

Readout of Higher-Level Processing in the Discharge of Superior Colliculus Neurons

EDWARD L. KELLER,^a KYOUNG-MIN LEE,^{a,b} AND ROBERT M. MCPEEK^a

^a*The Smith-Kettlewell Eye Research Institute, San Francisco, California 94115, USA*

^b*Seoul National University, Seoul, Korea*

ABSTRACT: The discharge of neurons in the deeper layers of the superior colliculus (SC) was studied while monkeys performed two visual discrimination tasks that required different amounts of cognitive processing. In a search paradigm the animal's task was to saccade to the location of an odd-colored stimulus located in an array of distractors of uniform color (pop-out visual search). The visual stimuli remained on the screen as the discrimination process distinguished target from distractors. In a choice response task the color of a central cue signaled which stimulus from a previously presented array of colored stimuli was to be the target of a saccade. The stimulus array was turned off well before the central cue was presented. Most neurons showed activity aligned on both the visual input and the motor response in single-target tasks. Many of these same neurons showed additional discharge that was correlated with the required higher-level decision processes in both of these more natural visual tasks. In the case of pop-out search the SC has been shown to be functionally involved in the decision processes. The cue-aligned activity in SC in the choice response task is surprising because no transient visual stimulus appeared in the response field of the neuron.

KEYWORDS: saccades; superior colliculus; frontal eye fields; search paradigm; choice response paradigm

INTRODUCTION

The traditional view of the discharge of many neurons in the deeper layers of the primate superior colliculus (SC) is that they show a burst of activity aligned on the onset of a visual stimulus that is presented in the response field of the neuron and another burst of activity aligned on a saccade that moves the line of sight onto this stimulus.¹ This visuomotor response is seen most clearly in a delayed saccade paradigm in which monkeys are required to withhold the saccadic movement after the visual target is presented until a fixation point is turned off. The period of time between the onset of the visual target and the offset of the fixation point is called the delay period. The delay period can be several hundred milliseconds or more in duration and produces a clear separation between the early activity associated with a visual response to the peripheral target and the later activity associated with the sac-

Address for correspondence: Edward L. Keller, Smith-Kettlewell Eye Research Institute, 2318 Fillmore Street, San Francisco, CA 94115. Voice: 415-345-2102; fax: 415-345-8455. elk@ski.org

Ann. N.Y. Acad. Sci. 1039: 1–11 (2005). © 2005 New York Academy of Sciences.
doi: 10.1196/annals.1325.019

cade. Normally neurons in the superficial layers of the SC only show activity associated with the appearance of the target (a visual response), whereas some cells in the deeper layers only discharge just before and during a saccade to the target (a motor response). The introduction of the delay period has also shown that many neurons in the SC discharge at lower and irregular rates during this period. The magnitude of this delay period activity has been used to separate neurons in the deeper layers of the SC into two subpopulations of cells. Cells with a high level of delay-period activity have been called buildup cells, whereas those with no or minimal amounts of activity in this period have been called burst cells.^{2,3}

Based on results obtained when single visual target presentations are used, it has been suggested that delay-period activity in the SC is correlated with readiness to make the saccadic movement.^{2,4} When multiple potential targets were used, activity in the delay period was shown to be correlated with higher-level visual processing mechanisms, for instance, the discrimination of target from distractors.³⁻⁵ Nevertheless, paradigms with instructed delays are rather unnatural in enforcing a delay in generating a saccade after target selection has been made. We have recently used two different paradigms that involve target or response selection, but encourage reaction-time saccades to be made. In these tasks the saccade can be generated as soon as information specifying a particular target is made available. One paradigm was a pop-out visual search task in which the target is distinguished by its odd color from a set of distractors of an alternative color. In the other task, which we call a choice response paradigm, a central color cue indicated which of an array of stimuli was the target. These paradigms allow investigations of SC neuron discharge that may be correlated with higher-level discrimination processes under more natural conditions in which an eye movement is made immediately after selection of a behaviorally significant object in its visual field.

