12 Commands for Coordinated Eye and Head Movements in the Primate Superior Colliculus

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CONTENTS

12.1 INTRODUCTION

Results of recent experiments have modified concepts of how neurons in the intermediate and deeper layers of the superior colliculus (SC) represent commands for

orienting movements of the eyes and head. This chapter explores the implications of these new findings for three important problems associated with collicular function: the spatial-to-temporal transform problem, population coding, and the types of feedback signals received by collicular neurons.

12.2 KEY QUESTIONS

12.2.1 SPATIAL-TO-TEMPORAL TRANSFORM PROBLEM (STTP)

Electrical stimulation of the intermediate and deeper layers of SC of monkeys with their heads restrained produces conjugate, contralateral saccades with amplitudes and directions that depend on the site of collicular stimulation.[1] When different regions of the colliculus are activated, the direction and amplitude of the stimulation evoked movements change systematically,[1] revealing a motor map that is in anatomical register with the retinotopic map found in the overlying superficial layers.[2] Early studies reported that variations in the parameters of stimulation (intensity, frequency, pulse width, and train duration) had no effect on the direction, amplitude, or velocity of the stimulation-evoked movements.[1,2] Thus, it was concluded that the spatial distribution of activity within the SC encodes information about the characteristics of a saccade, and that neither the level nor duration of collicular activity plays an important role in saccade execution.

Downstream from the SC, both the level and duration of motor command signals are important. Excitatory burst neurons (EBNs) in the pons generate activity that is primarily responsible for the horizontal component of a saccade. Similarly, EBNs located in the midbrain produce activity responsible for vertical and torsional components of saccades. The temporal characteristics of EBN activity are related to the temporal features of the saccade. Burst rate is highly correlated with saccade velocity and saccade duration is tightly coupled to burst duration.[3–6] EBN signals are conveyed monosynaptically to motoneurons innervating extraocular muscle fibers. The motoneurons display a pulse-step discharge pattern. The transient increase in muscle tension needed to move the eye at saccadic velocity results from a pulse of innervation and the steady state tension needed to hold the eye at its new location in the orbit is due to a step change in the firing rate of motoneurons.[7–12] The amplitude and duration of the pulse affect the size and speed of saccades.

How are the place coded command signals observed in SC translated into the temporally coded signals observed in premotor neurons located in pons and midbrain? This question,[1] called the spatial-to-temporal transform problem (STTP), remains one of the most important problems in the neural control of gaze. The related problem of extracting separate signals for the horizontal and vertical burst generator circuits is known as the vector decomposition problem. The transformed signals must control both saccade direction and amplitude.

The amplitude of saccades evoked by collicular stimulation increases as the stimulation site moves more caudally. A rostrocaudal gradient of the number of tectal neurons projecting to pontine and midbrain burst neurons could be an important aspect of controlling saccade amplitude. Such a gradient in the number of neurons projecting to the region surrounding the abducens nucleus was described in an early

experiment,[13] but was not observed in subsequent studies.[14–16] In retrospect, the failure to replicate the early observation is understandable because, in fact, a simple rostrocaudal gradient is not the pattern of connectivity required. Collicular neurons coding for movements having a 5û horizontal component reside in many different locations in the motor map. Cells discharging before 5û purely horizontal movements do reside in rostral SC, but those discharging maximally before movements with a 30û vertical component and a 5û horizontal component reside in caudal SC. The amplitude lines on Robinson's motor map represent vectorial amplitude, not the amplitude of the horizontal or vertical components.

