Reward-Dependent Gain and Bias of Visual Responses in Primate Superior Colliculus

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Summary

Eye movements are often influenced by expectation of reward. Using a memory-guided saccade task with an asymmetric reward schedule, we show that visual responses of monkey SC neurons increase when the visual stimulus indicates an upcoming reward. The increase occurred in two distinct manners: (1) reactively, as an increase in the gain of the visual response when the stimulus indicated an upcoming reward; (2) proactively, as an increase in anticipatory activity when reward was expected in the neuron's response field. These effects were observed mostly in saccade-related SC neurons in the deeper layer which would receive inputs from the cortical eye fields and the basal ganglia. These results, together with recent findings, suggest that the gain modulation may be determined by the inputs from both the cortical eye fields and the basal ganglia, whereas the anticipatory bias may be derived mainly from the basal ganglia.

Introduction

The superior colliculus (SC) is equipped with sensorimotor mechanisms by which spatial information contained in sensory signals is converted into orienting movements of the eyes and the head (Meredith et al., 1992; Sparks, 1986; Wurtz and Albano, 1980). The sensorimotor conversion is competitive because incoming sensory signals are abundant and complex while orienting movements are made one at a time. Successful behavior, then, requires an efficient selection mechanism. The simplest solution would be to select the object that is physically the most conspicuous among all (Itti and

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Koch, 2001). However, the most conspicuous object may not be the most desirable object to orient to. How should an animal determine which object is the most desirable? The answer cannot be derived from incoming sensory inputs alone but is likely to be derived from past experience, especially past experience of reward. An object or position that was previously associated with reward is more likely to be selected, and consequently, the animal is more likely to orient to the position of the object (Glimcher, 2001; Lauwereyns et al., 2002b). However, it is unclear whether these hypothetical processes occur in the SC. There have been some studies suggesting that the SC is involved in selection by attention (Gattass and Desimone, 1996; Kojima et al., 1996; Robinson and Kertzman, 1995) or stimulus probability (Basso and Wurtz, 1998; Dorris and Munoz, 1998), but the exact mechanism is unknown. Furthermore, it is unknown whether the selection by reward and the selection by attention are carried out by the same neural mechanisms.

To investigate whether the SC is involved in the selection of visual targets by reward, we used a memory-guided saccade task with an asymmetric reward schedule (one-direction-rewarded task [1DR]) (Kawagoe et al., 1998) (Figure 1). In this task, the subject is required to make a saccade to a remembered cue position but is rewarded only after the saccade to one particular position. The cue was chosen out of two positions: one inside the neuron's response field (RF) and the other outside the response field (nonRF), mirror-symmetric to the RF stimulus. The rewarded position was switched to the other in the next block. In one block, the rewarded position was located in the RF (RF-rewarded block); in the other block, the rewarded position was located outside the RF (nonRF-rewarded block). We found that visual responses of SC neurons to the RF cue stimulus were frequently larger when the cue indicated an upcoming reward than when the cue indicated no reward.

Results

We recorded 179 neurons from superior colliculus in two male Japanese monkeys (*Macaca fuscata*). Among these, 156 neurons (87%) reliably responded to the cue stimulus (Mann-Whitney U test, $p < 0.01$). We found that the visual response changed in magnitude depending on the reward condition. This feature is illustrated in Figures 2–4 for three SC neurons. Visual responses were invariably stronger when the cue stimulus in the RF indicated future reward (left, RF-rewarded block) than when it indicated no reward (right, nonRF-rewarded block) (Mann-Whitney U test, $p < 0.01$). However, the nature of the reward-contingent modulation varied between neurons.

