LYNCH, J. C., V. B. MOUNTCASTLE, W. H. TALBOT, and T. C. T. YIN, 1977. Parietal lobe mechanisms for directed visual attention. *J. Neurophysiol.* 40:362–389.

MACKAY, W. A., and A. RIEHLE, 1992. Planning a reach: Spatial analysis by area 7a neurons. In *Tutorials in Motor Behavior 2*, G. Stelmach and J. Requin, eds. New York: Elsevier.

MAUNSELL, J. H. R., and D. C. VAN ESSEN, 1983. The connections of the middle temporal visual area (MT) and their relationship to a cortical hierarchy in the macaque monkey. *J. Neurosci.* 3:2563–2586.

MAYS, L. E., and D. L. SPARKS, 1980. Dissociation of visual and saccade-related responses in superior colliculus neurons. *Science* 43:207–232.

MAZZONI, P., R. A. ANDERSEN, and M. I. JORDAN, 1991a. A more biologically plausible learning rule for neural networks. *Proc. Natl. Acad. Sci.* 88:4433–4437.

MAZZONI, P., R. A. ANDERSEN, and M. I. JORDAN, 1991b. A more biologically plausible learning rule than backpropagation applied to a network model of cortical area 7a. *Cerebral Cortex* 1:293–307.

MAZZONI, P., R. M. BRACEWELL, S. BARASH, and R. ANDERSEN, 1992. *Soc. Neurosci. Abstr.* 18:148.

MOUNTCASTLE, V. B., J. C. LYNCH, A. GEORGOPOULOS, H. SAKATA, and C. ACUNA, 1975. Posterior parietal association cortex of the monkey: Command function for operations within extrapersonal space. *J. Neurophysiol.* 38:871–908.

NEWSOME, W. T., R. H. WURTZ, and H. KOMATSU, 1988. Relation of cortical areas MT and MST to pursuit eye movements: I. Differentiation of retinal from extraretinal inputs. *J. Neurophysiol.* 60:604–620.

PECK, C. K., J. A. BARO, and S. M. WARDER, 1992. Eye position effects on visual responses in the superior colliculus. *Invest. Ophthalmol. Vis. Sci. (Suppl.)* 33:1357.

ROBINSON, C. J., and H. BURTON, 1980a. Organization of somatosensory receptive fields in cortical areas 7b, retroinsular postauditory and granular insula of *M. fascicularis*. *J. Comp. Neurol.* 192:69–92.

ROBINSON, C. J., and H. BURTON, 1980b. Somatic submodality distribution within the second somatosensory (SII), 7b, retroinsular, postauditory and granular insular cortical areas of *M. fascicularis*. *J. Comp. Neurol.* 192:93–108.

ROBINSON, D. L., M. E. GOLDBERG, and G. B. STANTON, 1978. Parietal association cortex in the primate: Sensory mechanisms and behavioral modulations. *J. Neurophysiol.* 41:910–932.

ROBINSON, D. L., J. W. MCCLURKIN, and C. KERTZMANN, 1990. Orbital position and eye movement influences on visual responses in the pulvinar nuclei of the behaving macaque. *Exp. Brain Res.* 82:235–246.

SAKATA, H., H. SHIBUTANI, and K. KAWANO, 1980. Spatial properties of visual fixation neurons in posterior parietal association cortex of the monkey. *J. Neurophysiol.* 43:1654–1672.

SNYDER, L. H., P. R. BROTCHIE, and R. A. ANDERSEN, in press. World-centered encoding of location in posterior parietal cortex of monkey. In *Proceedings of Neural Control of Movement Third Annual Meeting*.

WAGMAN, I. H., 1964. Eye movements induced by electric stimulation of cerebrum in monkeys and their relationship to bodily movements. In *The Oculomotor System*, M. B. Bender, ed. New York: Harper & Rows, pp. 18–39.

ZIPSER, D., and R. A. ANDERSEN, 1988. A back-propagation programmed network that simulates response properties of a subset of posterior parietal neurons. *Nature* 331:679–684.

34 Role of Monkey Superior Colliculus in Control of Saccades and Fixation

ROBERT H. WURTZ AND DOUGLAS P. MUNOZ

ABSTRACT Saccadic eye movements and the intervening periods of visual fixation represent one of the simplest behavioral systems that have been studied in the primate. The superior colliculus (SC) is a key structure in both systems, although it is only part of a system extending from cerebral cortex to the pons. Recent experiments on the control of saccades have identified two types of collicular cells that discharge in relation to saccades. *Burst cells* have a discrete burst of activity before onset of saccades. Many have a discharge whose end coincides closely with the end of the saccade, a clipped discharge. A modified feedback system controlling the position of the eyes is consistent with key aspects of the discharge of these cells and the initiation of saccades by the SC. Other cells show a slow buildup of activity before the onset of a saccade and, during a saccade, show a moving wave front of activity across the SC. These *buildup cells* are proposed also to be inside a feedback loop controlling the amplitude of the saccade. The control of visual fixation between saccades depends on the activity of *fixation cells* within the anterior colliculus whose activity increases during such active fixations. Initial studies of the interaction between these systems of saccade and fixation control are consistent with the idea that one inhibits the other.

Rapid eye movements and the intervening periods of visual fixation represent a simple behavioral system in primates. Saccades move the eyes rapidly from one point of interest to another. Little visual information is available during these movements, which usually last no more than 40 ms. It is in the periods of fixation following saccades, in which the fine-grained foveas of the eyes are directed at the objects of interest, that we obtain nearly all visual information. In this chapter, we consider some of the underlying neuronal mechanisms that control these saccadic eye movements and visual fixation.

Monkeys, like humans, also make saccadic eye movements separated by periods of visual fixation, and this behavioral similarity between the two species of primates has made the monkey a superb model for analysis of the neuronal systems underlying the control of visual fixation and saccadic eye movements. The parts of the brain related to the generation of saccades have been studied extensively, and a series of areas extending from cerebral cortex to the pons have been identified as part of the system that controls the generation of saccades (Wurtz and Goldberg, 1989). These areas include the posterior parietal cortex, the frontal and supplementary eye fields in the frontal lobe, the caudate nucleus and substantia nigra pars reticulata in the basal ganglia, the superior colliculus (SC) on the roof of the midbrain, and regions of the mesencephalic and pontine reticular formation that are closely related to the motor nuclei driving the extraocular muscles. In this chapter, we concentrate on the role of the monkey SC in the control of visual fixation and saccadic eye movements.[1]

Organization of superior colliculus

The SC, a layered structure on the roof of the midbrain, receives important input from the cortical and deep telencephalic areas and, in turn, projects to the pontine and mesencephalic gaze centers. The alternating fiber and cell body layers clearly have different functions, as indicated by the differential relation of neuronal activity in these layers to visual stimulation

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and the generation of saccadic eye movements. A cell in the superficial layers increases its discharge rate following the onset of a visual stimulus in a particular part of the visual field, the visual receptive field of the cell. The receptive fields of these cells form a retinotopically coded map of the contralateral visual field.

The discharge of the cells in the intermediate layers of the SC is tightly linked to the occurrence of saccades (Sparks, 1978). These saccade-related cells also frequently begin to discharge at a fixed latency after visual stimulation but discharge more vigorously before the onset of saccadic eye movements. The increased discharge rate of saccade-related cells accompanies saccades made to points within the area of the visual field that define the movement field of the cell (Wurtz and Goldberg, 1972). The movement field of each saccade cell has a central region with a maximal discharge and a gradient of response that fades away as the saccade vector deviates from this central area (Wurtz and Goldberg, 1972; Sparks and Mays, 1980).

Cells in different parts of the colliculus have movement fields that represent different amplitudes and directions of saccades. If we accept that the central point of each cell's movement field gives the maximum discharge of the cell, we can look at this point for many cells throughout the intermediate layers and see a map of preferred saccade directions and amplitudes—a movement map (figure 34.1). By electrically stimulating the SC, Robinson (1972) demonstrated that the amplitude of the saccade increases along a line running from the rostrolateral pole to the caudomedial pole of the SC, as shown on the map in figure 34.1, with the smallest saccades represented in the rostral SC and the largest in the caudal SC. Upward and downward directions are represented medially and laterally, respectively.