Contemporary anatomical methods were used to reexamine the rostrocaudal gradient of SC connections to abducens nucleus using an approach that takes the details of the collicular map into account. Grantyn and colleagues[17] injected rabies virus into the lateral rectus muscle of rhesus monkeys and measured the retrograde transneuronal transport of the virus to SC to determine the density of neurons projecting to abducens nucleus. If the relative density of projection neurons is an important part of the STTP, the number of horizontal eye movement-related SC neurons should increase with distance from the rostral pole of the SC and decrease as a function of distance from the representation of the horizontal meridian. Counts of the number of labeled neurons in the intermediate SC layers located inside a 1mm-wide band that matched the horizontal meridian of the collicular motor map were plotted against distance from the rostral SC pole. Caudal sites contained more neurons, but the experimentally observed density gradients were not as steep as the gradient produced by models in which the density of collicular output neurons was the critical factor accounting for the increase in saccade amplitude. The distributions of cell densities in the intermediate SC layers representing saccades of equal vectorial amplitudes but different directions were also examined. Concentrations of labeled cells were highest in the vicinity of the horizontal meridian but decreased more sharply toward the periphery than predicted by models. Thus, the authors conclude that the density gradients of cells projecting to motoneurons cannot fully account for the amplitude of a pure horizontal saccade or for the amplitude of the horizontal component of oblique saccades. The retrograde labeling method permits a description of the relative number of cells projecting to abducens nucleus, but possible differences in the synaptic efficacy of each labeled cell's output are more difficult to quantify.

Moschovakis and colleagues[18] stimulated different regions of the collicular map, noted the amplitudes of the horizontal and vertical components of the stimulation-evoked movement, and then made small injections of biocytin into the stimulated areas. They counted the number of boutons labeled in the paramedian pontine reticular formation (PPRF) after anterograde transport of the biocytin for each injection. A significant positive correlation was observed between the normalized number of labeled boutons and the amplitude of the horizontal component of movements evoked by stimulation. This differential weighting of anatomical projections from different parts of the collicular map to PPRF must be a critical aspect of the STTP. However, additional processing is probably required to account for the site specific maximal amplitudes observed with collicular stimulation. With a simple weighting of synaptic connections, the effects of strong stimulation at a rostral site could be equivalent to weaker stimulation at more caudal site.

12.2.2 POPULATION CODING

The receptive and movement fields of collicular neurons are large and coarsely tuned.[19–21] Initially, it was assumed that neurons with such coarsely tuned receptive and movement fields could not generate accurate saccades and, therefore, that the SC was not involved in coding the exact location of a visual target or in specifying the exact distance and direction of the saccade required to look to the target. Instead, it was proposed that the activity of collicular neurons merely facilitated movements that directed gaze to a broad area of the visual field.[21] Later, researchers realized that information about the precise parameters of an impending saccade could be coded spatially — the location of the active population of neurons within the SC could specify, precisely, saccade metrics. A number of schemes by which this information could be extracted from a spatial or anatomical code were suggested.[20,22–25] In these schemes, each member of the active population contributes to the movement but the exact trajectory of a saccade is determined by the average or sum of the population activity.

Results of experiments in which small subsets of the active population were reversibly inactivated or activated,[26,27] supported a population averaging hypothesis. The vector averaging model of Sparks and colleagues,[20] assumes that the region of collicular neurons active before a given saccade occupies a symmetrical area within the motor map. Only the neurons in the center of the active population discharge maximally before the programmed movement. But, for each subset of active neurons producing a movement tendency with a direction and amplitude other than the programmed movement, a second subset of neurons producing an opposing movement tendency will be active. The resultant of the two movements will have the programmed direction and amplitude. The vector-averaging hypothesis does not require neurons with sharply tuned movement fields in order to generate accurate saccades.

According to the vector-averaging hypothesis, a predictable pattern of errors should be observed when a small region of colliculus is inactivated and animals are required to make saccades of different directions and amplitudes. The predicted pattern of errors was observed after small injections produced a local reversible inactivation of collicular neurons.[27] Further evidence for a vector-averaging model was obtained in experiments in which saccades were evoked by microstimulation of the frontal eye field (FEF) before and after local inactivation of neurons in SC. When SC inactivation affected only a subset of the neurons that would normally be active during the FEF evoked saccades, the direction and amplitude of the evoked saccade shifted in a manner that was consistent with the SC inactivation removing a component of a vector average.[28]