METHODS

Five male rhesus monkeys (*Macaca mulatta*) were used in this study, three in the visual search task and two in the choice response task. All experimental protocols were approved by the Institutional Animal Care and Use Committee at the Smith-Kettlewell Eye Research Institute and complied with the guidelines of the Public Health Service policy on Humane Care and Use of Laboratory Animals. The surgical implants and data-collection techniques have been described extensively in a recent publication.⁶ Data collection and storage were controlled by a custom real-time program running on a laboratory computer. Eye position and velocity were sampled at 1 kHz and digitally stored on disk. A Macintosh computer, which was interfaced with the PC, generated the visual displays with software constructed using the Video Toolbox library.⁷ Visual stimuli were presented on a 29-inch color CRT (Viewsonic GA29) in synchronization with the monitor's vertical refresh. The monitor had a spatial resolution of 800 by 600 pixels and a noninterlaced refresh rate of 75 Hz. The monitor was positioned 33 cm in front of the monkey and allowed stimuli to be presented in a field of view of approximately $\pm 32^\circ$ along the horizontal meridian and $\pm 30^\circ$ along the vertical meridian.

The monkeys were seated in a primate chair with their heads restrained for the duration of the testing sessions. They executed behavioral tasks for liquid reward and

were allowed to work to satiation. Records of each animal's weight and health status were kept, and supplemental water was given as necessary.

FIGURE 1 shows the spatial and temporal arrangement of the two visual tasks in schematic form. In the search task (FIG. 1A) the monkey fixated a central point. After a random interval the fixation point went off and an array of visual stimuli (target and distractors) was presented simultaneously. The array consisted of four colored disks, one of which was an odd color. In each trial the colors of the target and distractors were randomly chosen to be red or green. The stimuli locations were all at the same eccentricity and were separated from each other by angles of 90° . The four locations were adjusted for each neuron so that one of the stimuli fell near the center of the neuron's response field. In this short communication we will only contrast the activity of SC neurons for the cases when the odd-colored stimulus (the target) was in the response field (FIG. 1A, upper inset) or at the opposite array location (lower inset). The animal was required to saccade to the odd-colored target to receive a liquid reward. On some trials, selected at random, when the fixation point went off, only a single visual stimulus appeared at one of the four potential locations. In another block of trials a single target appeared in every trial at one of the same array locations used in the search task selected at random. In both types of single-target cases the animal was rewarded for saccading to the location of this single visual target.

FIGURE 1B shows the choice response task. The animal fixed a white, central disk for a random interval, and after this delay, an array of potential targets appeared in the peripheral visual field. The array consisted of equiluminant disks of different colors, either one, two, or four in number. In the present paper we will only discuss results for the two-stimulus condition. The two locations were adjusted for each neuron so that one of the stimuli fell near the center of the neuron's response field. After a short interval (as the animal maintained fixation) the colored stimuli were replaced with two white stimuli at the same locations. These mask stimuli were equiluminant with the colored stimuli that they replaced. After another interval the fixation point was replaced by a colored disk that matched one of the stimuli in the original array. The appearance of the colored cue instructed the animal to saccade to the remembered location of the visual stimulus with the same color as the cue. We will only contrast the activity of SC neurons for the cases when the matching-color stimulus was in the response field (the case shown in FIG. 1B) or at the opposite array location (not shown). Trials were run in blocks so that colors used in the array and their locations were fixed. Thus, in both paradigms the animal was able to make a saccade as soon as the information required to make the discrimination of target from distractor was available.

Off-line analysis of the eye movement data was performed with algorithms that used velocity and acceleration criteria to detect the beginning and end of saccades. Data from each trial were visually inspected to verify the accurate identification of saccades. We analyzed only those trials in which the monkey made a single correct saccade to the target. In order to analyze the neural data we generated a spike density function for each trial by convolving the spike train with a Gaussian of sigma 4 ms.⁸ We aligned the trials on the presentation of the stimulus array, on the onset of the saccadic response, and in the case of the choice response paradigm, on the onset of the cue.

