Neuron, Vol. 43, 575–583, August 19, 2004, Copyright ©2004 by Cell Press

Manipulating Intent: Evidence for a Causal Role of the Superior Colliculus in Target Selection

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Summary

The superior colliculus (SC) is well known for its role in the motor control of saccades. Recent work has shown that it also plays a role in the selection of saccades, but a causal role in the process of target selection has not been demonstrated. We applied subthreshold microstimulation to the SC while monkeys performed a task requiring them to select a stimulus as the target for a pursuit or saccade movement. Stimulation increased the proportion of selections toward the stimulus that appeared contralateral to the site of stimulation and also decreased their latencies. For pursuit, this stimulation-induced contralateral response bias was with respect to the initial target location and not the direction of eye movement, demonstrating a causal effect on target choice distinct from any effect on motor preparation. These results show that the SC helps decide the object of the next movement, beyond its traditional responsibility of saccade production.

Introduction

The superior colliculus (SC) has long been regarded as part of the mechanism responsible for specifying the timing and endpoints of saccades. Microstimulation in the SC can evoke saccades, the amplitudes of which are largely determined by the position of the electrode within an ordered topographical map of saccade endpoints (Robinson, 1972; Stryker and Schiller, 1975). Subthreshold stimulation can alter the trajectory of visually guided saccades due to an averaging of the visual saccade vector with the vector of the stimulated region (Glimcher and Sparks, 1993). Local inactivation of the SC can also alter the latency and the metrics of saccades (Hikosaka and Wurtz, 1985; Lee et al., 1988; Schiller et al., 1987). Single-unit recording studies have documented the response fields of neurons in the SC corroborating the topographical architecture of this structure as well as its time-locked burst of activity several milliseconds prior to saccade onset (Sparks and Hartwich-Young, 1989; Wurtz and Albano, 1980).

More recent work supports the idea that the SC is involved not only in the motor production of saccades but also in the selection of saccades. For example, several studies have shown that presaccadic activity in the SC, which can precede the movement by hundreds of milliseconds, is related to target selection for saccades (Basso and Wurtz, 2002; Horwitz and Newsome, 1999, 2001; Krauzlis and Dill, 2002; McPeek and Keller, 2002a, 2002b). Altering activity in the SC with microstimulation or pharmacological agents can also alter saccade trajectories and endpoints as well as the selection of saccade targets (McPeek et al., 2003; McPeek and Keller, 2004).

What remains unclear is whether the SC is causally involved in target selection itself, beyond its role in the selection and preparation of saccades. One approach to this problem is to examine the SC during smooth-pursuit eye movements. Recent studies have shown that SC activity is linked with the control of smooth-pursuit eye movements (Krauzlis, 2003; Krauzlis et al., 1997, 2000, 2002) and, in particular, that premotor activity in the SC can predict target choice for pursuit as well as for saccades (Krauzlis and Dill, 2002). Unlike saccades, pursuit is primarily driven by stimulus motion rather than stimulus location, making it possible to dissociate target selection from movement preparation. For example, if a subject chooses and makes a saccade to a stationary target located to the left, target selection and the eye movement are both directed leftward. However, if that same target moves smoothly to the right, target selection remains leftward but the eye movement is now directed rightward. If the SC plays a causal role in target selection, then manipulating SC activity with weak microstimulation should increase the proportion of choices toward stimuli that appear in the hemifield contralateral to the site of stimulation, independent of the direction of eye movement required to acquire the target. We tested this hypothesis by microstimulating in the intermediate/deep layers of the SC, using currents that were subthreshold for evoking saccades, while the monkeys selected one of two stimuli as a target for pursuit or saccade eye movements in a two-alternative forced-choice task.

Results

We trained monkeys to select one of two grayscale bars as the target of a pursuit or saccade eye movement in a luminance discrimination task (Figure 1). In a match-to-sample design, a gray or white cue was presented during fixation to indicate the identity of the upcoming rewarded target. The two stimuli (one white and one gray) then appeared in opposite visual hemifields at a fixed eccentricity, which varied from session to session depending on our electrode location in the SC. The difference in luminance between the two stimuli was adjusted so that the monkeys were below asymptotic performance (~99% correct). During pursuit trials (Figure 1B), the two stimuli traveled toward the midline of the screen at a fixed velocity and then crossed into the opposing hemifields at the time of pursuit latency, giving rise to saccade-free pursuit (Rashbass, 1961). On half of the trials, we microstimulated at an intermediate or deep site in the SC with currents that were subthreshold for eliciting a saccade during free viewing. We set the

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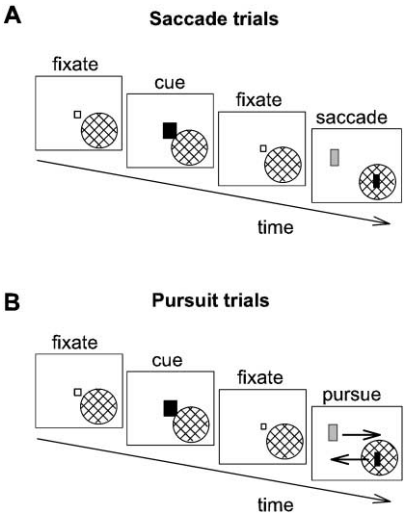

Figure 1. Sequence of Events on Saccade and Pursuit Trials

The monkey fixated the small central square and larger square cue before making an eye movement to the matching stimulus after the fixation square was extinguished. On saccade trials (A), target and distractor stimuli were stationary. On pursuit trials (B), stimuli moved at a constant speed (9°–46°/s) in the directions indicated by the arrows. The crosshatched region represents the visual location corresponding to the site of stimulation in the SC.

initial locations of the stimuli so that one of the two bars appeared at a position in the visual field matching that of our stimulation site in the SC. Target identity (white/gray), target location (left/right), trial type (pursuit/saccade), and stimulation condition (with/without) were all randomly interleaved.