12.2.3 THE ROLE OF FEEDBACK

Most current models assume that saccades, once considered to be ballistic or pre-programmed movements, are under feedback control. What is the source of the putative feedback signal? It is not visual. A saccade ends before signals from the retina reach central visual areas that could provide feedback about accuracy. Necessary feedback

signals are not derived from sensory receptors in extraocular muscle fibers. Saccadic accuracy is not affected significantly by elimination of proprioceptive feedback.[29] Zee and colleagues[30] hypothesized that a copy of a motor command (corollary discharge) could be used as a feedback signal for controlling saccade amplitude and almost all contemporary models of the saccadic system use a corollary discharge signal for feedback. This is possible because the load confronting the control system is relatively constant. Changes in the mechanical properties of the plant associated with trauma or aging would not prevent the use of this computational strategy if the gain of the critical signals is modifiable.

Some models of the saccadic system assume that the SC is within a dynamic feedback loop so that the locus[31,32] or level[33] of collicular activity continuously changes as a saccade is executed. Munoz and colleagues hypothesized that during a large saccade, a population of neurons in the caudal colliculus will discharge first. As the eye moves (reducing the difference between the desired displacement of the eye and the current eye position), the site of neural activity migrates rostrally in the SC until, finally, neurons at the rostral pole of the colliculus encoding a motor error of zero become active. If the distribution of activity within the SC is represented as a relief map, the nested contours of increasing activity can be thought of as a *hill* that, according to the hypothesis, migrates rostrally during the course of the movement. According to this hypothesis, motor error is mapped dynamically by the location of active cells within the motor map found in the deeper layers of the SC.

Initial evidence offered in support of this hypothesis was evaluated as either inconsistent with the model or subject to plausible alternative explanations.[34] Subsequent quantitative analyses of the distribution of activity within SC during a saccade have not been consistent with the notion of a systematic and sequential shift from caudal to rostral SC.[35–37]

Waitzman and colleagues hypothesized that saccade dynamics are controlled by the discharge profiles of SC neurons.[33] In this model, the locus of activity in the SC encodes the desired eye movement and the level of activity represents the dynamic motor error. The evidence supporting this hypothesis is meager. The hypothesis was based upon a correlation (observed for a subset of collicular cells) between the decay in spike discharge at the end of a burst and the reduction in vectorial motor error occurring during a saccade. There is no direct evidence that the decay in collicular activity causes the decay in motor error. Moreover, the methods used to obtain this correlation are problematic and other necessary lines of supporting evidence are missing.

Waitzman et al.[33] obtained a heavily filtered estimate of the decay in spike frequency of collicular cells with saccade-related activity by obtaining a spike density function that was the average of several trials. The spike density function was generated by substituting a Gaussian pulse of variable width for each action potential. The temporal waveform of this average spike density function was compared to the time course of dynamic motor error by shifting one of the waveforms to optimize the fit between the curves, rather than shifting the function by a fixed time. One concern with this analysis is based upon the fact that saccades are highly stereotyped and the bursts generated by neurons in different regions of the SC are quite similar.[19] Thus, the relationship between dynamic motor error and the decay in spike discharge

could be an epiphenomenon that emerges when two stereotyped decay functions are filtered and time-shifted to maximize the optimal fit. Large gaze shifts that involve coordinated movements of the eyes and head extends the time in which a relationship between frequency of cell discharge and motor error can be examined. The activity of cells in caudal SC of monkeys that discharge during combined eye/head gaze shifts is poorly correlated with dynamic motor error.[38] It should also be noted that Bozis and Moschovakis developed a model of the saccadic system that generated a monotonic relationship between motor error and the instantaneous discharge of collicular burst cells without placing the SC within a feedback loop.[39]

A second concern is that the analysis of Waitzman et al. ignores all members of the active population, except those in the center. Compared to the entire active population, only a few cells reside in the center of the active population and they may contribute very little to the total population output. Although surrounding cells may discharge less vigorously and with a different time course, because the number of cells is so large, their contribution to the population output may actually be greater than the contribution of the few cells in the middle. Because the activity of cells on the periphery of the active population contribute to the each movement,[27] what needs to be computed to test the Waitzman et al. hypothesis is the time course of the population output - not the time course of the activity of the cells in the middle of the population. The relationship between the total population output and dynamic motor error is unknown.

