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Target Selection and Saccade Generation in Monkey Superior Colliculus

Nicholas L. Port and Robert H. Wurtz

Laboratory of Sensorimotor Research National Eye Institute National Institutes of Health Bethesda, Maryland USA

Abstract

The superior colliculus (SC) of the monkey has been shown to be involved in not only initiation of saccades but in the selection of the target to which the saccade can be directed. The present experiments examine whether SC neuronal activity related to target selection is also related to saccade generation. In an asynchronous target task, the monkey was required to make a saccade to the first of two spots of light to appear. Using choice probability analysis over multiple trials, we determined the earliest time at which neurons in the SC intermediate layers indicated target selection. We then determined how closely the neuronal selection was correlated to the saccade onset by using our asynchronous reaction time task, which allowed the monkey to make a saccade to the target as soon as the selection had been made. We found that the selection became evident at widely differing times for different neurons. Some neurons indicated target selection just before the saccade (close to the pre-saccadic burst of activity), others did so at the time of the visual response, and some showed an increase in their activity even before the target appeared. A fraction of this pre-stimulus bias resulted from a priming effect of the previous trial; a saccade to the target in the movement field on the previous trial produced both a higher level of neuronal activity and a higher probability for a saccade to that target on the current trial. We found that most of the neurons (76%) showed a correlation between selection time and reaction time. Furthermore, within this 76% of neurons, many indicated a selection very early during the visual response. There was no evidence of a sequence from target selection first and saccade selection later, but rather that target selection and saccade initiation are intertwined and are probably inseparable.

Keywords

Target Selection; Superior Colliculus; Saccades; Priming

INTRODUCTION

A salient feature of all primates is the ability to examine the visual world with high acuity vision. To accomplish this, the high resolution foveas of the eyes are redirected as frequently as three times per second from one target to another in the visual field. The brain systems that select these targets and generate saccades to them are becoming better understood as the flow of information has been examined while monkeys make such selections. Neuronal activity has been identified extending from higher order visual-motor processing in the parietal (Shadlen and Newsome 2001; Roitman and Shadlen 2002) and frontal cortex (Thompson et al. 1996; Kim and Shadlen 1999; Schall 2002; Gold and Shadlen 2003) through the basal ganglia (Hikosaka et al. 2000) to the visual-motor neurons in the superior colliculus (SC).

Neurons in the intermediate layers of the SC have long been known to have a visual response and increased activity before saccadic eye movements (see review by Sparks and Hartwich-Young 1989). More recently they have been shown to be critically involved in the selection of visual targets for these saccades. With tasks that depended on visual motion discrimination (Horwitz and Newsome 1999; Horwitz and Newsome 2001b; Horwitz and Newsome 2001a; Horwitz et al. 2004), color in visual search (McPeck and Keller 2002b; McPeck and Keller 2002a; Keller et al. 2005; Kim and Basso 2008), or the target for pursuit or saccades (Krauzlis and Dill 2002), these SC neurons showed changes of activity during target selection. These changes were frequently in the prelude or buildup activity that develops between the initial visual and final saccade related activity. Both uncertainty during selection (Basso and Wurtz 1998) and competition between stimuli (Li and Basso 2005) altered SC activity. When multiple targets were present, the saccade curvature towards the selected target was correlated with the activity of SC neurons (McPeck et al. 2003; Port and Wurtz 2003b). Finally, subthreshold SC stimulation biased selection towards a target (Carello and Krauzlis 2004; Dorris et al. 2007), and inactivation altered the target selection in the visual search task (McPeck and Keller 2004; McPeck 2008). There can be little doubt from these previous studies that SC neuronal activity is closely related to target selection as well saccade initiation.

In the present experiments we concentrate on how closely related target selection is to the generation of the saccade to that target. We first looked at when an SC neuron indicates the selection. One possibility is that the target selection occurs early in the visual motor sequence in the SC, namely, at the time of the visual response. At the other extreme, target selection might occur later, for example at the time of the presaccadic activity. In either case, identifying the time of target selection across these SC neurons would provide a critical clue as to how closely associated the selection is to the visual and saccade related responses. Furthermore, a better understanding of this timing permits a more definitive test of the relation of target selection to saccade generation because a neuron's time of target selection can be correlated with the saccadic reaction time over a series of trials. A close correlation would indicate an intertwining of target selection and saccade generation, while a low correlation would be more consistent with a target selection process that is separable from saccade generation.