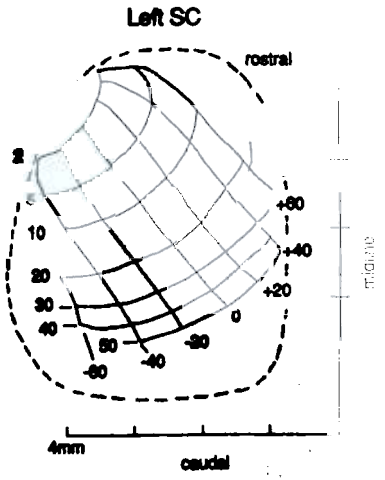

FIGURE 34.1 Map of saccade vectors throughout the intermediate layers of the SC. (After Robinson, 1972.)

An impending saccade is preceded by neural activity in one area of the SC movement map. Saccades to different parts of the field are accompanied by activity in different areas of the map. The activity of one cell does not determine the amplitude and direction of a saccade, but the population of all active cells does (Lee, Rohrer, and Sparks, 1988; Sparks and Mays, 1990).

Two types of saccade cells

Whereas neurons concentrated in the intermediate layers of the monkey SC discharge in relation to saccadic eye movements, two types of cells with different activity patterns recently have been described (Munoz and Wurtz, 1992). One population of neurons, *burst cells*, discharged a high-frequency burst of action potentials immediately prior to saccade onset. A second population of saccade-related cells had a slow buildup of activity in addition to movement-related activity; we refer to these neurons as *buildup cells*.

We distinguish the two classes of saccade cells by using several different saccade tasks, including the visually guided saccade task in which the monkey makes a saccade to a visual target that appears as the fixation point disappears (figure 34.2). The left column of the figure shows the cell discharge aligned on the onset of the visual target, and the right column shows the same discharge aligned on the onset of the saccade. Both the burst cell (figure 34.2A) and the buildup cell (figure 34.2B) began to discharge approximately 60–70 ms after target onset (figure 34.2, left) and then generated a more vigorous discharge in association with saccade onset (figure 34.2, right). The burst cell paused briefly between its presumed visual- and movement-related responses, whereas the buildup cell demonstrated no clear pause.

To determine whether the discharge of the buildup cell was related to the preparation for the saccade or to the presence of the visual stimulus, we used a memory-guided saccade paradigm in which the target was flashed briefly and the monkey had to make a saccade to the spatial location of the target after the offset of the fixation point. In this task, burst cells gave only weak responses to the target flash and then exhibited a burst of activity in association with the saccade to the remembered location of the target flash. In contrast, the

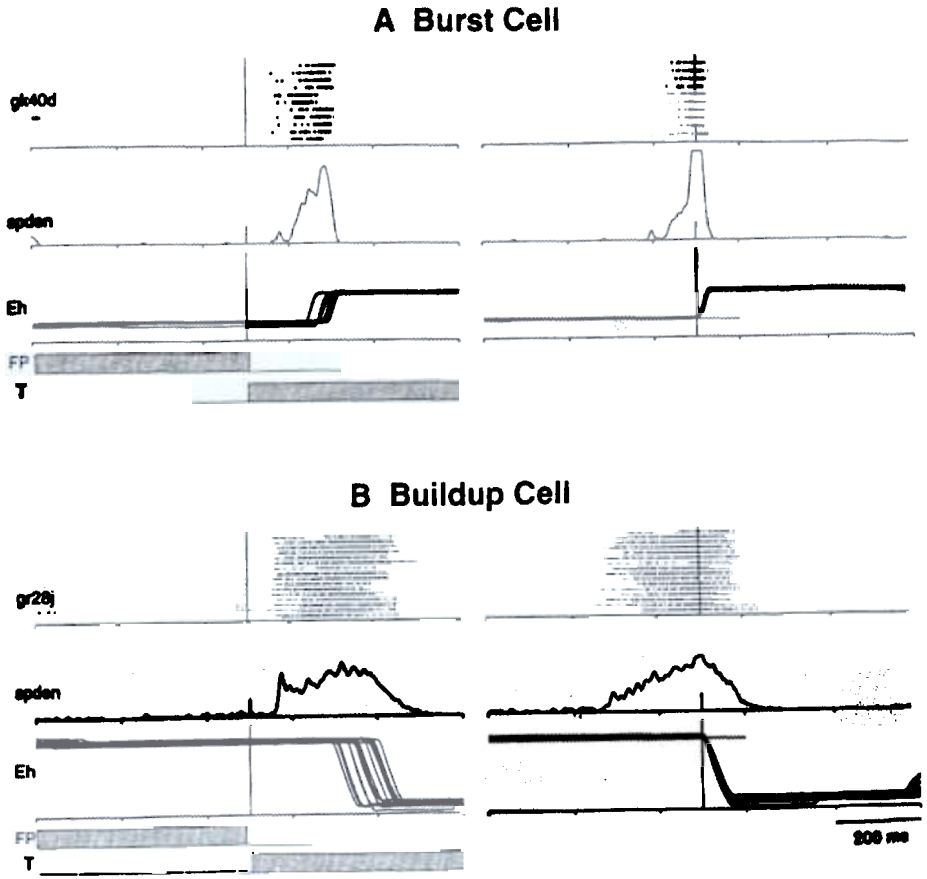

FIGURE 34.2 Discharge of burst and buildup cells. Shown in each panel are the individual rasters, the spike density profile (spden), and the horizontal eye position traces (Eh) for 8 to 10 trials. The traces in the left column are aligned on target onset, and the same data are aligned on saccade onset in the right column. Saccade direction and amplitude were selected for the strongest movement-related response. (A) Burst cell. The discharge shown for this cell is for the optimal saccadic amplitude and direction of 10° to the right. This cell was classified as a burst cell rather than a preparatory cell because the presaccadic activity consisted only of the burst before the saccade. (B) Buildup cell. Discharge is for saccades 25° to the left. The buildup of activity is independent of the visual stimulus. FP, fixation point; T, target. (From Munoz and Wurtz, 1994)

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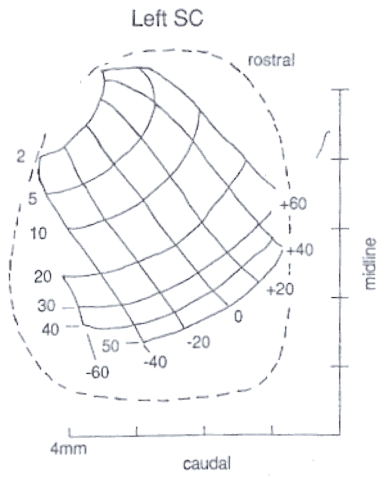

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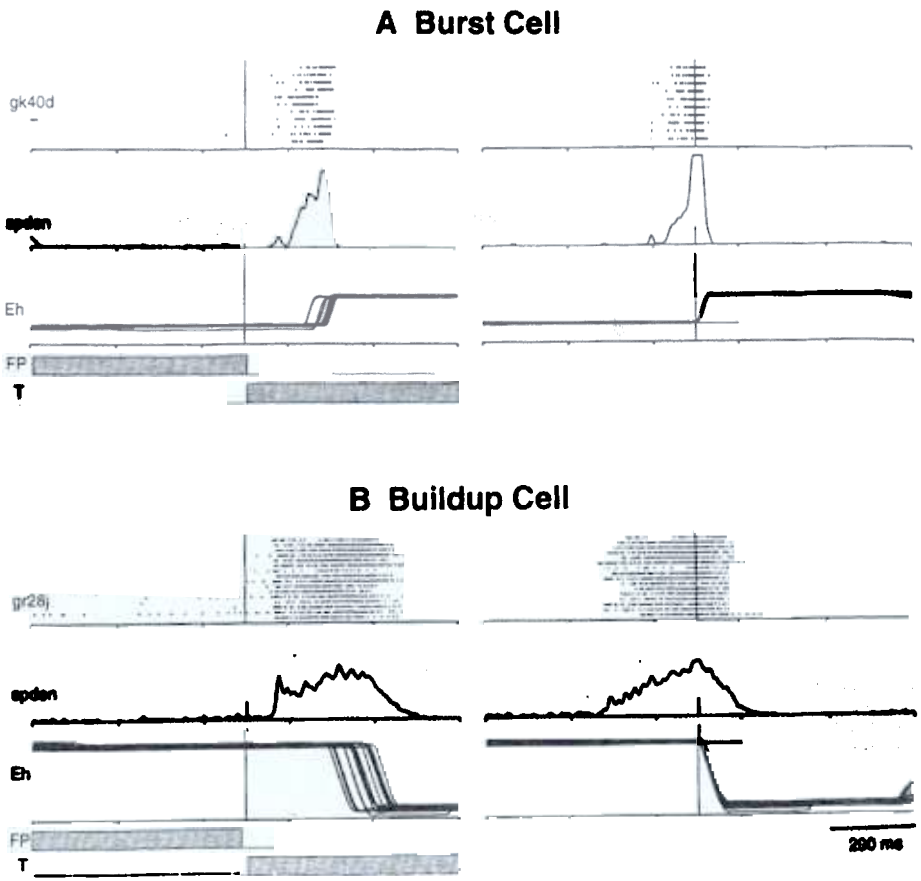