The results from a single representative session from the left SC can be seen in Figure 2. For saccade trials, we measured the endpoint of the first saccade. When the saccade target appeared on the left side (i.e., ipsilateral to the site of stimulation), in the absence of stimulation the monkey's percentage of correct leftward saccades was 93% (Figure 2A, No Stimulation). The percentage dropped to 82% with stimulation (Figure 2A, Stimulation). When the saccade target appeared on the right side (i.e., contralateral to the site of stimulation), in the absence of stimulation the monkey's percentage of correct rightward saccades was 82% (Figure 2C, No Stimulation). The percentage rose to 99% with stimulation (Figure 2C, Stimulation). For pursuit trials, we measured the eye velocity of the first 100 ms of pursuit. When a pursuit target appeared on the left side, in the absence of stimulation the monkey correctly pursued it (in the rightward direction) 90% of the time (Figure 2B, No Stimulation). The percentage dropped to 65% with stimulation (Figure 2B, Stimulation). When a pursuit target appeared on the right side, in the absence of stimulation the monkey correctly pursued it (in the leftward direction) 83% of the time (Figure 2D, No Stimulation). The percentage rose to 91% with stimulation (Figure 2D, Stimulation). Thus, for this site, both pursuit and saccades showed an increase in percent correct during stimulation when the targets appeared contralateral to the site of stimulation and a decrease in percent correct when the targets appeared ipsilateral to the site of stimulation.

We found similar effects across our sample of 35 sites (Figure 3). Note that in the case of pursuit, there was a dissociation between the direction of eye movement and the initial stimulus location from which it derived, such that a contralaterally appearing target gave rise to ipsiversive pursuit and vice versa. Nevertheless, for both pursuit and saccades, the contralateral increase in percent correct (and corresponding ipsilateral decrease) was with respect to target onset location, not the direction of the resulting eye movement. Specifically, stimulation resulted in a significant increase in the percentage of correct responses ($p < 0.05$, assuming a binomial distribution) for contralateral targets in 26/35 sessions for saccades (filled circles, Figure 3A) and 16/34 sessions for pursuit (Figure 3B). Conversely, stimulation significantly decreased the percentage of correct responses for ipsilateral targets in 19 sessions for saccades (Figure 3C) and 22 sessions for pursuit (Figure 3D).

As documented in the Supplemental Data (http://www.neuron.org/cgi/content/full/43/4/575/DC1), microstimulation did not have any appreciable effect on the corrective saccades that accompanied pursuit or on the metrics of pursuit itself. In particular, there was no increase in the frequency of saccades, as might be expected if the microstimulation facilitated saccade production, and all of the corrective saccades that accompanied pursuit occurred too late to influence the pursuit choice.

In order to see the collective ipsilateral and contralateral effect for each session, we plotted the two against each other. Increases in percent correct for contralateral targets occurred concurrently with decreases in percent correct for ipsilateral targets during most sessions (Figures 4A and 4B). Therefore, the effect of microstimulation on pursuit and saccade choices was not simply a general increase or decrease in task performance, nor was it the result of having caused different types of effects at different sites. Instead, the changes in percent correct were the result of the monkeys choosing the contralateral stimulus more often on trials with stimulation than without, whether that stimulus was a target (resulting in a percent correct increase for contralateral targets) or a distractor (resulting in a percent correct decrease for ipsilateral targets).

The effect of microstimulation also showed some degree of spatial specificity. When the site of stimulation overlapped the target location (radial distance between SC site and target less than 2°), we found significant effects at 64% of the sites for pursuit and 60% of the sites for saccades. However, when the site of stimulation did not overlap the target but was still in the same visual hemifield (radial distance greater than 2°), we found significant effects at only 10% of the sites for pursuit and 37% of the sites for saccades.

The histograms in Figure 4 summarize the changes in percent correct found for contralateral and ipsilateral targets across all sessions for saccades (C) and pursuit (D) and also separates the data according to whether the target identity was white or gray. A two-way ANOVA of the mean change in percent correct across all sessions confirms that the mean change in contralateral target percent correct was significantly different from the mean change in ipsilateral target percent correct for saccades and pursuit (Tukey test, $p < 0.001$). A closer