To do these experiments we recorded from SC intermediate layer neurons that increased their activity before saccades (saccade-related neurons). First, to estimate the time at which the activity of an SC neuron indicates target selection, we used a choice probability method based on receiver operating characteristic (ROC) analysis. Second, we determined how closely this neuronal selection time was correlated with the saccade onset by using a reaction time task in which the monkey could make a saccade as soon as selection had been made.

We found no single early or late times at which neuronal selection became evident but rather that different neurons indicated the selection over a range of times extending from the visual response to the presaccadic activity. Regardless of this selection time, we found that it was correlated with saccade onset. We conclude that target selection and saccade generation are not sequential but rather are temporally intertwined in the SC.

Abstracts of this work have appeared previously (Port et al. 1999; Port and Wurtz 2003a).

METHODS

Behavioral and Physiological Procedures

The same two monkeys used in previous experiments (Port and Wurtz 2003b) were used in the present experiments, and the same procedures were used for behavioral control, recording of eye position, and recording from pairs of SC neurons. All animal care and experimental

procedures were approved by the Institute Animal Care and Use Committee and complied with Public Health Service Policy on the humane care and use of laboratory animals.

In the current study, rather than analyzing the burst activity before saccades, we analyzed the visual and delay activity during fixation that precedes these bursts in the saccade related neurons in the SC intermediate layers. Although the neurons were recorded in pairs, for this study we analyzed the activity of each neuron individually. We recorded from 70 neurons (35 neuron pairs). Eighteen neurons (9 pairs) were removed from analyses because their visual - movement fields included both targets, making it impossible to determine to which target the neuronal activity was related. From the 52 neurons remaining (26 pairs of which 13 pairs were included in Port and Wurtz 2003b), another neuron was removed from the data set because it had a very poor saccade related burst of action potentials (< 50 spikes/s), leaving a final sample of 51 neurons. For these 51 neurons, the two targets were in the same contralateral hemifield for 33 neurons and across the vertical meridian from each other for the other 18 neurons.

After isolating a neuron we tested its activity in two behavioral tasks. First, in order to see how its activity was related to the visual target and saccade initiation, we used a visually guided delayed saccade task described previously (Port and Wurtz 2003b). The monkey then performed the asynchronous target task described in the same previous report. In this task, we required the monkey to choose between two targets - one lying in the visual and movement field of the neuron and the other lying outside of this field. The monkey obtained a water reward for making a saccade to the target that appeared first. The targets were positioned at two points in the visual field as shown schematically in Fig. 1A, with the targets located in the centers of the movement fields of the two SC neurons being studied. The interval between the appearance of the first and second targets (Fig. 1B) was randomized on successive trials as was the order in which they appeared. The order of the target presentations were systematically varied so that target #1 preceded target #2 at four different intervals, target #2 preceded target #1 at four different intervals, and one presentation was simultaneous. Each target was also presented alone for a total of 11 trial types. These trial types were repeated without replacement 50 times for a total of 550 trials per experiment. In the simultaneous condition the monkeys were randomly rewarded 50% of the time. The 4 asynchronous times were in multiples of X ms, so that for $X = 5$, the four asynchronous time values were 5, 10, 15, and 20 ms. During the experiments, X was usually 15 to 20. ms.

A major factor that affected the value of X was target positioning. More peripheral and widely spaced targets were more difficult for the monkey because a small asynchrony (eg. 15 ms) is easier to perceive near the fovea than in the periphery. Variations in target positions (which were dictated by the location of the movement fields of the SC neurons being studied) therefore required changes in the asynchronies used. At the beginning of each experimental session the value of X was adjusted so that the monkey made the saccade to the correct target on about two-thirds of the trials, and the value of X remained the same for the rest of that experimental session.

Determination of Selection Times

The activity of each neuron was evaluated to determine the time at which its firing rate indicated the target selected was in the movement field of the neuron as opposed to outside of it. In the first step we converted the neuronal spike trains into spike density functions (MacPherson and Aldridge 1979; Richmond et al. 1987) in order to produce a continuous function of neuronal activity throughout a trial. Each spike was replaced with a Gaussian (usually 10 ms) and trials were then grouped into those on which the monkey made a saccade to the target into or out of the movement field. Fig. 2A, C, and E show spike density curves for three example neurons. This separation was made regardless of the asynchrony between the targets or whether the

saccade made was to the “correct” target for that trial; the asynchrony was essentially a relatively simple way of requiring the monkey to make saccades to each of the two targets.