For the neuron in Figure 2, the phasic visual response ("gross visual response," see Experimental Procedures) was larger in the RF-rewarded condition (top left) than in the nonRF-rewarded condition (top right) (Mann-Whitney U test, $p < 0.01$). There was no significant change
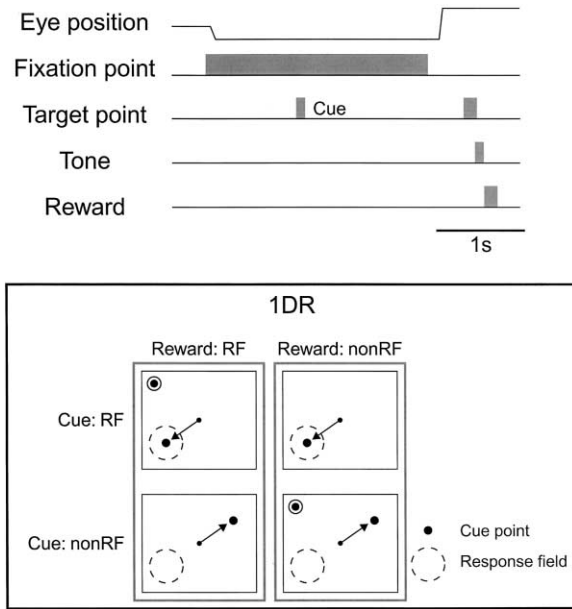
Figure 1. Memory-Guided Saccade Task in One-Direction-Rewarded Condition

(Top) Timing of stimulus presentation and eye movements. (Bottom) The cue stimulus was presented either inside the neuron's response field (RF) or opposite to the RF (nonRF). In the RF-rewarded block (left), only the RF cue indicated that reward would be given after the correct saccade (as indicated by a dotted circle). In the nonRF-rewarded block (right), only the nonRF cue indicated reward. We compared the visual response to the RF cue when it indicated reward (top left condition) and when it indicated no reward (top right condition). See Experimental Procedures for details.

ever, the increase seemed dependent on the preceding anticipatory activity. Interestingly, the anticipatory activity was present in the RF-rewarded condition (left) but not in the nonRF-rewarded condition (right). In other words, although the "net visual response" (see Experimental Procedures) showed no significant change, the "gross visual response" increased in the RF-rewarded condition because the "base activity" increased (Mann-Whitney U test, $p < 0.01$). In this neuron, then, the level of the visual response to the RF stimulus was influenced by the reward-oriented anticipatory bias. The neuron was thus classified as "bias type."

The neuron in Figure 4 showed both effects: both the net visual response and the base activity were higher, and consequently, the gross visual response was higher in the RF-rewarded condition (left) than in the nonRF-rewarded condition (right). This neuron, then, would be classified as "gain and bias type."

The reward-contingent increase of the visual response was quite common among SC neurons. Among 156 cue-responsive neurons, 56 (36%) showed significantly higher activity in the RF-rewarded condition than in the nonRF-rewarded condition (Mann-Whitney U test, $p < 0.01$). In other words, the visual response was positively modulated by reward expectation. We found only six neurons (4%) that showed statistically significant negative reward modulation. Among 56 neurons with positive reward modulation, 18 neurons (32%) were classified as gain type, 24 neurons (43%) were classified as bias type, and 14 neurons (25%) were classified as gain and bias type. Figure 5 shows four examples (top four rows) and the population activity for each type (bottom row).

To examine whether the three types of reward-modulated neurons form distinct classes, we made a scatterplot based on the net visual response (ordinate) and the base activity (abscissa) for each neuron (Figure 6A). The base activity was generally high for bias type neurons, low for gain type neurons, and intermediate for gain and bias type neurons. On the other hand, there was no clear difference in the net visual responses among these types. To illustrate the reward-dependent nature of the net visual response and the base activity,

in the "base activity" (mean firing rate in a peri-cue period, see Experimental Procedures). In this neuron, then, the gain of the visual response to the RF stimulus increased with reward. The neuron was thus classified as "gain type" (see Experimental Procedures).