We used two methods to determine when a statistically significant target discrimination was present in the activity of a neuron. Discrimination was defined for the

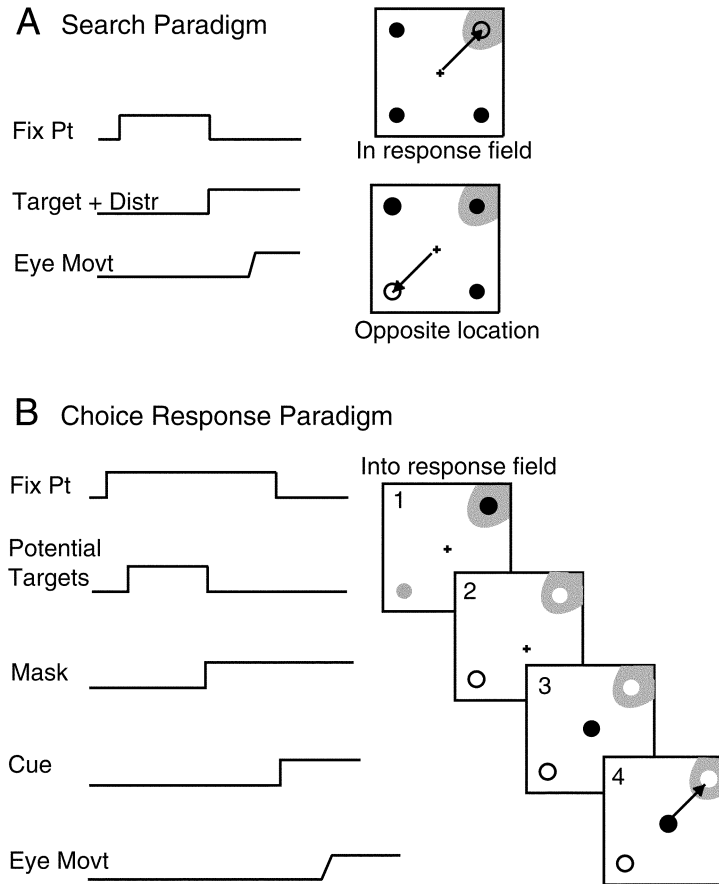


FIGURE 1. Schematic representations of the two paradigms used in the present report to study the activity of SC neurons under more natural viewing conditions. **(A)** The temporal order of events in the visual search paradigm is shown on the left. Spatial plots of the arrangement of the stimulus array are shown on the right. The shaded regions in the upper right corner of these plots show the location of the response field of the neuron being studied. In the upper plot the odd-colored stimulus (*open circle*) appears in the response field simultaneously with the appearance of three distractors (*filled circles*). The odd-colored stimulus is the goal of a rewarded saccade shown by the *arrow*. The *small cross* is the fixation point. In the lower plot the target appears at the array location directly opposite the response field. **(B)** The temporal order of events in the choice response paradigm is shown on the left. Spatial plots of the arrangement of the stimulus array, mask, and cue are shown on the right. (Response field convention the same as **(A)**.) In frame 1 a red stimulus (*filled circle*) appears in the response field, while the alternate choice is marked by a green stimulus (*lightly shaded circle*) at the opposite location. The fixation point (*small cross*) remains on. In frame 2 a mask (*open circles*) is applied at the locations of the colored array. Fixation remains on. In frame 3 a red cue replaces the fixation point. This instructs the animal to make a saccade to the former location of the red target. In frame 4 the animal makes the correct choice and saccades to the location where the red target had appeared. The other choice response would be the same except that a green stimulus would replace the fixation point and the correct choice would be to saccade in the direction opposite to the response field.

case when the target was present in the cell's response field in comparison with its activity when the target was present at the location opposite the response field. For cells studied with the search paradigm we used signal detection theory⁹ as modified to analyze discrimination at the single neuron level.^{6,10} For the choice response paradigm a nonparametric Kruskal-Wallis ANOVA test was used to determine discrimination between the same two conditions.

RESULTS

Activity in the Superior Colliculus Correlated with Target Selection in the Search Paradigm