In the next step we searched for the time at which the curves separated for saccades into the movement field and out of the movement field. For this we used the now well established choice probability technique developed by Britten et. al. (1996) based on computing the receiver operating characteristic (ROC). This has previously been used to determine the time of saccadic choices in both FEF and SC (Thompson et al. 1996; Krauzlis and Dill 2002; McPeck and Keller 2002a; Kim and Basso 2008). For the example neurons in Fig. 2B, D, and F the ordinate shows the choice probability indicating that the upcoming saccade will go into the movement field each ms from 500 ms before target onset to 400 ms after target onset, aligned on target onset. Like the spike density curves, these choice probability plots show a rise after target onset and a greater rise before the later saccade onset.

While the plots in Fig. 2B, D and F indicate the successive probabilities of the saccade going into the movement field for each ms, they do not indicate when that probability is above chance. To determine this probability, we used a resampling statistic that enabled us to compare the choice probability at each ms to what would have occurred by chance (Britten et al. 1996; Dodd et al. 2001; Horwitz and Newsome 2001b). In this permutation test the observed choice probability was compared to the resampled distribution. We then applied the evaluation of significance to each ms on the choice probability curve and indicated the ms periods that reached a significance of less than 0.001 by a blue dot. On many curves, there were cases for which one point was significant but subsequent points were not. We therefore required five successive choice probabilities in a row to reach significance before we identified the first point as the time of neuronal discrimination.

All analyses were written in MATLAB (www.mathworks.com). The ANOVA was done in SPSS (www.spss.com). The mean firing rates in the ANOVA were square root transformed in order to normalize the Poisson like distribution of neural firing rates and to stabilize the variance (Georgopoulos et al. 1989; Snedecor and Cochran 1989; Prince et al. 2002).

RESULTS

Neuronal Selection Times

The time at which the saccade related neurons predicted which target the monkey would select fell along a continuum from just before saccade onset to before the target even came on. Figure 2 shows the response of three example neurons illustrating this range, although we consider this to be a continuum rather than three separate classes of neurons. The left column shows the spike density functions aligned with onset of the target in the movement field for saccades to the target (green trace) and those to the target outside of the movement field (red trace). The right column shows the time of neuronal discrimination as indicated by the choice probability plot. The blue dots indicate the decision time at the 0.001 significance level; the orange dots indicate the decision time at the 0.01 level.

For the first example neuron, the spike density curves (Fig. 2A) separate so close to the onset of the saccade as to be essentially indistinguishable from the onset of the saccade related burst of action potentials (which peaked on average 23 ms before the saccade in our sample of neurons). On the choice probability plot, the decision occurred 134 ms after target onset (0.001 level in Fig. 2B). For the second example neuron (Fig. 2C) the spike density curves separated much earlier – closer to the time of the peak visual response to the target. The time of neuronal discrimination was 66 ms on the choice probability plot (0.001 level, Fig. 2D). Finally for the third neuron, the activity indicated the selected target even before the appearance of the two target stimuli. For this neuron the level of activity increased before target onset (Fig. 2E) in

contrast to the absence of any background activity before target onset for the neurons in Fig. 3A and C. This activity indicated the time the target was selected, which in this case was time *before* target onset. Note, however, that the exact time of decision (-339 ms, 0.001 level, Fig. 3F) is affected by our randomization of when the first target came on (400 - 800 ms after fixation). The point, however, is that the selection clearly preceded target onset.

We determined the selection time for all of the 51 neurons in our sample (Fig. 3). Eleven neurons indicated the selection before the target even came on, and we will refer to these neurons as *pre-stimulus bias neurons*. For the remaining neurons the selection fell along a *continuous* range of times after target onset. For convenience of presentation, we found it useful to divide the rest of the neurons into two groups based on whether the selection occurred during the visual or saccadic burst of action potentials. We found that a trough between the two bursts occurred at about 120ms, and we used this value as our division. Those in which the selection was evident during the visual response, we refer to as *visual selection neurons* (27 neurons), and those in which the decision became evident after the visual response, we refer to as *saccade selection neurons* (13 neurons). The mean times of neuronal discrimination for the three groups of neurons were -236 , $+75$, and $+151$ ms from target onset and -453 , -119 and -73 ms before saccade onset. Thus, about 22% of the neurons indicated the selection before the targets came on and about 75% indicated the decision by the end of the visual response (120 ms).