The gross visual response of the neuron in Figure 3 was also larger in the RF-rewarded condition (top left) than in the nonRF-rewarded condition (top right). How-
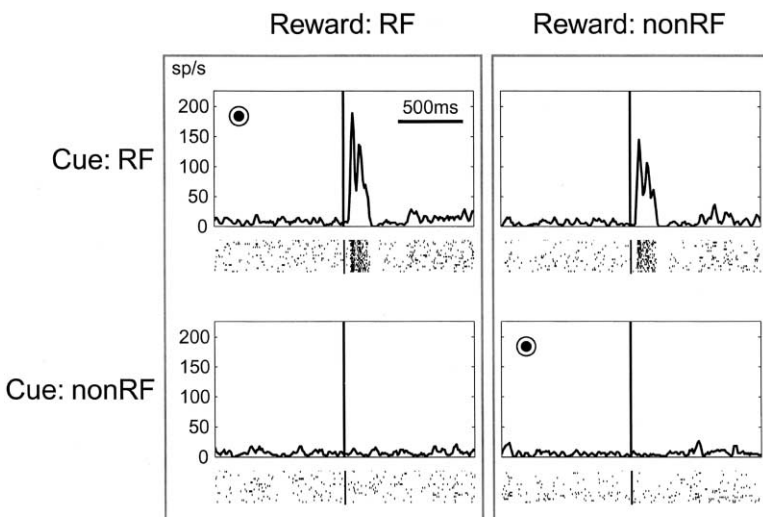

Figure 2. Reward-Contingent Increase of Visual Responses of SC Neurons: Gain Type

Raster and histograms are aligned on the onset of the cue stimulus (vertical line), separately for the RF stimulus (top) and for the nonRF stimulus (bottom). The experiment was done in two blocks: when the RF cue indicated reward (RF-rewarded block, left) and when the nonRF cue indicated reward (nonRF-rewarded block, right). A dotted circle in the histogram indicates rewarded condition.

Reward: RF   Reward: nonRF
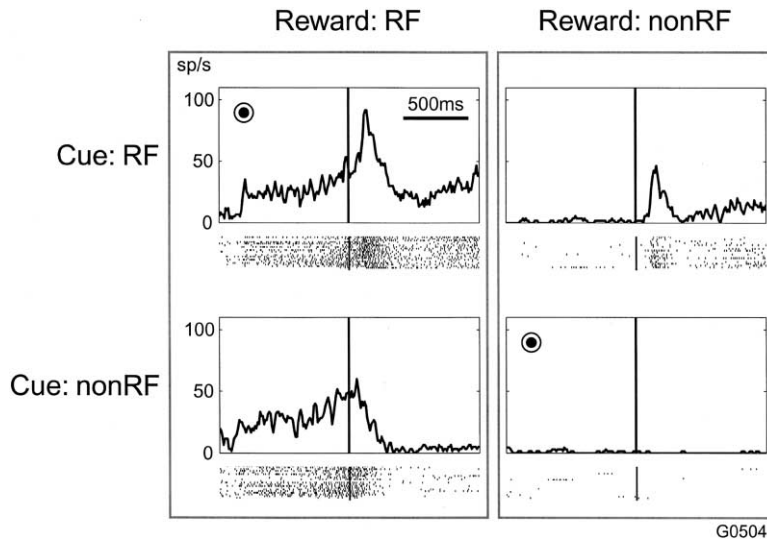
Cue: RF

Cue: nonRF

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Figure 3. Reward-Contingent Increase of Visual Responses of SC Neurons: Bias Type

The same format as in Figure 2.

we subtracted the activity in the nonrewarded condition from the activity in the rewarded condition for each neuron (Figure 6B). For the bias type, the reward modulation occurred mostly for the base activity; for the gain type, the reward modulation occurred for the net visual response. However, we found no clear segregation between these types of neurons in either scatterplot. The gain and bias type appear to bridge the gain type and the bias type.

We found that neurons with and without reward modulation were differentially distributed in the SC (Figure 7). In Figure 7A, we plotted the reward modulation index of each neuron (abscissa) according to its depth in the SC (ordinate). Positive or negative reward modulation is indicated by, respectively, a positive or negative value. The data in Figure 7A are summarized in Figure 7B as frequency histograms relative to depth, separately for the nonmodulated type and the modulated types (gain, bias, and gain and bias type). In the upper part of the SC (0–500 μm), most of the visually responsive neurons were of the nonmodulated type. This part corresponded to the superficial layer where few neurons showed pre-

saccadic activity (Figure 7C). On the other hand, most reward-modulated neurons were distributed below 500 μm, where saccadic activity became comparable to or stronger than visual responses. In fact, most reward-modulated neurons also showed presaccadic activity (overall: 46/56, 82%; gain type: 11/18, 61%; bias type: 23/24, 96%; gain and bias type: 12/14, 86%). Some of them, especially bias type neurons, also showed prelude activity ($>$20 spikes/s 200–100 ms before saccade onset) (overall: 12/46, 26%; gain type: 1/11, 9%; bias type: 10/23, 43%; gain and bias type: 1/12, 8%). On the other hand, presaccadic activity in nonmodulated neurons was less common (68/100, 68%) and a small number of them showed prelude activity (5/68, 7%).

