Tonic Activity during Visuo-oculomotor Behavior in the Monkey Superior Colliculus

Jun Kojima

Department of Physiological Sciences, School of Life Sciences,
Graduate University for Advanced Studies

Laboratory of Neural Control, National Institute for
Physiological Sciences

Tonic Activity during Visuo-oculomotor Behavior in the Monkey Superior Colliculus

SUMMARY

1. The superior colliculus plays a key role in the sensory-motor conversion of orienting behavior (Schneider 1969, Ingle 1973). However, it is unclear that whether the superior colliculus is involved in intermediary cognitive processes such as attention, memory, and movement preparation. To answer this question, we recorded single cell activities in the superior colliculus of monkeys trained to perform a series of visuo-oculomotor tasks.
2. In an overlap saccade task (SACO), a peripheral target light appeared while the monkey was fixating on the central fixation spot. When the central fixation spot went off, the monkey was required to make a saccade to the visible peripheral target. In a delayed saccade task (SACD), the monkey was required to make a saccade to remembered position of peripheral light spot (target cue) which was cued during fixation. In an attention task (ATT) the monkey was required to respond, without making an eye movement, to the dimming of the spot by releasing a lever.
3. We recorded 141 neurons showing tonic activities related to the tasks. Neurons without saccadic activity (n=33) were considered to be in the superficial layer, while neurons with saccadic activity (n=108) were considered to be in the intermediate layer. This assumption was later supported histologically.
4. Depending on the predominance of the activities among the three tasks (SACO, SACD, and ATT), we classified the tonic neurons into four types: (1) visuomotor (activity was significantly greater in SACO), (2) mnemonic motor (SACD dominant), (3) visual attention (ATT dominant), and (4) nonspecific.

   These tonic activities had a preferential retinotopic field, which

was similar to the visual receptive field and movement field of the same neurons and of neighboring neurons.

5. In the intermediate layer a fair number of neurons were found to be selective for the tasks: visual attention (n=13), visuomotor (n=13), and mnemonic motor (n=15). The other 67 neurons were of non-specific type. Specific types were less common in the superficial layer: visual attention (n=3), visuomotor (n=4). Mnemonic motor type was not found. The other 26 neurons were of non-specific.
6. In conclusion, the tonic activities in the superior colliculus involve information of memory of the target location, the preparation of saccade and the peripheral attention. These signals may be sent to the phasic responsive neurons in the superior colliculus and/or the brainstem saccade generators, and modulate saccadic eye movement. Furthermore, they may be sent to the thalamic neurons, to which the neurons in the intermediate layer project. The superior colliculus might participate in the processes in which memory-, preparation-, and attention-related signals are maintained.

CONTENTS

- INTRODUCTION
  - I. Two visual systems
    - (1) geniculo-striate system
    - (2) retino-tectal system
  - II. Superior Colliculus
    - (1) Anatomy of the superior colliculus
    - (2) Functional roles of the superior colliculus
      - (a) The superficial layer
      - (b) The intermediate and deep layers
    - (3) Tonic neurons
  - III. Purpose of this study
- METHODS
  - I. Surgery
  - II. Behavioral paradigms
  - III. Experimental procedures
  - IV. Histology
  - V. Data analysis
- RESULTS
  - I. Difference between superficial and intermediate layers
  - II. Classification of the tonic neurons in the superior colliculus
    - (1) Visuomotor type
    - (2) Visual attention type
    - (3) Mnemonic motor type
    - (4) Nonspecific type
  - III. Directional selectivity
  - IV. Histological data
- DISCUSSION
- CONCLUSION
- REFERENCES
- ACKNOWLEDGEMENTS

INTRODUCTION

The superior colliculus is unique in its dual role in sensory and motor functions. It receives visual inputs directly from the retina (Hendrickson et al 1970, Wilson and Toyne 1970) and indirectly from the visual cortical areas (Kuypers and Lawrence 1967, Kadoya et al. 1971) and at the same time sends oculomotor output to the brainstem saccade generators (Harting et al 1980). It is thus thought that the superior colliculus plays a key role in sensory-motor conversion, as seen in orienting response (Schneider 1969, Ingle 1973). However, a motor action is not always an immediate consequence of sensory inputs; it can be selected, remembered, and prepared (Andersen et al 1987, Goldman-Rakic 1987, Hikosaka et al 1989c, Goldberg and Bruce 1990). The objective of the present research was to examine whether the superior colliculus is involved in such intermediary cognitive processes.

I will firstly present a historical background and current concepts on the function of the superior colliculus, which will make clear the purpose of our study.

1. Two visual systems

Based on lesion studies, Schneider (1969) proposed a two visual system hypothesis: the geniculo-striate system participates in the identification of the visual stimulus, while the retino-tectal system is involved in the detection and localization of events in visual space.

(1) Geniculo-striate system

Visual information originating in the retina is, partially, sent to the striate cortex through the lateral geniculate nucleus (indicated by the dotted arrow lines in Figure 1A). It is well known that patients with lesions in the striate cortex become blind (Pöppel 1977). After a focal lesion of the striate cortex, the monkey cannot identify the shape and pattern of a visual stimulus only when it is presented in the corresponding visual receptive field (Mohler and Wurtz 1977).

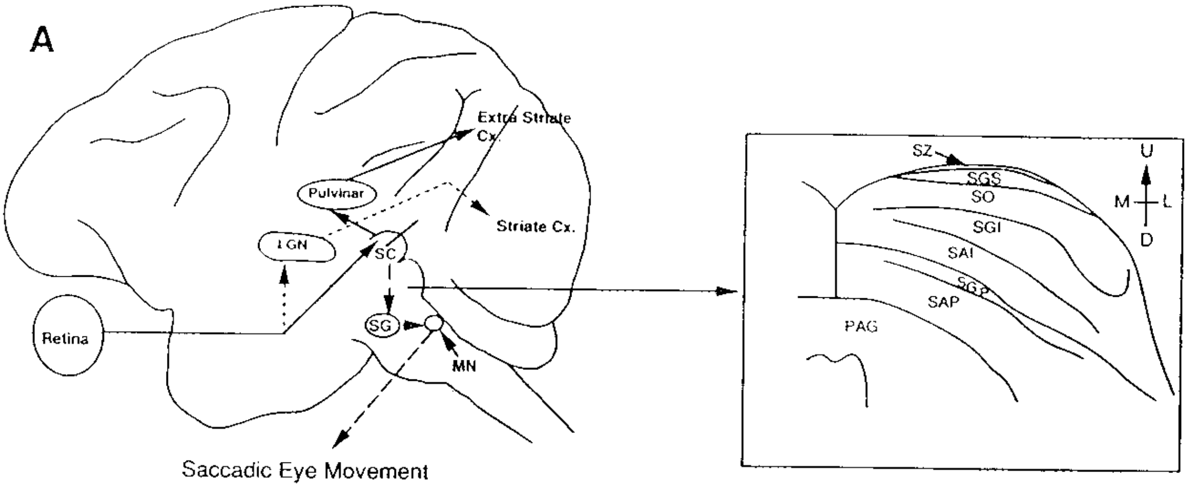


Figure 1. Anatomy of the monkey superior colliculus.
A: Schematic location of the superior colliculus and signal flows of the two visual systems. Abbreviations: SC, the superior colliculus; LGN, lateral geniculate nucleus; SG, saccade generator; MN, oculomotor motoneuron. Solid arrow line, the retino-tectal pathway; dotted arrow line, the geniculo-striate pathway; dashed arrow line, a signal flow of saccadic eye movement. Solid line stuck into SC indicates the cutting plane which is shown in B.
B: Line drawing of the section of the right superior colliculus (based on Kanaseki and Sprague 1974). Abbreviations: SZ, stratum zonale (zonal layer); SGS, stratum griceum superficiale (superficial gray layer); SO, stratum opticum (optic layer); SGI, stratum griceum intermedium (intermediate gray layer); SAI, stratum album intermedium (intermediate white layer); SGP, stratum griceum profundum (deep gray layer); SAP, stratum alubum profundum (deep white layer); PAG, periaqueductal gray matter.

Interestingly, however, the cortically blind patients and animals could orient their eyes or head to a salient visual object (Pöppel et al 1973, Singer et al 1977). The human patients can do so even though they are unable to tell the identity of the object (Pöppel et al 1973). This residual ability, blindsight, is generally attributed to the function of the superior colliculus (a homologue of the optic tectum in the lower mammals and vertebrates) and related visual areas (Pöppel 1977).

(2) Retino-tectal system

The above idea is supported by the anatomical connection involving the superior colliculus (solid arrow lines in Figure 1A). The information in the superior colliculus is transmitted down to the brainstem reticular formation where generators for saccadic eye movement are located (dashed lines of Figure 1A) (Hepp et al 1989). Deficits in visual perception are also noted by lesions of the superior colliculus. For example, perception of luminance contrast was impaired in a patient suffering from congenital malformation of the superior colliculus (Zihl and Cramon 1979). The ablation of the superior colliculus of the monkey produced neglect for the contralateral half of the visual field (Denny-Brown 1962, Wurtz and Goldberg 1972b). Thus, the retino-tectal system would be directly involved in the detection and localization of events in visual space. The projection from the superior colliculus to the extrageniculate cortex through the pulvinar (solid arrow lines of Figure 1A) may underlie this aspect of visual function.

II. The superior colliculus

(1) Anatomy of the superior colliculus

The superior colliculus is located in the midbrain, in its dorsal part (Figure 1A). It consists of seven layers (Figure 1B) which are determined by cyto- and myeloarchitectural examination (Kanaseki and Sprague 1974). These layers are usually grouped into three functional layers: (a) superficial layer (SZ, SGS, SO), (b) intermediate layer (SGI, SAI), and (c) deep layer (SGP, SAP).

(2) Functional roles of the superior colliculus

(a) Superficial layer

In the primate superior colliculus, neurons in the superficial layer respond almost exclusively to visual stimulus. Each neuron responds to a visual stimulus in a restricted area (visual receptive field) in the hemifield contralateral to the side of the neuron. It responds to onset and/or offset of a visual stimulus. The response is usually phasic, with a latency of 40-80 msec. The visual neurons are differentially sensitive to a stimulus size, but not to stimulus shape, orientation, wavelength (Cynader and Berman 1972). They respond to a moving visual stimulus as well, but they usually lack a direction selectivity.

A notable feature in these visual neurons is their dependence on saccadic eye movement. This historical discovery was made by Goldberg and Wurtz (1972) who used alert, trained monkeys. Some of the visual neurons showed enhancement of a visual response when the monkey made a saccade to the stimulus. When the monkey fixated on a central fixation point and a stimulus came on in the neuron's receptive field (fixation task), the neuron showed a weak irregular response. In contrast, when the monkey was required to make a saccade to the same visual stimulus after the fixation point went off, the neuron showed a clearer and more consistent response. There was no response to the saccadic eye movement

This phenomenon, called 'saccadic enhancement', was thought to reflect 'selective attention' which would precede the initiation of a saccade (Goldberg and Wurtz, 1972). In later studies, however, the same authors concluded that the enhancement is specific to the initiation of saccadic eye movement, because selective attention without eye movement (similar to one of our tasks 'ATT') was not associated with an enhancement (Wurtz and Mohler 1976a).

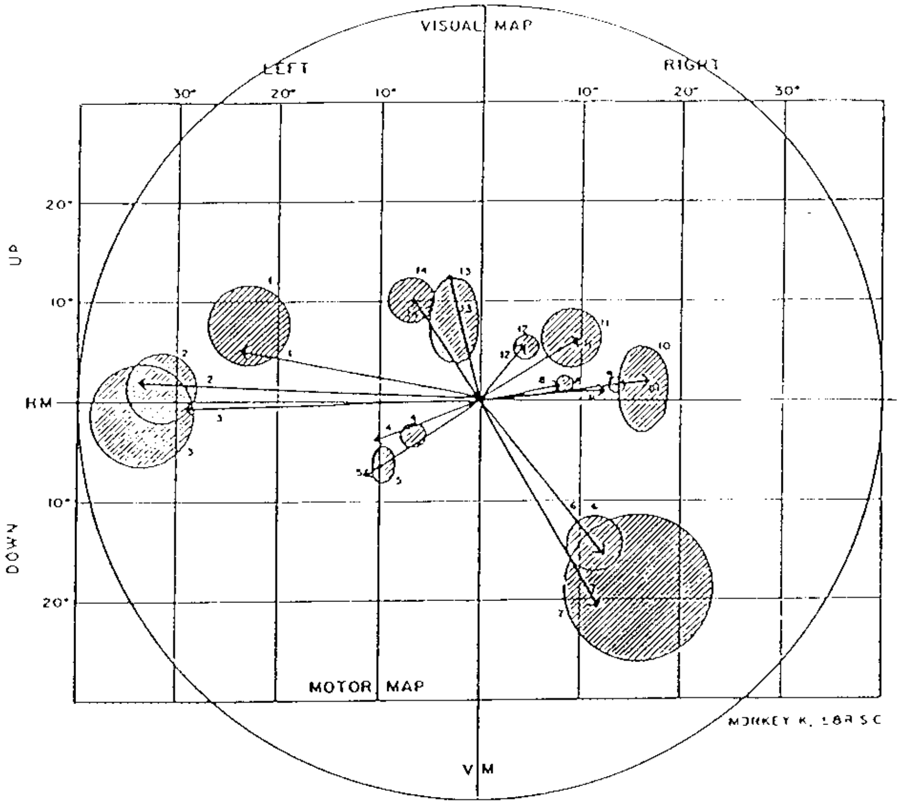


Figure 2. Neural activity and stimulation effects in the superficial layer of the monkey superior colliculus. Hatched circles indicate the visual receptive fields of 14 units. Arrows from the center indicate the direction and amplitude of saccades elicited by electrical stimulation at each of the 14 sites. Abbreviations: HM, horizontal meridian; VM, vertical meridian. (Schiller and Stryker, 1972)

The relationship of the visual responses in the superficial layer and saccadic eye movement was more directly shown by Schiller and Stryker (1972) (Figure 2). It had been known that chemical or electrical stimulation of the superior colliculus induced contraversive saccadic eye movements (see also Figure 3). Schiller and Stryker examined the superior colliculus of an alert monkey by using single-unit recording and electrical stimulation. They compared the location of single cell's visual receptive field and the vector (amplitude and direction) of a saccade evoked by the electrical stimulation. At every site in the superficial layer there was striking correspondence between the receptive field position and the saccade vector which was presented in the intermediate and deep layers.

Summary of the superficial layer: (1) the neurons respond phasically to the visual stimulus, (2) visual receptive fields are restricted in the contralateral hemifield, and (3) retinotopic organization in the superficial layer is corresponded to the organization of the saccade vector in the intermediate and deep layers.

(b) Intermediate and deep layers

The relationship to eye movement becomes clearer in the intermediate and deep layers, as demonstrated by Robinson (1972) in the first systematic stimulation study using alert monkeys (Figure 3). Eye positions were measured by the search coil method which he developed and is now widely used. A train of electric pulses was necessary to elicit a saccade. He found that the threshold current for evoking a saccade was much lower in the intermediate and deep layers than in the superficial layer.

Another important feature was the retinotopic arrangement of the evoked saccades. In Figure 3A, the direction and amplitude of evoked saccades are indicated by arrows, their locations indicating the sites of stimulation in the left superior colliculus. The results are summarized in Figure 3B. Stimulation at the medial sites produced upward saccades, while lateral stimulation produced downward saccades. Large saccades were evoked from more caudal site, while smaller saccades from more rostral sites. The evoked saccades were all-or-none in nature and their amplitude and direction depended solely on where the superior colliculus was stimulated and not how it was stimulated. The Robinson's study suggested that both the intermediate and deep layers are closely related to saccadic eye movements.