In this section we describe the activity of visuomotor (VM) neurons recorded in the SC during the search paradigm. Neurons were placed in this class by their characteristic activity in a delayed saccade paradigm. In this paradigm the onset of the visual target is widely separated in time from the onset of the saccade made to the target. When the activity of the cell is aligned alternatively on these two events, a burst of activity trailing target onset by about 50 ms and another separate burst of activity leading the saccade by about 30 ms clearly appear. The activity of VM cells during the delay period was quite variable. Some showed almost no activity, whereas others showed a variable or sustained rate of discharge that bridged the stronger activity present in the visual- and saccade-related bursts. However, in the search paradigm all of our VM cells showed a considerable amount of activity in the short period of time between the visual and motor events. FIGURE 2A and 2B, which are aligned on the onset of the visual array, show that this cell produces an early biphasic response followed by a saccade-related response (when the saccade was directed to the upper right quadrant) in the search task. These early biphasic response profiles were seen in a subset of VM neurons that we recorded in the SC during the search paradigm. A comparison of the spike density trace in FIGURE 2A (average activity for trials in which the target was in the cell's response field) and that in FIGURE 2B (for trials in which the target was at the array location opposite to the response field of the cell) indicates that the initial transient visual response was nearly the same in amplitude and duration for the two cases. However, the second visual response reached higher amplitude when the target was in the response field. Signal detection theory analysis determined when in time this higher discharge made a statistically significant discrimination of the target in the response field compared with that at the opposite location. The discrimination was significant at those times indicated by the thick bars below FIGURE 2A. The cell began to discriminate between the two target locations at about 110 ms after array onset, lost this discrimination for a brief period near the end of the second burst of activity, and then again discriminated the different target locations at the time of the saccadic movement, as expected. Here, the cell fired a motor-related third burst of activity when the movement was directed into the response field of the cell. About half the VM cells we recorded showed a significant target selection signal that was better aligned with the onset of the array than with the saccade. This subset of VM neurons contains signals that discriminate the target from distractors at a fixed delay after array onset, regardless of eventual saccade latency.

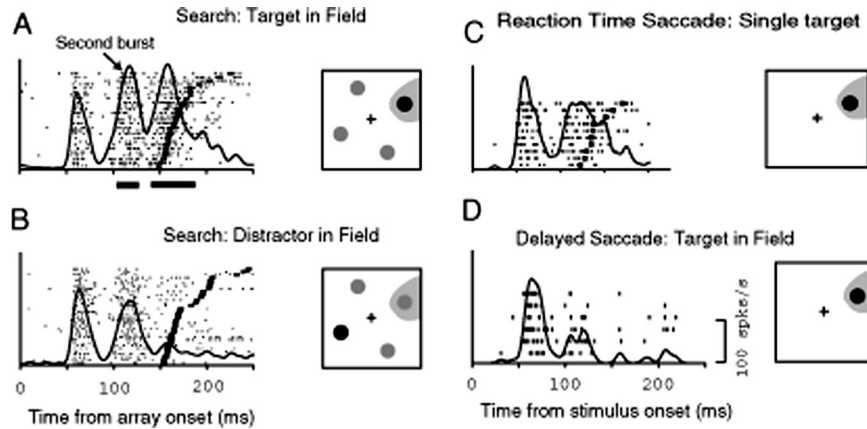


FIGURE 2. Activity of a VM neuron with a biphasic visual response in the search paradigm. The center of this cell's response field was located in the upper right visual field. (A) A spike density curve showing the average activity present in the neuron is superimposed over a raster display that shows the individual discharges of the cell for each trial. In each of this set of trials the odd-colored visual stimulus appeared in the response field (inset on the right). Trials were aligned on the onset of the visual array. The time of saccade onset is shown in each trial by the thick horizontal tick mark. Trials were ordered from bottom to top, based on the latency of saccade onset, shortest latency at the bottom. (B) Same arrangement as (A), but in each trial in this set the odd-colored stimulus appeared at the position in the array that was directly opposite the location of the response field. Times when the activity present with the target in the response field was significantly higher in comparison to that present when the target appeared out of the response field are shown by the *thick horizontal lines* below (A). (C) Activity of the cell for a set of trials in which a single target appeared in the center of its response field and a saccade was made immediately to this stimulus. Raster and average spike density aligned on single-target onset. (D) Activity of the cell during a set of delayed saccade trials in which a single target appeared in the center of its response field, but the fixation point remained lit for a random time. The saccades (not shown) were delayed until after the fixation point was extinguished. Data aligned on target onset.