FIGURE 34.2 Discharge of burst and buildup cells. Shown in each panel are the individual rasters, the spike density profile (spden), and the horizontal eye position traces (Eh) for 8 to 10 trials. The traces in the left column are aligned on target onset, and the same data are aligned on saccade onset in the right column. Saccade direction and amplitude were selected for the strongest movement-related response. (A) Burst cell. The discharge shown for this cell is for the optimal saccadic amplitude and direction of 10° to the right. This cell was classified as a burst cell rather than a preparatory cell because the presaccadic activity consisted only of the burst before the saccade. (B) Buildup cell. Discharge is for saccades 25° to the left. The buildup of activity is independent of the visual stimulus. FP, fixation point; T, target. (From Munoz and Wurtz, 1994)

buildup cells discharged in a sustained manner from the time of the flash until the saccade was made, even though the target was no longer visible.

This sustained discharge could also be elicited in the absence of any retinal stimulation as the discharge occurred before the visual target had been presented in a gap saccade paradigm. In this latter task, the fixation point went off, leaving a period of darkness preceding target onset; the buildup cell was silent until after fixation point offset and then began to discharge in the period of darkness, even though the target had not yet appeared. The intensity of this anticipatory activity was similar to that seen in the memory-guided task when the target had appeared but the saccade was delayed. The buildup cell then increased its discharge after onset of the target and continued to discharge until the monkey made the saccade to the visible target. In contrast, the burst cell remained silent during the period of darkness between fixation point offset and target onset and then discharged a brief phasic burst approximately 60–70 ms after target onset, followed by a second, more robust burst of spikes synchronized with saccade initiation.

Although there is a continuum of cell types extending from those with burst cell characteristics to those demonstrating a buildup of activity, we have divided cells into these two groups. In general, we classified neurons as burst cells if they lacked significant sustained activity in the interval between the visual- and movement-related bursts seen in the visually guided task and during the instructed delay period in the memory-guided tasks. Neurons that had, in addition to a movement-related response, a sustained response related to preparation to make the saccade were classified as buildup cells.

Another major difference between burst and buildup neurons was in their movement fields. Figure 34.3 compares the discharge of a burst cell and a buildup cell associated with various amplitude saccades whose directions matched the optimal direction of each cell. The optimal saccade amplitude for the cells was approximately 8°. The burst cell (figure 34.3A) discharged maximally for saccades that were close to the optimal amplitude and, when saccade amplitude was greater or less than optimal, the discharge of the cell diminished. The saccade-related responses of the buildup cell (figure 34.3B) diminished if either the amplitude of the saccade was smaller than optimal or the direction deviated from optimal. However, buildup cells continued to discharge for saccades of optimal direction whose amplitudes were greater than optimal. In net, the burst cell had a movement field that was closed—that is, the response field had a distal border because the cell did not discharge for saccades significantly larger than optimal. In contrast, the buildup cell had an open-ended movement field: The cell discharged for all saccades of optimal direction that were equal to or greater than the optimal amplitude.

The latency between the onset and termination of the saccade to the peak of the cell discharge also differed for the burst and buildup cells. The timing of the peak discharge of burst cells relative to saccade onset did not vary with saccade amplitude; it always occurred around the time of saccade onset. For buildup cells, however, the occurrence of peak discharge relative to saccade onset depended on saccade amplitude; as saccade amplitude increased, the time from saccade onset to peak discharge also increased.

Several other characteristics of these cells should be noted. The saccade-related discharge patterns just described for both burst and buildup cells occurred regardless of whether the saccade was made to a visual target (as in figure 34.2) or to a remembered target. The saccade-related portion of both cell types' discharge was similar whether or not the target was visible during the movement. There were also no differences in the shapes of the movement fields for saccades made under these two conditions. The activity recorded from buildup cells during saccades that were larger than the optimal amplitude was not related to the programming of subsequent corrective saccades. With large saccades, cells with open-ended movement fields were active, regardless of whether there was a subsequent corrective saccade.

We determined the relative location of burst and buildup cells below the collicular surface. The depth of each cell was determined relative to the depth of the first multicell visual responses that we encountered on that penetration as the electrode entered the superficialmost layers of the SC. The visual cells, lacking saccade-related activity, were located in approximately the first millimeter of the SC; burst cells were found immediately beneath the visual cells, approximately 1–2 mm below the dorsal surface; the buildup cells were located ventral to and somewhat intermingled with the burst cells, approximately 1.5–2.5 mm below the dorsal surface of the SC. Both types of saccade-related cells were in the intermediate layers of the SC, with the buildup cells lying deeper than the burst cells.

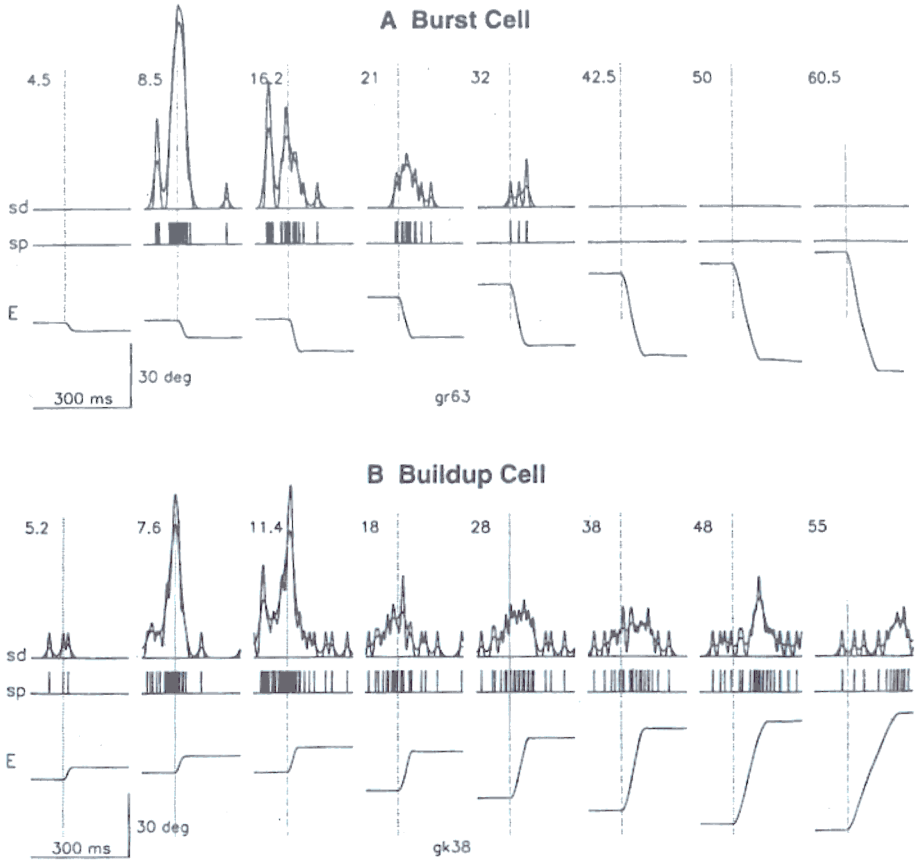


FIGURE 34.3 Movement fields of SC burst cell (A) and buildup cell (B). Saccade amplitude was systematically varied along the optimal direction across the movement field of the cell. The optimal saccade amplitude for both cells was approximately 8°. Shown in each panel is a single trial with two spike density profiles (sd), the individual action potentials (sp), and the radial eye position (E). The burst cell had a discrete movement field, whereas the buildup cell had an open-ended movement field. (From Munoz and Wurtz, 1994)