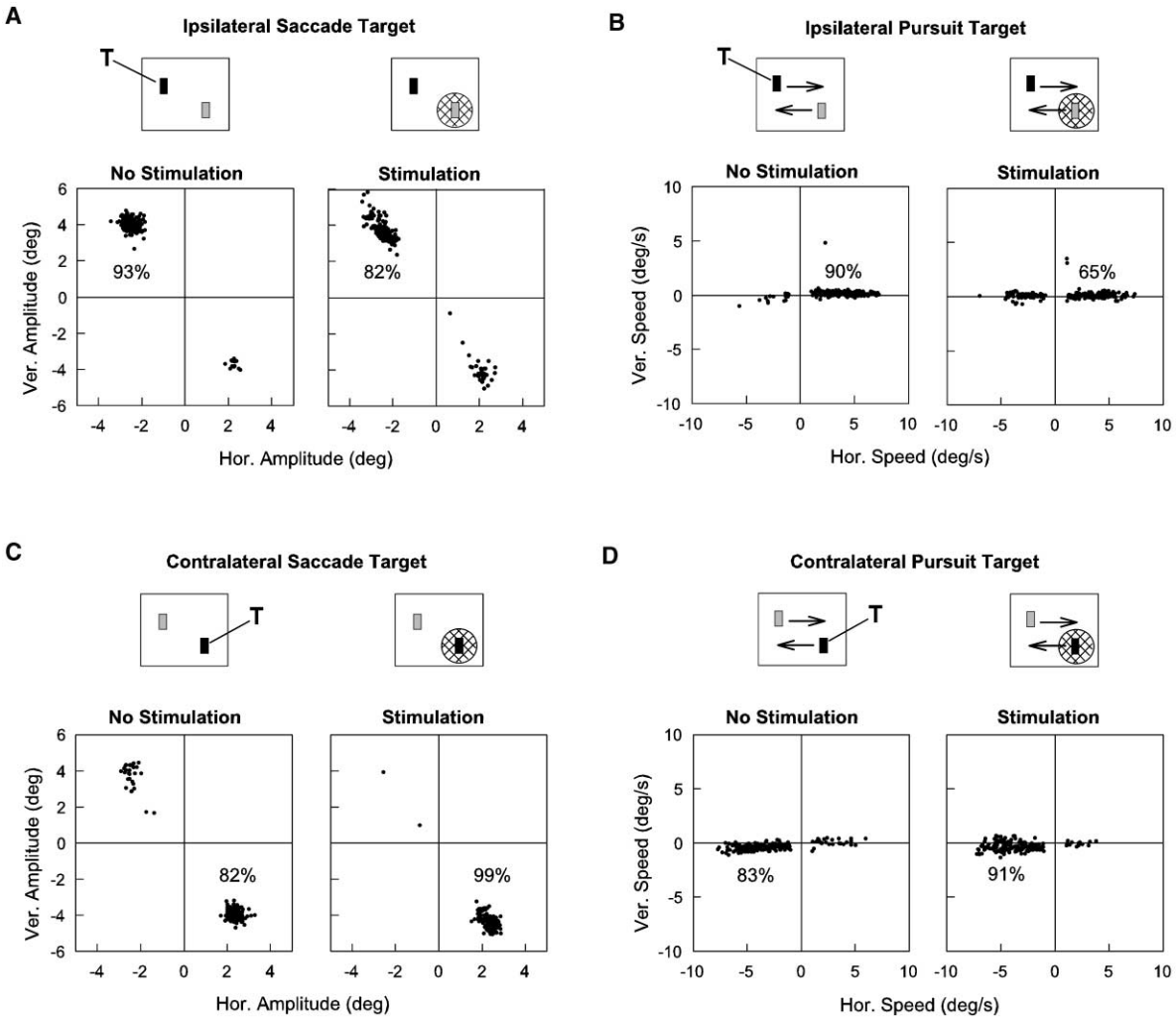

Figure 2. Changes in Target Choice Caused by SC Stimulation during a Representative Session

The experimental conditions are identified by the icons at the top of each panel: the black bar (labeled "T") represents the target onset location, and the crosshatched region indicates the visual location corresponding to SC stimulation. For saccade conditions, the endpoints of the first saccade from every trial are plotted for targets appearing ipsilateral (A) and contralateral (C) to the site of SC stimulation. For pursuit conditions, the horizontal and vertical velocities over the first 100 ms of pursuit are similarly plotted for targets appearing ipsilateral (B) and contralateral (D). The pair of plots within each panel shows the results from trials with (right) and without (left) stimulation, and the inset values report the percentage of correct responses for each condition.

examination revealed a difference between saccades and pursuit: the effects for contralateral targets were significantly bigger than those for ipsilateral targets for saccades (two-way ANOVA of the absolute value of the mean change in percents correct, $p = 0.026$), whereas the opposite was true for pursuit ($p = 0.002$). This difference might be due to the mismatch between stimulation site and stimulus location that emerged on pursuit trials, as the retinal position of the pursuit stimulus changed over time but the stimulation site remained fixed. However, there was no difference in the effects based on target luminance for either saccades (two-way ANOVA, $p = 0.37$) or pursuit ($p = 0.88$).

The combined contralateral and ipsilateral effects show that stimulation increased the frequency of choices to stimuli that appear on the contralateral side of the screen, regardless of the target's identity. Signal detection theory provides a compact way of quantifying the amount of spatial bias a monkey exhibits by comparing the proportion of hits and false alarms made to a particular location (Macmillan and Creelman, 1991). The same analysis can also be used to assess the monkeys' overall ability to discriminate the two stimuli (sensitivity, measured as d') (Macmillan and Creelman, 1991). In practical terms, bias and sensitivity measurements collapse ipsilateral and contralateral information into a single data point each, allowing one to see the overall effect for every session without having to compare data from two spatially disparate locations.