Discussion

Using an asymmetrically rewarded version of the memory-guided saccade task, we demonstrated that the visual response of SC neurons often increased when a cue stimulus indicated an upcoming reward. There were two types of increase: one due to a change in the gain

Reward: RF   Reward: nonRF
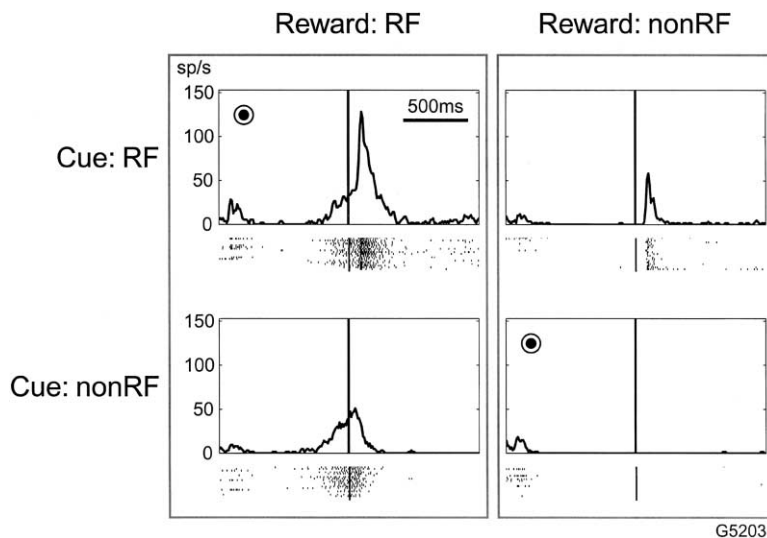
Cue: RF

Cue: nonRF

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Figure 4. Reward-Contingent Increase of Visual Responses of SC Neurons: Gain and Bias Type
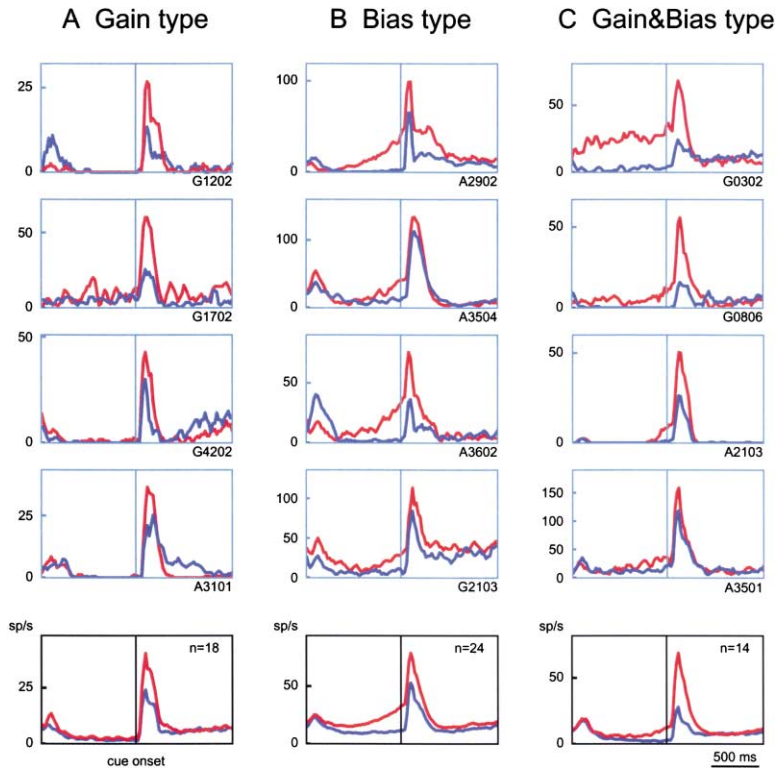
The same format as in Figure 2.