Fixation cells in rostral superior colliculus

On the saccade map of the SC (see figure 34.1), large-amplitude saccades are represented caudally and small saccades are represented rostrally. Some cells in the rostral pole, however, do not increase their discharge rate before saccades but instead do so during periods of active fixation. This observation was made in the SC of the cat (Munoz and Guitton, 1989, 1991) and, more recently, in the monkey (Munoz and Wurtz, 1993a, b, c). Figure 34.4 shows the discharge of such a

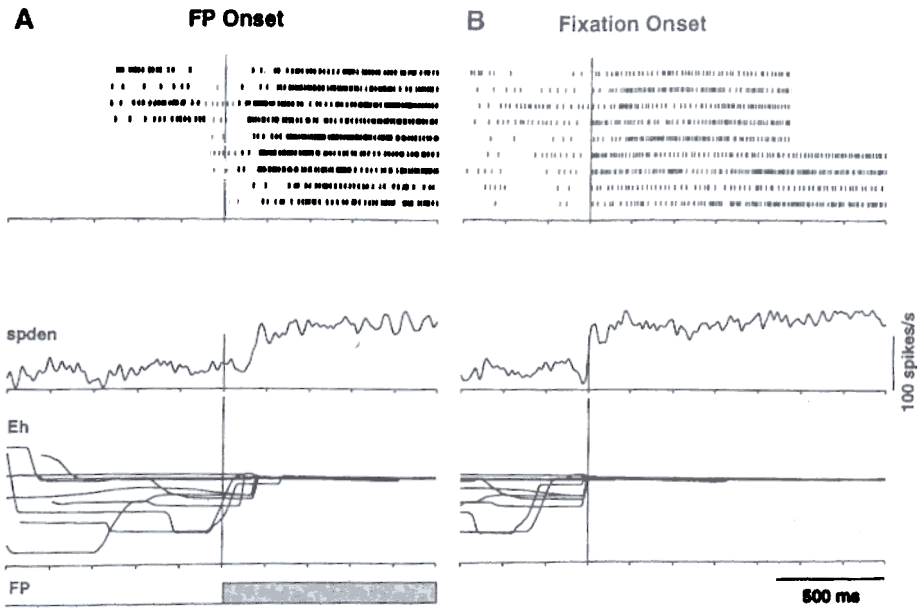


FIGURE 34.4 Example of the discharge of a fixation cell during active fixation. Rasters are aligned on (A) the onset of the fixation target (fixation point [FP] onset) and (B) the time when the eye entered the computer-controlled fixation window (fixation onset). The traces shown from top to bottom are the individual rasters, the spike density function (spden), and the horizontal eye position traces (Eh). (From Munoz and Wurtz, 1993a)

fixation cell while the monkey was looking about in the experimental room and then after it made a saccade to the visual target. In figure 34.4A, the raster and spike density display are aligned on this onset of the target, whereas in figure 34.4B they are aligned on the time when the monkey achieved fixation of the target. The discharge rate of the cell went up with acquisition of the target, not with target onset. In addition, the discharge was low while the monkey fixated a point on the blank screen but increased with active fixation of the target.

These fixation cells in the monkey have a number of other characteristics. The discharge was not simply the result of the visual stimulus falling on the foveal receptive field of a visually sensitive neuron. When we blinked the target off briefly, but the monkey continued to fixate, the cell continued to discharge. We have used this continued discharge as a criterion for the identification of fixation cells. In contrast, the discharge of other cells lying in the anterior colliculus more dorsal to fixation cells does pause with removal of the fixation point, indicating that the response of these cells is a visual one.

Another salient characteristic of collicular fixation cells is that they pause during saccades between actively fixated targets. Just as the duration of saccades increases with saccade amplitude, the duration of the pause also increases with larger saccadic amplitudes. Thus, the fixation cells and the saccade cells have patterns of discharge that are reciprocal: Fixation cells (figure 34.5, left) are active during fixation and silent during saccades, whereas saccade cells (figure 34.5, right) are silent during fixation but burst at the time of the saccades.

Fixation cells were located in the rostral pole of the SC at a depth similar to that of the buildup cells. We consider fixation cells as the extension of the buildup cell layer into the rostral pole.

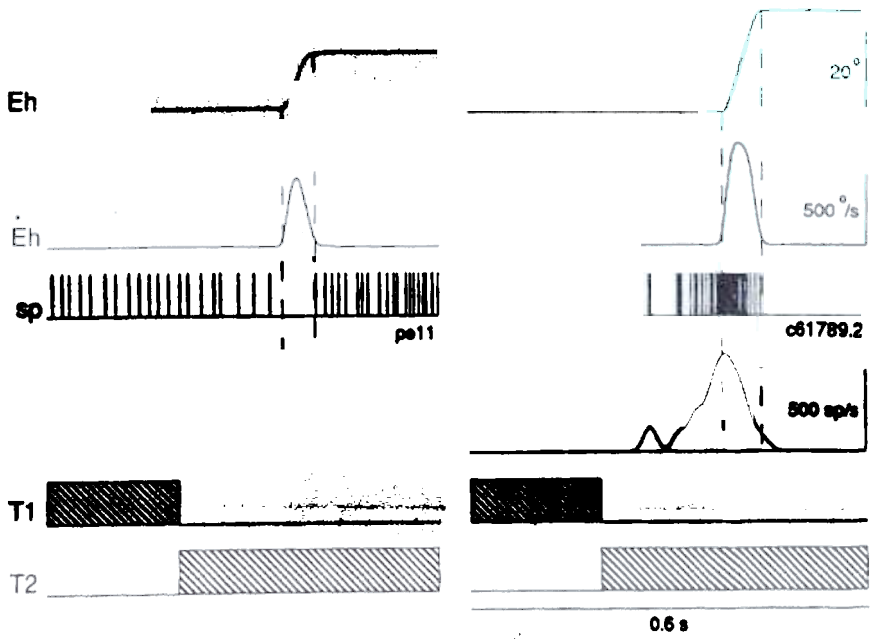


FIGURE 34.5 Comparison of the discharge of a fixation cell located in the anterior pole of the SC (left) and a saccade cell located in the caudal left SC (right). Same conventions as in figure 34.2. (From Munoz and Wurtz, 1993c)

Interaction between fixation and saccades

The reciprocal relationship of activity between saccade and fixation cells within the SC suggests that they might be mutually inhibitory. This mutual inhibition, in turn, suggests that if the activity of the fixation cells were artificially altered, the frequency of the saccades might be changed. We both increased and decreased the activity of the fixation cells to test the effect of this on the generation of saccades.

Figure 34.6 shows the logic of our experiments. Our hypothesis, like that developed for the cat (Munoz and Guitton, 1991), is that fixation cells in the rostral pole of the SC exert control over the saccadic system by inhibiting the saccade cells in the SC as well as by activating the brainstem omnipause neurons that gate the burst neurons in the paramedian pontine reticular formation. Though we show only the interaction of the fixation cells with the rest of the SC in figure 34.6, the effect of the fixation cells on these other midbrain and pontine areas should be regarded as being represented on the schematic drawing by the rest of the SC. Our strategy was to alter the activity of fixation cells in the rostral SC while leaving the rest of the SC undisturbed and then to test subsequent saccade generation. We first increased the activity in the fixation zone by applying low-frequency electrical stimulation (figure 34.6B) to increase activity of cells adjacent to the site of stimulation. According to our hypothesis, this manipulation should lead to increased activity in the fixation zone of the SC and decreased activity in the rest of the SC related to saccades.

Figure 34.7 illustrates the effect of stimulating both fixation zones simultaneously while the monkey made saccades in the visually guided saccade paradigm.