A number of factors might influence these observations and we investigated the following ones.

Width of sigma for spike density functions—We used a sigma of 10 ms for the spike density function for each trial, and it is possible that a sigma this wide leads to an early estimate of the time of neuronal discrimination. For the neurons showing decisions during visual and saccade related activity, the decision time was about 5 to 10 ms later with a 3 ms sigma. There was an increase in the percentage of pre-stimulus bias neurons from about 22% to 24% with the shift to a sigma of 3 ms, which is likely to be due to the increased level of noise introduced by using a smaller sigma.

Significance level—To see the effect of relaxing our significance level from $p < 0.001$, we tested the effect using the $p < 0.01$ level. The effect was a systematic shift to an earlier identification of the decision. This change in decision time does not affect our basic conclusion that the decision becomes evident in different SC neurons at different times.

Target presentation order—So far we have grouped together trials in which the saccade went to the target in the movement field regardless of whether that target was the first of the two targets to appear on that trial. If we instead compared trials in which the target appeared first in the movement field to those in which the other target appeared first, we might find further differences in the time of neuronal discrimination. To see if there was such a difference, for each neuron, we split our data set into two groups based on target order, repeated our analysis on each of the two groups, and tested for an effect of target order. There was no systematic difference in the time of neuronal discrimination (Wilcoxon sign rank test, $p = 0.26$) for trials in which the target appeared first in the movement field compared to when it appeared second.

Decision time and delay activity—We also explored whether the time of neuronal discrimination was related to the magnitude of the delay activity in these SC neurons as had been reported in previous experiments (Horwitz and Newsome 2001b; McPeck and Keller 2002a). We determined the magnitude of the delay activity using a delayed-saccade task, which was run on 44 neurons. The time of neuronal decision was not related to the magnitude of the

delay activity (data not shown) even if we looked at only those 32 neurons that had a substantial discharge during the delay period (50 spikes/s).

Neuronal decision and behavioral asymmetry—The examples of neuronal decision shown so far are from experiments in which the monkey made a substantial number of saccades to each target so that the neuronal decision was independent of any asymmetry in target choice behavior. The behavior in these cases closely matched a Weibull function fitted to the psychophysical performance (Fig. 4A). In other experiments, however, the monkeys showed a preference for selecting one of the targets (Fig. 4B). One possible explanation for the response differences across experiments could lie in the location of the two targets in the visual field (determined by the movement field locations). The monkey may have had a tendency to make a saccade to the closer target. To quantify any such effect, we compared the monkey's response bias to the asymmetry of the target locations. To quantify the response bias, we used those trials in which the targets appeared simultaneously, and computed a response bias index which went from 0 to 1, with 0 indicating a small bias and 1 indicating a large bias (see Fig 4C, ordinate). The response bias index for the equal choice in Fig. 4A was 0.05 and that for the heavily biased choice in Fig. 4B was 1.00. For the index for target asymmetry (see Fig 4C, abscissa), 0 indicates targets with equal distances from the fixation point and 1 indicates targets with large asymmetry in target distances. We found a modestly significant correlation between the target-asymmetry index and the bias index ($r = 0.43$, Pearson $p = 0.03$) indicating that the position of the targets in the field probably does make a contribution to the asymmetry in target selection.

The next issue is whether the neurons that had an early decision time were those recorded on days when the monkey had a strong tendency to select the target that was in the movement field being studied. For this comparison we used a similar but signed bias index that indicated a bias toward or away from the movement field and compared this to the selection of the target in or out of the movement field. Fig. 4D plots the time of decision for each neuron on the abscissa and the signed response bias index for the monkey's behavior during that recording session on the ordinate. If the response bias influenced the time of neuronal decision we would expect that a strong response bias (numbers greater than +0.5 or less than -0.5 on the signed bias axis) would be accompanied by early decisions. No such relationship is evident in Fig. 4D. Although we see response biases by the monkey toward one target or the other that are likely to be related to target eccentricity (Fig. 4C), this does not seem to have a significant influence on the time of target selection (Fig. 4D).