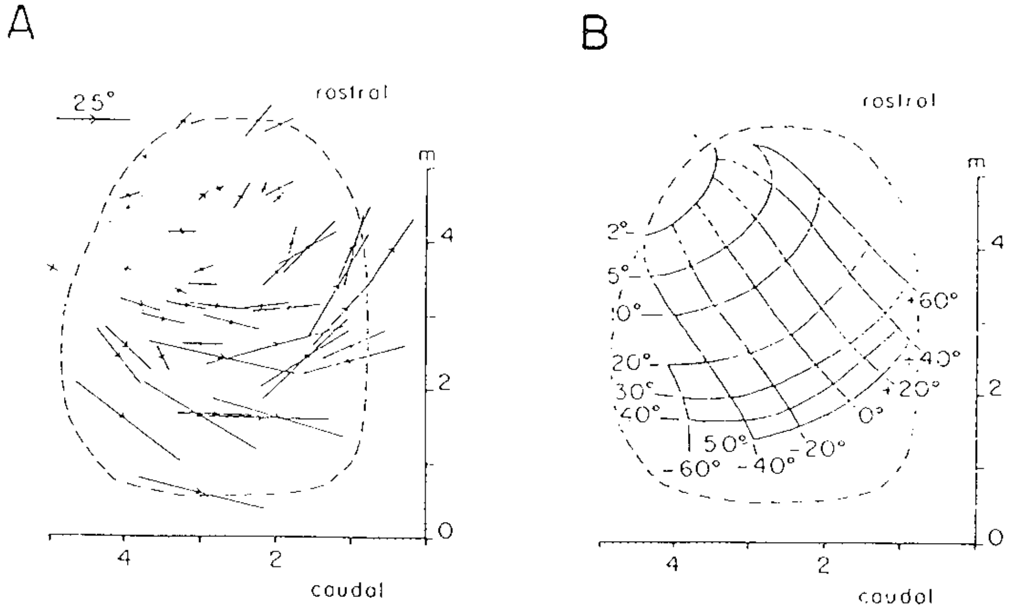


Figure 3. Maps of saccade direction and amplitude on a dorsal view of the left superior colliculus of the monkey.
A: A composite of the saccades evoked by microstimulation. Each arrow indicates the direction and amplitude of the saccade evoked at the corresponding site. Dotted line is the reconstructed boundary of the superior colliculus.
B: Smoothed contours of equal amplitudes (from 2 ° to 50 °) and directions (from -60 ° to +60 °) of saccades forming a motor map on the superior colliculus. Scale is in mm; m indicates the midline.
(Robinson, 1972)

The oculomotor, rather than visual, function of these deeper layers is also indicated by spike activity of single neurons. They show a characteristic burst of spikes before a saccade (Goldberg and Wurtz 1972, Sparks and Mays 1980, Sparks and Jays 1986) (Figure 4). For each trial, the monkey made a saccade from a central fixation point to a peripheral target presented at a random location. This neuron (in the left superior colliculus) showed a vigorous burst of activity before a saccade only when the saccade was made to a restricted region in the lower-right quadrant. Within the responsive region (now commonly called 'movement field'), the responses decreased as the saccades were deviated away from its center.

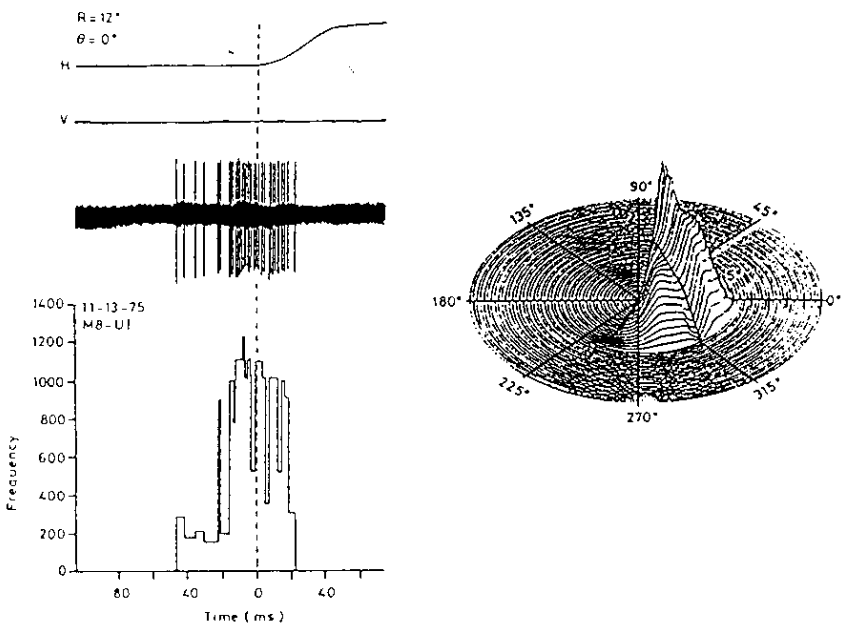


Figure 4. Saccade related burst neuron in the intermediate layer of the monkey superior colliculus.
Left: Discharge pattern recorded from a typical saccade-related neurons. Top: H, horizontal eye position; V, vertical eye position. Middle: Tracing of the spike discharge. Bottom: Instantaneous spike frequency.
Right: Three-dimensional representation of the number of spikes as a function of the direction and amplitude of saccades. The center of movement field of the neuron was 1° amplitude at a direction 40° downward. (Sparks and Jay, 1986)

In general, neurons responsive to small saccades have small and sharply tuned fields, while those responsive to large saccades have less tuned movement field. Neurons discharging prior to small saccades were located rostrally, while neurons discharging prior to large saccades were located caudally. This result corresponded to the oculomotor map obtained by the stimulation studies (see Figure 3).

Many of the presaccadic burst neurons show a visual response as well. In some neurons termed 'visuomotor neurons' (Wurtz and Goldberg, 1972a, Mays and Sparks 1980), the saccadic activity is dependent on the presence of a visual target; they show no activity when the saccade is made spontaneously without a visual target.

Figure 5 shows the activity of a typical visuomotor cell (Wurtz and Goldberg 1972a). The monkey first fixated on the fixation point (FP), and when one of the targets (1-5) appeared he made a saccade to it. When a saccade occurred in response to the visual stimulus, both phasic visual and saccade responses were observed (1A, 2A). The neuron also responded phasically when a spot of light came on in its receptive field even though no eye movement occurred (1B, 2B). The movement field (solid line) roughly matched the visual receptive field (dashed line), though the movement field was usually larger than the visual receptive field.

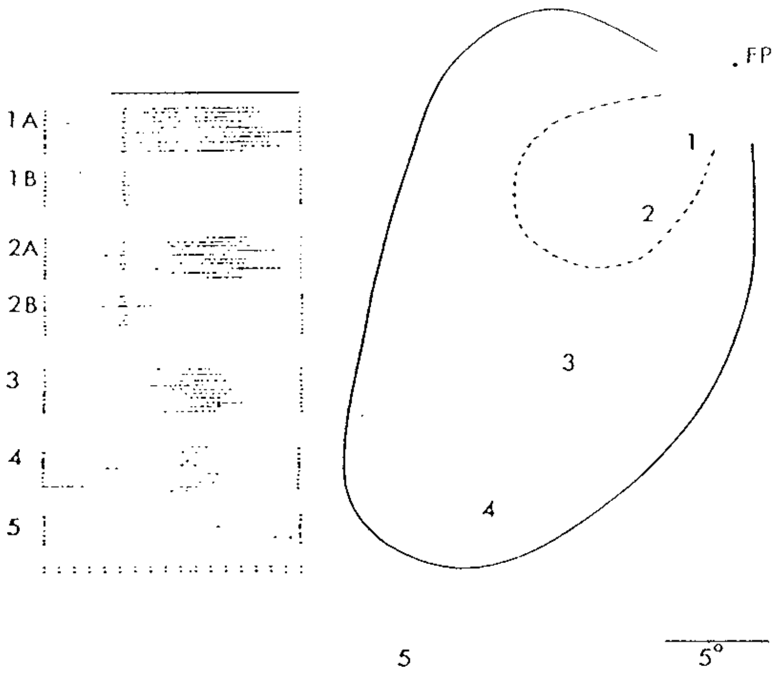


Figure 5. A visuomotor neuron in the intermediate layer. The monkey fixated on a fixation point (FP). When the fixation point went off and another target spot appeared, the monkey was required to make a saccade to the target.
Right: Each number (1-5) indicate the position of the target. Solid line shows the movement field of the neuron; dashed line the visual receptive field.
Left: Responses at target point 1-5 are shown as the same number of the raster display. The cell discharge is shown when the monkey made a saccade to the spot of light (1A, 2A), and when the monkey did not make a saccade to it (1B, 2B). Solid line on the raster indicates duration of the target on. Time interval between successive dots at the bottom of the raster display is 50 msec. (Wurtz and Goldberg, 1972)

Summary of the intermediate and deep layers: (1) electrical stimulation produces saccadic eye movement and the evoked saccades are retinotopically arranged, (2) the neurons respond phasically to the saccadic eye movement and have movement field, and (3) some neurons in the intermediate layer also respond to visual stimuli.

(3) Tonic neurons

All of the above neurons in the superior colliculus show phasic responses which are either sensory (visual) or motor (saccadic). In order to orient to an object, the sensory signals must be converted into the motor signal. It is expected therefore that there are some activities bridging the two. A candidate for such intermediary activity has been described by Mays and Sparks (1980). Using a double saccade task (following described) they found neurons showing sustained response to stimuli (tonic activity) which they called "quasi-visual cell".

Figure 6 shows the schematic representation of visual, quasi-visual, and saccade related cell activity on a double-saccade task. The monkey was required to make double saccades, first from the center to a peripheral target, and then back to the center. When the monkey fixated on the central target (O), another peripheral target (B) appeared briefly (100 msec) on the right side at 20°. As soon as the central fixation point disappeared, the monkey was required to make a first saccade to the target B, and to make a second saccade to the center O. Note that either B or O was no longer present when the saccade occurred; the second saccade, especially, was guided by the memory of the central fixation point.

On the right side of Figure 6 are summarized the types and locations of neurons which would become active in this task. The appearance of target B would elicit a visual response in a group of superficial layer cells on the left side of the superior colliculus (site 1). Neurons in the intermediate layer just beneath the active visual neurons (site 4) would then show a burst of spikes, which produces a saccade to target B.

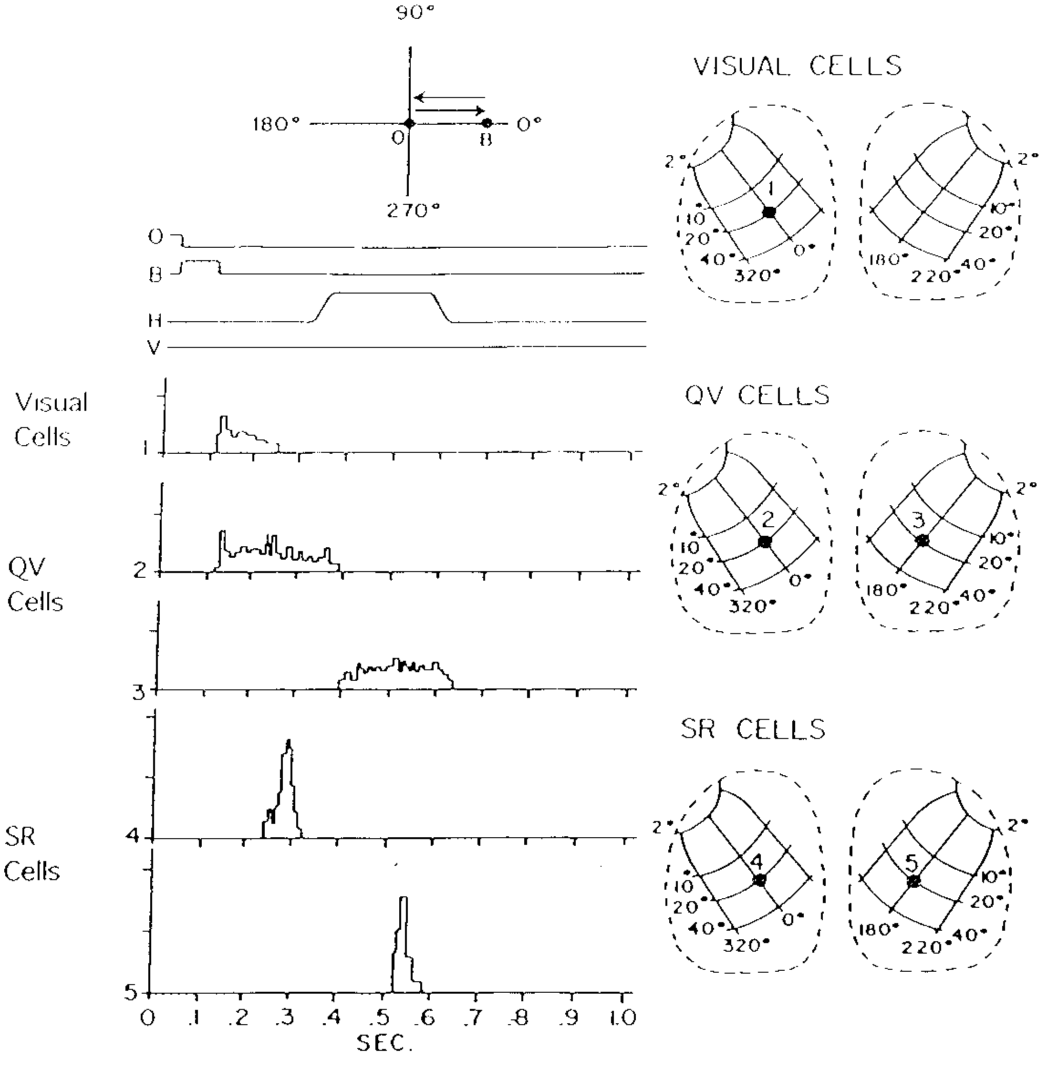


Figure 6. Schematic representation of visual, Quasi-visual (QV) and saccade-related (SR) cell activity during a double saccade task.

Schematic dorsal view of the superior colliculus was shown on the right side: each number on the filled circle shows the location of neuron. The neuron activity in each number was represented by the same number on the left side of traces of instantaneous spike frequency.

On the left side, Top: scheme of the task and the target location (for details, see Introduction); Middle: durations of fixation point (O) and target point (B), horizontal eye position (H) and vertical eye position (V). Bottom: Cell activity is shown as trace of instantaneous spike frequency.

During the fixation period (O), another target (B) appeared briefly. A visual cell responded phasically to the target (trace1, site1) and QV cell responded tonically before saccade to the target (trace2, site2). When the monkey made a saccade to the target, a SR cell responded phasically to the saccade (trace4, site4). After the saccade to the target, the monkey was required to return his gaze back to the center (O). A QV cell on the opposite side (trace3, site3) responded tonically between the fixation of the target (B) and the saccade to the center (O), both of which were now invisible. Another SR cell responded phasically to the saccade to the center. (Mays and Sparks, 1980)

Quasi-visual cells were found in the neighborhood of the saccadic burst cells. They showed a sustained discharge which ended with the saccade without a burst (site 2). A unique feature of the quasi-visual cells was revealed during the period before the second saccade to the center. At the symmetric position in the superior colliculus (site 3) the quasi-visual cells started discharging immediately after the eye reached the target B and the spike activity continued until the recentering saccade. Thus, the quasi-visual cells discharged before saccades in the absence of appropriate visual stimulation.

On the left side of the superior colliculus, neural activity appears to be started off by a visual response in the superficial layer and relayed by quasi-visual cells to the presaccadic cells. On the right side, there is no visual response preceding the sustained activity in the quasi-visual cells.

III. Purpose of this study

The presence of quasi-visual cells suggests that neural activity in the superior colliculus could be initiated by non-visual signals and can be maintained for future eye movement. But the detailed nature of the tonic activity is still unknown. Is it related to memory of target location? Is it related to preparation of eye movement? Or is it related to attention to the target? These are the questions fundamentally important for the mechanism underlying the initiation of voluntary movement in general.

In order to differentiate between the above three possibilities we trained the monkeys to perform the following visuooculomotor tasks (Their details and additional tasks will be explained in Methods and Figure 7) and recorded single cell activities in the superior colliculus.

(1) Delayed saccade task: The monkey was required to make a saccade to a remembered position of a peripheral target light which had been cued a

few second before (Hikosaka and Wurtz 1983a, Matsumura et al. 1992). If a neuron is related to short term memory, it should respond tonically between the presentation of the target cue and the saccade onset (Hikosaka and Wurtz 1983a, Hikosaka et al 1989).

(2) Saccade task with overlap target: Unlike in the delayed saccade task, a peripheral target light remained on, and the monkey was required to make a saccade to the visible target a few seconds later. If a neuron is related to the preparation of saccade, it should show sustained activity between the target onset and the saccade onset (Hikosaka and Wurtz 1983a, Hikosaka et al. 1989b).

(3) Attention task: The monkey was required, while keeping his gaze on the central fixation point, to respond to the dimming of a peripheral target light by releasing a lever(Wurtz and Mohler 1976a, Robinson et al. 1978). If a neuron is related to attention, it should respond tonically between the target onset and its dimming (Petersen et al. 1985).

METHODS

We studied single-cell activities in the superior colliculus of three Macaca fuscata monkeys (Body weight 6.5 kg, 6.5 kg and 8.0 kg). The monkeys were kept in separate primate cages (1mX1mX1m) in an air-conditioned room. At each experimental session, they were brought to the experiment room. The monkeys were given restricted fluid before recording or training. Their health conditions, such as body weight and appetite, were checked daily. Supplementary water and food were provided daily.