Also unknown is whether the subset of cells displaying the putative monotonic decay in spike discharge, rather than the cells that do not display this relationship, are those that project to downstream premotor circuits. Equally critical to the hypothesis is a demonstration that the necessary feedback signal actually reaches the putative collicular dynamic motor error cells. As Waitzman et al. point out, this requires an inverse temporal-to-spatial transform in which the inhibitory feedback from the resettable integrator is arranged topographically and weighted according to the termination point in SC.

Finally, in a number of recent experiments a variety of methods have been used to modify the time course of saccades while recording the activity of neurons in SC. Convincing evidence that the activity of SC neurons codes dynamic motor error by instantaneous firing rate has not been obtained in any of these experiments.[37,40,41]

12.3 RECENT FINDINGS

12.3.1 The Level and Duration of Collicular Activity

The traditional view that the direction and amplitude of a saccade are determined solely by the site of collicular activity and that the level or duration of collicular activity plays no role in saccade execution is not supported by the results of recent experiments. Stanford and colleagues[42] repeated the early microstimulation experiments but systematically varied the duration and frequency of the stimulation trains over a wider range than used in the early experiments. In contrast to the results of the earlier studies, they found that both the site of stimulation and the parameters of stimulation were important factors in determining the properties of stimulation-

induced eye movements. Discrepancies with earlier results are probably due to differences in the ranges over which stimulation parameters were varied. Consistent with early findings, the site of stimulation within the collicular motor map determines the largest movement that can be produced. But, for any stimulation site, movement amplitude depends upon the duration of the stimulation train. As train duration increases, movement amplitude increases monotonically until it reaches the site-specific limit. Within the range over which amplitude can be modulated, movement offset is tightly linked to the offset of the stimulation train. Truncation of the movement is detectable if collicular stimulation ends prematurely. This finding strongly suggests that collicular activity must be sustained throughout the execution of the movement if the amplitude specified by the site of collicular stimulation is to be achieved. Additionally, the peak velocity of an evoked movement is influenced by the frequency of stimulation; higher frequencies produce movements with higher velocities. This finding is consistent with the hypothesis that the peak velocity of a saccade is determined, at least in part, by the level of collicular activity. The effects of train duration and frequency can be traded to produce movements that have comparable amplitudes but different velocity profiles. Movements with high velocity and short duration can be produced by high-frequency, short duration stimulation trains. Stimulation with low frequency, long duration trains produces low-velocity movements of long duration. Thus, the parameters of collicular stimulation can be adjusted to provide independent control over saccade amplitude and saccade velocity.

The findings of Stanford and colleagues, summarized above, are remarkably similar to observations made in several nonprimate species.[43–46] Consequently, the older view that the functional organization of the primate SC is fundamentally different from the organization of the SC or optic tectum of other species is no longer warranted. Moreover, these findings require a revised view of the function of the primate SC — a view in which, in addition to the site of collicular activity, the duration and level of activity contributes to determining the amplitude, velocity and duration of saccadic eye movements. Ongoing collicular activity sustains the movement until the desired displacement is accomplished while the level of collicular activity influences movement velocity. Stanford and colleagues[42] concluded that at least three independent signals are derived from the spatial and temporal pattern of collicular activity — one specifying the desired displacement, another related to saccadic velocity, and a third involved in the initiation of a saccade.

Several other lines of evidence also challenge the notion of a purely topographic motor representation of saccades within the primate SC. Pharmacological inactivation of collicular regions by injection of lidocaine[27,47] or muscimol[48] causes dramatic decreases in the velocity of visually guided saccades without necessarily modifying the amplitude of the movement.[27] In a systematic study extending earlier microstimulation results, Van Opstal and colleagues reported movement amplitude to be an increasing, but saturating, function of current strength.[49] Assuming that variations in current strength influence the size and vigor of the active collicular population, they suggested that the computation of desired displacement does, in fact, depend on the level of collicular activity. They also noted that differences in the effects of inactivation and current strength might be reconciled by considering the possibility that the duration of collicular activity is important. In agreement with the inactivation

studies, Van Opstal and colleagues reported decreases in movement velocity with decreases in current strength and suggested that reductions in amplitude might reflect a failure to compensate for decreases in velocity with suitable increases in the duration of collicular activation.[49]