We used the constant criterion method for calculating bias (see Experimental Procedures) and arbitrarily defined a positive value to represent a bias in the contralateral direction. Microstimulation resulted in an increase in bias toward the contralateral stimulus for both saccades

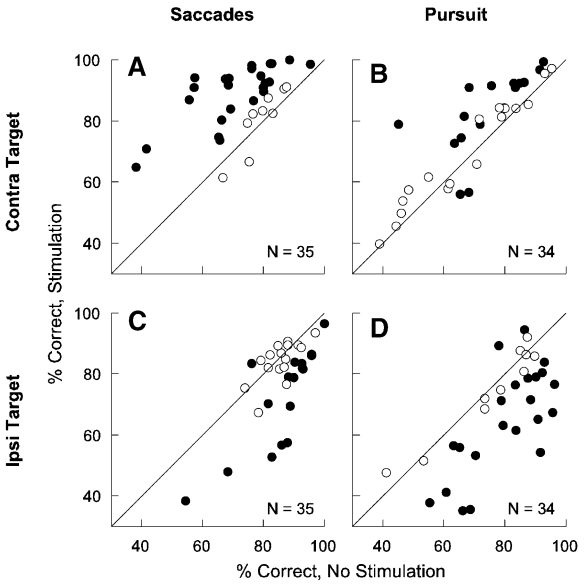

Figure 3. Changes in Target Selection Caused by SC Stimulation

The percentage of correct responses on trials with stimulation (% Correct, Stimulation) is plotted as a function of the percentage of correct responses without stimulation (% Correct, No Stimulation). Data are plotted separately for saccade (A and C) and pursuit (B and D) trials and for targets initially appearing contralateral (A and B) and ipsilateral (C and D) to the site of SC stimulation. Each symbol shows data from a single session (n = 35 sessions; one session run as saccade-only). Filled circles indicate sessions for which stimulation caused a significant change in percent correct. A few data points are not visible, as they fell beyond the plot axes (percent correct < 40%).

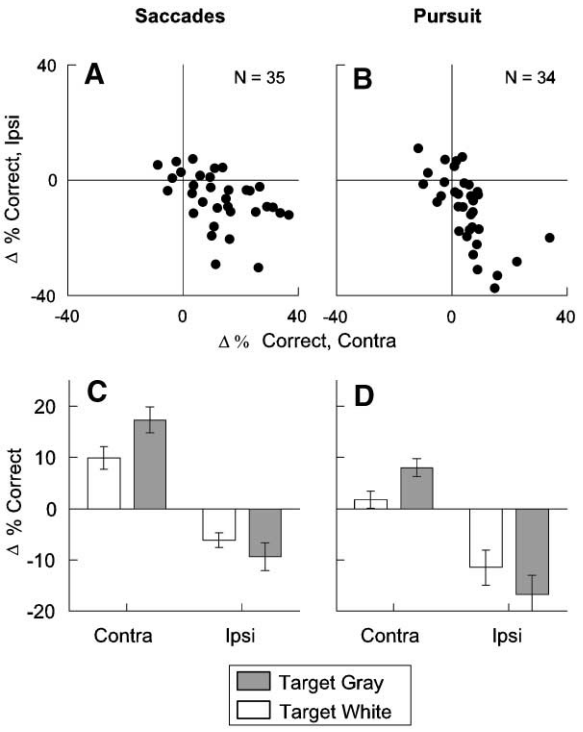

Figure 4. Comparison of Changes in Target Selection for Ipsilateral and Contralateral Targets

Change in percent correct for ipsilateral targets is plotted as a function of change in percent correct for contralateral targets for saccades (A) and pursuit (B). Mean change in percent correct across all sessions for contralateral and ipsilateral targets for saccades (C) and pursuit (D). Gray bars represent trials on which the target identity was the darker of two stimuli; white bars represent trials on which the target identity was the lighter stimulus. Error bars indicate the standard error of the mean. Two-way ANOVA showed a significant main effect of target onset location (contralateral/ipsilateral) on change in percent correct ($p < 0.001$) for both pursuit and saccades, but no effect of target luminance.

and pursuit (Figures 5A and 5B). The effect on sensitivity (d') differed between the two: saccade performance exhibited an increase in sensitivity during stimulated trials (Figure 5C); pursuit tended to show a decrease in sensitivity (Figure 5D). Bias calculations also revealed an interesting indirect effect of microstimulation. On saccade trials with no stimulation (abscissa, Figure 5A), bias was negative (i.e., in favor of the ipsilateral stimulus) during most sessions (28/35); this proportion was significantly different from that expected by chance if the monkey were unbiased (χ^2, $p = 0.023$). This effect might reflect a voluntary compensatory strategy. Because the monkeys were overtrained on the task, they were accustomed to an equal number of leftward and rightward targets and may have responded to the increased number of contralateral saccades during the experiment by developing a bias for ipsilateral saccades during unstimulated trials. Pursuit showed a similar trend, although the proportion of sessions that showed a negative bias (20/34) was not significantly different from chance (χ^2, $p = 0.62$).

Figure 6 summarizes the effects of microstimulation on the average changes in bias and sensitivity across all sessions. As with percent correct, the changes in bias and sensitivity (Figures 6A and 6B) showed no significant differences based on the luminance of the target (two-way ANOVA, $p = 0.42$ for saccades, $p = 0.45$ for pursuit). Both pursuit and saccades showed an increase in bias for stimuli that appeared on the contralateral side. The two differ in the effects on sensitivity, with saccades showing an increase in sensitivity with stimulation and pursuit showing a decrease in sensitivity. The relative magnitude of effects on pursuit and saccades were not significantly different from each other (Student's t test, $p = 0.91$ for bias, $p = 0.79$ for sensitivity). The increase in bias was, however, stronger than the change in sensitivity for both pursuit and saccades (two-way ANOVA, $p < 0.001$). In summary, microstimulation increased the likelihood that the monkeys would select the stimulus that appeared on the contralateral side of the screen as an object for a saccade or pursuit, irrespective of whether that stimulus was a distractor, a target, white, or gray.