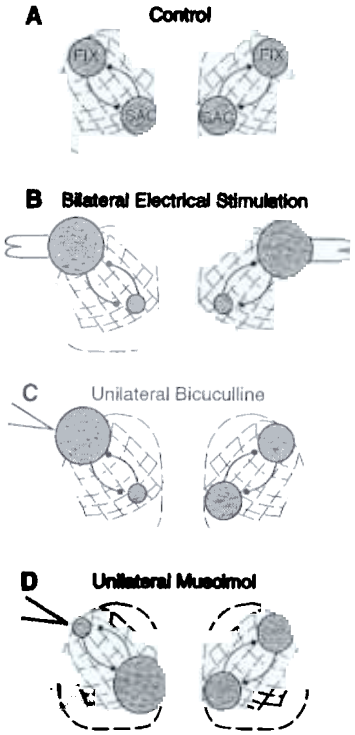


FIGURE 34.6 (A) Schematic motor map of the deeper layers of the monkey SC showing the putative connections between the collicular fixation zone (FIX) and the saccade zone (SAC). See text for details. (B) Activation of FIX cells in both colliculi with bilateral electrical stimulation would lead to increased inhibition of SAC cells. (C) Artificial activation of FIX cells with a unilateral injection of GABA antagonist (bicuculline) would lead to increased activity in the FIX zone and then to increased inhibition of SAC cells. (D) Artificial inhibition of FIX cells with a unilateral injection of a GABA agonist (muscimol) would lead to decreased activity in the FIX zone and then disinhibition of SAC cells. (From Munoz and Wurtz, 1993b)

Stimulation trials (solid traces) were interleaved with control trials during which no stimulation occurred (dotted traces). The small vertical tick on the eye position and velocity traces indicates the cue for the monkey to initiate the saccade (simultaneous offset of the fixation point and onset of the peripheral target). The monkey made saccades approximately 200 ms after target onset in the control condition to targets 20° to the left or right. A long-duration, low-frequency train of stimulation (500 ms, 150 Hz, 30 μA, marked by the horizontal bar under the eye position traces) delayed saccade initiation. The monkey could generate the saccade to the new target only after the stimulation ceased. All centrifugal saccades were affected as were centripetal saccades. Even with the delay in initiation, the saccades reached the target, as indicated by the equal amplitude of the normal and delayed saccades in figure 34.7. This accuracy endured even if the target was no longer present after the stimulation ended, as was the case when the monkey made a saccade to the remembered location of the target. When we applied stimulation to the fixation zone during the saccade, saccades were interrupted in midflight.

When we positioned the electrode outside the location on the motor map where fixation cells were recorded, the effect was not evident. Also, when we stimulated at locations above, below, or rostral to the location of fixation cells with similar parameters, no effect was seen on saccade generation.

Whereas electrical stimulation allowed us to increase activity within the fixation zone, injection of GABAergic drugs allowed us either to increase the activity with a GABA antagonist (bicuculline, figure 34.6C) or to decrease activity with a GABA agonist (muscimol, figure 34.6D). We found that bicuculline and muscimol injections had a profound effect on the monkey's ability to fixate a target and make saccades to a new target. Application of bicuculline increased saccade latencies, whereas muscimol reduced latencies and led to instability of fixation.

The effect of reducing fixation activity with muscimol is illustrated in figure 34.8. We used a memory-guided saccade task to maximize the requirements for fixation. In this saccade task (figure 34.8A), we flashed a spot of light (T2) for 80 ms at a point in the contralateral visual field, but we required the monkey to continue fixating until after the fixation point (T1) went off several hundred (400–800) milliseconds later. If the monkey delayed the saccade until after offset of the fixation point (T1), it was rewarded as a correct response, but if the saccade occurred earlier, it was not rewarded for this incorrect response. The histograms at the top of figure 34.8B show that the normal monkey easily made almost entirely correct saccades. Most of

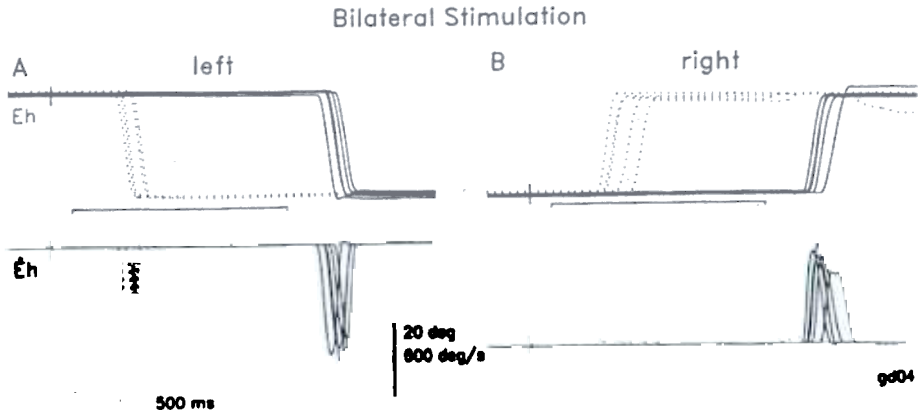


FIGURE 34.7 Suppression of saccades by bilateral stimulation of both fixation zones simultaneously. Five control trials (dotted traces) and five stimulation trials (solid traces) are superimposed in each panel as the monkey made visually guided saccades. The vertical tick on the eye position traces indicates the time of target onset, and the horizontal bar under the eye position traces indicates the time of stimulation. Low-frequency, long-duration stimulation (500 ms, 150 Hz, 30 μA) of both fixation zones prevented the initiation of centrifugal saccades. (Eh, horizontal eye position traces.) (After Munoz and Wurtz, 1993b)

these saccades were initiated approximately 200 ms after T1 offset. After injection of muscimol into the rostral colliculus (bottom of figure 34.8B), the monkey had difficulty delaying initiation of the saccade after the flash of the target, and many saccades occurred just after the flash. Note that these saccades on the incorrect trials were to the right target but at the wrong time. Thus, the execution of the saccade was not disrupted—it was simply delayed—exactly as we would expect if we had removed an inhibition on saccade generation.

The incorrect saccades shown on the frequency histograms in the lower half of figure 34.8B not only occurred before the fixation point went off, but many occurred within a latency of 80–100 ms after the target light flashed. Such a short regular latency is characteristic of express saccades previously observed in the monkey (Fischer and Boch, 1983). Of particular relevance to the fixation cells in the SC is the proposal (Fischer, 1987) that express saccades occur most frequently when fixation has already been broken, which is exactly what we propose is the consequence of the functional removal of the rostral SC.

The fixation cells that we have identified are almost certainly part of a larger system within the brain, as cells whose discharge is modified by fixation under some conditions have been observed in parietal cortex (Mountcastle, Andersen, and Motter, 1981) and substantia nigra pars reticulata (Hikosaka and Wurtz, 1983). Extrastriate cortical lesions also alter the frequency of express saccades, which is consistent with the role of cortex in the control of visual fixation (Weber and Fischer, 1990).

Burst cells temporally related to saccades

The most intensively studied saccade-related cells have been the burst cells (see figures 34.2A, 34.3A). The work on these cells has been summarized recently by Sparks and Hartwich-Young (1989). Occurrence of the burst is highly correlated with occurrence of the saccade (Sparks, 1978), and each saccade is accompanied by activity at a specific location on the SC movement map that specifies the amplitude and direction of the saccade. The sum of activity from all cells presumably is responsible for bringing the saccade on target.

In fact, bringing the eye on target has been a vexing problem for models of the saccadic system, and fitting the SC into these models has been even more difficult.

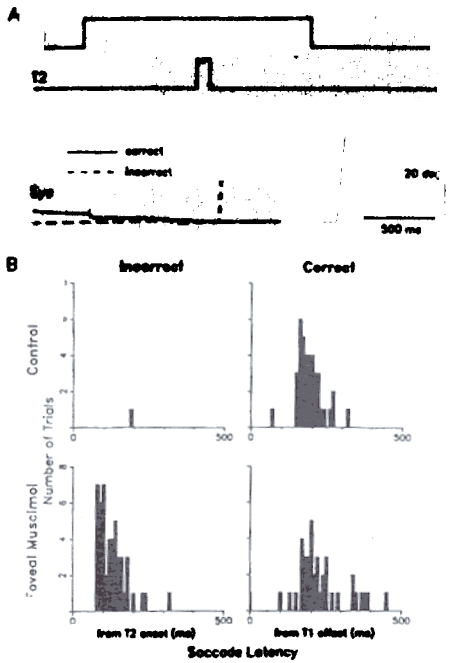


FIGURE 34.8 Shortening of saccade latency as a result of inactivation of fixation cells. (A) Examples of saccades occurring after the fixation point goes off (T1; correct) and shortly after the flash in the peripheral field (T2; incorrect). (B) Frequency of occurrence of these two types of saccades before (top) and after (bottom) the injection of muscimol. (From Munoz and Wurtz, 1993c)

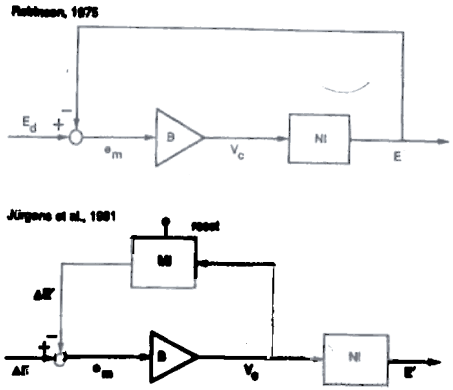


FIGURE 34.9 Two models of feedback control of saccadic amplitude. (Top) Robinson model. (Bottom) Jürgens, Becker, and Kornhuber model. Both are simplified to show only essential elements related to the negative feedback hypothesis (see text for details). E', new eye position; ΔE', change in E'; E_d, desired eye position; e_m, error signal; B, burst cells; MI, model integrator; V_c, velocity command; NI, neural integrator. (From Wurtz and Munoz, in press.)