12.3.2 GAZE, NOT EYE OR HEAD, COMMANDS?
12.3.2.1 Microstimulation Experiments

How many command signals are generated by collicular neurons? Microstimulation of the optic tectum/superior colliculus in a number of nonprimate species produces coordinated movements of the eyes, head, pinnae, vibrissae, and body. But the results of early experiments in which coordinated movements of the eyes and head were not observed following microstimulation of the SC in monkeys[50] were interpreted as evidence that the monkey SC is not involved in the coordination of eye and head movements. This conclusion was reinforced by the failure to find single cell activity in the monkey SC related to head movements.[51] Thus, the primate SC was thought to be involved in the production of saccadic movements of the eyes but not in the implementation or coordination of combined eye-head movements that occur during large gaze shifts.

Freedman and colleagues stimulated the SC of rhesus monkeys with completely unrestrained heads while systematically varying the site and parameters of micro-stimulation.[52] In contrast to earlier primate experiments that failed to observe coordinated orienting movements of the eyes and head, they found that collicular stimulation produces high velocity, combined eye-head gaze shifts that are remarkably similar to naturally occurring visually guided gaze shifts of comparable amplitude and direction. The failure of earlier workers to obtain similar findings can be attributed to the restricted range of stimulation parameters and/or stimulation sites used in those studies.

The amplitude and velocity of stimulation-induced gaze shifts depends on the site of stimulation and on the parameters (frequency, current level, and duration of the stimulation train) of stimulation. Increases in the duration of the stimulation train systematically increases the amplitude of evoked gaze shifts until a site-specific maximal amplitude is reached. The frequency of stimulation affects the velocity of evoked gaze shifts; peak velocity increases when higher frequencies are used. The head contribution to stimulation-induced gaze shifts depends on the positions of the eyes in the orbit at the onset of stimulation. The head contribution increases and the latency to head movement onset decreases when the eyes are deviated in the direction of the ensuing gaze shift. The head contribution to stimulation-induced gaze shifts also depends upon the direction of the gaze shift, contributing less for gaze shifts with more vertical components.

Stimulation drives the eyes to approximately the same orbital position regardless of whether the head is restrained or unrestrained. Movements produced when the head is restrained are reduced in amplitude by approximately the amount that the head would have contributed if free to move. Consequently, when the head is restrained, there may be a dissociation between the *desired* gaze amplitude specified by the locus of collicular activity and the stimulation-induced movement that actually

occurs. Also, during head restrained stimulation, the observed movement may be only a portion of the movement encoded by the locus of collicular activity. Thus, the collicular *motor map* defined using microstimulation in head restrained subjects is grossly distorted.

Which neuronal signals are being activated by collicular stimulation? Stimulation of a particular site using constant stimulation parameters produces gaze shifts with relatively constant amplitudes and directions. This does not depend upon a particular eye movement always being coupled with a particular head movement. Rather, stimulation-induced gaze shifts of similar directions and amplitudes are accomplished with many combinations of eye and head components, depending on the initial positions of the eyes in the orbits and the direction of the gaze shift. The most parsimonious interpretation of this finding is that microstimulation is activating neurons generating a command for a change in gaze angle — signals that are separated into eye and head components below the level of the SC. It is more difficult to explain this pattern of results if one assumes that the combined eye-head movements produced by microstimulation result from activating one subset of cells generating an eye command and another subset of cells generating a command to move the head.

12.3.2.2 Recording Data

Freedman and Sparks also recorded the activity of single neurons in the intermediate and deep layers of the monkey SC during combined eye-head gaze shifts made to visual targets.[53] The cells were studied in conditions in which: (1) the amplitude and direction of gaze movements was relatively constant, but the eye and head components varied over a wide range; and (2) either the eye or head contribution was fixed but the direction and amplitude of gaze changed over a large range. Thus, the activity of collicular neurons was studied under conditions in which gaze and the eye and head contributions to gaze were dissociable.