FIGURE 2C provides insight into why the biphasic burst of visually aligned activity in SC neurons has received little attention previously. The data in FIGURE 2C were collected during a block of trials in which only a single target appeared at one of the four array locations used in the search task. Only those trials in which the single target appeared in the response field of the cell were used to construct FIGURE 2C. On these single-target trials the cell discharged a transient burst of visual activity at the same time that it did in the search trials (FIG. 2A and 2B). The amplitude of the visual burst of activity in the single-target case is somewhat larger than that when the visual search array appeared. We and others have shown previously a significant decrease in the magnitude of the initial visual response in the search task when compared with the single-stimulus task.^{3,6} In further tests in which the single-target trials were interleaved at random with the trials in which the search array appeared, we showed that this reduction was primarily due to lateral inhibition between neurons with response fields in distant regions of the visual field rather than to a top-down inhibition that was set up in the context of the search task.⁶ The latency of the saccades in the

single-target task was generally shorter than in the search task. This is seen by comparing the temporal location of the saccade onset indicators on individual trials in FIGURE 2A and 2B with those in FIGURE 2C. Because saccade latency was shorter in the single-target trials, the saccadic response (the third burst seen in FIG. 2A and 2B) also moved to shorter latencies and merged with the visual response. The result was that it was impossible, in the single-target case, to distinguish a second peak of visual activity from the discharge related to the execution of the saccade.

FIGURE 2D shows that the second burst of the cell's visual response is still present in the delayed saccade task, but it was greatly diminished in the latter task. This was a general finding: the appearance of a second burst of visual activity was largely suppressed in the delayed-saccade task.

Activity in the Superior Colliculus Correlated with Choice in the Choice Response Paradigm

We recorded in two additional monkeys to determine whether activity related to the selection processes would also appear in VM cells in the SC in a task that requires more cognitive input than the search task. Although we collected data in separate blocks of trials with one, two, and four alternate target choices, we will report results here only for the two-alternate choice trials. FIGURE 3 shows typical results recorded in one VM neuron. This neuron's response field was located in the lower right visual field. This neuron showed separate visual- and motor-related bursts of activity in the delayed saccade paradigm when the single target was presented in its response field (not shown). It also produced a considerable amount of irregular discharge in the delay period in this paradigm. In the data shown in FIGURE 3, the visual array on each trial consisted of the simultaneous presentation of a red disk in the response field of the neuron and a green disk in the field directly opposite the response field. During this presentation the animal maintained fixation on the center, white fixation point. When the fixation point turned into either a red or green color, the animal made a saccade to the location of the colored stimulus that had previously been the same as the cue now at the fovea.

The data in the left column of FIGURE 3 are aligned on array onset. The spike density traces in the lower plot show that this cell produces the expected burst of activity beginning at about 60 ms for both response choices, because one of the colored stimuli is always located in the cell's response field. Further, a second burst of visually aligned activity is seen that begins at about 160 ms. Thus, this cell's early response closely resembles that shown for the cell used to illustrate FIGURE 2 in the search task. The biphasic response of the cell aligned on array onset did not discriminate the final choice requirement as expected because no information was available at this time to make this choice. The data shown in the middle column in FIGURE 3 are aligned on the onset of the cue. At this time information is available to make the correct choice, and the animal is free to saccade as soon as possible. Thus, in terms of information content this alignment point is similar to the onset of the search array in the previous section, but the neural processes required to make a correct choice are quite different. The spike density traces in the lower plot show that a small burst of activity, beginning at about 110 ms, occurs when the cue to saccade to the former position of the red target (location in the response field) is presented. Furthermore, this early response statistically discriminates between the two choice responses and

is missing in the trials in which the correct choice is to the location opposite to the response field of the cell. The data shown in the column on the right are aligned on saccade onset. The spike density traces in the lower plot show a large burst of activity that occurs for trials to the response field of the cell, whereas little or no activity occurs for saccades in the opposite direction.

In a similar fashion to the second visual burst observed in some VM neurons in the search task, we found about one-third of VM cells showed a transient increase of