Robinson (1975) proposed a local feedback model to solve this problem. The essential features of his model are shown in the upper half of figure 34.9. A burst of activity (a velocity command, V_c) from pontine burst cells (B) drives the saccade, and the same V_c signal is integrated by a neural integrator (NI) to hold the eye at the new position. At the same time, an internal representation of this position signal (E') is fed back for comparison with the desired eye position (E_d). As long as a difference persists between these values, an error signal (e_m) is generated that continues to drive the burst generator (V_c). When the difference (e_m) reaches zero, the activity driving the eye stops, and the eye reaches the target.

One problem with this model, however, is that the E_d signal is in cranial or head-centered coordinates rather than the eye-movement (retinotopic) coordinates of the map of movement fields layed out on the SC (see figure 34.1). The saccade cells discharge the same burst regardless of whether the monkey began the saccade close to the center of the visual field or from one side or the other. If this map were in spatial coordinates, where the eye starts should substantially alter the discharge of the cell (Jürgens, Becker, and Kornhuber, 1981).

A subsequent model by Jürgens, Becker, and Kornhuber (1981) offered a resolution between the feedback model of Robinson (1975) and the retinotopic coordinate system seen in the SC (figure 34.9, bottom). These investigators added a second integrator (a model integrator [MI]) that was reset after each saccade so that the feedback was an internal feedback of *change* in eye position (ΔE') rather than absolute eye position (E'). This internal representation of change in position ΔE' was compared with the change in eye position required (ΔE), and any difference is the e_m that would drive the eye to the new position, as in the Robinson model.

This placement of the system in retinotopic coordinates made the signals at the summing junction consistent with the retinotopic coordinate system of the SC and inspired a reinvestigation of the SC to determine whether these signals could be found. The change in eye position required (ΔE) should be present and remain throughout the saccade, whereas the feedback signal (ΔE') should be present during the saccade and should be reset after it. The difference signal (e_m) is maximal at saccade onset and decreases during the saccade to approach zero as the saccade reaches the target.

Waitzman and coworkers (1988, 1991) found that many saccade-related burst cells in the SC demonstrated clipped responses—that is, the intense burst portion of the discharge came to an end at the time the eye stopped moving. For example, the discharge of the burst cell in figure 34.2A ended close to the time the saccade ended (its response was clipped off by the saccade). Furthermore, the dynamics of the change in discharge in many clipped cells revealed a nearly linear decline over the duration of the saccade and a reduction in motor error (Waitzman et al., 1991).

With this previously unappreciated observation that many burst cells ended as the saccade ended, Waitzman's group (1988, 1991) constructed a modified Becker and Jürgens model of the saccadic system that incorporated the SC specifically into the model (figure 34.10). The retinotopic map of burst or clipped cells in the SC is now envisioned as conveying the e_m signal so that the SC is *inside* the feedback loop. The ΔE signal may be the increased activity in one region of the visual map in the superficial layers of the SC or in the inputs from cortex to SC. No correlate of ΔE' is evident; the signal may be conveyed by the terminals ending on the clipped cells. The e_m signal in the model would be conveyed to the brain stem by the clipped cells in the SC.

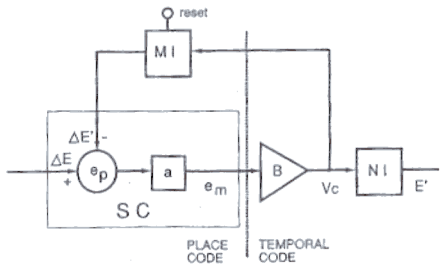


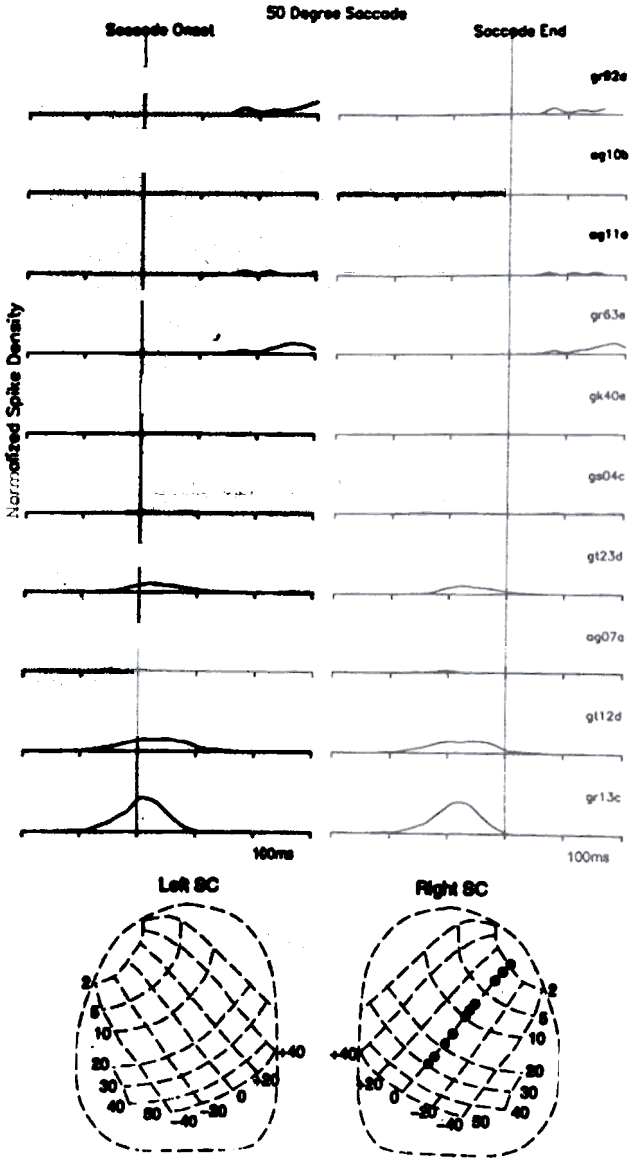
FIGURE 34.10 Model of negative feedback system for control of saccadic amplitude with SC in the feedback loop. a, scale factor; e_p, collicular locus; other abbreviations as in figure 34.9. (From Waitzman et al., 1991.)

A consequence of this model is worth noting. A change in eye position is controlled by the feedback loop, and only errors in position after the output of the summing junction are controlled. Any changes of cell activity within the colliculus would be expected to be associated with changes of eye velocity because they would influence the strength of the burst but not the final eye position controlled by the loop. Thus, a relation between eye velocity and cell discharge (Rohrer, White, and Sparks, 1987) and the effect on eye velocity of chemical lesions of SC (Hikosaka and Wurtz, 1985) both would be consistent with the model.

Finally, note that the SC is in retinotopic coordinates and the preferred change in eye position is conveyed by activity within this map, a place code. The projections from the SC, however, go from this place code to the temporal code that is used eventually to drive the eye muscles. Although we do not know how this conversion occurs, a reasonable hypothesis is that areas within the SC where a hill of neuronal activity is related to large saccades have a stronger innervation onto the pontine bursters than do those associated with small saccades (Edwards and Henkel, 1978; Wurtz and Albano, 1980). The temporal code also must be translated back into a spatial code in the feedback loop, but whether this translation starts from a position signal (Waitzman et al., 1991) or a velocity signal (Lefevre and Galiana, 1990; Droulez and Berthoz, 1991) is not known.