Pre-stimulus Bias and Priming

Since our pre-stimulus bias neurons predict the target to be selected before the target stimulus even comes on, they seem particularly likely to reflect an effect of previous trials. Such a priming effect, in which the movement performed or reward received on a previous trial influences the amount of neuronal activity on a current trial, has been reported by several investigators (Platt and Glimcher 1999; Dorris et al. 2000; Coe et al. 2002; Lauwereyns et al. 2002). We next investigated to what extent the activity of the pre-stimulus bias neurons resulted from such a priming effect.

For the 11 neurons that showed a pre-stimulus bias, we divided the current trials into four types according to whether the target selected on the previous trial was into or away from the movement field and whether it was to or away from the field on the current trial. Figure 5A shows a clear and orderly progression of the magnitude of the neuronal activity for these four types of trials. Type1 trials, in which both the previous and current saccades were into the movement field (in – in, blue line in Fig. 5A), have the highest level of activity during the pre-stimulus, visual response, and pre-saccadic periods. This is consistent with a positive priming

effect: if the saccade on the preceding trial went into the movement field, the strength of the neuronal activity is greater on the current trial. In contrast, in Type 2 trials where the previous saccade went out of the movement field but the current trial went into the movement field (out – in, red line in Fig. 5A) less activity is seen. For Type 3 trials, in which the saccade on the previous trial entered the movement field but the current saccade did not, the neuronal activity is further reduced (in – out, green line in Fig. 5A). Finally, trials in which saccades on both the previous and current trials go to the other target (Type 4) have the lowest level of activity (out – out, black line in Fig. 56). In order to quantify this effect we did a two-way ANOVA in which the dependent variable was the neuronal activity during an epoch, and the two factors were the saccades on the previous trial (in or out of the movement field) and the saccade on the current trial (in or out of the movement field). We tested for significance in the three epochs: the pre-stimulus epoch, the mean activity for the last 10 ms before target onset; the visual period, the mean visual activity in a 5 ms epoch centered on the peak visual response; and the pre-saccade period, the mean saccade activity in a 10 ms epoch centered on the time of the peak of the saccade related burst. For all three epochs, a significant effect of both the previous and current trial was observed on the level of the neuronal activity (ANOVA, $p < 0.0001$).

We repeated the analysis on the visual selection and saccade selection neurons taken together (Fig. 5B). Starting around the time of the visual response, the priming effect was very similar to that seen in the pre-stimulus bias neurons, namely an orderly relationship from in – in trials to out – out trials. A two-way ANOVA yielded a significant effect of both factors (previous saccade and current saccade) on the mean level of activity for the visual epoch and saccade epoch ($p < 0.0001$).

The priming effect of the previous trial saccade, however, does not account for all of the bias activity. For example, if the level of activity were due to priming alone, the in–in and in–out trials in Fig. 5A should have the same level of activity; instead there is an orderly relationship of both the previous and the current trial on the level of activity. One possible other source of priming is the reward on the previous trial and previous experiments on the SC have demonstrated such an effect (Ikeda and Hikosaka 2003). We looked for such priming by reward on the previous trial, but no effect was evident under our experimental conditions.

Neuronal Selection Time and Reaction Time

Having determined the time at which SC neurons indicated a monkey's selection of one target over the other, we next determined how closely that neuronal time related to the behavioral time for making the saccade. To do so, we first divided the individual trial results for each neuron into three groups based on the reaction time of the saccade on that particular trial, using the same general procedures used previously in analyses of the FEF (Thompson et al. (1996) and the SC (McPeck and Keller (2002a)). The fastest reaction times were up to 0.33 of a cumulative reaction time distribution and the slowest were in the 0.67 to the peak of the distribution. To ensure that the monkey did not have a warning from the onset of the other target, in this analysis we included only those trials with the target appearing first in the movement field. This reduced our number of trials by approximately 45% in comparison to the analyses in Figs. 2 –5, and produced a corresponding increase in data noise. We therefore increased the number of successive points required to reach significance level before identifying the time of neuronal selection from the 5 (used in Figs 2 – 5) to 10. Figure 6A plots the neuronal activity for an example saccade selection neuron for the early (red), middle (blue), and late (green) reaction time groups for trials entering (thick lines) and not entering (thin lines) the neuron's movement field. Figure 6B shows the neuron's choice probability for the three reaction time groups. The time of neuronal selection is clearly affected by the separation of the data set by reaction time; the early reaction time group has an early time of neuronal selection and the late reaction time group has a late time.