For all of the cells in their sample for which these analyses could be performed, motor-related activity was best correlated with the amplitude and direction of the gaze shift, and only weakly correlated with eye or head components of gaze. Gaze shifts having similar amplitudes and directions were associated with similar motor-related bursts. They conclude that cells in the superior colliculus generate commands related to the displacement of the line of sight, and that this activity is not directly related to the individual components of the orienting gaze shifts.[53] These findings provide further support for the hypothesis that a desired gaze displacement signal is derived from the locus of collicular activity, and is decomposed into separate eye and head signals downstream from the SC.

12.4 IMPLICATIONS OF RECENT FINDINGS

12.4.1 Population Coding

Previous studies of population coding of motor commands in SC have examined animals with their heads restrained (for example, see References 26 and 27). As a

consequence, little is known about how large populations of broadly tuned SC neurons encode precise gaze shifts and population coding of motor commands in SC needs to be re-examined under more natural, head unrestrained conditions.

If the activity of collicular neurons specifies a change in the direction of gaze rather than a change in eye position, then population coding schemes must be modified to account for coordinated movements of the eyes and head. Currently, no published studies have determined whether or not the vector averaging scheme of Sparks and colleagues[20] can be extended to the more natural, head-unrestrained condition. A simple extension of the vector averaging hypothesis to coordinated eyehead movements predicts that local inactivation of collicular neurons should cause the SC to output an erroneous signal for desired gaze displacement (except when the area affected by the injection coincides with the center of the activated region of SC) that would also affect the velocity of the gaze shift. Other than the velocity effect, the injection should have no direct effect upon ability of the animal to execute eye or head movements of any direction or amplitude. Thus, the relative contributions of the eyes and head to these erroneous gaze shifts should match the ratio observed for similar (but normometric), naturally occurring gaze shifts. As mentioned above, the starting position of the eyes influences this ratio. Systematically manipulating initial orbital position would make it possible to test the population coding hypothesis over a wide range of behavioral conditions.

12.4.2 STTP AND FEEDBACK
12.4.2.1 Gaze Direction

In retrospect, one of the reasons the STTP has been so intractable is that the question is ill-posed. For the primate, the original statement of the problem is based upon erroneous conclusions about both *which* signals are represented in the SC and *how* the signals are represented. New findings indicate that the location of collicular activity encodes a signal of desired gaze displacement rather than a signal of desired eye displacement. While the site of activity in the SC sets the limit on the maximal gaze shift that will occur, the time course and level of activity are also important. Collicular activity must be sustained for a movement to continue and the level of activity is a determinant of the speed of a movement.

This new perspective has important consequences for experimental attempts to solve the STTP. For example, more experiments are needed to provide additional detail about how projections from different regions of the collicular map differ in terms of the ratio of synaptic drive to neurons controlling the horizontal and vertical movements of the eyes. But parallel experiments must also examine the ratio of synaptic drive to neurons involved in the control of head movements.[54] In this context, a recent study of the patterns of neck muscle activity following SC stimulation in head-restrained monkeys[55] provides insights into how the locus of collicular activity could specify which neck muscles are activated and influence the temporal pattern of neck muscle activity. Corneil and colleagues found that the drive to neck muscle motoneurons is widely distributed throughout almost the entire SC and that there is a clear topography to the stimulation-evoked neck muscle EMG responses.