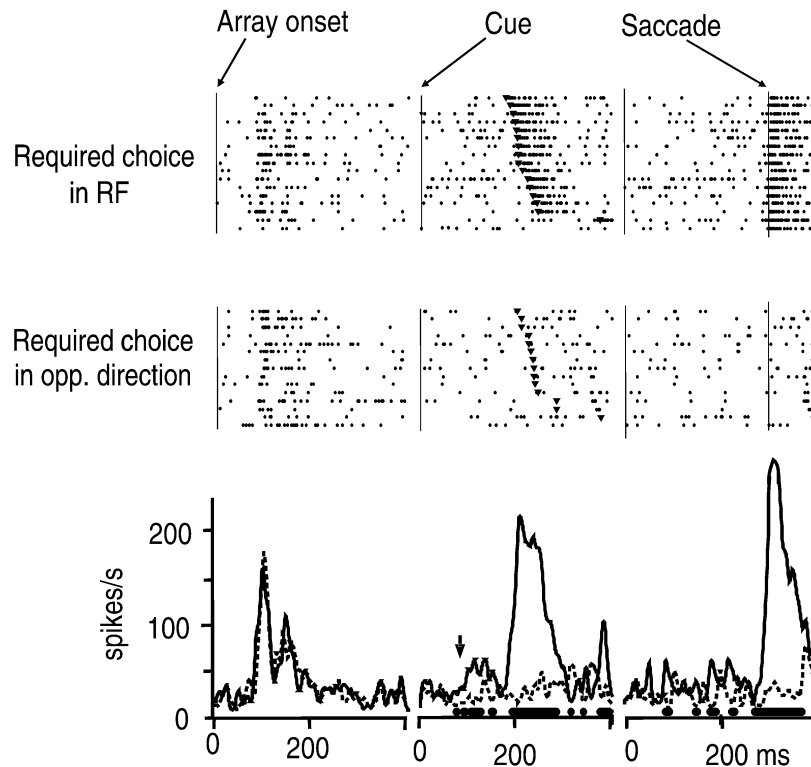


FIGURE 3. Activity of a VM neuron with a biphasic visual response in the choice response paradigm. Raster displays show the individual discharges of the cell for each trial in the upper two rows of plots. The trials are sorted so that trials in which the cue directed that the choice response be made to the location of the stimulus formerly in the response field of the cell are sorted into the upper row of plots. Trials in which the response was to be directed to the opposite location are sorted into the lower row of raster plots. Data are aligned on array onset (*left*), cue onset (*middle*), and saccade onset (*right*). In the middle raster plots the onset times of the saccades are indicated by the *heavier symbols*. Spike density curves showing the average discharge are plotted below. *Solid curves* indicate activity associated with choices to the cell's field, and *dashed curves* indicate activity associated with the opposite directed responses. The *arrow* above the spike density curve in the middle row points to the transient increase in activity that occurs when the activity is aligned on the onset of the cue and when the cue requires a saccade to the response field of the cell. The *thick lines* below the spike density traces indicate the times when activity is significantly different between the two choice conditions.

activity shortly after the presentation of the cue in the choice response task. This increase in activity was statistically larger in about a third of these cells and, thus, was correlated with the required choice response. The onset time of this activity aligned with the cue was about the same time as that of the second burst of activity in VM cells for the search paradigm.

DISCUSSION

The delayed saccade paradigm has traditionally been used to differentiate the visual- and motor-related discharge in deeper layer cells in the SC. In addition, recent studies have shown that activity in the delay period can be correlated with a number of higher-level visual processing mechanisms, including target selection and prior probability of a stimulus becoming the target.³⁻⁵ In the present communication we describe the results obtained with two paradigms that produce relatively short-latency saccades once the discrimination criteria are presented, in comparison with the enforced long latency present in the delayed saccade paradigm. We show that about half of the collicular VM cells we recorded show a transient increase in activity shortly after a discrimination becomes possible. In many of these cells this transient increase in activity discriminates between the cases when the target or the correct response is in or opposite to the response field of the cell.

However, the additional time required to make a visual discrimination in the search task or to access working memory in the choice response task resulted in longer average saccade latencies in both our paradigms in comparison with that seen in the traditional single-target paradigm. This small increase in saccade latency allowed us to better separate the transient early activity that was correlated with the discrimination or selection process from the later motor response of the cell.

The choice response task involves enforced delays like the delayed saccade paradigm, but like the search task, once the visual information is presented that allows the animal to make a correct selection of response, the task generates reaction-time saccades. The correct response in the search task requires a selection process to distinguish the target from distractors, but the process can be accomplished by visual processing as the target and distractors remain on the screen as the animal makes the selection. Saccade response and the target selection are identical in the spatial domain. Interestingly, similar to what has been found in the FEF,¹⁰ the results obtained in the search paradigm for cells in the SC showed that target selection occurred earlier and independently in time from the later saccadic response. In the choice response task no change in the visual stimulus occurred in the response field of the neuron after the application of the mask. The cue was presented at the fovea, which was not in the response field of any of the neurons tested. Correct response choice in this paradigm requires access to working memory, where a map of the location of the different colored stimuli would be located, but the cue is not represented in this map except by a comparison in color space. Presumably, this task requires much more cognitive processing than that required in the search task. Nevertheless, early transient activity that reflected the discrimination process appeared in SC cells at about the same time in both paradigms.