To determine whether this relation of neuronal decision time and behavioral reaction time was true across our largest sample of neurons (visual and saccade selection neurons) we used the time at which the choice probability indicated a difference in choice in each of the reaction time groups, and calculated the slope of a least-squares fit line through the three points for each neuron (Fig. 6C). The time of decision for the three reaction time groups for the example neuron in Fig. 6B is indicated by the three colored diamonds in Fig. 6C. We could do this for only 26 neurons because the division of the trials into three groups reduced the significance level for decision below $p < 0.001$ for a number of neurons. A positive *slope* for almost all of the neurons (Fig. 6C) indicates that they show a relationship between time of decision and saccade latency. The unity line in the Fig. 6C shows the time at which neuronal decision time equals saccadic latency. It is worth noting that the data points fell below the unity line, meaning that the time of neuronal selection occurred before movement onset. Figure 6D shows a histogram of the slopes in Fig. 6C; only four of the 26 neurons included in this analysis have a slope below 0.5.

We performed the analyses in Fig. 6C and 6D so that our results could be directly compared to those of Thompson and colleagues (1996) and McPeck and Keller (2002). However, this analysis has a flaw, namely one is performing a least squares regression fit when both variables are subject to error (Draper & Smith, 1998). Thus we repeated the analysis by using a ratio rather than a regression, a method that has been applied to the FEF (Sato et al, 2001). In this analysis the two points showing the early and late neuronal discrimination times are plotted as a function of the saccadic reaction time (Fig. 6E). We then created a ratio index for each neuron that is the ratio of the change of neuronal discrimination over the change of reaction time (Fig. 6F). The results are similar to those of the regression analysis: across the sample there is a 50% or greater increase in reaction time as a function of the time of neuronal selection. We conclude that the time of selection across this sample of neurons is related to the time at which the saccade is subsequently made.

DISCUSSION

Selection Times

Using a simple visual reaction time task and choice probability analysis, we determined when each of the 51 saccade related SC neurons indicated whether the monkey would make a saccade to the stimulus inside or outside of its movement field. Our goal was to determine whether there was a limited window in the sequence of processing from visual response to presaccadic activity when these movement-related neurons indicated which target was selected and which saccade was to be made. We found that individual SC neurons predicted the target selected across the full range of times (Figs. 2 - 3) from just before the pre-saccadic burst (saccade selection neurons) through the initial visual response (visual selection neurons) to the pre-stimulus period before the targets had even appeared (pre-stimulus bias neurons).

The activity of a quarter (13/51) of the neurons accurately predicted which target would be selected at a mean time of 73 ms before saccade onset (151 ms following target onset). If all SC neurons indicated the choice this late in the sequence, we would probably regard the selection and saccade related neuronal activity as essentially the same event. However, approximately half of the SC neurons (27/51) predicted the upcoming target on average 75 ms following stimulus onset (119 ms before saccade onset), and all the visual selection neurons did so within 120 ms of target onset, or long before saccade initiation.

SC neuronal choice times in previous experiments have tended to be closer to the time of saccade generation, and while it is difficult to compare across very different experiments, the major difference might lie in the nature of the decision demanded of the monkey. For example, the task used by Krauzlis and Dill (2002) required a choice between two colored targets and between saccade and pursuit, that used by McPeck and Keller (2002a) entailed choices among

four colored targets, and that of Horwitz and Newsome (1999; 2001a; 2001b) required discrimination of motion direction masked by visual noise. Since neurons in the intermediate layers of the SC have not been shown to discriminate color (Ottes et al. 1987) and motion discrimination has been shown to require MT cortex (Newsome and Pare 1988), the discriminations in these previous tasks presumably require substantial processing in brain areas that are afferent to the SC. In the absence of a complex discrimination task, the contribution of the SC saccade related neurons to target selection might be more apparent. Our finding that choice can occur as early as the visual response indicates that neurons in the entire visual motor interval contribute to the selection, and not just those close to the pre-saccadic activity.