EMG activation became faster, stronger, and more prevalent for more caudal stim ulation locations.[55]

12.4.2.2 Initial Eye Position

Gaze shifts of the same direction and amplitude are accomplished by many different combinations of eye and head contributions, depending upon the initial positions of the eyes in the orbits and the direction of the gaze shift.[56] Even when the head is immobilized, the tonic component of the activity of several dorsal neck muscles is highly correlated with the horizontal position of the eyes during spontaneous eye movements and during vestibular nystagmus.[57–59] The relationship between neck muscle activity and horizontal eye position is nonlinear. Very little, if any, neck muscle activity is observed until the eye reaches a threshold position in the orbit. Then, neck muscle activity increases linearly as a function of eye position until the recruitment of additional motor units makes it difficult to isolate individual units. The relationship between tonic levels of neck muscle activity and eye position is greater when the head is fixed. When the head is free, neck muscle activity is usually related to head position, but muscle activity is phasically modulated during saccadic eye movements and head accelerations. In head restrained animals, neck EMG responses evoked by collicular stimulation are systematically influenced by the positions of the eyes in the orbits at the onset of the stimulation train.[55]

12.4.2.3 Gaze Amplitude

Most models of the coordinated eye-head movements occurring during large gaze shifts assume that gaze direction and amplitude are under feedback control. Results of experiments in which head movements were perturbed by the application of an external force during a large gaze shift have been interpreted as evidence that gaze is controlled by feedback mechanisms. In a variety of conditions[60–65] gaze amplitude is unaffected by perturbations in head trajectory. However, one model[66] of the gaze system compensates for mechanical perturbations of the head without using dynamic feedback control of gaze amplitude.

The microstimulation experiments summarized above[42,43,45,52] demonstrate that collicular activity must be sustained for a movement to continue (see previous discussion). Accordingly, one possible way of controlling the duration (and indirectly, the amplitude) of a gaze shift is to control the duration of collicular activity. For large gaze shifts, the cessation of the movement-related activity of collicular neurons is highly correlated with the end of a gaze shift[53] (because the end of the gaze shift and the end of the eye movement are coupled tightly, the end of the motor burst also is highly correlated with the end of the eye movement). The observation that this correlation does not depend on the amplitude and direction of movements relative to the movement field center suggests that there is a general cessation of motor activity over large regions of the collicular motor map associated with the end of the gaze shift. These findings seem consistent with models[60,67,68] in which gaze, rather than eye or head, displacement is under feedback control and the SC is located within the feedback loop. However, a causal relationship between the ces-

sation of collicular activity and the end of a gaze shift has not been established and other experimental findings are difficult to explain using such a model.

If the eye and head components of large gaze shifts are under feedback control and if neurons in SC are located inside the feedback loop, then electrical stimulation of output fibers will produce a nonzero output signifying a mismatch between actual gaze displacement and the desired gaze displacement. Gaze position should continue to change for as long as the stimulation train continues to activate the output neurons or until the displacement of the eyes and/or head reaches a physiological limit. This is what occurs for eye movements with stimulation of the MNs or PPRF (unpublished observations), but not what happens with stimulation of SC. One possible explanation for the failure to see continued changes in gaze position with sustained collicular stimulation is that the stimulation becomes ineffective, through fatigue or otherwise. However, over the range of stimulation train durations that have been studied, the head continues to move as long as the stimulation train continues, even though gaze stops when it reaches the site specific limit and the eyes begin to counter-rotate at that time to compensate for the continued movement of the head.

If the comparator resides downstream from the SC, then collicular stimulation produces a signal that specifies a particular desired displacement, depending upon which site in the motor map is activated. This signal serves as a reference signal to the downstream comparator and when the actual displacement matches the desired displacement, the movement stops, even if the stimulation train continues. This is what appears to happen when collicular neurons are stimulated with long trains.

12.5 SUMMARY

Despite much progress in understanding the role of the SC in the control of orienting movements of the eyes and head, much remains to be learned. Important issues have not been resolved. Is gaze under feedback control? If so, how and where are signals of the eye and head components of the gaze shift combined? Where are signals of desired and actual gaze displacement compared? How is the result of this comparison used to control the direction and amplitude of eye and head movements? How and where is the desired gaze displacement command observed at the level of SC decomposed into signals appropriate to control the eye and head components? Is the head component of the gaze shift under feedback control? What is the status of the VOR during large gaze shifts? Is the VOR equally active during the entire gaze shift? When does the reduction in VOR gain end? How are reductions in VOR gain implemented? These and other questions about the neural control of coordinated eye and head movements bring a different perspective to studies of the role of the SC in the control of gaze.

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