Figure 5. Reward-Contingent Increase of Visual Responses of SC Neurons

(A) Gain type, (B) bias type, and (C) gain and bias type. For each type, spike frequency histograms are shown for four neurons (top four rows) and averaged for all neurons belonging to the type (bottom row). The histograms are aligned on the onset of the RF cue stimulus (bin width: 20 ms). They are shown in two conditions: when the RF cue indicated reward (RF-rewarded block, red) and when the RF cue indicated no reward (RF-nonrewarded block, blue). These neurons showed no response to the nonRF cue stimulus (data not shown).

of the visual response to the RF stimulus (gain type) and the other due to a bias in the level of anticipatory activity before cue onset (bias type). However, these two types of reward modulation do not seem to be expressed by distinct groups of SC neurons, since a considerable number of neurons showed both effects (gain and bias type) and there was no clear clustering in the scatterplots of neuronal activities (Figure 6).

The gain effect has been described in previous studies (Goldberg and Wurtz, 1972; Kojima et al., 1996; Dorris et al., 2002). A pioneering experiment was done by Gold-

berg and Wurtz (1972). They found that visual responses of SC neurons were often enhanced when the monkey was about to make a saccade to the stimulus. Kojima et al. (1996) found that some SC neurons showed increased visual responses when only covert attention was deployed. In both cases, the enhancement seemed to reflect a genuine increase in the phasic visual response, similar to the gain type in our study.

In addition to the gain effect, we observed a new type of increase—the bias type. Pre-cue anticipatory activity was present when the cue stimulus in the response field
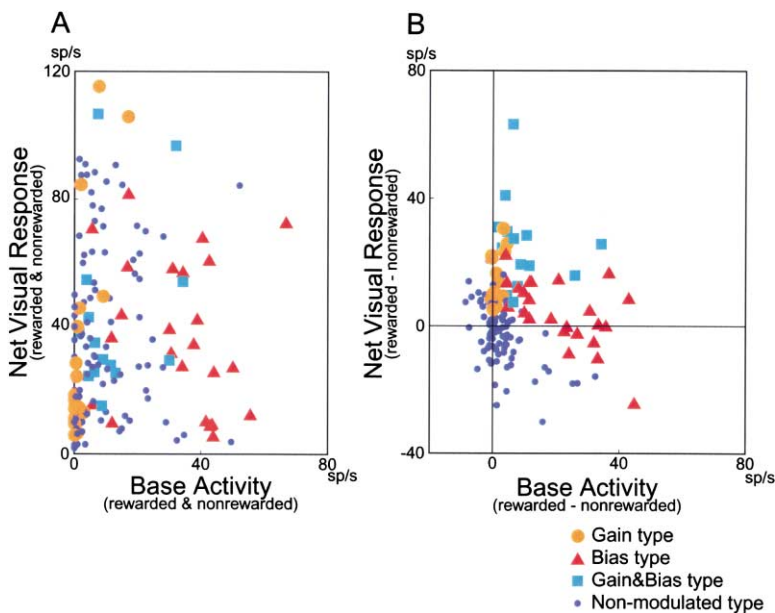

Figure 6. The Relationship between the Net Visual Response and the Base Activity for Each Neuron