Because the effects of stimulation were the same whether the target was white or gray, the results are not likely due to the introduction of a visual luminance increment (or decrement) onto the contralateral stimulus as has been seen from stimulation of cortical areas (Girvin et al., 1979). In such a case, one would expect opposite effects for the two target colors (a luminance increment would make a white target more discriminable, but a gray target less discriminable). However, to further address the possible influence of visual stimulus alterations (or phosphenes), we performed control experiments in which we stimulated in the superficial layers of

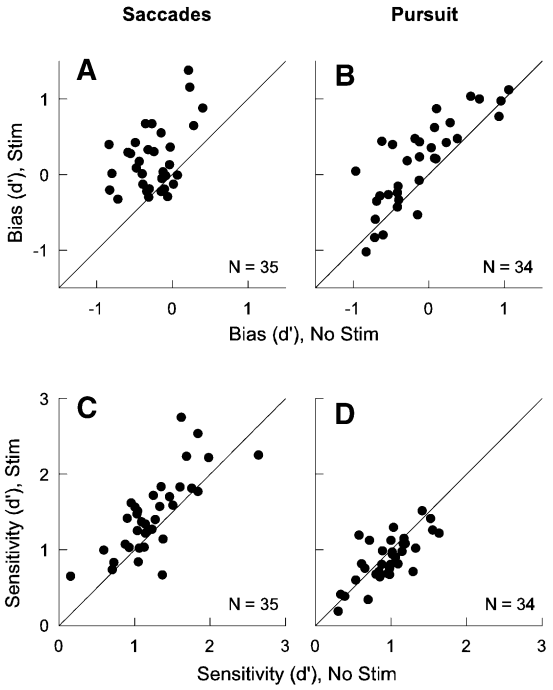

Figure 5. Changes in Bias and Sensitivity Caused by SC Stimulation

Bias (A and B) and sensitivity (C and D) on trials with stimulation are plotted as a function of the values obtained on trials without stimulation, separately for saccade (A and C) and pursuit (B and D) conditions. Each symbol shows results from a single session. Note that the axes for bias and sensitivity have different ranges but the same scale.

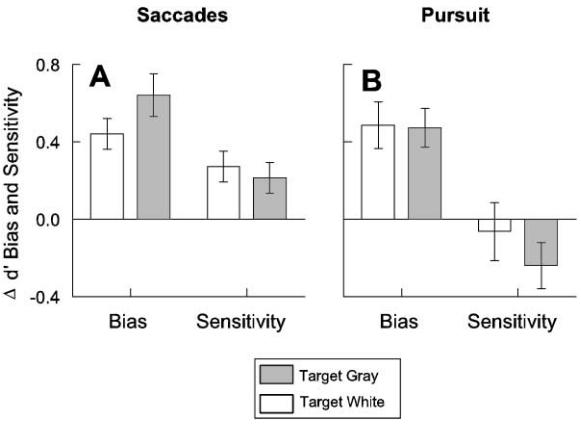

Figure 6. Mean Changes in Bias and Sensitivity Across All Sessions for Saccades and Pursuit

Gray bars represent trials in which the target identity was the darker of two stimuli; white bars represent trials in which the target identity was the lighter stimulus. Error bars indicate the standard error of the mean. Two-way ANOVA reveals a significant difference between the magnitude of bias and sensitivity effects ($p < 0.001$) for both pursuit and saccades. There was no significant difference based on target luminance.

the SC (which contain visual but not movement-related cells) during the same task. We confirmed our placement in the superficial layers by recording visual activity from single and multiple units prior to conducting these control experiments. There were no changes in percent correct, bias, or sensitivity when we stimulated the superficial layers ($n = 4$ sessions).

A simple explanation for our results is that microstimulation shifted SC activity toward response threshold at the stimulated location. If so, one might expect not only changes in bias or percent correct but also changes in latency, because the shift in activity would alter the time it takes to reach threshold (Asrress and Carpenter, 2001; Carpenter, 1981; Carpenter and Williams, 1995; Hanes and Carpenter, 1999; Logan, 1994; Logan et al., 1984; McGarry et al., 2003; Osman et al., 1986). Figure 7A schematically illustrates the level of net activity between the left and right SC. In this example, the upward deflection represents a gradual increase in net activity for an impending contralateral response, and the point at which the activity reaches threshold determines the latency. The stimulation trace shows a contralateral bias in net activity. Because this biased trace is closer to the contralateral threshold, contralateral responses would be expected to have shorter latencies. Conversely, ipsilateral responses should have longer latencies.

As predicted, the effect of stimulation on pursuit and saccade latency depended on whether the eye movement was made to a contralaterally or ipsilaterally appearing stimulus. Figure 7 shows the mean latency for saccades (B and D) and pursuit (C and E) for those sessions that exhibited a significant change in percent correct. The latency interaction between stimulation and the hemifield in which the selected stimulus appeared was significant for both movement types and both monkeys (two-way ANOVA, $p < 0.001$), with selections made to stimuli appearing on the ipsilateral side (open circles) during stimulation having longer latencies than unstimulated trials. Conversely, selections made to stimuli that appeared on the contralateral side (filled circles) had shorter latencies during stimulation compared to unstimulated trials, except for monkey W's contralateral saccades that had similar latencies in the presence or absence of stimulation. These results show that, in general, eye movements evoked by objects at locations that matched the site of stimulation (i.e., appeared contralateral) had shorter latencies, whereas eye movements evoked by objects at discordant locations (i.e., appeared ipsilateral) had longer latencies.