1. Surgery

Monkeys were anesthetized with a pentobarbital sodium while the following surgical procedures were performed with aseptic techniques in an operation room. Twenty acrylic screws were implanted on the skull. These screws were fixed with acrylic resin and acted as anchors for a derlin head holder which was used to restrain the head during the experiment. A derlin chamber for microelectrode recording was also fixed to the skull with acrylic resin. The chamber was tilted back 45° from vertical in the midsaggital plane so that the electrode tracks passed through the superior colliculus approximately perpendicular to its rostral-caudal orientation.

Eye positions were monitored by the screral search coil technique (Robinson 1963). Search coil of teflon-coated stainless-steel wire was implanted monocularly under the conjunctiva using a method by Matsumura et al. (1992). The animals received an antibiotic (sodium ampicillin 25 mg/kg intramuscularly each day) after the operation.

II. Behavioral paradigm

Before unit recordings, the monkeys were trained to perform five visuo-oculomotor tasks (Figure 7). The monkey sat on a primate chair with his head fixed in a dimly lit and sound attenuated room. When the monkey pressed a lever on the chair, the center fixation point came on in front of the tangent screen (57cm from his face). In the eye movement tasks, he had to make a saccade to the target spot after the center fixation point off. In the no-eye movement tasks he had to keep fixating the central fixation point. After a random period of time (1.5-2.5 sec) the light spot (target or fixation point) dimmed. If monkey released the lever within a short period of dimming time (0.5-1.0 sec), he was rewarded with a drop of water. The center fixation point and the target point were backprojected spots of light by projectors which use light-emitting diode (LED). The spots had a diameter of 3 mm. The location of the fixation and target point were controlled by an X-Y galvanometer mirror system under the control of a microcomputer.

We used two types of eye movement tasks, (1) the delayed saccade task (SACD) and (2) the saccade task with overlap target (SACO), and three types of no-eye movement tasks: (3) the attention task (ATT), (4) the fixation task with stimulus (FXS) and (5) the fixation task with long stimulus (FXS_LG).

(1) Delayed saccade task (SACD)

This task was designed to elicit a memory guided saccade. When the monkey was fixating on the center fixation point, another spot (target cue) came on briefly (50 ms), indicating the location of a future target point. The monkey was not allowed to look to the cue stimulus and was required to keep fixating for 2-3 sec until the fixation point went off. When the center fixation point went off, the monkey was allowed to make a saccade to the remembered location of the cue stimulus. The target came on 600 ms later, and the monkey was required, to obtain reward, to release the lever immediately after the target dimmed (Hikosaka and Wurtz 1983a, Matsumura et al. 1992).

(2) Saccade task with overlap target (SACO)

While the monkey was fixating the central fixation point, a target spot appeared, but unlike in SACD, it stayed on. The monkey had to keep fixating while the fixation point was present. Only after the fixation point went off, he was allowed to make a saccade to the visible target point. The rest was the same as SACD: reward was given if the monkey released the lever in response to the dimming of the target (Hikosaka and Wurtz 1983a, Hikosaka et al. 1989a).

(3) Attention task (ATT)

The initial stimulus condition was the same as in SACO. The fixation point, however, remained on until the end of the trial, and thus the monkey was not allowed to make a saccade to the target. The monkey's task was to detect the dimming of the peripheral target spot, not the fixation pint, by releasing the lever (Wurtz and Mohler 1976a, Robinson et al. 1978).

We used two additional tasks for control.

(4) Fixation task with stimulus (FXS)

The initial stimulus condition was the same as the SACD. But the fixation point remained on until it became dim, to which the monkey had to respond. The monkey was thus encouraged neither to remember the target position (unlike in SACD) nor to pay attention to the target (unlike in ATT).

(5) Fixation task with long stimulus (FXS_LG)

The initial stimulus condition was the same as SACO and ATT. The fixation point remained on (unlike in SACO) and became dim (unlike in

ATT). The monkey was thus encouraged not to pay attention to the target (unlike in ATT) and was not required to prepare for a saccade (unlike in SACO).

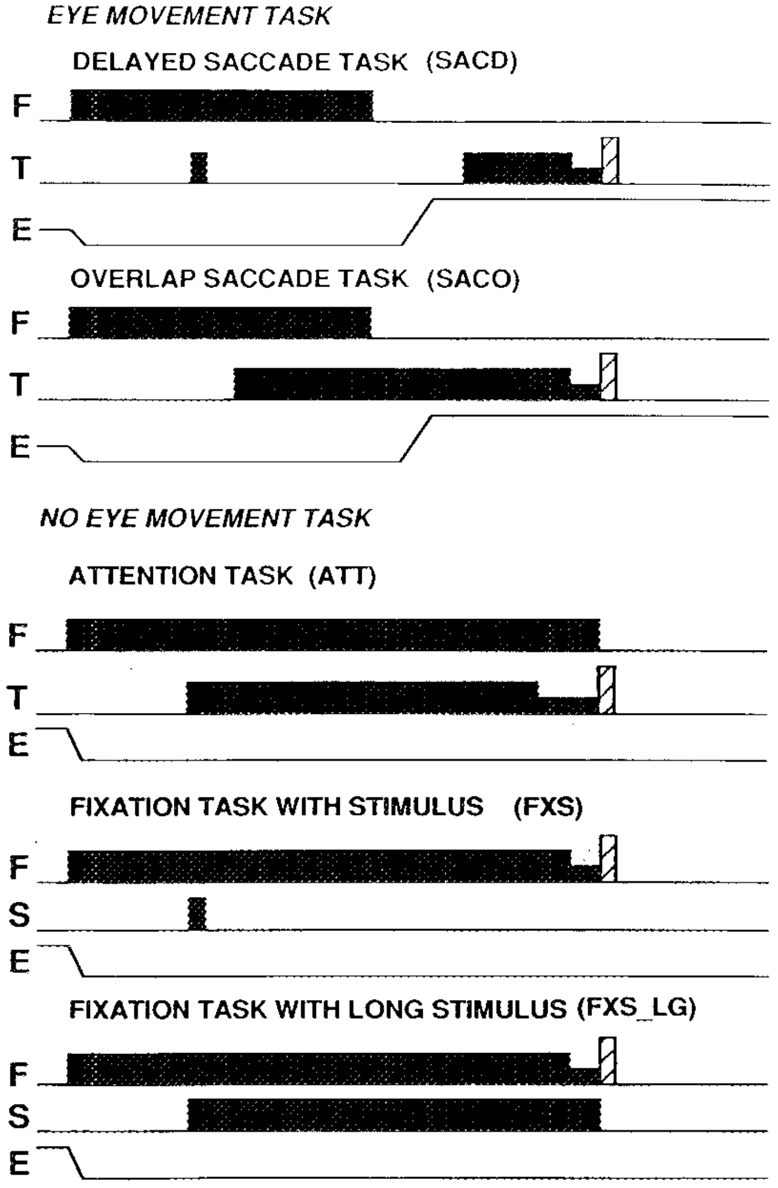


Figure 7. Behavioral paradigms. F, fixation point: a central spot of light that monkey must fixate to start a trial. S, stimulation point: a spot of light that was used as a stimulus to study visual responses. T, target point: a similar spot of light that appeared as a final target on the screen. Filled area: time during which the spot of light was on. Depression at the end of filled area indicates dimming of the spot, which was followed by delivery of reward (hatched area) if the monkey released the lever. E, schematic eye position.

III. Experimental procedure.

The entry of the electrode into the superior colliculus was signified by the characteristic spontaneous activity (irregular low frequency). First, we used the FXS task to determine the visual receptive field of nearby neurons, while changing of the visual stimulus at each trial. The best position to the visual stimulus was determined by the activity of phasic visual on-responses by using a sound monitor of unitary spike discharges. After the determination of the visual receptive field, the target was fixed to its center. Second, we used the SACO task to search for tonic activity which would appear after the presentation of the target. Once a tonic neuron was isolated, the five visuooculomotor tasks were applied, each as a block of 20 trials.

The layer of the recorded neuron was determined tentatively based on the following criteria and was confirmed, when possible, by a later histological examination (see below). If the activity of the tonic neuron and neighboring neurons did not show a phasic increase in activity with a saccade in any direction, the neuron was determined to be in the superficial layer. If the tonic neuron showed saccadic activity, it was determined to be in the intermediate layer.

IV Unit recording

We used glass-coated Elgiloy (RMO, U.S.A.) electrode for single unit recordings (Suzuki and Azuma 1976, 8-12 MΩ measured at 10 Hz, exposed tips 15-20 μm). The electrodes were driven by a hydraulic micro-manipulator (Narishige, MO-95, Japan) with an X-Y coordinate which was attached to the chamber. We used the magnetic search-coil technique for eye movement recording (Enzanshi-Kogyo, MEL2U, Japan).

The eye positions were measured and digitized at 500 Hz, and stored during the whole block of trials. The neural spike events were collected with a resolution of 1 milliseconds. The unit activities were led through the window discriminator and digitized. At each trial, these data, as well as the eye position data, were displayed on the CRT. We monitored on the computer display the raw activity signal, the window discriminator output by an oscilloscope, an audiomonitor, and a quick raster display of the units shown on the computer monitor. The behavioral tasks, storage of data and display of data were controlled by a 32 bit computer (PC 9801 RA21, NEC, Japan).

V. Histology

In 14 different penetrations we made marking lesions where typical tonic cells were recorded. These lesions were placed by passing positive current (5 μA, 200 sec) through the recording electrode. At the end of the experiments, the monkey was perfused transcardially with saline followed by 4% paraform aldehyde under deep anesthesia (sodium pentobarbital, I.V.). The cut plain of the mid-brain area was tilted back by 45° from vertical, parallel to the electrode penetrations. The brain was postfixed for two weeks. Serial sections (thickness: 50 μm), parallel to the electrode penetrations, were cut on a cryotome and stained with cresyl violet.

Some histological data which were related to marking lesions were projected on clear sheets, on which the outlines of the brain stem area, the marking lesions and the electrode tracks were drawn. Each marking lesion was identified based on the stereotaxic X-Y coordinate system and on the distance from the surface of the superior colliculus.

VI. Data analysis

(1) Spike raster and Histogram

Two types of data storage files were collected. Event buffer files contained the time of each discriminated action potential, the time of events such as the appearance and disappearance of visual cues, the times of the saccade onset and dim on, and the location of the cues and the target. Analog buffer files contained records of eye position at every 2 msec. Using the stored event buffer files and analog buffer files, we performed offline data analyses. Discriminated action potentials were displayed by rasters aligned on different events. Each dot on the rasters indicates a single action potential and each line indicating a single trial of task. On the basis of the raster, the histograms, aligned on each different event, were calculated and displayed.

(2) Between task comparison of neural activity

Figure 8 shows a typical tonically active neuron of the intermediate layers of the superior colliculus in SACD task. There were three phases: visual response (a), tonic activity (b), and presaccadic activity (c). Tonic neurons were so defined as having activity of a long duration (> 400 msec) in either of the three main tasks (SACD, SACO, and ATT). This criteria was thought to be reasonable, because the duration of phasic response, whether visual or saccadic, were usually less than 200 msec. Most of the tonic neurons in fact responded tonically till the onset of saccade or the offset of the target.

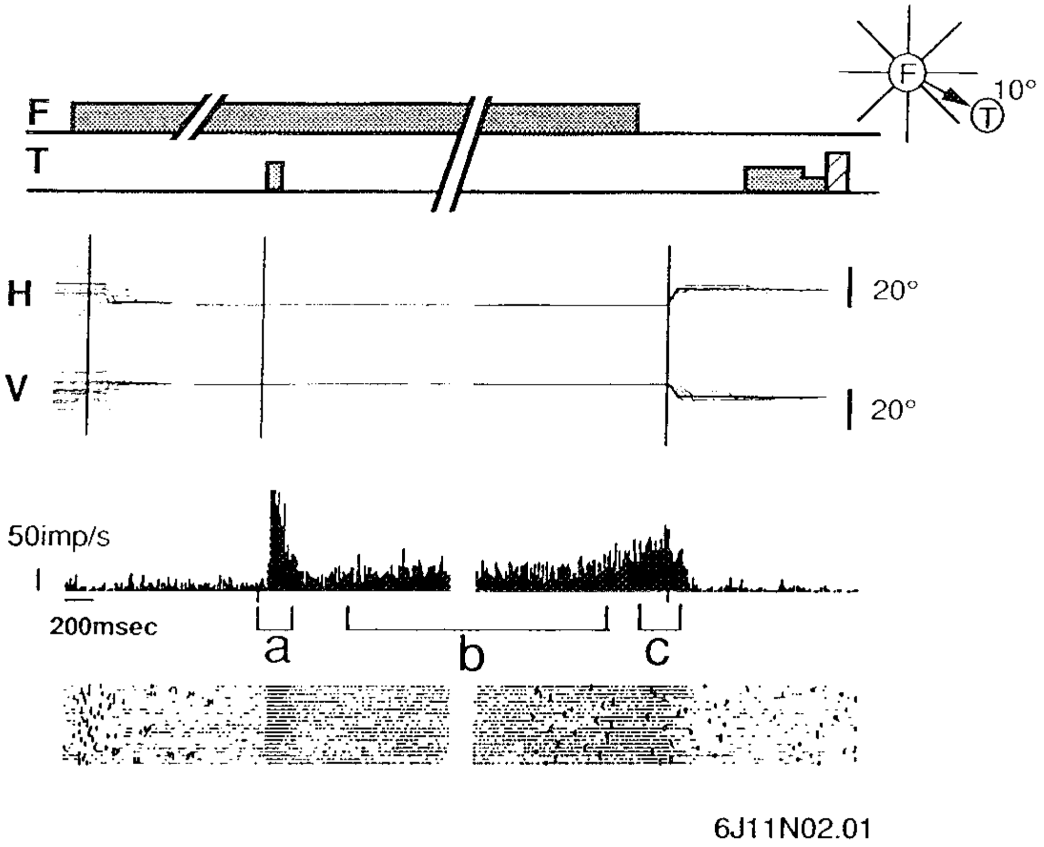


Figure 8. A typical neuron with tonic activity in SACD task. Top: durations of fixation point (F) and of target point (T) or visual stimulus point (S). The target presented at 10° to the right and 40° down from the center. Middle: horizontal eye position (H, up: rightward, down: leftward), vertical eye position (V, up: upward, down: downward), Eye position traces for all trials were superimposed. Bottom: Cell activity is shown as raster display, each dot indicating a single action potential and each line indicating a single trial of task(for details, see Methods). Averaged activity is shown above the raster display as a spike time histogram. Left side of raster and histogram are aligned on target cue onset and right side on saccade onset. Small vertical ticks on the left side of raster indicate the onsets of fixation point. Those on the right side indicate the offset of fixation point and the onset of target point. All subsequent figures use these conventions unless otherwise stated.

We concentrated on the tonic activity which was elicited by visuo-oculomotor tasks. Tonic activity in each task may represent different character of saccade. In SACD task, it may indicate the memory of the target location. In SACO task, it may indicate the preparation of the accurate saccade. In ATT task, it may indicate the peripheral attention.

In order to classify into each category, we compared the numbers of spikes which occurred in the three tasks. We set two windows on the raster displays (600 msec in duration), one for the control period (background activity) and the other for the test period (tonic activity), and counted the number of spikes which occurred within each window for each task trial (Figure 9). The control period was set just before the onset of the fixation point. For the two eye movement tasks (SACD and SACO), the test window was set so that its end was 200 msec before the saccade onset; this was to avoid possible inclusion of presaccadic activity. For the attention task (ATT) the test window started 200 msec after the target onset so as not to include a phasic visual response.

'Response magnitude' was defined for each task trial by subtracting the number of spikes within the control period from the number of spikes within the test period.

Response magnitude = N (test) - N (control)

(Here 'N' indicates the number of spikes for each trial.)

We then compared the response magnitude between all possible pairs of tasks (SACD, SACO, ATT and, if necessary, FXS_LG) by using Mann-Whitney's U test (unpaired comparison). The number of trials for each task (SACD, SACO, ATT and FXS_LG) was always set to 20. If the response magnitude was significantly stronger in one task than in other tasks, the neuron was classified into one of three specific types (see table 1).

Otherwise, the neuron was classified into nonspecific type.