In (A), the activity averaged across the RF-rewarded block and the nonRF-rewarded block is plotted. In (B), a difference (RF-rewarded block − nonRF-rewarded block) is plotted.
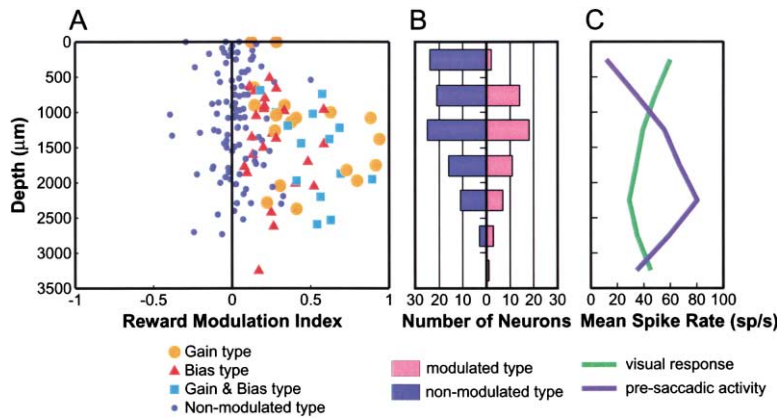
Figure 7. Distribution in Depth of Reward-Contingent Modulation of Visual Responses in the SC

(A) For each neuron, the reward modulation index (abscissa) is plotted against its depth from the top of the SC (ordinate). The reward modulation index was defined as (VR − VNR)/(VR + VNR), where VR is the mean visual response in RF-rewarded condition and VNR is the mean visual response in nonRF-rewarded condition. Reward-modulated neurons (gain, bias, and gain and bias type) and reward-nonmodulated neurons are shown in different symbols.

(B) The numbers of reward-modulated neurons (right) and reward-nonmodulated neurons (left) are shown for each 500 μm depth.

(C) The mean firing rates of all neurons in post-cue period (50–150 ms after cue onset: visual response) and presaccadic period (50 ms period before saccade onset: presaccadic activity) are shown for each 500 μm depth.

(RF stimulus) indicated an upcoming reward, but not when the RF stimulus indicated no reward. Consequently, the visual response to the RF stimulus was elevated when it indicated the presence of reward, but not when it indicated the absence of reward. Such a linear increase of the visual response can be regarded as an additive scaling effect. It has been reported that SC neurons may become active before the onset of a visual target or cue (Basso and Wurtz, 1998; Dorris and Munoz, 1998; Glimcher and Sparks, 1992). This resembles the bias effect shown in our study but is fundamentally different. In the previous studies, the anticipatory activity was higher when an RF stimulus was more likely to occur compared with other stimuli. Such probability-dependent anticipatory activity would not produce a selective bias in our paradigm, because the RF stimulus and the non-RF stimulus appeared equally likely both in the RF-rewarded block and the nonRF-rewarded block. In contrast, the bias effect reflects a mechanism that associates position and reward, which has not been examined previously for SC neurons.

How is the anticipatory activity generated? Previous studies from our research group showed that neurons in the basal ganglia—caudate nucleus (CD) (Takikawa et al., 2002a; Lauwereyns et al., 2002a) and the substantia nigra pars reticulata (SNr) (Sato and Hikosaka, 2002)—exhibit pre-cue anticipatory changes in activity in the same task, 1DR. It was then suggested that the changes in activity of basal ganglia neurons lead to the changes in saccade behavior (Takikawa et al., 2002b) through the serial connections from the CD to the SNr, directly or indirectly, and from the SNr to the SC (Hikosaka et al., 2000). CD pre-cue activity would inhibit the rapid firing of SNr neurons, and therefore SC neurons would be released from the tonic inhibition by the SNr. However, for this scheme to be valid, it was critical to demonstrate that SC neurons also exhibit pre-cue anticipatory activity. We now show that this is true. Our demonstration of the bias effect in SC neurons supplies the crucial missing link between the neuronal activity in the basal ganglia and saccade behavior. These results together provide strong evidence that the basal ganglia contribute to the generation of the bias effect in SC neurons.

This hypothesis is further supported by the locations of the bias type neurons in the SC. It has been well known that the SNr-SC connection terminates mostly in the intermediate layer of the SC where saccadic neurons prevail (Graybiel, 1978; Hikosaka and Wurtz, 1983b; Jayaraman et al., 1977; Karabelas and Moschovakis, 1985). Any influence from the SNr-SC input would most likely show up in SC neurons in the intermediate layer. Indeed, most of the bias type neurons were located in the relatively deeper layer where saccadic activity was prominent. However, it is unclear whether such anticipatory activity is created entirely in the basal ganglia. Anticipatory activity preceding target onset has been found in the cortical eye fields, especially the supplementary eye field (Coe et al., 2002), when the expected amount of reward was biased spatially. The cortical signal may be conveyed to the SC directly or indirectly through the basal ganglia.