Neuronal Selection Time and Saccadic Reaction Time

We evaluated the functional relation of SC neurons to saccade generation by looking at the correlation between the neuronal target selection time determined by the choice probability analysis and the monkey's directly measured saccadic reaction time as has been done previously in the frontal eye fields FEF (Thompson et al. 1996). If there were a high correlation between early selection times and short saccadic latency for a given neuron, we could infer that there is a close relationship between the activity of that neuron and the generation of the saccade. In the FEF the time of selection in a visual search task was not closely related to the saccadic latency (Thompson et al. 1996) indicating that FEF activity was more closely related to target selection (although subsequent experiments showed that in a more difficult task, selection time was related to reaction time, Sato et al. 2001). In similar visual search tasks, the selection time of some SC visual-motor neurons was closely related to reaction time and for others it was not (McPeck and Keller 2002a). Taken together these results support the inference that there is a sequence of processing from target selection in FEF neurons and in some SC neurons to saccade selection in other SC neurons.

In our experiments, however, we found no evidence of such an orderly sequence. Most of the neurons in our sample (76%) showed a correlation between neuronal selection time and saccadic reaction time. These neurons included many that indicated a selection during the visual response. This difference in findings is unlikely to be the result of different analytical methods because one of the two procedures we used (Fig. 6C and D) was nearly identical to that of the cited FEF and SC studies. As we have already noted, we think it is more likely that difference between behavioral tasks contributed to our unique results.

At the same time, we see similarity between the early neuronal selection in our simple reaction time task and the role of SC early visual activity that Edelman & Keller (1998) suggested contributes to the short reaction times of express saccades (but see also Sparks et al. 2000). Both our asynchronous target task and the express saccade task require little visual discrimination, might depend largely on processing within the SC, might lead to saccades based on the sum of activity in all SC saccade-related neurons, and reveal an essentially overlapping process of target and saccade selection. We speculate that tasks requiring substantial visual processing related to discriminations between targets might reveal a sequence of processing within the SC by providing a pre-processed input to a subset of SC neurons. A similar revelation of a sequence is evident when a delay is imposed such as in the experiments of Horwitz and Newsome (1999; 2001a; 2001b) and in the experiments on the characteristics of delay activity (Glimcher and Sparks 1992; Munoz and Wurtz 1995; Dorris and Munoz 1998).

Rather than indicate that the SC is related to target selection instead of saccade selection, we think the more parsimonious conclusion is that in the SC these two steps are intertwined, and that these functions are simply not separable in a structure designed to produce specific saccades to selected targets. Under this scenario, the SC closely combines target selection with saccade initiation, a feature that may have been less evident in previous experiments because

of the more demanding discriminations placed on the selection process at levels preceding the SC.

Priming in Pre-stimulus Neurons

A few SC saccade-related neurons (11/51) indicated the choice to be made in their level of activity even prior to the presentation of the target stimuli. Horwitz and Newsome (1999; 2001b) reported a relatively weak bias effect in direction-selective neurons that was usually measurable across the sample but not in single neurons. In contrast, we observed a highly significant bias ($p < 0.001$, permutation test) that was measurable at the single neuron level.

The analysis in Fig. 5 indicates that this pre-stimulus bias can be regarded as at least in part as a priming effect from events on the previous trial. A saccade to the target in the movement field on the previous trial produced a higher probability for a saccade to that target on the current trial and a higher level of neuronal activity. This priming is similar to that of Dorris and Munoz (2000), who found that SC activity during a gap task was higher and the reaction time shorter when the preceding trial was into the movement field. Bichot and Schall (2002) also reported an effect of priming in FEF on the timing of neuronal discrimination, and Curnow et al. (2003) found a priming effect on the firing rate of MT neurons while a monkey discriminated ambiguously rotating cylinders.

The salient point, however, is that from the activity of a subset of visual-motor neurons in the SC, we can predict which of two targets the monkey will select hundreds of ms before the targets even come on. While we cannot read out the monkey's intent on a trial by trial basis from a single neuron, over a block of trials we can accurately predict the decisions to be made.

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Figure 1.

The two-target task. **A.** Schematic layout of the two targets (Tar #1, Tar #2) in relation to the fixation point (Fix.) in the center of the screen. Target #1 fell in the movement field of the neuron being studied; target #2 was outside the movement field. **B.** Task time line. The monkey was required to make a saccade to the target that came on first. The time between target onsets was adjusted as the monkey became more proficient on the task as described in the Methods.

Figure 2.