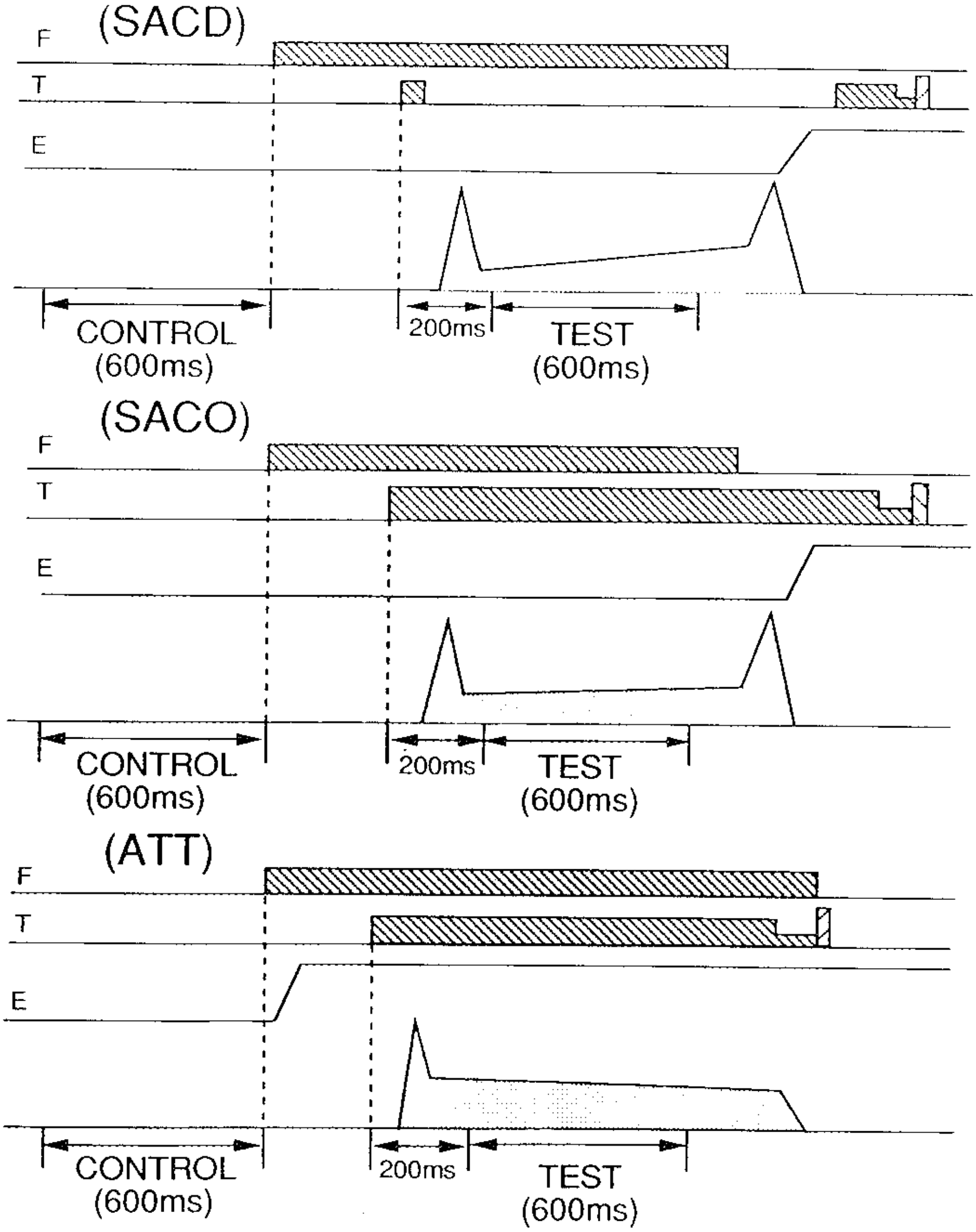


Figure 9. Schema showing control and test windows for 3 tasks (SACD, SACO, and ATT) to quantify response magnitude (see Methods for details). Top: durations of fixation point (F) and target point (T). E: schematic eye position. Middle: schematic histogram of neuronal activity during each task. Bottom: locations of control and test windows.

(3) Directional tuning curve

Like the visual and saccadic responses, the tonic activity generally showed directional selectivity. To quantify this selectivity we presented the target randomly at one of 8 directions and compared the tonic activity among the 8 directions. The tonic activity for each direction (not for each trial) was represented by 'activity ratio' defined as follows.

Activity ratio = Total N (test) / Total N (control)

(Here 'Total N' indicates the sum of the number of spikes across trials. The two windows (control and test) were the same as those used for the response magnitude.)

In addition to the tonic activity, we calculated the activity ratio for the visual response and the saccadic activity. The test window for the visual response started with the visual stimulus onset and was 200 msec in duration; the test window for the saccadic activity started 100 msec before saccade onset and was 200 msec in duration. The control window was set at the 200 msec before the onset of the fixation point.

We then plotted the activity ratio on the axes of eight directions, which we call 'direction tuning curve'.

RESULTS

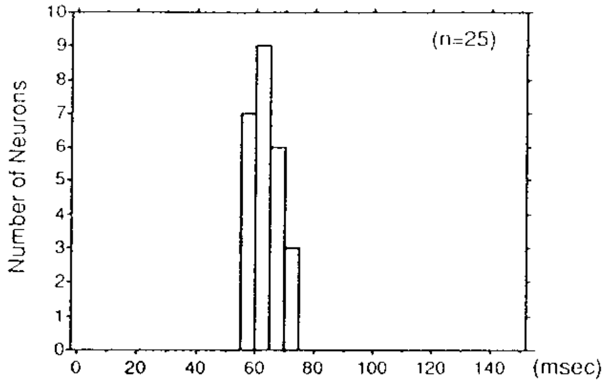
In the present study we concentrated on the tonic neurons in the superior colliculus. Although many neurons showing only phasic responses were encountered along electrode penetration, we did not attempt to isolate their activity for further analysis. Neurons were determined to be tonic in nature if its activity was sustained for more than 400 msec in either one of the main tasks (SACO, SACD, and ATT). A total of 141 tonic neurons were recorded from the superior colliculus in three monkeys.

I. Difference of neural activity between superficial and intermediate layers

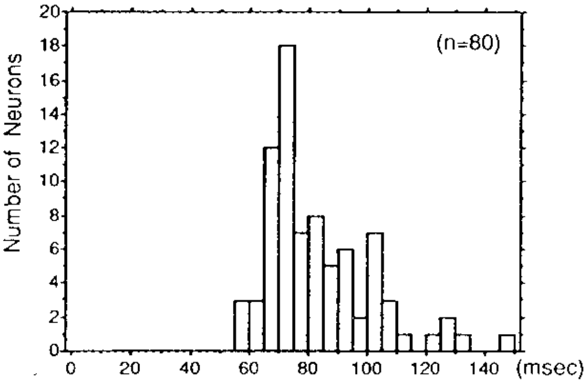
We found tonic neurons in both the superficial and intermediate layers. At the time of experiment, the layer of each tonic neuron was determined tentatively depending on the presence or absence of saccade-locked activity: (1) superficial layer if saccadic activity was absent, and (2) intermediate layer if saccadic activity was present. This classification was based on many previous studies and now seems unanimously accepted (Goldberg and Wurtz 1972, Mays and Sparks 1980). Our determination was later confirmed by histological examination of the marking sites of tonic neurons. Thirty three neurons were in the superficial layer, and the other 108 were in the intermediate layer.

The difference between the layers was also seen in the latency of visual responses (Figure 10). The latencies in the superficial layer ranged from 51 to 74 msec (mean 65.6 msec, SD 6.3), while in the intermediate layer they ranged from 55 to 144 msec (mean 84.1 msec, SD 22.3). The difference was statistically significant (Mann-Whitney's U test, $P<0.05$).

However, there were no significant differences among different types (visuomotor, mnemonic motor, visual attention and nonspecific) of tonic neurons (shown in Table 1).



A Superficial Layer



B Intermediate Layer

Figure 10. Latencies of visual responses of tonic neurons recorded in the superficial layer (A) and intermediate layer (B).

III. Classification of the tonic neurons in the superior colliculus

Table 1 summarizes the types of tonic neurons. We used the SACD, SACO, ATT (and FXS_LG, if necessary) tasks to classify the tonic neurons. They were classified into four types: (1) *visuomotor type*, if tonic activity in the SACO task was significantly stronger than those in the other tasks; (2) *visual attention type*, if tonic activity in the ATT task was significantly stronger than those in the other tasks; (3) *mnemonic motor type*, if tonic activity in the SACD task was significantly stronger than those in the other tasks; (4) *nonspecific type*, if the neuron could not be classified into either of the above three types. Neurons of the non-specific could be classified into several sub-types; some neurons showed significantly enhanced activity in two or three of the four tasks; some neurons showed no significant difference among the four tasks.

Table 1 **Classification of Tonic Neurons**

Types of Neurons	Superficial Layer	Intermediate Layer
Visuomotor	4	13
Visual Attention	3	13
Mnemonic motor	0	15
Nonspecific	26	67
Total	33	108

The results can be summarized as follows. First, a majority of tonic neurons were of non-specific type. Second, the specific types were more common in the intermediate layer, where the three specific types were similarly common. Third, in the superficial layer no cell was classified to be of mnemonic motor type. In fact, among the superficial layer neurons, none showed significant activity in the SACD task, whereas most tonic neurons in the intermediate layer showed some tonic activity in this task.

(1) Visuomotor type

(a) Superficial layer

Four out of 33 superficial layer neurons were classified as visuomotor type. Figure 11 shows activity of a typical visuomotor type neuron in the superficial layers. During the three tasks (SACO, ATT and FXS_LG), the target location was fixed at the center of the visual receptive field and the intensity of the stimulus was not changed.

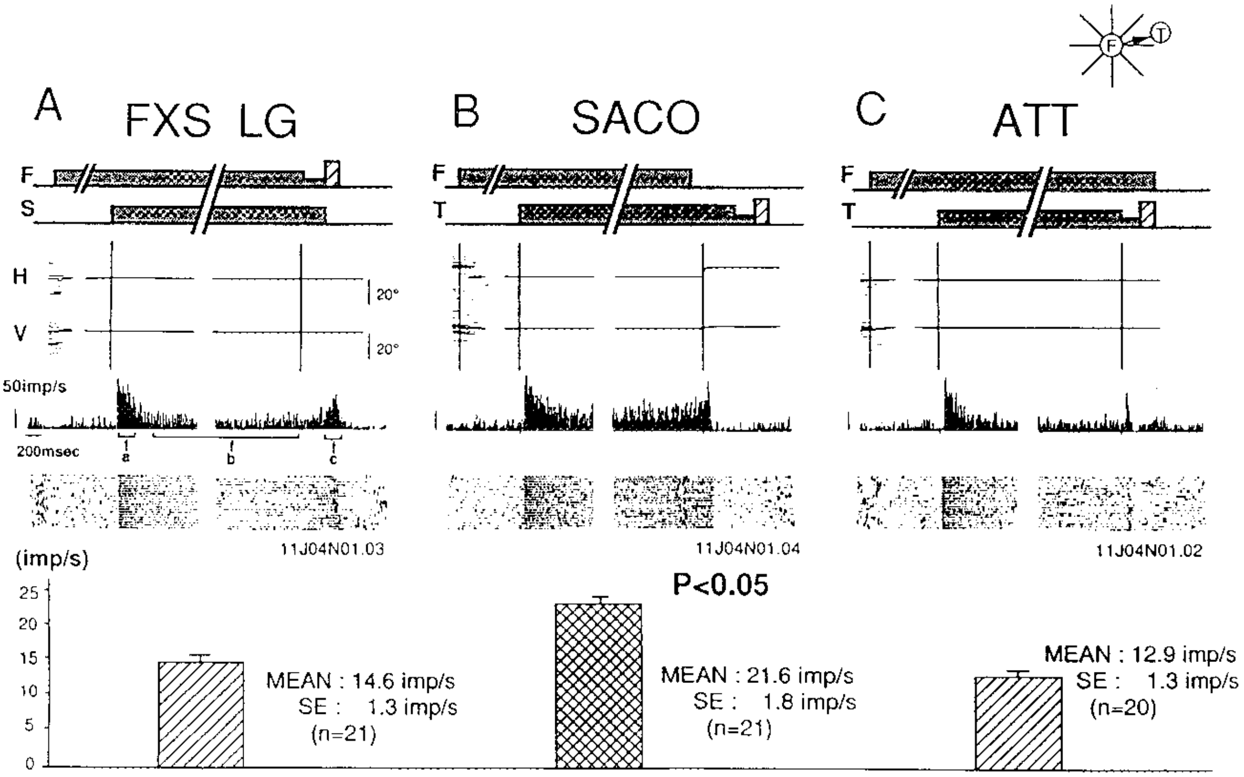


Figure 11. A neuron of visuomotor type in the superficial layer. Its activity is compared between 3 tasks: FXS_LG (A), SACO (B), and ATT (C). Top: durations of fixation point (F) and target point (T) or visual stimulus point (S). The target presented at 9° to the right and 10° up from the center. Middle: horizontal eye position. The left half of the raster-histogram in A is aligned at stimulus onset and those in B and C are aligned at target onset. The right halves in A and C are aligned at dim onset, and that in B is aligned at saccade onset. Bottom: comparison of response magnitudes of tonic activity of the neuron (see Methods for detail).

In the FXS_LG task (Figure 11A), in which a peripheral spot (S) had no behavioral significance, this neuron showed a strong visual on-response (indicated by arrow-a), irregular tonic activity during visual stimulation (arrow-b), and a brief off-response (arrow-c). The tonic activity, not the visual response, was enhanced in the SACO task (Figure 11B) in which the monkey made a saccade later to the same spot (T). Since the stimulus conditions were identical in these two tasks as long as the monkey was fixating, the enhancement of the tonic activity may be attributed to the fact that the monkey was preparing for a saccade to the stimulus. Alternatively, the enhancement could be due to the fact that the monkey was simply paying attention to the stimulus. The latter possibility, however, was not supported by the experiment using the ATT task (Figure 11C) in which the monkey was required to attend to the stimulus, without making an eye movement; the tonic activity became much less.

To confirm the difference of the tonic activity among the three tasks, we calculated the response magnitude for each task trial and compared them between the tasks using by Mann-Whitney's U test (see Methods). At the bottom of Figure 11 are shown the mean and SE of the response magnitudes for each task. The response magnitude was strongest in the SACO task in comparison with either of the other two tasks (Mann-Whitney's U test, $P<0.05$). No significant activity was seen in the SACD task (not shown). We thus concluded that the tonic activity of this neuron reflects the process in which visual information is converted to oculomotor information.

As for the phasic visual on response, there seems no significant difference among the three tasks. We did not examine the difference in detail, because our interest was the tonic activity in this study.

(b) Intermediate layer

Thirteen out of 108 tonic neurons in the intermediate layer were classified as visuomotor type. Figure 12 shows an example. In the SACO task (Figure 12B) this neuron showed a visual on-response (indicated by arrow-a), tonic activity during visual stimulation (arrow-b), and the presaccadic response (arrow-c). It was thus suggested that the tonic activity was related to preparation of a future saccade. In the SACD task (Figure 12A) a similar saccade was prepared, but now to a remembered position; yet the tonic activity was significantly weaker. The relation to attention was also excluded by the experiment using the ATT task (Figure 12C). Statistical comparison confirmed the difference: the tonic activity was strongest in the SACO task among the three tasks (Mann-Whitney's U test, $P<0.05$).

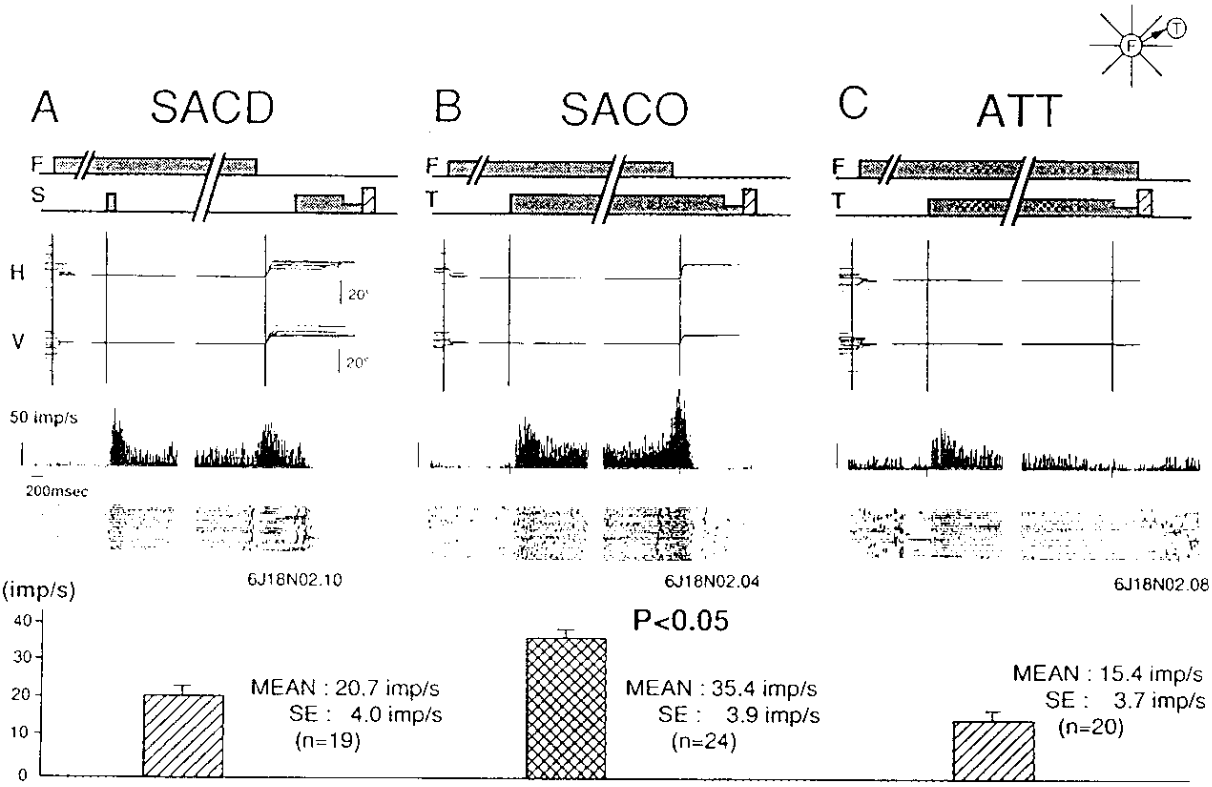


Figure 12. A neuron of visuomotor type in the intermediate layer. The target presented at 12° to the right and 28° up from the center. Its activity is compared between three tasks: SACD (A), SACO (B), and ATT (C). The left half of the raster-histogram in A is aligned at target cue onset and the right half in A at saccade onset.