In contrast, the gain effect may be derived, at least partly, from outside of the basal ganglia. The latencies of visual responses in SC neurons (40–80 ms) observed in this and previous studies (Wurtz and Albano, 1980) were generally shorter than the latencies of visual responses in SNr or CD neurons (90–200 ms) (Hikosaka et al., 1989; Hikosaka and Wurtz, 1983a). Although the gain of visual responses is modulated by expectation of reward in CD neurons (Kawagoe et al., 1998) and SNr neurons (Sato and Hikosaka, 2002), the effects would not be early enough to modulate the early portion of visual responses of SC neurons. Earlier visual responses may occur in neurons in the cortical areas related to saccade initiation (or cortical eye fields) (Barash et al., 1991; Goldberg and Bushnell, 1981; Schall, 1991). The gain of these cortical visual responses is modulated by reward expectation: frontal eye field (Kobayashi et al., 2002; Leon and Shadlen, 1999), supplementary eye field (Coe et al., 2002), and area LIP in the parietal cortex (Platt and Glimcher, 1999). Hence, the gain modulation in SC neurons may first be induced by the direct inputs from the cortical eye fields (Paré and Wurtz, 2001; Segraves and Goldberg, 1987; Shook et al., 1990; Sommer and Wurtz, 2000), followed by the input from the basal ganglia (Hikosaka and Wurtz, 1983b).

Most of the reward-modulated neurons were found in the deeper layer of the SC (Figure 7) and showed presaccadic activity as well. There are two types of saccadic neurons in the primate SC: neurons that exhibit

only a presaccadic burst (burst neurons) (Schiller and Koerner, 1971; Sparks et al., 1976; Wurtz and Goldberg, 1971) and neurons that exhibit prelude or buildup activity (buildup neurons) (Munoz and Wurtz, 1995) which is often followed by a presaccadic burst (prelude bursters) (Glimcher and Sparks, 1992). We found that bias type neurons tended to show prelude or buildup activity compared with the other two types. However, it is premature to conclude that bias type neurons correspond to buildup neurons, especially because only 3 among 23 bias type neurons were qualified to be buildup neurons according to a criterion by Munoz and Wurtz (1995) (>30 spikes/s >100 ms before saccade onset).

Based on the present results, we propose that the gain signal and the bias signal originate from different brain regions and are distributed to single SC neurons selectively (gain type and bias type) or together (gain and bias type). The gain modulation, which occurs after visual onsets, would be induced primarily by the cortical inputs, whereas the bias modulation, which occurs before visual onsets, would be induced mainly by the basal ganglia input. With these mechanisms, the SC would bias the animal to orient toward a reward-expected location, both proactively and reactively. However, it remains to be studied how selectively the cerebral cortex and the basal ganglia contribute to the gain and bias modulations.

Experimental Procedures

General

We used two male Japanese monkeys (*Macaca fuscata*). Detailed methods were described elsewhere (Takikawa et al., 2002a). After anesthesia using pentobarbital sodium, we implanted a head holder, a chamber for unit recording, and an eye coil under surgical procedures. Surgical procedures were conducted in aseptic conditions. A scleral eye coil was implanted in one eye for monitoring eye position (Robinson, 1963; Judge et al., 1980). The recording chamber was placed over the frontoparietal cortices. All surgical and experimental protocols were approved by the Juntendo University Animal Care and Use Committee and were in accordance with the National Institutes of Health Guide for Care and Use of Animals.