There was also a saccade latency difference of the opposite sign during unstimulated saccade trials, reflecting the compensatory ipsilateral bias the monkeys adopted in the absence of stimulation. Contralateral saccades had a significantly longer latency than ipsilateral saccades for both monkeys (Figures 7B and 7D) during those trials in which we did not stimulate (independent t test, $p < 0.001$). Pursuit showed the opposite effect, with acquisition of ipsilateral stimuli having a significantly longer latency than contralateral stimuli during unstimulated trials for monkey A (Figure 7C, $p < 0.001$) and a similar but not significant trend for monkey W (Figure 7E, $p = 0.097$).

Discussion

The primary finding of this study is that microstimulation in the SC biased the monkeys' pursuit and saccadic eye movement choices toward the stimuli that appeared on the contralateral side. This manipulation of the monkeys'

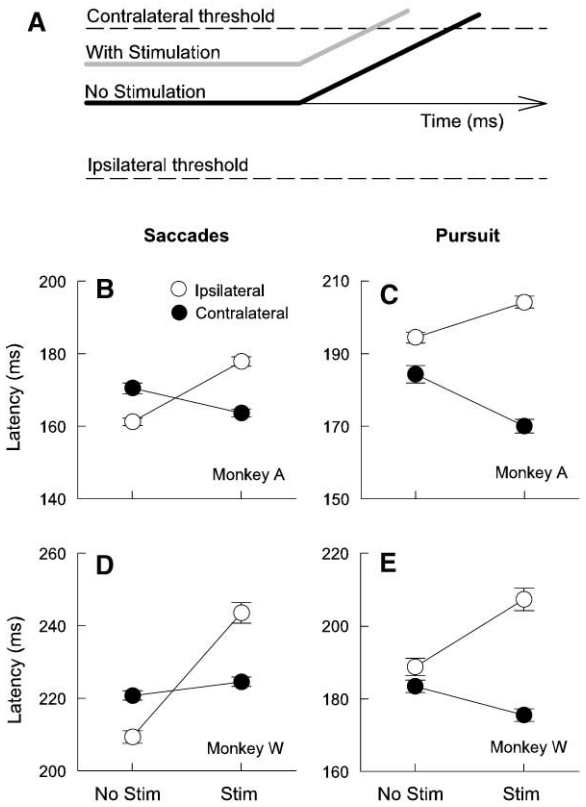

Figure 7. Changes in Saccade and Pursuit Latency Caused by SC Stimulation

(A) Schematic representing activity in the net SC during an impending contralateral response. The gray line represents a schematic response in the presence of microstimulation. The black line represents a similar trial in the absence of stimulation. (B–E) Latency measurements grouped according to the starting location of the stimulus that evoked a particular direction of eye movement. (B and D) Saccade latency is plotted as a function of stimulation condition (Stim, No Stim), separately for each monkey. Filled circles represent contralateral saccades; open circles represent ipsilateral saccades. (C and E) Pursuit latency is plotted as a function of stimulation condition. Filled circles represent pursuit of the stimulus appearing on the contralateral side; open circles represent pursuit of the stimulus appearing on the ipsilateral side. Error bars indicate the standard error of the mean. Stimulation increased the latencies of both saccades and pursuit for stimuli that appeared on the side ipsilateral to the site of SC stimulation ($p < 0.001$) and decreased the latency for eye movements to stimuli that appeared on the contralateral side ($p < 0.001$), except for monkey W's contralateral saccades, which were slightly increased.

choices shows that the SC plays a role in choosing the next target, in addition to its well-known role in the motor preparation and execution of saccades (Sparks and Mays, 1990; Wurtz and Albano, 1980). These results build upon a body of work over the past several years that has suggested a connection between premotor activity in the SC and target choice. Increasing the probability that a saccade target would fall within a neuron's response field by decreasing the number of potential target locations has been shown to increase premotor activity in the SC (Basso and Wurtz, 1998). Premotor activity has also been shown to discriminate targets from distractors (McPeek and Keller, 2002a) and to predict saccade target choice (Horwitz and Newsome, 1999, 2001). It has also recently been demonstrated that inactivation of the SC produces striking deficits in saccade target selection (McPeek and Keller, 2004). However, the saccade results alone, in the present study and others, leave open the possibility that premotor activity in the SC is related to motor preparation rather than target selection. Because target location largely determines the saccade endpoint, premotor activity in the SC might represent a partially formed plan for a saccade, rather than an evolving decision about the target.

The effects of stimulation on pursuit target choice are particularly important for concluding that the SC has a role in target selection per se, because they provide a clear dissociation between the location of the stimulus and the metrics of the eye movement. These results complement our previous findings that the selection of targets for pursuit is associated with changes in the activity of SC neurons (Krauzlis and Dill, 2002; Krauzlis, 2003). As in the current results, those earlier experiments employed a step-ramp paradigm (Rashbass, 1961) in which the target appeared in one visual hemifield before moving smoothly toward and into the opposite hemifield. Neurons in the SC increase their activity when the initial step is into their response field (i.e., contralateral) even when the subsequent pursuit moves the eyes in the opposite direction. Similarly, we found that microstimulation introduced a response bias for the stimulus contralateral to the SC site, even though this choice for pursuit resulted in an eye movement directed away from the target location. Thus, microstimulation of the SC manipulated the monkeys' choices based on the location of the target, not the direction of the pursuit eye movement used to acquire the target. This allows us to reject the notion that stimulation merely accelerated motor preparation for a particular eye movement vector, in favor of the idea that it instead marked a particular (contralateral) object for an upcoming movement.