(2) Visual attention type

(a) Superficial layer

Three out of 33 superficial layer neurons were classified as visual attention type. Figure 13 shows an example. The tonic activity in the ATT task (Figure 13C) was clearly stronger than that in the SACO task (Figure 13B), suggesting that this activity was not related to eye movement. Further, the tonic activity was much weaker in the FXS_LG task (Figure 13A) in which, unlike in the ATT task, the monkey was not required to attend to the stimulus. As shown in the bottom half of the Figure 13, the enhancement of tonic activity in the ATT task was confirmed statistically by using Mann-Whitney's U test (P<0.05). This neuron was thus judged to be related to the peripheral attention.

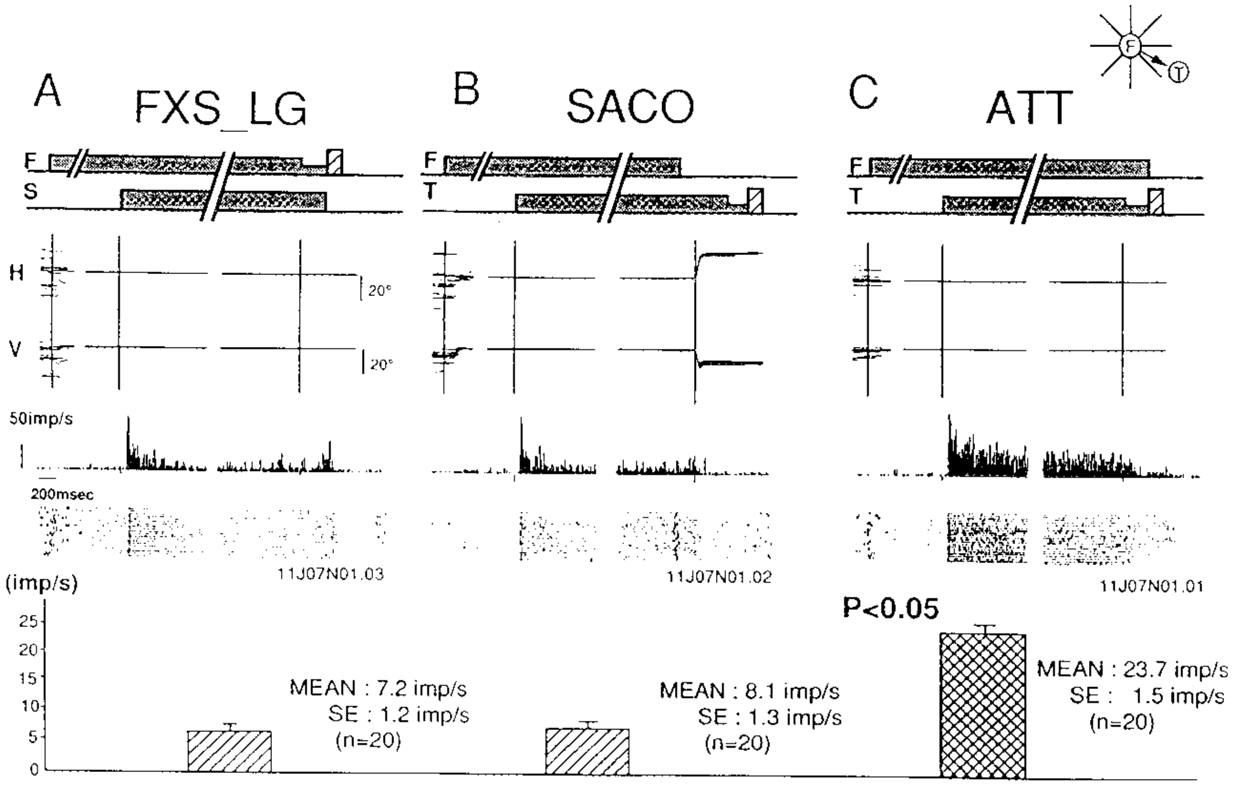


Figure 13. A neuron of visual attention type in the superficial layer. The target presented at 19° to the right and 15° down from the center. Arrangements of each raster and histogram are the same as Figure 11.

(b) Intermediate layer

Thirteen out of 108 intermediate layer neurons were classified as visual attention type. Figure 14 shows an example. The activity started with a visual response, and lasted to before saccade in the SACO task (Figure 14B). On the other hand, tonic discharge in the SACD task was smaller than that in the SACO task (Figure 14A). Thus, the tonic activity may reflect the visual information associated with saccade. However, the tonic activity in the ATT task was further enhanced compared with the SACO task (Figure 14C). The enhancement in the ATT task was confirmed statistically (Mann-Whitney's U test, P<0.05). This neuron was judged to be related to peripheral attention rather than eye movement.

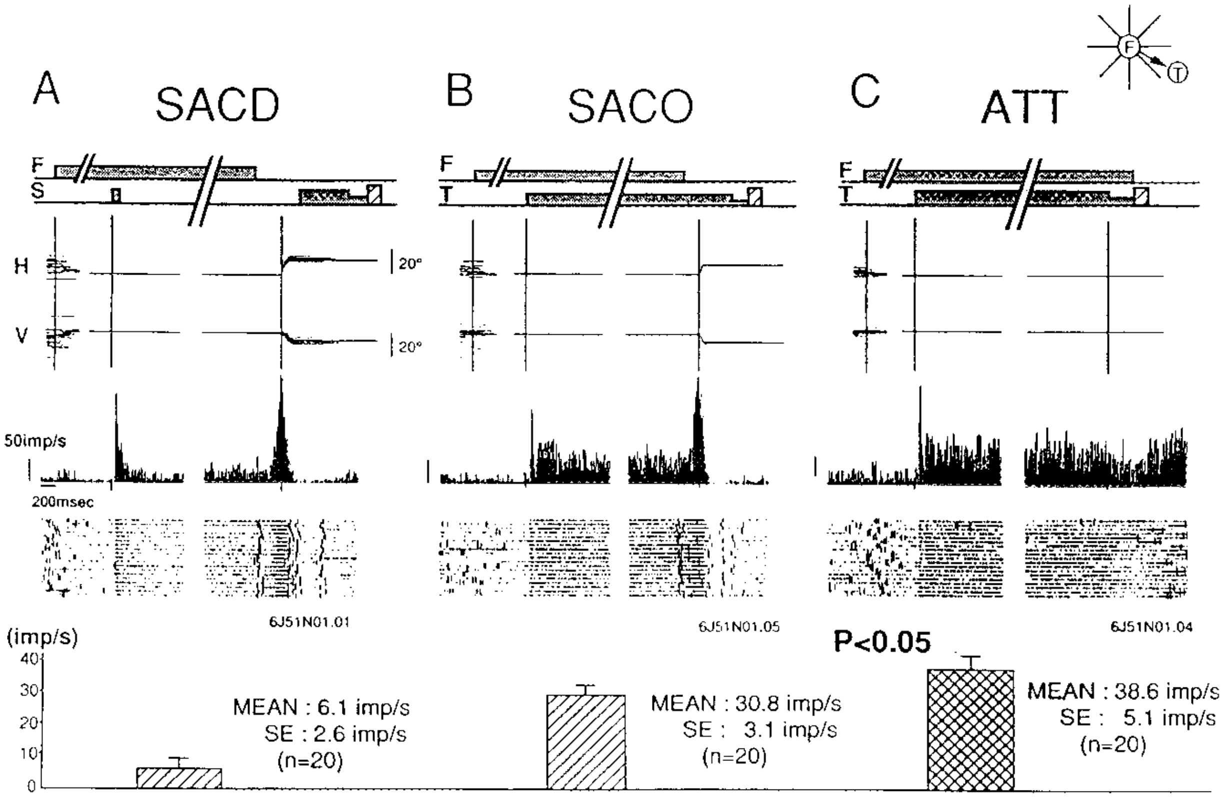


Figure 14. A neuron of visual attention type in the intermediate layer. The target presented at 10° to the right and 40° down from the center. Arrangements of each raster and histogram are the same as Figure 12.

(3) Mnemonic motor type

(a) Superficial layer

There was no neuron in the superficial layer which showed significant tonic activity in the SACD task.

(b) Intermediate layer

Fifteen out of 108 intermediate layer neurons were classified as mnemonic motor type. Figure 15 shows an example. The tonic neurons did not show a strong response in either the SACO (Figure 15B) or ATT task (Figure 15C), in both of which the target was continuously present. The neuron showed the strongest tonic activity in the SACD task, in which the monkey had to memorize the location of the target (Figure 15A). This was confirmed statistically (Mann-Whitney's U test, $P<0.05$).

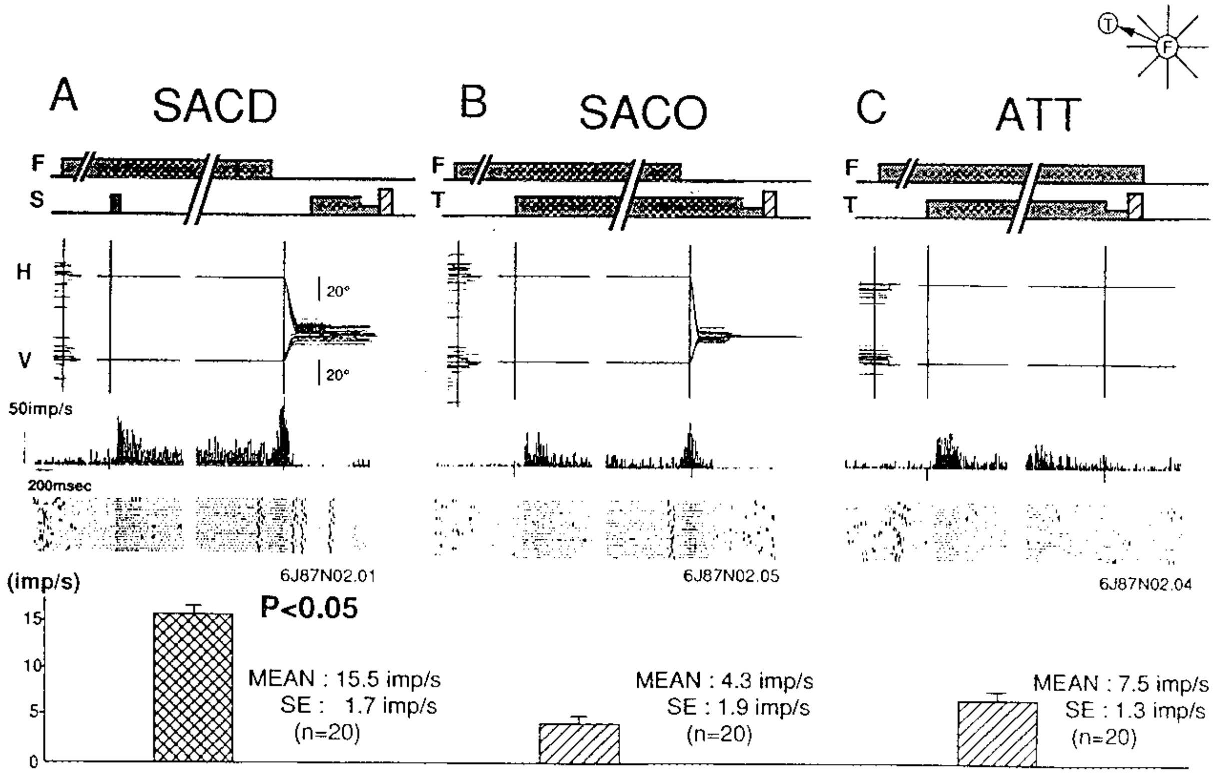


Figure 15. A neuron of mnemonic motor type in the intermediate layer. The target presented at 36° to the left and 15° up from the center. Arrangements of each raster and histogram are the same as Figure 12.

(4) Nonspecific type

Twenty-six out of 33 superficial layer neurons were classified as nonspecific type. Figure 16 shows an example. The tonic activity was roughly the same among three tasks (FXS_LG, SACO, and ATT). Tonic activity was absent only in the SACD task, which was a general feature among superficial layer neurons.

Sixty-seven out of 108 intermediate layer neurons were classified as non-specific type. They usually showed a roughly equal degree of activity in the SACD task.

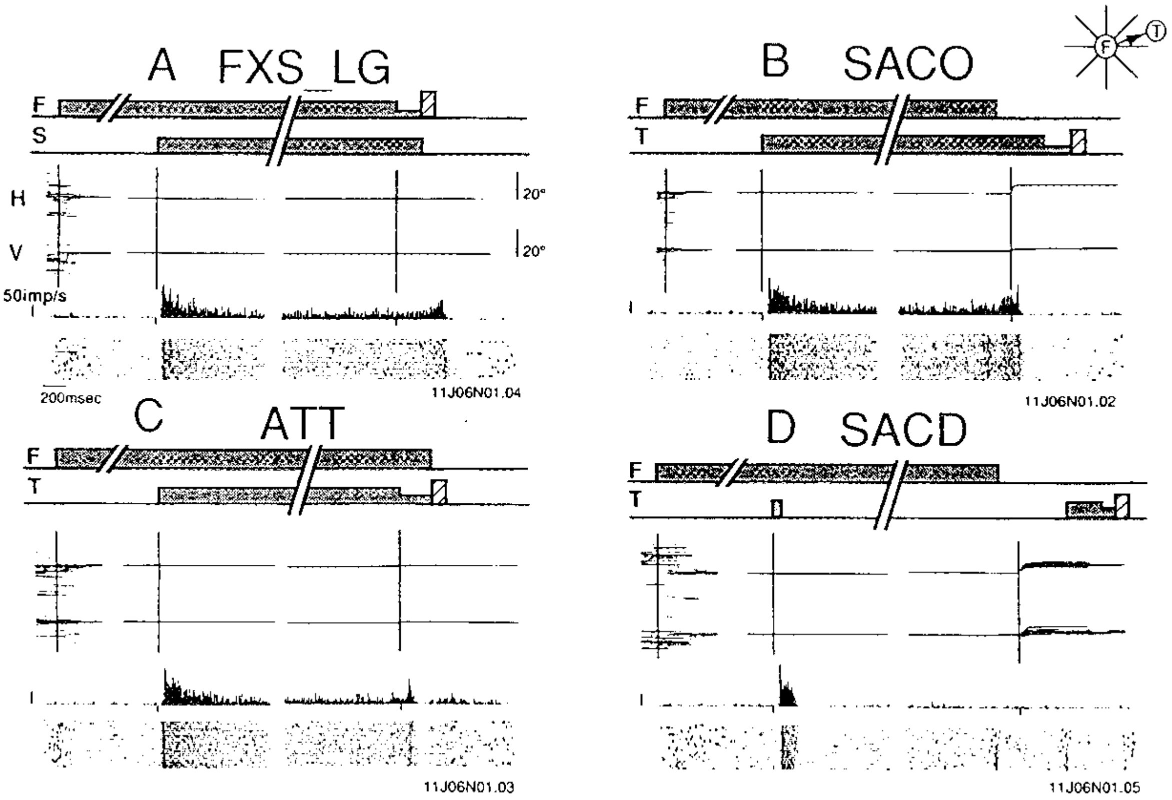


Figure 16. A neuron of nonspecific type of neuron in the superficial layer. The target presented at 7° to the right and 17° up from the center. Arrangements of each raster and histogram are the same as Figure 11.