Buildup cells spatially related to saccades

A salient distinction between burst cells and buildup cells in the SC is a difference in the pattern of activity in the cells lying at different positions on the SC motor map. Figures 34.11 and 34.12 illustrate this by showing the normalized spike density profiles of cells in each of the burst and buildup cell layers. The cells have different optimal saccade amplitudes and are located in dif-



ferent locations within the SC, which are shown schematically by filled circles on the SC motor map. The discharge for each cell is that accompanying a 50° saccade. The peak discharge of the caudalmost cells in both layers occurred near the time of saccade onset. In the burst cell layer (see figure 34.11), only cells in the caudal SC discharged with the 50° saccade, and cells lying more rostral to the initially active zone remained silent. The level of discharge of burst cells in the initially active zone simply diminished so that by saccade termination, these neurons were almost silent. However, the buildup cells lying rostral to the initially active cells were activated sequentially at some point during the 50° saccade (see figure 34.12). Looking at the left column in figure 34.12, where cell responses are aligned on saccade onset, the peak discharge began before the 50° saccade for the caudalmost cell and gradually moved later for more rostrally located cells. A clear-moving front of activity is therefore visible beginning in the caudal SC and moving to the rostral SC. Again, looking at the burst cell layer, no such movement is evident.

In the rostral SC (see figure 34.12, top), activity was confined to the fixation cells 200 ms before the onset of the 50° saccade. As activity began in the buildup cell layer and then later in the burst cell layer, fixation-related activity in the rostral pole simultaneously diminished. At saccade onset, fixation-related activity had ceased and cells in both layers of the caudal SC were maximally active. The fixation cells began to discharge again at the end of the saccade.

Thus, the buildup cells seem to differ from the burst cells in the activity contained in various parts of the movement map. In the burst cell layer, the neural activity hill reaches peak height at saccade onset and diminishes in size during the saccade. This characteristic contributed to the formation of the model for saccade generation that includes the SC in a feedback loop controlling saccade amplitude, as described previously. In the buildup cell layer, the activity in the buildup cells seems to change as if a front of activity were moving across the SC during the course of the saccade. At the start of a large-amplitude saccade, neural activity is centered in the caudal SC but, as the vector error between the current position of the visual axis and the target decreases during the saccade, cells located progressively more rostral in the SC (i.e., those preferring smaller and smaller amplitude gaze shifts) begin to discharge.

This observation of a shift in activity across the SC during a saccade was first made for movement-related cells in the cat SC (Munoz, Guitton, and Pélisson, 1991) and also led to the conclusion that the SC is within the feedback loop controlling the amplitude of saccades but for reasons quite different from those described earlier. Munoz, Guitton, and Pélisson (1991) argued that when this shifting activity reached the fixation cells located in the rostral SC, the saccade was terminated, thus closing a loop. The location of the SC in relation to a feedback control system for the amplitude of saccades had remained a puzzle for almost two decades, but these two sets of experiments both reached the conclusion that the SC was in the feedback loop.

Conclusions

Our understanding of a system within the brain that controls the generation of saccadic eye movements has developed substantially over the past 20 years, but the SC has remained a central structure in this system. The recognition that burst cells within the colliculus discharge in a manner consistent with their location within a feedback loop that governs the amplitude of the saccade has allowed the spatial map within the colliculus to be more readily understood in the *spatial-to-temporal* transition that is necessary to activate the temporally driven eye muscles. The study of a second set of saccade-related cells, the buildup cells, that appear to have a moving front of activity across the SC during a saccade, has contributed a second map of movement-related activity. Although there many facets have yet to be worked out, these observations further constrain the position of the SC in any model of the control of saccades.

In contrast to the long-standing recognition of a saccadic system, the recognition of a system for active fixation is relatively recent (Munoz and Guitton,

FIGURE 34.11 Independence of burst cells from sequential activation. Each curve is for one cell that is located progressively further caudally in the SC, as indicated by the dots on the SC map at bottom of figure. Activity was obtained when the monkey made 50° saccades. Same discharge is aligned on saccade onset (left column) and on saccade end (right column). Only cells in the caudalmost SC were activated during the 50° saccade. (From Munoz and Wurtz, 1994.)

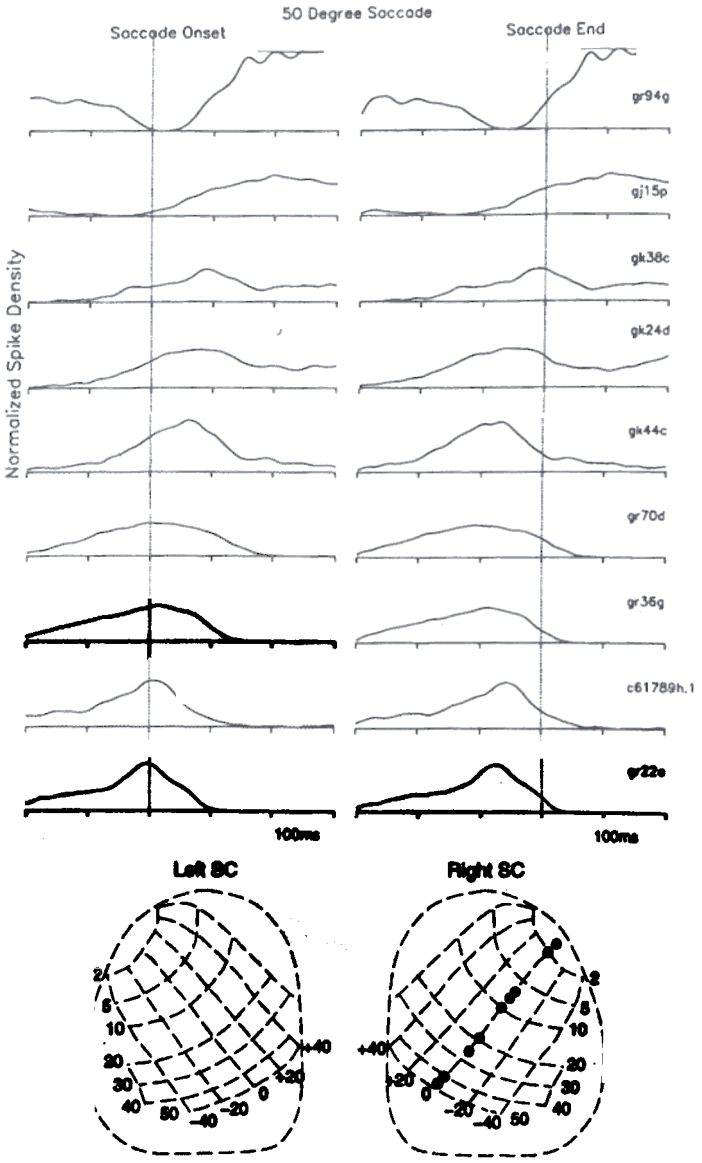


FIGURE 34.12 Successive activation of buildup cells whose fields are located progressively closer to the anterior pole of the SC. Same organization as in figure 34.11. (From Munoz and Wurtz, 1994.)

1989). The role of the rostral colliculus in this function is now becoming established in both the cat and the monkey. Interaction between this fixation system and the saccadic system at the level of the SC allows us to study the integration of these two systems in a relatively simple environment. The factors involved in such an interaction may aid in our understanding of such integration in other more complex sensorimotor systems.

NOTE

The experiments reported in this chapter are based largely on the original research reports of Waitzman and colleagues (1991) and Munoz and Wurtz (1993a, b, c). The chapter is also derived from a recent summary of the SC (Wurtz and Munoz, in press).

REFERENCES

DROULEZ, J., and A. BERTHOZ, 1991. The concept of dynamic memory in sensorimotor control. In *Motor Control: Concepts and Issues*, D. R. Humphrey and H.-J. Freund, eds. Chichester, Engl.: Wiley, pp. 137–161.

EDWARDS, S. B., and C. K. HENKEL, 1978. Superior colliculus connections with the extraocular motor nuclei in the cat. *J. Comp. Neurol.* 179:451–468.

FISCHER, B., 1987. The preparation of visually guided saccades. *Rev. Physiol. Biochem. Pharmacol.* 106:1–35.

FISCHER, B., and R. BOCH, 1983. Saccadic eye movements after extremely short reaction times in the monkey. *Brain Res.* 260:21–26.

HIKOSAKA, O., and R. H. WURTZ, 1983. Visual and oculomotor functions of monkey substantia nigra pars reticulata: II. Visual responses related to fixation of gaze. *J. Neurophysiol.* 49:1254–1267.

HIKOSAKA, O., and R. H. WURTZ, 1985. Modification of saccadic eye movements by GABA-related substances: I. Effect of muscimol and bicuculline in monkey superior colliculus. *J. Neurophysiol.* 53:266–291.