In the case of the search paradigm many VM cells showed an early biphasic response that was aligned with the onset of the search array. Cells with such responses

have been reported before in the frontal eye fields and the SC.^{11,12} Our analysis has shown that although the first burst of activity in these SC cells may be visual, the second burst has a significant component of its activity correlated with target/distractor discrimination processes. The early transient activity present in the response of some SC neurons in the choice response task was even more clearly driven by top-down neural processing, because it was elicited without a change in the visual stimulus within the response field of the cell.

Although the early transient activity was correlated with the higher-level processes underlying target selection or response choice in both our paradigms, it could be that these blips of activity merely represent hiccups of discharge in the SC due to the latter structure's direct connection to the frontal eye fields where the processes generating selection may actually take place. It has been shown in another experiment in our laboratory that the activity in the SC in the search task is functionally related to the discrimination processes.¹³ It remains to be demonstrated that the early activity in the SC aligned to the onset of the cue in the choice response task is functionally related to the alternative response selections.

ACKNOWLEDGMENTS

This research was supported by NIH grant EY08060 to E.L.K., by NIH grant EY014885 to R.M.M., the Visiting Scholar Program of The Smith-Kettlewell Eye Research Institute, and a grant (M103KV010021-03K2201-02120) from the Brain Research Center of the 21st Century Frontier Research Program funded by the Ministry of Science and Technology of the Republic of Korea to K.M. L.

REFERENCES

1. SPARKS, D.L. & R. HARTWICH-YOUNG. 1989. The deep layers of the superior colliculus. *In* The neurobiology of saccadic eye movements, Reviews of Oculomotor Research, Vol. III. R.H. Wurtz & M.E. Goldberg, Eds.: 213–256. Elsevier. Amsterdam.
2. MUNOZ, D.P. & R.H. WURTZ. 1995. Saccade-related activity in monkey superior colliculus. I. Characteristics of burst and buildup cells J. Neurophysiol. **73**: 2313–2333.
3. BASSO, M.A. & R.H. WURTZ. 1998. Modulation of neuronal activity in superior colliculus by changes in target probability J. Neurosci. **18**: 7519–7534.
4. GLIMCHER, P.W. & D.L. SPARKS. 1992. Movement selection in advance of action in the superior colliculus. Nature **355**: 542–545.
5. HORWITZ, G.D. & W.T. NEWSOME. 2001. Target selection for saccadic eye movements: prelude activity in the superior colliculus during a direction-discrimination task J. Neurophysiol. **86**: 2543–2558.
6. MCPEEK, R.M. & E.L. KELLER. 2002. Saccade target selection in the superior colliculus during a visual search task J. Neurophysiol. **88**: 2019–2034.
7. PELLI, D.G. 1997. The VideoToolbox software for visual psychophysics: transforming numbers into movies Spat. Vis. **10**: 437–442.
8. RICHMOND, B.J., L.M. OPTICAN, M. PODELL & H. SPITZER. 1987. Temporal encoding of two-dimensional patterns by single units in primate inferior temporal cortex. I. Response characteristics J. Neurophysiol. **57**: 132–146.
9. GREEN, D.M. & J.A. SWETS. 1966. Signal detection theory and psychophysics. John Wiley and Sons. New York.
10. THOMPSON, K.G., D.P. HANES, N.P. BICHOT & J.D. SCHALL. 1996. Perceptual and motor processing stages identified in the activity of macaque frontal eye field neurons during visual search. J. Neurophysiol. **76**: 4040–4055.

11. SCHALL, J.D., D.P. HANES, K.G. THOMPSON & D.J. KING. 1995. Saccade target selection in frontal eye field of macaque. I. Visual and premovement activation J. Neurosci. **15**: 6905–6918.
12. SOMMER, M.A. & R.H. WURTZ. 2004. What the brain stem tells the frontal cortex. I. Oculomotor signals sent from superior colliculus to frontal eye field via mediodorsal thalamus J. Neurophysiol. **91**: 1381–1402.
13. MCPEEK, R.M. & E.L. KELLER. 2004. Deficits in saccade target selection after inactivation of superior colliculus Nat. Neurosci. **7**: 757–763.