III. Directional selectivity

It is well known that neurons in the superior colliculus are spatially selective; both visual and saccadic responses had preferential fields, known as 'visual receptive field' and 'movement field' (Goldberg and Wurtz 1972, Schiller and Stryker 1972, Sparks and Jay 1986). Do the tonic neurons also have preferential fields? As shown above, the tonic neurons had three components of response: visual response, presaccadic response and tonic activity. Are the spatial selectivity for these components, if present, the same or different? To answer these questions we presented the target randomly out of 8 directions.

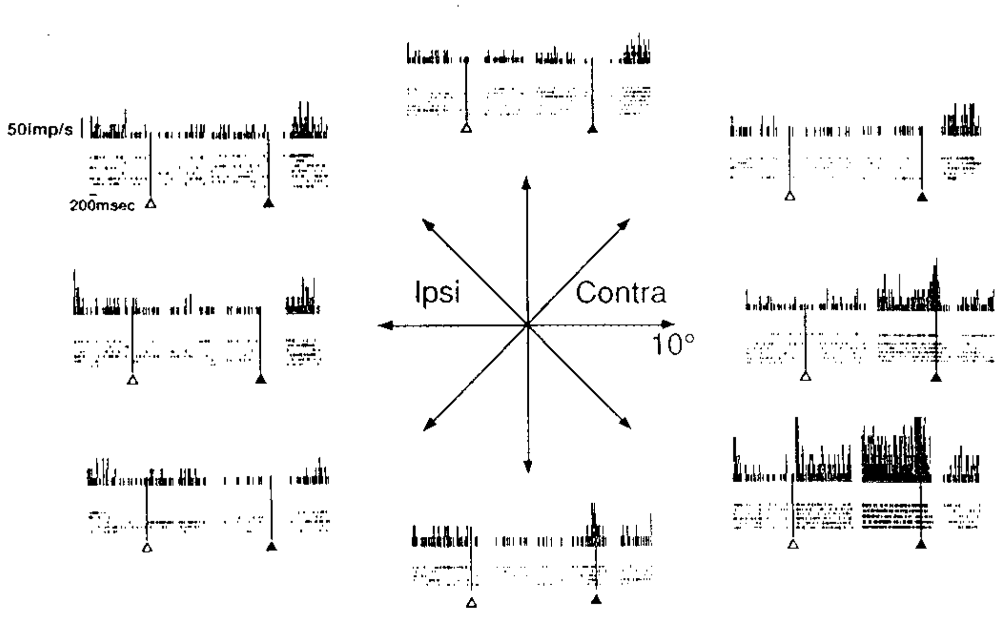
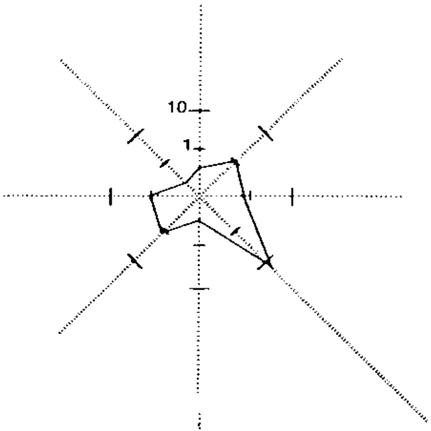


Figure 17. Directional differences of activity of a neuron in the intermediate layer of the left superior colliculus during SACD task. The eccentricity of the target was 10 degrees. Each raster and histogram show the averaged firing rate for each direction of the target relative to the center of the figure. In each raster and histogram, left side is aligned on stimulus onset (open triangle) and right side on saccade onset (filled triangle).

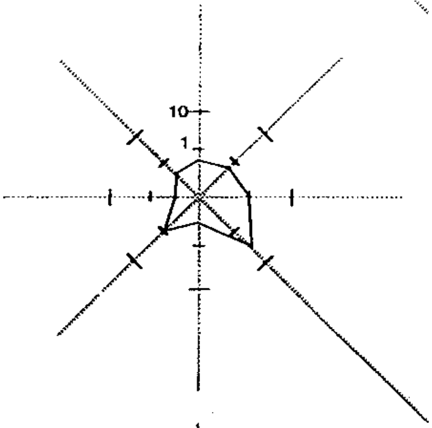
Figure 17 shows directional selectivity of a tonic neuron in the intermediate layer (recorded in the left superior colliculus). It is clear that all of the three components of response were directinally selective. The tonic activity was strongest in the right-downward direction; so was the visual response. The best direction for the saccadic response was also right-downward, but it was seen also in the direction of down, downward to right and right. Further, there appears some inhibition associated with saccades to the ipsilateral side (left, upward to left).

To analyze the directional selectivity quantitatively, we calculated the activity ratio for each of the three components and drew a directional tuning curve, as shown in Figure 18 (the same neuron shown as in Figure 17). The directional tuning curves of the visual responses and tonic activity were similar. There may be some inhibitions for the upward/leftward directions. The directional selectivity for the saccadic response was less sharp, and the inhibition in the upward/leftward directions were more consistent.

Visual Response



Tonic Activity



Saccade Reasponse

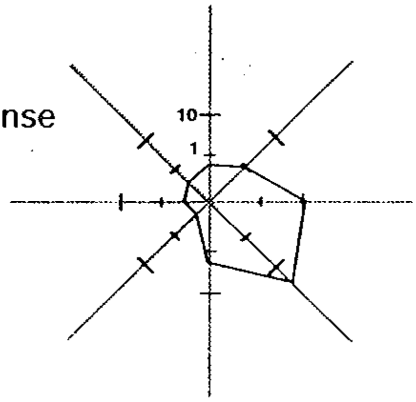


Figure 18. Directional tuning curve of each phase of the activity (visual response, tonic activity, and saccade response) obtained for the same neuron illustrated in A. Activity ratios (see Methods) are plotted in polar coordinates. Tick marks on the straight lines radiating from center indicate the activity ratios of 1 and 10 (plotted in log scale).

IV. Histological data

It was crucial, especially in this study, to have an accurate estimate of the depth of the neuron recorded. Since the superior colliculus, more than other brain areas, tends to be depressed when an electrode is inserted, we took the following care. When the electrode entered the superficial layer, we again pulled up the electrode while recording neural activities. We determined the surface of the superior colliculus at the point where visual responses disappeared, which was significantly shallower than the first visual response obtained after the first entry of the electrode.

To confirm the location of each tonic neuron we then made small marking lesions at some of the typical tonic neurons. All of these marks were identified later by histological examination. It was however difficult to relate each of the functionally identified neuron to one of the marks. The following values obtained at the time of experiment were useful for this purpose: (1) the X-Y coordinates of the electrode position read from the electrode manipulator, and (2) depth of the neuron estimated as described above. The visual receptive field or movement field of the recorded neuron was also helpful for the reconstruction; for they are known to indicate the location of the recording site (Robinson 1972, Schiller and Stryker 1972).

Figure 19 shows a photomicrograph of a histological section showing a plane of the superior colliculus roughly perpendicular to its surface. All of the histologically identified marks are shown in Figure 20, as projected onto a representative plane. All of the tonic neurons, which we judged to be in the intermediate layer, were actually located in the intermediate layer except for one, which was in the deep layer. There is no tendency for differential distribution among different types of tonic neurons. The tonic neuron in the deep layer was located on the caudal part of the superior colliculus. All of tonic neurons judged to be in the superficial layer were located in the superficial layer (Figure 20).

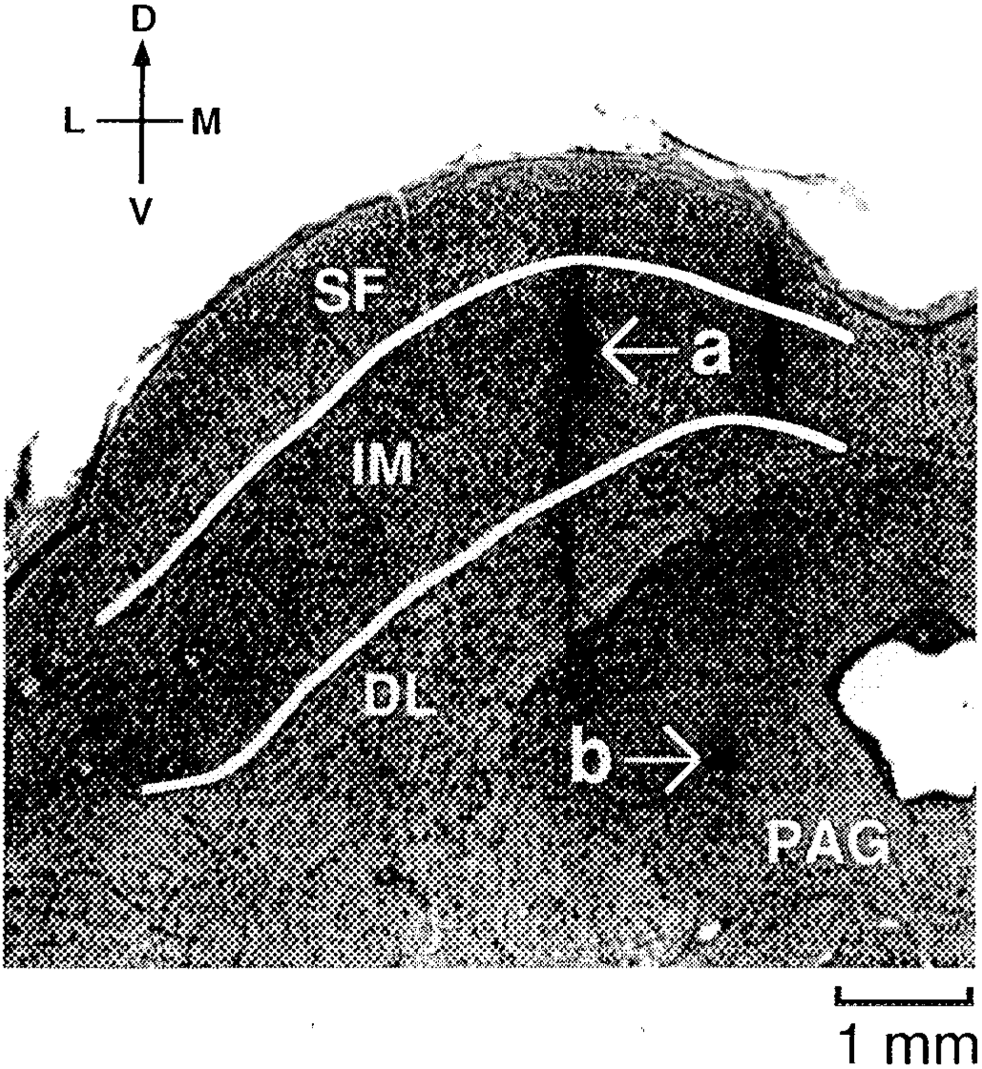


Figure 19. Photomicrograph of a coronal section showing the superior colliculus. Arrow a, a marking site where a nonspecific type neuron was recorded; arrow b, a marking site of 3 mm below the site where a visuomotor type neuron was recorded. Abbreviations: SF, the superficial layer; IM, the intermediate layer; DL, the deep layer; PAG, periaqueductal gray matter; D, dorsal; V, ventral; M, medial; L, lateral.

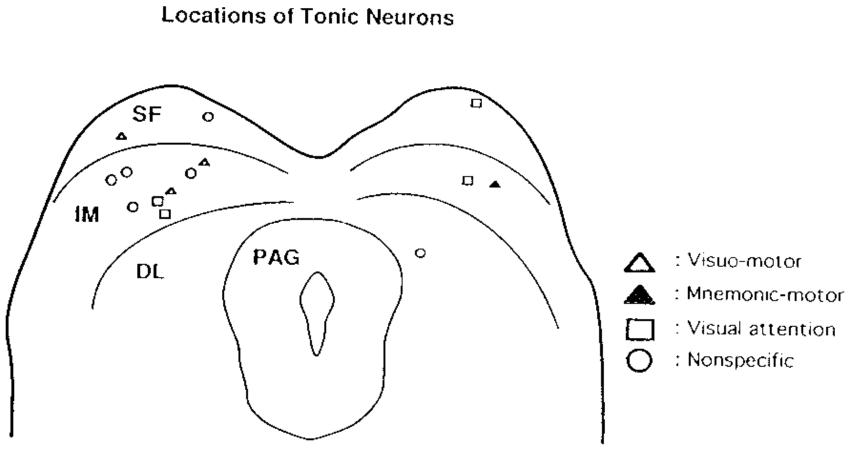


Figure 20. Marking sites indicating the locations of tonic neurons; visuomotor type (open triangle), mnemonic motor type (filled triangle), visual attention type (filled square), nonspecific type (open circle). Abbreviations: SF, the superficial layer; IM, the intermediate layer; DL, the deep layer; PAG, periaqueductal gray matter.

DISCUSSION

We examined the nature of information carried by 'tonic neurons' in the superior colliculus, which are relatively few in number but have distinct characteristics. For this purpose we recorded the tonic neurons while the monkey was performing different behavioral tasks, each of which would reveal a unique aspect of behavioral information. The experiments revealed that tonic neurons in the superior colliculus were classified into four types: visuomotor, visual attention, mnemonic motor and nonspecific types. A majority of neurons in the superficial layer were classified as nonspecific type, although some were of visuomotor and visual attention types. In contrast, nearly half of neurons in the intermediate layers were classified as specific types, either visuomotor, visual attention or mnemonic motor type. These findings suggest that the intermediate layer, rather than the superficial layer, of the superior colliculus may be more differentially related to preparation of saccade, peripheral attention and memory. In the following discussion we will concentrate on the tonic neurons in the intermediate layer.

COMPARISON WITH QUASI VISUAL CELLS

Like our tonic neurons, the quasi-visual cells also responded tonically during the delay period in the double saccade task (Mays and Sparks 1980). The situation at the second saccade in their task was similar to that in our SACD task: the monkey was required to make a saccade to the remembered target. It might be argued that the tonic activities in this study were recorded from the quasi-visual cells. We do not think so, however, because the quasi-visual cell did not show a saccade response. One might suggests that our tonic neurons are a special type of quasi-visual cell which are located in the superficial layer and thus do not respond to a saccade. However, the tonic neurons in the superficial layer did not show sustained activity during the delay period in SACD task. Therefore, we conclude that tonic neurons in this study are different from the quasi-visual cells.

POSSIBLE SOURCES OF THE INFORMATION OF MEMORY, PREPARATION OF SACCADE AND ATTENTION

If the tonic activity in the superior colliculus originates in other brain areas, similar tonic activities must be found in these areas. The candidates can be found in the cerebral cortex, basal ganglia, and thalamus. The frontal eye field (Bruce and Goldberg 1985, Goldberg and Bruce 1990), supplementary eye field (Schall 1991), and posterior parietal cortex (Andersen et al. 1987, Barash et al. 1991) are the three major cortical areas (Figure 21). The caudate nucleus (Hikosaka et al. 1989c) and substantia nigra pars reticulata (Hikosaka and Wurtz 1983b) are the two candidate regions in the basal ganglia (Figure 21). The intralaminar portion of the thalamus (Schlag and Schlag-Rey 1984) could also be involved.

Although some neurons in these areas show tonic activities, their detailed nature is often unclear since appropriate tasks were not used to differentiate several possibilities. It is important to know whether the tonic activities in these areas are selective for the tasks. We will discuss about the possible origins of each specific type of information on the basis of data currently available.

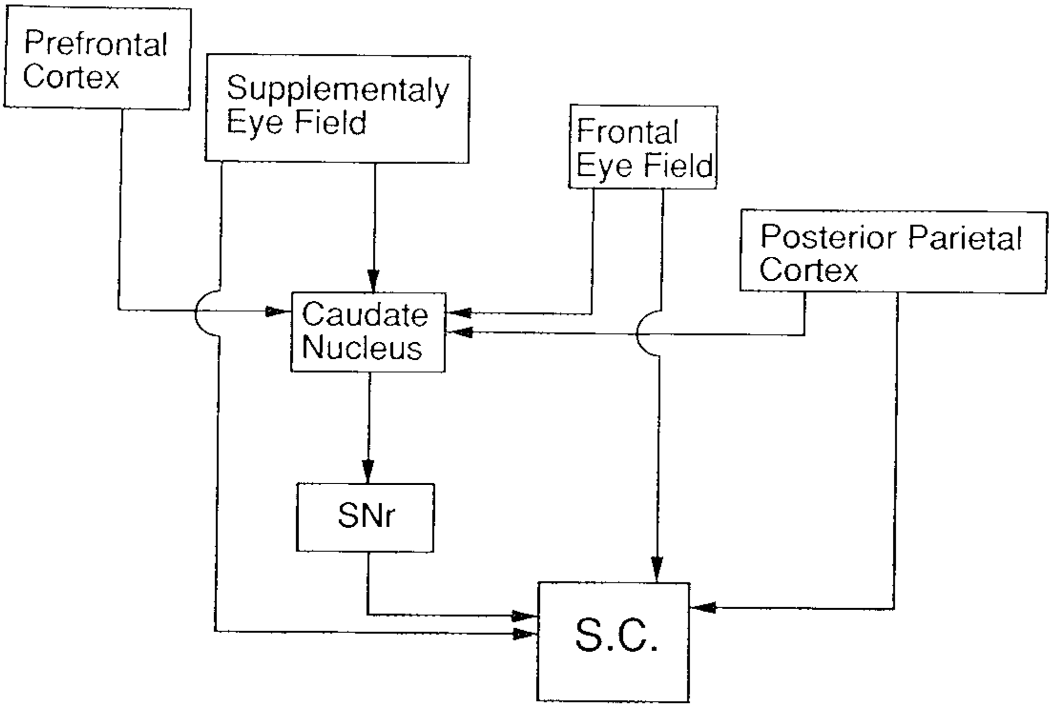


Figure 21. Possible source of tonic activity in the intermediate layer. Abbreviations: SNr, substantia nigra pars reticulata; S.C., superior colliculus.

