an extrinsic inhibitory nigrotectal

projection. The substantia nigra pars reticulata forms the primary output of the BG, a set of subcortical brain areas that act as an intermediate processing stage between frontal cortex and the intermediate layers of the SC for voluntary saccade control. The substantia nigra pars reticulata–SC projection is believed to regulate saccadic burst initiation by imposing a blanket of tonic GABAergic inhibition over the SC (Hikosaka, Takikawa, & Kawagoe, 2000), the release of which allows the SC to trigger the downstream saccade generator. There is evidence that neurons comprising the ipsilateral projection deliver spatially specific disinhibition to the SC (Jiang, Stein, & McHaffie, 2003), because they are tonically active and exhibit a discrete pause in discharge for contraversive saccades to a restricted region of the visual field (Hikosaka & Wurtz, 1983a). These neurons might carry a form of spatially specific top–down inhibition of the sort hypothesized in the current study. However, this mechanism cannot be responsible for inducing the kind of saccade deviation away that was observed in the current study because it would have been ultimately reflected in the sustained distractor-related SC discharge (see, e.g., Basso & Wurtz, 2002; Hikosaka & Wurtz, 1983b). This was not the case.

A second inhibitory mechanism in the SC is the well established intrinsic lateral inhibitory network that operates across the intermediate SC layers (Meredith & Ramoa, 1998; Munoz & Istvan, 1998). Here, neurons with different spatial tuning compete in a push-pull relationship, such that only one discrete population of neurons bursts for a saccade of a given direction and amplitude at any one time (Munoz & Fecteau, 2002). There is evidence that saccade deviation toward is associated with competition between simultaneously active SC sites around the time a saccade is launched (McPeek et al., 2003; Port & Wurtz, 2003). Given that the only correlation between saccade deviation and distractor-evoked discharge occurred during a very short perisaccadic window, deviation toward may be explained by lateral SC interactions, but it remains unclear from current models how deviation away may be explained via the same mechanism (Meeter, Van der Stigchel, & Theeuwes, 2010; Godijn & Theeuwes, 2002; Trappenberg, Dorris, Munoz, & Klein, 2001). One alternative to the hypothesis of top–down inhibition at the distractor-related locus is the possibility of a form of top–down excitation around the opposite side relative to the distractor. Although there was no stimulus for the eyes to latch onto here, we cannot rule out the possibility of some diffuse top–down excitatory signal in the opposite region of the distractor, which might shift the balance of activation in that direction and bias trajectories away. Unfortunately, we did not measure activity around the target or other locations where no stimulus was present, and in the absence of a stimulus, it is not certain that we would observe any measurable differences in spiking rate associated with diffuse excitation outside the stimulus locations. However, this hypothesis remains to be tested. In addition, there is much to be learned about the specific spatial and temporal parameters of lateral SC interactions, and whether these parameters may be shaped by top–down inputs to influence saccade trajectories. Computational models that propose explanations for saccade trajectory deviations could benefit from the current results and should be used to formulate detailed testable hypotheses that link neuronal activity to saccade trajectories.

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