JÜRGENS, R., W. BECKER, and H. H. KORNHUBER, 1981. Natural and drug-induced variations of velocity and duration of human saccadic eye movements: Evidence for a control of the neural pulse generator by local feedback. *Biol. Cybern.* 39:87–96.

LEE, C., W. H. ROHRER, and D. L. SPARKS, 1988. Population coding of saccadic eye movements by neurons in the superior colliculus. *Nature* 332:357–360.

LEFEVRE, PH., and H. L. GALIANA, 1990. Velocity versus position feedback to the superior colliculus in gaze control modelling. *Soc. Neurosci. Abstr.* 16:1084.

MOUNTCASTLE, V. B., R. A. ANDERSEN, and B. C. MOTTER, 1981. The influence of attentive fixation upon the excitability of the light-sensitive neurons of the posterior parietal cortex. *J. Neurosci.* 1:1218–1235.

MUNOZ, D. P., and D. GUITTON, 1989. Fixation and orientation control by the tecto-reticulo-spinal system in the cat whose head is unrestrained. *Rev. Neurol. (Paris)* 145:567–579.

MUNOZ, D. P., and D. GUITTON, 1991. Control of orienting gaze shifts by the tectoreticulospinal system in the head-free cat: II. Sustained discharges during motor preparation and fixation. *J. Neurophysiol.* 66:1624–1641.

MUNOZ, D. P., D. GUITTON, and D. PÉLISSON, 1991. Control of orienting gaze shifts by the tectoreticulospinal system in the head-free cat: III. Spatiotemporal characteristics of phasic motor discharges. *J. Neurophysiol.* 66:1642–1666.

MUNOZ, D. P., and R. H. WURTZ, 1992. Two classes of cells with saccade related activity in the monkey superior colliculus. *Soc. Neurosci. Abstr.* 18:699.

MUNOZ, D. P., and R. H. WURTZ, 1994. Saccade related activity in monkey superior colliculus. Manuscript in preparation.

MUNOZ, D. P., and R. H. WURTZ, 1993a. Fixation cells in monkey superior colliculus: I. Characteristics of cell discharge. *J. Neurophysiol.* 70:559–575.

MUNOZ, D. P., and R. H. WURTZ, 1993b. Fixation cells in monkey superior colliculus: II. Reversible activation and deactivation. *J. Neurophysiol.* 70:576–589.

MUNOZ, D. P., and R. H. WURTZ, 1993c. Superior colliculus and visual fixation. *Biomedical Res.* 14 Suppl 1:75–79.

ROBINSON, D. A., 1972. Eye movements evoked by collicular stimulation in the alert monkey. *Vision Res.* 12:1795–1808.

ROBINSON, D. A., 1975. Oculomotor control signals. In *Basic Mechanisms of Ocular Motility and Their Clinical Implications*, G. Lennerstrand and P. Bach-y-Rita, eds. Oxford: Pergamon, pp. 337–374.

ROHRER, W. H., J. M. WHITE, and D. L. SPARKS, 1987. Saccade-related burst cells in the superior colliculus: Relationship of activity with saccadic velocity. *Soc. Neurosci. Abstr.* 13:1092.

SPARKS, D. L., 1978. Functional properties of neurons in the monkey superior colliculus: Coupling of neuronal activity and saccade onset. *Brain Res.* 156:1–16.

SPARKS, D. L., and R. HARTWICH-YOUNG, 1989. The deep layers of the superior colliculus. In *The Neurobiology of Saccadic Eye Movements: Reviews of Oculomotor Research*, vol. 3, R. H. Wurtz and M. E. Goldberg, eds. Amsterdam: Elsevier, pp. 213–256.

SPARKS, D. L., and L. E. MAYS, 1980. Movement fields of saccade-related burst neurons in the monkey superior colliculus. *Brain Res.* 190:39–50.

SPARKS, D. L., and L. E. MAYS, 1990. Signal transformations required for the generation of saccadic eye movements. *Annu. Rev. Neurosci.* 13:309–336.

WAITZMAN, D. M., T. P. MA, L. M. OPTICAN, and R. H.

WURTZ, 1988. Superior colliculus neurons provide the saccadic motor error signal. *Exp. Brain Res.* 72:649–652.
WAITZMAN, D. M., T. P. MA, L. M. OPTICAN, and R. H. WURTZ, 1991. Superior colliculus neurons mediate the dynamic characteristics of saccades. *J. Neurophysiol.* 66: 1716–1737.
WEBER, H., and B. FISCHER, 1990. Effect of a local ibotenic acid lesion in the visual association area on the prelunate gyrus (area V4) on saccadic reaction times in trained rhesus monkeys. *Exp. Brain Res.* 81:134–139.
WURTZ, R. H., and J. E. ALBANO, 1980. Visual-motor function of the primate superior colliculus. *Annu. Rev. Neurosci.* 3:189–226.
WURTZ, R. H., and M. E. GOLDBERG, 1972. Activity of superior colliculus in behaving monkey: III. Cells discharging before eye movements. *J. Neurophysiol.* 35:575–586.
WURTZ, R. H., and M. E. GOLDBERG, 1989. *The Neurobiology of Saccadic Eye Movements: Reviews of Oculomotor Research*, vol. 3. Amsterdam: Elsevier.
WURTZ, R. H., and D. P. MUNOZ (in press). Saccadic and fixation systems of oculomotor control in monkey superior colliculus. In *Neuroscience: From Neural Networks to Artificial Intelligence. Proceedings of a U.S.-Mexico Seminar Held in the City of Xalapa in the State of Veracruz on December 9–11, 1991*, P. Rudomin, M. A. Arbib, F. Cervantes-Perez, and R. Romo, eds. Berlin: Springer-Verlag.

35 Contributions of Vision and Proprioception to Accuracy in Limb Movements

CLAUDE GHEZ, JAMES GORDON, MARIA FELICE GHILARDI, AND ROBERT SAINBURG

ABSTRACT We have studied movement errors in normal human subjects and in patients deafferented by large-fiber sensory neuropathy. In normals, movement extent and direction were subject to different sources of variable and systematic errors, suggesting that these parameters are programed independent. Moreover, vision of the hand and the target were necessary to program direction accurately. These data suggest that the planning of reaching movements takes place in an extrinsic, hand-centered coordinate system.

In deafferented patients, simple movements aimed to visual targets showed large errors in direction and extent because of failure to compensate for directional variations in limb inertia. In movements with direction reversals, distinctive errors appeared because of failure to program elbow muscle contractions in accord with interaction torques produced at the elbow by variations in acceleration of the upper arm. Both inertial and reversal errors were substantially reduced when patients had recently had the opportunity to monitor movements of their arm visually. We conclude that the programing of accurate trajectories requires a frequently updated internal model of the state and properties of the limb by proprioceptive input. It is proposed that such internal models are critical for the transformation from extrinsic to intrinsic coordinates used to plan the joint angle changes and torques needed to execute the movement.

It is generally understood that the accuracy of limb movements depends largely on precisely calibrated feedforward commands that direct the hand to the target (Georgopoulos, 1986). Although vision and proprioception are both essential if movements are to be accurate, the nature of the information provided by these two modalities is not fully understood. For example, it normally is taken for granted that vision simply provides information about the location of the target. Whether vision is needed also to determine the initial position of the hand is not known. Some investigators hypothesize that the relationship of the target to the limb is critical (Burnod et al., 1992; Flanders, Helms Tillery, and Soechting, 1992). For these authors, movement trajectories are driven by a motor error representing the difference between the intended final limb configuration and its initial configuration, determined proprioceptively. Whether the extent and direction of movement can, in fact, be programed accurately by the comparison of visual information obtained from a target and information about arm configuration obtained proprioceptively has not been examined in any detail.

Significant insights into the role of proprioception in trajectory formation have been obtained by studying the motor deficits of patients with large-fiber sensory neuropathy (Rothwell et al., 1982; Sanes et al., 1985; Forget and Lamarre, 1987; Forget and Lamarre, 1990; Ghez et al., 1990). In these patients, the selective degeneration of large-diameter afferent fibers may abolish completely all sense of joint position as well as stretch reflexes. Studies of such patients have documented the importance of proprioceptive input for the regulation of steady-state force and for detecting and correcting trajectory errors due to mechanical perturbations (Rothwell et al., 1982; Sanes et al., 1985). Evidence from such studies suggests that loss of proprioception does not alter or impair the strategies that subjects use to make single-joint movements: Like intact controls, deafferented patients produce move-

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