I. The information of the mnemonic motor type

Tonic neurons of mnemonic motor type are thought to carry information selective for memory, rather than movement preparation or attention. If such information derives from other areas, they also should show similary memory-selective information. Although memory-related information has been found, using similar saccade tasks, in the frontal eye field (Bruce and Goldberg 1985) and the posterior parietal cortex (Gnadt and Andersen 1988, Andersen et al. 1990, Barash et al. 1991), there has been no indication that it is specific to memory. For example, one type of neurons in the frontal eye field (visuomovement cell, Bruce and Goldberg 1985) exhibit tonic activity in addition to visual and movement responses, but its magnitude was similar between the two task situations comparable to SACO and SACD. The posterior parietal cortex neurons also show presaccadic tonic activity, which again is equally present in the two task situations (Andersen et al. 1987, Andersen et al. 1990).

The memory-specific nature has been found in the basal ganglia and the prefrontal cortex. Some neurons in the caudate nucleus show tonic activity which is specific to memory-guided saccades (Hikosaka et al. 1989c); it was absent before visually guided saccades. The memory-specific role of the basal ganglia was further suggested by the chemical lesion of the caudate nucleus of the monkey (Miyashita et al. 1991): after injection of MPTP which specifically denervates dopaminergic fibers, the monkey became unable to make memory guided saccades to the side contralateral to the lesion, although visually guided saccades were largely intact. Similar memory-specific saccadic deficits are observed in human patients of basal ganglia diseases (e.g., Parkinson's and Huntington's disease) (Crawford et al. 1989, Leigh et al. 1983).

The neural mechanism by which the caudate nucleus exerts influences on the superior colliculus has been clarified by anatomical and physiological studies. Caudate neurons project to the substantia nigra pars reticulata (SNr), which in turn projects to the intermediate layer of the superior colliculus (Jayaraman et al. 1977, Graybiel and Ragsdale 1979). These two serial connections are both inhibitory and GABAergic (Yoshida and Precht 1971, DiChiara et al. 1980, Araki et al. 1984). With its characteristic high spontaneous activity SNr neurons normally inhibit neurons in the intermediate layer of the superior colliculus (Hikosaka and Wurtz 1983a). Activity in caudate neurons would thus produce a pause in the sustained activity of SNr neurons. In fact, visual and saccadic responses seen in the SNr are always a decrease in firing (Hikosaka and Wurtz 1983a). Further, SNr neurons show a sustained decrease in discharge rate during the delay period of a memory guided saccade task (SACD) (Hikosaka and Wurtz 1983b). Hence, the tonic activity of caudate neurons would lead to a tonic disinhibition of the superior colliculus by suppressing the activity of SNr neurons.

The memory-related function of the prefrontal cortex has been widely accepted (Joseph and Barone 1987, Goldman-Rakic 1987). This view has further been elaborated by recent studies using saccade tasks similar to ours. After local injection of a selective antagonist of D1 dopamine receptor into the prefrontal cortex, the monkey became unable to make memory guided saccades, though visually guided saccade were unchanged (Sawaguchi and Goldman-Rakic 1991). The deficit was location-specific: saccades to a limited area in the visual field are selectively impaired by a small injection, and the impaired area depends on the injection site in the prefrontal cortex. Neural correlates of the memory-specific behavior were found by Funahashi et al. (1989): neurons in the prefrontal cortex show tonic activities in a memory guided saccade task (same as our SACD task). A comparison between the directional selectivity of visual response and that of delay-period activity showed a strong positive correlation of the preferred directions. The correlation is similar to that in the tonic neurons in the superior colliculus.

In sum, it is suggested that neurons of the prefrontal cortex and the caudate nucleus share memory-selective features with the tonic neurons of mnemonic motor type in the superior colliculus. Underlying this correlation may be the strong connection from the prefrontal cortex to the caudate nucleus (Künzle 1978, Jakobson et al. 1978). We would suggest that the information related to short-term memory in the prefrontal cortex is transmitted to the caudate nucleus, and the activity of the mnemonic motor type in the superior colliculus may reflect the activity of the caudate nucleus neurons through the SNr.

II.The information of the visuomotor type

The origin of this type of signal must be those neurons which would show tonic activity before visually guided saccades rather than memory-guided saccades. In the frontal eye field, visuomovement cells may also respond tonically during the interval between the target onset and the saccade onset (Bruce and Goldberg 1985). There are some neurons within this group whose tonic activity is stronger before visually guided saccades (SACO) than before memory-guided saccades (SACD) (Goldberg and Bruce 1990).

The role of the frontal eye field in visually guided initiation of saccade is strongly supported by its massive connection to the superior colliculus, especially to the intermediate layer (Fries 1984, Huerta et al 1986, Segraves and Goldberg 1987, Stanton et al. 1988a). Thus, the visuomotor type neurons in the superior colliculus may reflect tonic neurons in the frontal eye field.

III. The information of the attention type

Attention is the process by which sensory processing is selectively facilitated. At the neuronal level, attention is revealed by an enhancement of sensory response. This was first described in the superior colliculus by Goldberg and Wurtz (1972). They compared the magnitude of visual response between two situations which are physically identical but behaviorally different. In a fixation task, the monkey was required to detect dimming of the central fixation point, ignoring a peripheral visual stimulus (as in our FXS task); in a saccade task, the monkey was required to make a saccade to the same stimulus upon its onset. Phasic visual response of superficial layer neurons was enhanced when the monkey made a saccade to the stimulus.

Subsequent studies showed that a similar saccadic enhancement of visual response is seen in other brain areas: frontal eye field (Wurtz and Mohler 1976b), posterior parietal cortex (Robinson et al. 1977, Bushnell et al. 1981, Goldberg and Bushnell 1981), and caudate nucleus (Hikosaka et al. 1989b). However, it was found that the enhancement in the superior colliculus and frontal eye field was specific to saccade (Goldberg and Wurtz 1972, Wurtz and Mohler 1976b, Bruce and Goldberg 1985). Only in the posterior parietal cortex were found neurons that showed enhancement when the monkey attended to the target without making an eye movement (Goldberg and Bushnell 1981). Some of them also responded tonically to the presentation of a visual stimulus (Goldberg and Bushnell 1981, Andersen et al. 1987). Role of the parietal cortex in attention has also been suggested by lesion studies and clinical observations (Lynch et al. 1977, Lynch and McLaren 1989, Zihl and Cramon 1979).

These findings suggest that the activity of neurons of the posterior parietal cortex may be the source of the tonic activity of visual attention type in the superior colliculus.

FUNCTIONS OF TONIC ACTIVITY IN THE SUPERIOR COLLICULUS

The major output areas of the superior colliculus were classified into the following two areas: the oculomotor areas in the brain stem and the thalamus (Figure 22)(Harting 1977, Harting et al. 1980, Sparks and Hartwich-Young 1989).

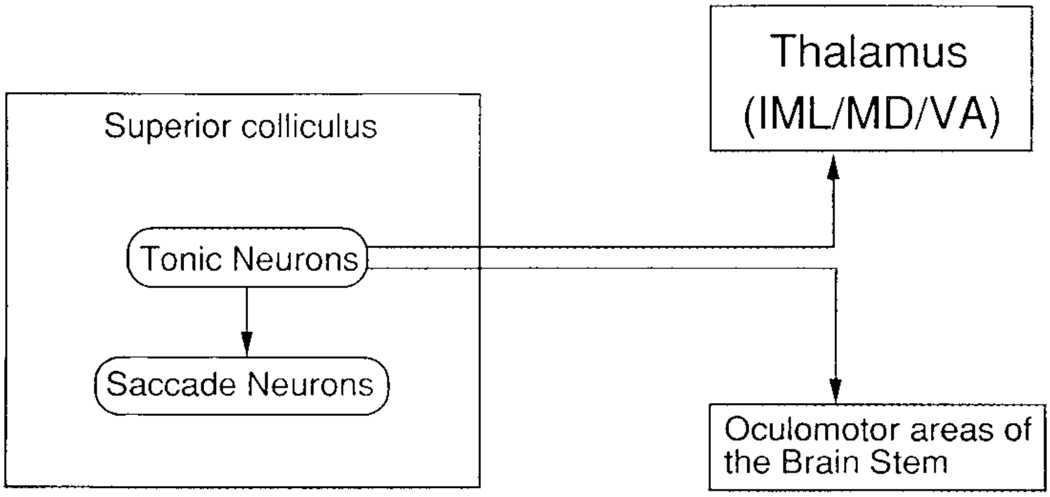


Figure 22. Hypothetical scheme of efferent connections of the tonic neurons in the intermediate layer. Abbreviations: IML, the internal medullary laminar nuclei; MD, the medial dorsal nucleus; VA, the ventral anterior nucleus.

The superior colliculus is well known to project to the oculomotor areas of the brain stem (Harting 1977) which contain burst neurons that drive ocular motoneurons directly to produce a saccade (Hikosaka et al. 1978, Grantyn et al. 1980, Igusa et al. 1980). It has been thought that saccadic burst neurons in the superior colliculus provide these brainstem burst neurons with a pulse-like signal (Sparks and Jay 1986, Sparks and Hartwich-Young 1989, Sparks and Mays 1990, Waitzman et al 1991). It appears unlikely that the tonic neurons also project to the brainstem burst neurons, because the burst neurons do not show sustained activity before a saccade. In the cat, however, visually responsive neurons in the superior colliculus project to the burst neuron area (Grantyn and Grantyn 1982). Similarly, the tonic neurons in the monkey superior colliculus might also project to the burst neuron area and influence their membrane potential; this influence may normally be damped by a strong inhibition from omnipause neurons (Keller 1974, Nakao et al. 1980). According to this scheme the tonic activity in the superior colliculus would change the subthreshold excitability of premotor burst neurons, and the selectivity of the tonic activity is preserved to some extent up to this level.

Another possible projection is to the thalamus, especially their subnuclei such as the ventral anterior (VA), the medial dorsal (MD), the internal medullary laminar nuclei (IML) (Benevento and Fallon 1975, Harting 1977). In IML and MD, there are neurons showing visual and saccadic responses (Schlag and Schlag-Rey 1984). There are also neurons that show tonic activity in response to a visual stimulus in their receptive fields or in response to visual fixation (Schlag and Schlag-Rey 1984). The IML and MD are mutually connected with the frontal eye field and posterior parietal cortex (Pearson et al. 1978, Barbas and Mesulam 1981, Stanton et al. 1988a). These nuclei also project to the caudate nucleus

(Jones and Leavitt 1974). The VA instead projects to the prefrontal cortex (Jacobson et al. 1978).

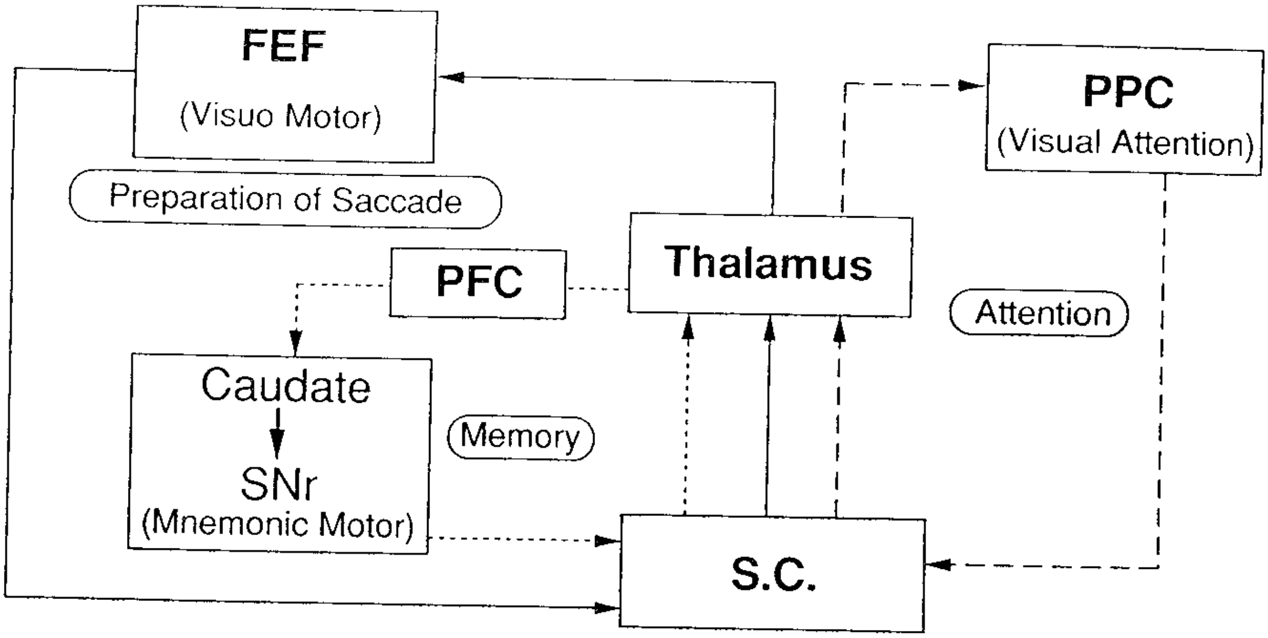


Figure 23. Hypothetical signal flows of the tonic neurons. Solid lines indicate the flow of the information for preparation of saccade. Dashed lines show the flow of the information for peripheral attention. Dotted lines show the the flow of the information for memory. Abbreviations: FEF, frontal eye field; PPC, posterior parietal cortex; PFC, prefrontal cortex; SNr, substantia nigra pars reticulata; S.C., the superior colliculus.

These anatomical findings, taken together, suggest that there are loop circuits which are formed by the superior colliculus, thalamus, cerebral cortex, and basal ganglia (Figure 23). And tonic activities are found in every area involved in the loops. It might be speculated that the tonic activities are maintained by such reverberating loop connections.

Furthermore, these loops might be divided into three: (1) thalamus (IML/MD) - frontal eye field - superior colliculus, (2) thalamus (VA) - prefrontal cortex - caudate nucleus - SNr - superior colliculus, and (3) thalamus (IML/MD) - posterior parietal cortex - superior colliculus. Based on the arguments in the previous section ('POSSIBLE SOURCES OF THE INFORMATION OF MEMORY, PREPARATION OF SACCADE AND ATTENTION'), we would suggest that these loops may convey different types of signals: preparation of saccade, short-term memory, and visual attention (Figure 23). And this may be the reason why there are specific types of neurons in the superior colliculus. Note, however, that a majority of superior colliculus neurons are non-specific, suggesting that these signals, to a considerable degree, converge onto single neurons in the superior colliculus.

Finally, there remains the possibility that the tonic neurons are interneurons (Behan and Appell 1987, Ma et al. 1990). If so, the relatively specific signals observed in the tonic neurons might further be integrated at the next stage, presumably presaccadic burst neurons in the superior colliculus, and then transmitted to saccadic burst neurons in the brain stem.

CONCLUSION

Most of the previous studies on single cell activities in the superior colliculus showed that neurons in the intermediate layer respond phasically to a visual stimulus and to a saccade (Wurtz and Goldberg 1972a, Mays and Sparks 1980). One exception is a type of neuron called quasi-visual cell (Mays and Sparks 1980). Therefore, it has long been thought that the function of the superior colliculus is sensory-motor and does not include more cognitive ones (Sparks and Hartwich-Young 1989).

We found, however, that there are a fair number of tonic neurons in the superior colliculus, and some of them are selective for short-term memory, preparation of saccade, and visual attention. Our findings suggest that the superior colliculus is one of the areas where such cognitive signals are translated into oculomotor information. Furthermore, the superior colliculus might participate in the processes in which memory-, preparation-, and attention-related signals are maintained; and this may be accomplished by multiple loop circuits formed with the cerebral cortex, thalamus, and basal ganglia.