In addition to biasing the monkeys' choices, microstimulation also changed the latencies of pursuit and saccades, providing additional evidence that the SC plays a causal role in target selection. The mechanism of selection is not yet fully understood, but models of reaction time generally assume that some internal signal varies over time and that the movement is triggered when this signal reaches a threshold value (Carpenter and Williams, 1995; Link and Heath, 1975; Ratcliff et al., 1999; Reddi and Carpenter, 2000; Schwarz, 1993). If microstimulation biased this internal signal toward the contralateral stimulus, then the latencies for contralateral stimuli should be decreased and the latencies for ipsilateral stimuli should be increased (Figure 7). Overall, that is exactly what we observed, with the exception of one monkey's contralateral saccades (Figure 7D, filled circles); this exception may reflect the fact that microstimulation is a coarse technique that disrupts as well as displaces the normal pattern of neuronal activity. Nonetheless, the effects of microstimulation on latency corroborate the previous findings that the latencies of saccades and pursuit are related to the firing rates of neurons in the SC (Basso and Wurtz, 1998; Dorris et al., 1997; Krauzlis and Dill, 2002; McPeek and Keller, 2002a).

Microstimulation also had some effect on the sensitiv-

ity (d') of the pursuit and saccade responses. The changes in sensitivity were more variable and differed between pursuit and saccades, which make them harder to explain. The changes may have been caused in part by an interaction between the primary effect on bias and the monkeys' own tradeoffs between speed and accuracy. Since reaction time can affect sensitivity, for instance, the stimulation-induced changes in contralateral and ipsilateral latency may have had differing effects on pursuit and saccades.

The etiology of these effects on target selection is unclear, but two types of mechanisms seem plausible. One possibility is that microstimulation directly shifted the balance of activity that determines the monkeys' response. The fact that we found larger and more consistent effects on response bias than on sensitivity (Figures 5 and 6) suggests that we may have altered the monkeys' decision criteria while leaving the visual processing of the stimuli relatively unperturbed. In particular, by elevating activity locally within the SC, we may have reduced the strength of signal required to trigger a response to the contralateral stimulus; this change in initial conditions would amount to a shift of the decision criterion in favor of the contralateral stimulus. The neural mechanisms that might apply this criterion to the triggering of pursuit and saccades are not known but could involve newly identified shared pathways in the brainstem (Keller and Missal, 2003; Krauzlis, 2004).

A second possibility is that microstimulation acted indirectly by causing a shift in visual attention, consistent with the premotor theory of attention (Rizzolatti et al., 1987; Sheliga et al., 1995). The visual responses of neurons in the SC are enhanced when the stimulus is the target of a saccade (Goldberg and Wurtz, 1972; Robinson and Kertzman, 1995; Wurtz and Mohler, 1976), providing early suggestions of a link between visual attention and SC activity. The "buildup" activity of saccade-related neurons is modulated by symbolic cues and stimulus probability, manipulations that also cause changes in reaction time (Basso and Wurtz, 1998; Kustov and Robinson, 1996). It has recently been shown that a subset of SC neurons, the visuomotor cells, is active during covert shifts of attention evoked by spatially precise cues but not by symbolic cues (Ignashchenkova et al., 2004). Furthermore, the endpoints of saccades evoked by SC stimulation are modified by shifts of attention (Kustov and Robinson, 1996). These results support the idea that the SC is part of a shared circuit for orienting attention and selecting targets for eye movements. Of course, such a circuit would not be restricted to the SC, and our stimulation results do not allow us to distinguish whether the selection signal arises within the SC or elsewhere. For example, an attentional effect has recently been demonstrated in another eye movement-related area—stimulation in the frontal eye fields increased the visual response of those V4 neurons that represent the stimulated area (Moore and Armstrong, 2003; Moore and Fallah, 2004). In our experiment, the response bias introduced by microstimulation, as well as the effects on eye movement latency, could be explained by a shift of attention toward the contralateral stimulus at the expense of the ipsilateral stimulus. Such a shift in activity could have the same effects on performance as a change in the decision criterion (Macmillan and Creelman, 1991).

The results from our experiment do not differentiate between the two types of selection mechanisms—spatial attention or response intention—because both are capable of producing a contralateral response bias, nor are the two mutually exclusive. Regardless of the exact mechanism or place of origin of the selection, our results show that the SC applies the selection signal toward choosing eye movement targets, even in the absence of saccades. Thus, in addition to its traditional role in the motor control of saccades, the SC is also involved in the preceding step of selecting which object will become the target of the next eye movement.

Experimental Procedures

Animal Preparation

We collected data from two adult rhesus monkeys (*Macaca mulatta*) that were 5 years of age and weighed 9–12 kg. All experimental protocols for the monkeys were approved by the Institutional Animal Care and Use Committee and complied with United States Public Health Service policy on the humane care and use of laboratory animals. The monkeys were prepared and studied using standard techniques for microstimulation, single-neuron recording, and eye movement recording that have been described previously (Basso et al., 2000; Krauzlis, 2003).