Behavioral Tasks

The monkey sat in a primate chair in a dimly lit and sound attenuated room with his head fixed. In front of him was a tangent screen onto which small red spots of light were backprojected using two LED projectors. We trained monkeys to perform a memory-guided saccade task with an asymmetrical reward schedule, a one-direction-rewarded version of a memory-guided saccade task (1DR) (Figure 1). A trial started with the onset of a central fixation point which the monkey had to fixate. A cue stimulus, a small red spot of light, came on 1 s after fixation onset for 100 ms. The monkey had to keep fixation and remember the cued location. The fixation point turned off after 1–1.5 s, and the monkey had to make a saccade to the cued location. The correct saccade was indicated by a tone stimulus. The cue stimulus was presented at one out of two possible locations: one was located in the response field (RF) of the recorded neuron; the other was located outside the RF in the mirror-symmetric position relative to the fixation point (Figure 1, bottom). The cue location was chosen pseudorandomly across trials such that every subblock of four trials contained two trials for each of the two locations randomly.

A unique feature of the 1DR task was that only one of the two locations was rewarded. The rewarded target position was fixed in a block of 40 to 60 successful trials. Thus, the 1DR task was done in two blocks: RF-rewarded block (the rewarded position was in the RF) and nonRF-rewarded block (the rewarded position was outside the RF). Even for nonrewarded trials, the monkeys had to make a correct saccade. If the saccade was incorrect, the same trial was repeated. For each recorded neuron, we obtained data on at least one set of the RF-rewarded block and the nonRF-rewarded block. The order of two blocks was randomized across neurons. We usually repeated the two blocks to confirm the reliability of the data.

Recording Procedure

Single-unit recordings were performed using tungsten electrodes (Frederick Haer). The electrode was inserted into the brain through a stainless steel guide tube (diameter: 0.8 mm) which was used to penetrate the dura. A hydraulic micro drive (Narishige, MO 95-S) was used to advance the electrode into the brain. To determine the depth of recording, we used electrophysiological measures. The entry of the electrode into the SC was indicated by a sudden appearance of multiunit neuronal activity or cell injury. We then backed up the electrode slowly until no neuronal activity was detected. We then advanced the electrode until any neuronal activity appeared. We determined this depth as the surface of the SC (see Figure 7). Eye movements were recorded using the search coil method (Enzanshi Kogyo MEL-20U) (Robinson, 1963; Judge et al., 1980; Matsumura et al., 1992). Eye positions were sampled at 500 Hz.

Data Analysis

We mainly analyzed visual responses of SC neurons to the cue stimulus. The presence of a visual response was determined by comparing the firing rate in a post-cue test period (duration: 100 ms, 50–150 ms after cue onset) between RF-cued trials and nonRF-cued trials (Mann-Whitney U test, $p < 0.01$). Both RF-rewarded and nonRF-rewarded blocks were included in this analysis. Our main interest was the comparison of SC visual responses between the RF-rewarded condition and the nonRF-rewarded condition. For this purpose, we used the following measures. First, "gross visual response" was simply the firing rate in the post-cue test period. The gross visual response was sometimes boosted by the preceding anticipatory activity. We calculated the mean firing rate in a peri-cue period (duration: 100 ms, 50 ms before and after cue onset) as "base activity." Then, we subtracted the base activity from the gross visual response to get "net visual response." These calculations were done for each trial.

Based on these measures, we classified visual neurons into four types. (1) Nonmodulated type: the gross visual response was not significantly different between the RF-rewarded condition and the nonRF-rewarded condition. If the gross visual response was significantly larger in the RF-rewarded condition than in the nonRF-rewarded condition, the neuron was judged to be reward modulated and was further classified into the following three types. (2) Gain type: the gross visual response was significantly larger in the RF-rewarded condition than in the nonRF-rewarded condition, while the base activity was not significantly different between the two conditions. (3) Bias type: the base activity was significantly larger in the RF-rewarded condition than in the nonRF-rewarded condition, while the net visual response was not significantly different between the two conditions. (4) Gain and bias type: both the base activity and the net visual response were significantly larger in the RF-rewarded condition than in the nonRF-rewarded condition. All these comparisons were statistically tested by Mann-Whitney U test ($p < 0.01$).

For each neuron, we also determined the presence of saccadic activity by comparing the firing rate in a presaccadic period (duration: 50 ms, before saccade onset) between RF-cued trials and nonRF-cued trials (Mann-Whitney U test, $p < 0.01$). To examine if the presaccadic activity was preceded by prelude or buildup activity, we calculated the discharge rate in the window (200–100 ms before saccade onset).

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