REFERENCES

Andersen RA, Essick GK and Siegel RM (1987) Neurons of area 7 activated by both visual stimuli and oculomotor behavior. Exp. Brain Res. 67: 316-322.

Andersen RA, Bracewell RM, Barash S, Gnadt JW and Fogassi L (1990) Eye position effects on visual, memory and saccade-related activity in area LIP and 7a of macaque. J. Neurosci. 10: 1176-1196.

Araki M, McGeer PL and McGeer EG (1984) Presumptive γ-aminobutyric acid pathways from the midbrain to the superior colliculus studied by a combined horseradish peroxidase-γ-aminobutyric acid transaminase pharmacohistochemical method. Neuroscience. 13: 433-439.

Barash S, Bracewell RM, Fogassi J, Gnadt W and Andersen RA (1991) Saccade-related activity in the lateral intraparietal area. I. Temporal properties; comparison with area 7a. J. Neurophysiology. 66: 1095-1108.

Barbas H and Mesulam MM (1981) Organization of afferent input to subdivisions of area 8 (frontal eye field) in the rhesus monkey. J. Comp. Neurology. 400: 407-431.

Behan.M and Appell.PP (1987) Local projections of neurons in the deep layers of the cat superior colliculus: A study using phaseolus vulgaris leucoagglutinin (PHA-L). Soc. Neurosci. Abstr. 13: 430.

Benevento LA and Fallon JH (1975) The ascending projections of the superior colliculus in the rhesus monkey. J. Comp. Neurology. 160: 339-362.

Bruce CJ and Goldberg ME (1985) Primate frontal eye fields. I. Single neurons discharging before saccades. J. Neurophysiology. 53: 603-635.

Bushnell MC, Goldberg ME and Robinson DL (1981) Behavioral enhancement of visual responses in monkey cerebral cortex. I. Modulation in posterior parietal cortex related to selective visual attention. J. Neurophysiology. 46: 755-772.

Crawford TJ, Henderson L and Kennard C (1989) Abnormalities of nonvisually guided eye movements in Parkinson's disease. Brain. 112: 1573-1586.

Cynader H and Berman N (1972) Receptive-field organization of monkey superior colliculus. J. Neurophysiology. 35: 187-201.

Denny-Brown D (1962) The basal ganglia and their relation to disorder of movement. Oxford university press.

DiChiara G, Morelli M, Porceddu ML and DelFiacco M (1980) Effect of discrete kainic acid-induced lesions of corpus caudatus and globus pallidus on glutamic acid carboxylase of rat substantia nigra. Brain Res. 189: 193-208.

Fisk JD, Goodale MA, Burkhart G and Barnett HJM (1982) Progressive supranuclear palsy: The relationship between oculomotor dysfunction and psychological test performance. Neurology. 32: 698-705.

Fries R (1984) Cortical projections to the superior colliculus in the macaque monkey: A retrograde study using horseradish peroxidase. J. Comp. Neurology. 230: 55-76.

Fuchs AF and Robinson DA (1966) A method for measuring horizontal and vertical eye movement chronically in the monkey. J. Appl. Physiol. 21: 1068-1070.

Funahashi S, Bruce CJ and Goldman-Rakic PS (1989) Mnemonic coding of visual space in the monkey's dorsolateral prefrontal cortex. J. Neurophysiology. 61: 331-349.

Gnadt JW and Andersen RA (1988) Memory related motor planning activity in posterior parietal cortex of macaque. Exp Brain Res. 70: 216-220.

Goldberg ME and Bushnell MC (1981) Behavioral enhancement of visual responses in monkey cerebral cortex. II. Modulation in frontal eye fields specifically related to saccades. J. Neurophysiology. 46: 773-787.

Goldberg ME and Bruce CJ (1990) Primate frontal eye fields. III. Maintenance of a spatially accurate saccade signal. J. Neurophysiology. 64: 489-508.

Goldberg ME and Wurtz RH (1972) Activity of superior colliculus in behaving monkey. II. Effect of attention on neuronal responses. J. Neurophysiology. 35: 560-574.

Goldman-Rakic PS (1987) Circuitry of primate prefrontal cortex and regulation of behavior by representational memory. In: Handbook of physiology. The nervous system. Bethesda, MD: Am. Physiol. Soc. vol. V, p. 373-417.

Graybiel AM and Ragsdale CW Jr. (1979) Fiber connection of the basal ganglia. In: Cuenod M, Kreutzberg GW and Bloom FE (Eds). Development and chemical specificity of neurons. Elsevier. Amsterdam, pp.239-283.

Grantyn R, Baker R and Grantyn A (1980) Morphological and physiological identification of excitatory pontine reticular neurons projecting to the cat abducens nucleus and spinal cord. Brain Res. 198: 221-228.

Grantyn A and Grantyn R (1982) Axonal patterns and sites of termination of cat superior colliculus neurons projecting in the tecto-bulbo-spinal tract. Exp. Brain Res. 46: 243-256.

Harting JK (1977) Descending pathways from the superior colliculus: An autoradiographic analysis in the rhesus monkey. J. Comp. Neurology. 173: 583-612.

Harting JK, Huerta MF, Frankfurter AJ, Strominger NL and Royce GJ (1980) Ascending pathways from the monkey superior colliculus: An autoradiographic analysis. J. Comp. Neurology. 192: 853-882.

Hendrickson A, Wilson ME and Toyne MJ (1970) The distribution of optic nerve fibers in macaca mulatta. Brain Res. 23: 425-427.

Hikosaka O, Igusa Y, Nakao S and Shimazu H (1978) Direct inhibitory synaptic linkage of pontomedullary reticular burst neurons with abducence motoneurons in the cat. Exp. Brain Res. 33: 337-352.

Hikosaka O and Wurtz RH (1983a) Visual and oculomotor functions of monkey substantia nigra pars reticulata. I. Relation of visual and auditory responses to saccades. J. Neurophysiology. 49: 1230-1253.

Hikosaka O and Wurtz RH (1983b) Visual and oculomotor functions of monkey substantia nigra pars reticulata. III. Memory-contingent visual and saccade responses. J. Neurophysiology. 49: 1268-1284.

Hikosaka O, Sakamoto M and Usui S (1989a) Functional properties of monkey caudate neurons I. Activities related to saccadic eye movements. J. Neurophysiology. 61: 780-798.

Hikosaka O, Sakamoto M and Usui S (1989b) Functional properties of monkey caudate neurons II. Visual and auditory responses. J. Neurophysiology. 61: 799-813.

Hikosaka O, Sakamoto M and Usui S (1989c) Functional properties of monkey caudate neurons III. Activities related to expectation of target and reward. J. Neurophysiology. 61: 814-832.

Huerta MF, Krubitzer L and Kaas JH (1986) Frontal eye field as defined by intracortical microstimulation in squirrel monkeys, owl monkeys, and macaque monkeys: I. Subcortical connections. J. Comp. Neurology. 253: 415-439.

Igusa Y, Sasaki S and Shimazu H (1980) Excitatory premotor burst neurons in the cat pontine reticular formation related to the quick phase of vestibular nystagmus. Exp. Brain Res. 39: 310-311.

Ingle D (1973) Evolutionary perspectives on the function of the optic tectum. Brain Behav. Evol. 8: 211-237.

Jakobson S, Butters N and Tovsky NJ (1978) Afferent and efferent subcortical projections of behaviorally defined sectors of prefrontal granular cortex. Brain Res. 159: 279-296.

Jayaraman A, Batton RR and Carpenter MB (1977) Nigrotectal projections in the monkey: An autoradiographic study. Brain Res. 135: 147-152.

Joseph JP and Barone P (1987) Prefrontal unit activity during a delayed oculomotor task in the monkey. Exp. Brain Res. 67: 460-468.

Jones EG and Leavitt RY (1974) Retrograde axonal transport and the demonstration of non-specific projections to the cerebral cortex and striatum from thalamic intralaminar nuclei in the rat, cat and monkey. J. Comp. Neurology. 154: 349-378.

Kadoya S, Massopust C Jr and Wolin LR (1971) Striate cortex-superior colliculus projection in squirrel monkey. Exp. Neurology. 32: 98-110.

Kanaseki T and Sprague JM (1974) Anatomical organization of pretectal nuclei and tectal laminae in the cat. J. Comp. Neurology. 158: 319-338.

Keller EL (1974) Participation of the medial pontine reticular formation in eye movement generation in monkey. J. Neurophysiology. 37: 316-332.

Kojima J and Hikosaka O (1991) Monkey superior colliculus may integrate memory- and attention-related signals to produce saccadic oculomotor command. Neuroscience Res. Suppl. 16: S112.

Künzle H (1978) An autoradiographics analysis of the efferent connections from premotor and adjacent prefrontal regions (area 6 and 9) in macaca fascicularis. Brain Behav. Evol. 15: 185-234.

Kuypers HGJM and Lawrence DG (1967) Cortical projections to the red nucleus and the brain stem in the rhesus monkey. Brain Res. 4: 151-188.

Leigh RJ, Newman SA, Folstein SE, Lasker AG and Jensen BA (1983) Abnormal ocular motor control in Huntington's disease. Neurology. 33: 1268-1275.

Lynch JC, Mountcastle VB, Talbot WH and Yin TCT (1977) Parietal lobe mechanisms for directed visual attention. J. Neurophysiology. 40: 362-389.

Lynch JC and Mclaren JW (1989) Deficits of visual attention and saccadic eye movement after lesions of parietooccipital cortex in monkeys. J. Neurophysiology. 61: 74-90.

Ma TP, Cheng HW, Czech JA and Rafols JA (1990) Intermediate and deep layers of the macaque superior colliculus: A Golgi study. J. Comp. Neurology. 295: 92-110.

Matsumura M, Kojima J, Gardiner TW and Hikosaka O (1992) Visual and oculomotor functions of monkey subthalamic nucleus. J. Neurophysiology. 67: 1615-1632.

Mays LE and Sparks DL (1980) Dissociation of visual and saccade-related responses in superior colliculus neurons. J. Neurophysiology. 43: 207-231.

Miyashita N, Matsumura M, Usui S, Kato M, Kori A, Gardiner TW and Hikosaka O (1990) Deficits in task-related eye movements induced by unilateral infusion of MPTP in the monkey caudate nucleus. Soc. Neurosci. Abstr. 16: 235.

Mohler CW and Wurtz RH (1976) Organization of monkey superior colliculus: Intermediate layer cells discharging before eye movements. J. Neurophysiology. 39: 722-744.

Mohler CW and Wurtz RH (1977) Role of striate cortex and superior colliculus in visual guidance of saccadic eye movements in monkey. J. Neurophysiology. 40: 74-94.

Moschovakis AK, Karabelas AB and Highstein SM (1988) Structure-function relationship in the primate superior colliculus. II. Morphological identity of presaccadic neurons. J. Neurophysiology. 60: 263-262.

Nakao S, Curthoys IS and Markham CH (1980) Direct inhibitory projection of pause neurons to nystagmus-related pontomedullary reticular burst neurons in the cat. Exp. Brain Res. 40: 283-293.

Pearson RCA, Brodal P and Powell TPS (1978) The projection of the thalamus upon the parietal lobe in the monkey. Brain Res. 144: 143-148.

Petersen SE, Robinson DL and Keys W (1985) Pulvinar nuclei of the behaving rhesus monkey: Visual responses and their modulations. J. Neurophysiology. 54: 867-886.

Pöppel E, Held R and Frost D (1973) Residual visual function after brain wounds involving the central visual pathways in man. Nature. 243: 295-296.

Pöppel E (1977) Midbrain mechanisms in human vision. In: Neuronal mechanisms in visual perception. Neurosci. Res. Prog. Bull. 15: 335-343.

Posner MI, Cohen Y and Rafal R (1982) Neural systems control of spatial orienting. Philosophical transactions of the royal society of London. B298: 187-198.

Rafal RD and Grimm RJ (1981) Progressive supranuclear palsy: Functional analysis of the response to methysergide and antiparkinsonian agents. Neurology. 31: 1507-1518.

Robinson DA (1963) A method of measuring eye movement using a scleral search coil in a magnetic field. IEEE Trans. Bio-Med. Eng. BME-10: 137-145.

Robinson DA (1972) Eye movements evoked by collicular stimulation in the alert monkey. Vision Res. 12: 1795-1808.

Robinson DL, Goldberg ME and Stanton GB (1978) Parietal association cortex in the primate sensory mechanisms and behavioral modulations. J. Neurophysiology. 41: 910-932.

Sawaguchi T and Goldman-Rakic PS (1991) D1 dopamine receptors in prefrontal cortex: Involvement in working memory. Science. 251: 947-950.

Segraves MA and Goldberg ME (1987) Functional properties of corticotectal neurons in the monkey's frontal eye field. J. Neurophysiology. 58: 1387-1419.

Schall JD (1991) Neuronal activity related to visually guided saccades in the supplementary motor area of rhesus monkeys. J. Neurophysiology. 66: 530-558.

Schiller PH and Stryker M (1972) Single-unit recording and stimulation in superior colliculus of the alert rhesus monkey. J. Neurophysiology. 35: 915-924.

Schiller PH and Koerner F (1971) Discharge characteristics of single units in superior colliculus of the alert rhesus monkey. J. Neurophysiology. 34: 920-936.

Schlag J and Schlag-Rey M (1984) Visuomotor functions of central thalamus in monkey. II. Unit activity related to visual events, targeting and fixation. J. Neurophysiology. 51: 1175-1195.

Schneider GE (1969) Two visual systems: Brain mechanisms for localization and discrimination are dissociated by tectal and cortical lesions. Science. 163: 895-902.

Sparks DL and Jay MF (1986) The functional organization of the primate superior colliculus: A motor perspective. In: Freund HJ, Buttner U, Cohen B and Noth J (Eds.). The oculomotor and skeletal-motor systems: Differences and similarities, Elsevier. Amsterdam. pp. 235-242.

Sparks DL and Hartwich-Young R (1989) The deep layers of the superior colliculus. In: Wurtz RH and Goldberg ME (Ed.). The neurobiology of saccadic eye movements. Elsevier science publishers, pp. 213-255.

Sparks DL and Mays LE (1980) Movement fields of saccade-related burst neurons in the monkey superior colliculus. Brain Res. 190: 39-50.

Sparks DL and Mays LE (1990) Signal transformations required for the generation of saccadic eye movements. Annu. Rev. Neurosci. 13: 309-336.

Stanton GB, Goldberg ME and Bruce CJ (1988a) Frontal eye field efferents in the macaque monkey: I. Subcortical pathways and topography of striatal and thalamic terminal fields. J. Comp. Neurology. 271: 473-492.

Stanton GB, Goldberg ME and Bruce CJ (1988b) Frontal eye field efferents in the macaque monkey: II. Topography of terminal fields in midbrain and pons. J. Comp. Neurology. 271: 493-506.

Suzuki H and Azuma M (1976) A glass insulted "Elgiloy" microelectrode for recording unit activity in chronic monkey experiments. Electroencephalogr. Clin. Neurophysiol. 41: 93-95.

Waitzman DM, Ma TP, Optican LM and Wurtz RH (1991) Superior colliculus neurons mediate the dynamic characteristics of saccades. J. Neurophysiology. 66: 1716-1737.

Wilson ME and Toyne MJ (1970) Retino-tectal and Cortico-tectal projections in macaca mulatta. Brain Res. 24: 395-406.

Wurtz RH and Goldberg ME (1972a) Activity of superior colliculus in behaving monkey. III. Cell discharging before eye movements. J. Neurophysiology. 35: 575-586.

Wurtz RH and Goldberg ME (1972b) Activity of superior colliculus in behaving monkey. IV. Effect of lesions on eye movements. J. Neurophysiology. 35: 587-600.

Wurtz RH and Mohler CW (1976a) Organization of monkey superior colliculus: Enhanced visual response of superficial layer cells. J. Neurophysiology. 39: 745-765.

Wurtz RH and Mohler CW (1976b) Enhancement of visual responses in monkey striate cortex and frontal eye fields. J. Neurophysiology. 39: 766-722.

Yoshida M and Precht W (1971) Monosynaptic inhibition of neurons in the substantia nigra by caudate-nigral fibers. Brain Res. 32: 225-228.

Zihl J and Von Cramon D (1979) The contribution of the 'second' visual system to directed visual attention in man. Brain. 102: 835-856.

ACKNOWLEDGEMENTS

I, Jun Kojima, express deep appreciation to Prof. Okihide Hikosaka. I thank Dr. Masaru Matsumura, Dr. Makoto Kato, Dr. Satoru Miyauchi, Dr. Masahiko Inase, Dr. Nobuo Miyashita, and Ms. Miya Kato Rand for their helpful discussion about this study. I also thank Mr. Morio Togawa, Miss Miki Yoshitomo and Mr. Osamu Nagata for their technical assistance.