Neuronal selection times for three example neurons. **A.** Spike density functions of a neuron that did not indicate the selected target until the saccade related burst of action potentials. Activity is aligned to the onset of the target with trials in which saccades were into the movement field of the neuron in green and those out of the movement field in red. The mean is in black and the thickness of the line indicates the (SE) standard error of the mean. The curves did not separate until close to the time of the saccade related burst of action potentials. The filled black circle and horizontal black line represent the mean and standard deviation (SD) of the distribution saccadic response times for the trial plotted in this graph. **B.** The choice probability of the neuron over time. The blue-dots indicating a choice probability significant at the 0.001 level and the orange dots indicate a significance at the 0.01 level (permutation-

test, shuffles = 2000). **C-D**. An example in which the neuronal decision became evident during the visual response. **E-F**. An example in which the neuronal activity predicts the selected target before the targets come on. Times of neuronal discrimination are for the 0.001 significance level. The mean saccade latency from onset of the first target was 247 ms for A, 261 ms for B, and 187 ms for C.

Figure 3.

Selection times for the sample of neurons. Averaged neuronal activity for the three groups of neurons. **A.** Saccade selection neurons, those whose activity did not predict the selected target until the saccade related burst of action potentials. Green traces show the mean activity for the trials that went into the movement field and red traces show the mean activity for trials that went out of the movement field. **B.** Visual selection neurons, those that predicted the selected target within 120 ms of target onset. **C** Pre-stimulus bias neurons, those whose activity predicted the selected target before the target came on.

Figure 4.

Behavioral bias in psychophysical performance. **A.** An example experiment in which the monkey demonstrated little bias between the two targets. The ordinate is the target selected, and along the abscissa are the 11 trial types: (1) #1 target alone, (2- 5) target #1 appears first with intervals from large to small, (6) simultaneous, (7 - 10) target #2 first with intervals from small intervals to large, (11) #2 target alone. The symmetrical psychophysical performance with target selection closely matched the timing of the target asynchrony. **B.** The psychophysical performance from another experiment in which the monkey exhibits a behavioral response bias. Note that when the targets come on at the same time the monkey goes to target #2. **C.** The relation of response bias to target asymmetry resulting from target

position in the visual field. The response bias index (ordinate) was 1 minus the number of trials on which the monkey went to one target divided by the number of trials it went to the other target, with the smaller number in the numerator. The target asymmetry index (abscissa) was 1 minus the distance between one target and the fixation point divided by the distance between the other target and the fixation point, with the smaller number in the numerator. On the graph, the stars are monkey #1 and points are monkey #2. The correlation is low but significant. **D.** Time of neuronal decision and the signed response bias index for that experiment. Abscissa is the time of neuronal discrimination in the asynchronous target task (zero is target onset), and the ordinate is the signed response bias index for that experiment. There appeared to be no relationship between the amount of response bias and the time of decision.

Figure 5.

Effect of priming. The mean neuronal activity as a function of time for the pre-stimulus bias neurons (**A**) and the visual and saccade selection neurons (**B**). Neuronal activity is subdivided into whether the saccade on the previous trial was into or out of the movement field of the neuron and whether the current saccade was in or out of the movement field. The color key indicates the division of the trials.

Figure 6.

Relationship of the neuronal decision time to reaction time. **A.** The mean neuronal activity of an example neuron for early (red), middle (blue), and late (green) saccades for trials into (thick lines) and out of (thin lines) the movement field of this neuron. **B.** The choice probability as a function of time for the early (red), middle (blue), and late (green) saccade groups. The small dots indicate significant choice probabilities (permutation-test, $p < 0.001$, shuffles = 2000). **C.** The relationship of the time of neuronal discrimination to reaction time across the sample of neurons. The times of neuronal discrimination from the example neuron in A and B are indicated by the red, blue and green diamonds. The lines are the least-square fit through the three points from each neuron. **D.** Histogram of the slopes of a least-squares fit line of each

neuron in **C**. Bin width is 0.1. Of the 26 neurons, 22 have a slope greater than 0.5 indicating a substantial relationship between reaction time and the time of neuronal discrimination. **E**. The relationship of the time of neuronal discrimination to reaction time plotting the neuronal discrimination time and corresponding mean reaction time for *only* the early and late reaction groups (no fitting involved). **F**. Histogram of the ratio index of the change of neuronal discrimination time over the change of reaction time, e.g. (late neuronal discrimination time – early neuronal discrimination time) / (mean late RT group – mean early RT group).