Recording and Stimulating Procedures

Single-neuron recordings and microstimulation were performed in the intermediate and deep layers of the SC (1–3.5 mm below the surface), and electrode tracks were guided by structural MR images. For microstimulation, biphasic currents (10–30 μA, 100–200 Hz) were applied through tungsten microelectrodes (Frederick Haer) with impedances between 0.1 and 3.5 MΩ measured at 1 kHz, using a Grass S11 stimulator and PSIU6 isolation units (Astro-Med, Inc.). To determine the characteristic saccade vector associated with each SC site, we applied microstimulation for a duration matching that of the upcoming experiment (360 ms for monkey A and 460 ms for monkey W) immediately after a fixated spot stimulus was extinguished. Staircases of saccades were typically evoked with 10–15 μA applied at 200–250 Hz. To determine the parameters for subthreshold microstimulation, the strength of applied current was systematically reduced (10–30 μA, 91–200 Hz) until we no longer evoked saccades characteristic of the site. At some sites, saccades much smaller than the characteristic saccade were observed during stimulation, but these comprised fewer than 30% of the trials (the stimulation parameters in these cases resulted in few or no saccades during the actual experimental task).

Behavioral Paradigms

After the stimulation parameters for a given site were set, tests of the effects of stimulation on target selection started. At the beginning of each experimental trial, the monkey fixated a small spot stimulus (0.2° diameter) that appeared at the center of the display for a randomized duration (2–2.5 s). During this fixation interval, a centrally located 0.4° × 0.4° square precue appeared 1–1.5 s before the two target stimuli appeared and lasted for 600 ms; its luminance (either white or gray) indicated the identity of the upcoming target. At the end of the fixation period, two 0.2° × 0.4° stimuli appeared (one white and one gray) on opposite sides of the extinguished fixation point at a fixed eccentricity (1°–15° horizontal, 0.3°–8° vertical), which varied from session to session depending on the electrode location. On half the trials the stimuli remained stationary (saccade trials), and on the other half (pursuit trials) the stimuli moved toward the midline of the screen at a fixed speed (9°/s to 46°/s, one speed per session based on the stimulus onset eccentricity for that session). The stimulus parameters for pursuit were practiced during behavioral training sessions prior to the beginning of the stimulation experiments so that the pursuit responses during any given session were quite regular and reproducible, with minimal corrective saccades

during pursuit initiation (see the Supplemental Data [http://www.neuron.org/cgi/content/full/43/4/575/DC1]). The monkey was given a small juice reward for tracking the stimulus that matched the luminance of the precue. The onset locations for pursuit and saccade stimuli were adjusted so that one of the two appeared at a position in the visual field matching (or in the vicinity of) our stimulation site. Microstimulation was applied on half of the trials as described above beginning 100 ms prior to target and distractor onset and lasting 360 ms for monkey A and 460 ms for monkey W (durations were adjusted based on monkeys' eye movement latencies and sensitivity to stimulation-evoked saccades). Each session consisted of ~1200 trials.

Data Analysis

The occurrence of saccades was detected using eye velocity and acceleration criteria (Krauzlis and Miles, 1996). The onset of pursuit was estimated from traces of eye velocity on individual trials using a linear regression technique described previously (Adler et al., 2002). To confirm that this technique provided reliable estimates of pursuit onset, it was corroborated by a second test. We compared the mean velocity during pursuit onset (the first 100 ms after the estimated latency) to the mean velocity during fixation (a fixed 100 ms window starting 100 ms prior to target onset). We accepted the latency estimate only if the mean velocity during pursuit onset was significantly greater than that during fixation (Student's t test, $p < 0.05$).

Although stimulation-evoked saccades did occasionally occur, it is unlikely that these influenced our results. First, when present, stimulation-evoked saccades occurred on only about 10% of the trials. Second, these saccades were easily identified based on their very small amplitudes (0.5°–1°) and their short and stereotyped latencies; all such saccades were excluded from our calculations of percent correct. Third, the visual consequences of such small saccades were relatively minor. Because the saccades were very small, they brought the eyes no more than 1° closer to either stimulus. Fourth, control experiments simulating the visual effects of such displacements showed no change in performance. In these control sessions without microstimulation ($n = 2$), all objects on the screen were displaced by 1° on randomly selected trials at a random time within a temporal window matching the timing of stimulation-evoked saccades. The visual displacement occurred on 25% of the trials—a frequency much higher than the actual occurrence of stimulation-evoked saccades during any experimental session. These control experiments showed no effect on the monkeys' choice behavior.

To test the significance of the difference in performance on trials with and without microstimulation, we performed a one-tailed t test using the binomial distribution to compute the standard error ($p < 0.05$).

Bias was calculated in units of d' assuming a constant criterion, based on methods from signal detection theory (Macmillan and Creelman, 1991). In brief, correct selection of a contralateral target was scored as a "Hit" and incorrect selection of a contralateral distractor was scored as a "False Alarm". Bias (c) was then defined as the sum of the z-transformed Hit rate (H) and False Alarm rate (FA) values, divided by -2:

$$c = -0.5[z(H) + z(FA)].$$

Similarly, sensitivity was measured in units of d' using the same Hit rate and False Alarm rate values. Sensitivity (d') was defined as the difference of the z-transformed Hit rate and False Alarm rate, divided by the square root of 2:

$$d' = [1/\mathrm{sqrt}(2)][z(H) - z(FA)].$$

Except where noted otherwise, all group comparisons between mean values of latency, percent correct, bias, or sensitivity were tested for significance using two-way ANOVAs and post hoc Tukey tests of multiple comparisons.

Acknowledgments

We thank L. Chukoskie, G.A. Fowler, Z. Hafed, and D.B. Liston for their comments on a previous draft of this paper; and N. Dill and K. Kornylo for technical assistance. This work was supported by NIH grant EY12212 and a McKnight Scholar Award to R.J.K.

Received: March 1, 2004
Revised: July 16, 2004
Accepted: July 22, 2004
Published: August 18, 2004

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